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One Day National Conference on
Recent Trends in Chemical Sciences Research
[RTCSR-2024]

Date : 20th Jan 2024

Organized By
Department of Chemistry, M.S.P. Mandal's Balbhim Arts, Science and Commerce College, Beed – 431122, Maharashtra, India

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Modified Natural Silica Catalysed One-Pot Synthesis of Benzimidazole Derivatives

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ABSTRACT
Modified natural silica catalyzed an efficent synthesis of benzimidazole derivatives using benzaldehydes, o-phenylenediamines in ethanol at refluxed condition. We have modified natural silica using treatment of 1N sulfuric acid (H2SO4) solution. Natural silica shows the poor catalytic activity after modification which enhance the catalytic activity. Present catalytic materials shows many advantages such as high yields, non-toxic, simple work up procedure, clean and catalyst can be successfully recycle reused several times.
Keywords: Natural silica, Modified natural silica, Benzimidazole.

I. INTRODUCTION

Catalysis is a process in which the rate of a chemical reaction changes due to the participation of a substance called a catalyst. Catalysts may be in gaseous, liquid, or solid state. In homogeneous catalysis, the catalyst is molecularly dispersed in the same phase (usually gaseous or liquid) as the reactants. In heterogeneous catalysis the reactants and the catalyst are in different phases, separated by a phase boundary. Most commonly used heterogeneous catalysts are solids and the reactants are gases or liquids. Heterogeneous catalytic reactions occur on the surface of solid catalysts and involve elementary surface chemical processes such as adsorption of reactants from a reaction mixture, surface diffusion and reaction of adsorbed species, and desorption of reaction products. The acceleration of a chemical reaction is due to the high reactivity of surface atoms that facilitates bond breaking and bond rearrangement of adsorbed molecules [1].

Now days, development of environmentally benign protocols have been gaining an importance in chemical processes. Generally, organic reactions are carried out using inorganic acids such as H_2SO_4, HCl, and HNO_3 as well as on other hand by using Lewis acids like $AlCl_3$ and BF_3 [2]. Despite its high selectivity, these homogeneous classical acid catalysts offer several disadvantages like high toxicity, corrosive nature and generation of maximum waste, tedious recovery and reusability procedure. In view of enviro-economic aspects, it is necessary to replace these toxic acid catalysts by newer solid heterogeneous catalysts as an excellent alternative source over the conventional acid catalysts, as they can be in expensive, non-toxic, non-corrosive, easy to recover and reuse. Accordingly, various solid acid catalysts, such as heteropolyacids, ion exchange resins, zeolites and clays have been investigated. However, the main disadvantage associated with the hetero polyacids and ion exchange resins is poor thermal stability and loss of catalytic activities at high temperatures [3,4].

Benzimidazoles moieties are a very important class of heterocyclic compounds that have great applications in drug discovery [5]. Recently, researchers have done a wide varieties of researches on benzimidazole derivatives due to the fact that these derivatives have shown various spectrum of pharmacological activities; including, vitamin B12 [6], anti-ulcer, anti-tumour and anti-viral [7], anti-microbial [8], anti-cancer [9], anti-helminthic [10], anti-hypertensive [11], anti-oxidant [12], anti-tubercular [13], anti-inflammatory [14], anti-malarial [15], selective inhibition of the platelet-derived growth factor receptor [16], etc. The most prominent benzimidazole in nature which is N-ribosyl-dimethyl benzimidazole serves as an axial ligand for cobalt in vitamin B12 [17], a proton pump inhibitor [18], and omeprazole, pantoprazole and lansoprazole [19]. In recent years, several methods have been reported for the synthesis of benzimidazoles using various catalysts such as rose Bengal [20], p-toluenesulfonic acid/graphite and N,N-dimethyl aniline/graphite [21], NH_4Cl [22] and ytterbium perfluorooctane sulfonates ($Yb(OPf)_3$) [23]. Generally, the condensation of o-phenylenediamines with aldehydes in the presence of acid [24], base or metal catalyst [25] produces benzimidazoles. Other methods include condensation of o-phenylenediamines with carboxylic acids, nitriles and ortho-esters under dehydrating conditions [26], the dehydration of N-acylated, o-phenylenediamines using acetic acid [27], p-TSA [28] or amberlyst-15 which also produces benzimidazoles. However, some of these methods are plugged by one or other kind of drawbacks such as long reaction time, use of volatile organic solvents, low yields, and harsh reaction conditions. Therefore, it is necessary to develop an improved route for Synthesis of Benzimidazole derivative.

In advantages of heterogeneous catalyst we have synthesized new heterogeneous catalyst for the synthesis of bioactive heterocycle [29, 30]. Herein, we report a modified natural silica catalysed one-pot synthesis of Benzimidazole derivatives using aromatic aldehydes, o-phenylenediamines under mild reaction conditions.

II. EXPERIMENTAL WORK

All Chemicals were purchased either from Merck or Fluka and used without further purification. Melting points were taken in an open capillary and are uncorrected. Thin layer chromatography was performed on Merck pre-coated silica gel 60-F254 plates. 1H NMR spectra were recorded on an 300 MHz FT-NMR spectrometer in $CDCl_3$ as a solvent and chemical shifts values are recorded δ (ppm) relative to tetramethylsilane (Me4Si) as an internal standard.

2.1 Preparation of natural silica (SiO_2)

In present the study, naturally occurring silica was collected from sonai region of Ahmednagar district, of Maharashtra (India), in the form of silicate like material (Figure 1). The natural silica crystals separated from rock samples. It was subsequently washed with distilled water and acetone several times, dried, crushed and sieved to obtain fine powder. The powder was refluxed with de ionized water to remove soluble impurities. It was then decanted and dried in an oven for 2 h to obtain fine crystalline powder.

Figure 1 image of natural silica (SiO_2)

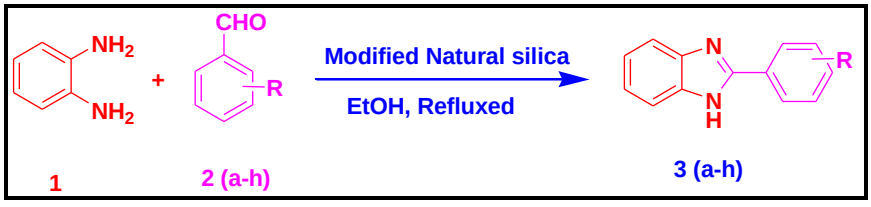
2.2 Modified natural silica

Natural silica was modified by following method. To the 1 gm powder of natural silicate materials 30 ml of 1N H_2SO_4 added and stirred for 12 h. Then sulphuric acid adsorbed on the surface of natural silica. The resultant product was filtered and washed with distilled water and dried 2 h in an oven to obtain modified natural silica (figure 2).

Figure 2 image of modified natural silica

2.3 General procedure for the synthesis of benzimidazoles Derivatives

A mixture of aldehydes (1 mmol), o-phenylenediamines (1 mmol), and modified natural silica (0.1gm) was heated in ethanol at refluxed in appropriate time. The progress of the reaction was monitored by TLC (n-hexane/ethyl acetate, 1:2). After completion of the reaction, the mixture was washed with cold ethanol and the crude product was recrystallized by ethanol to obtain the pure benzimidazole derivatives in 90-93% yields (Scheme 1).



Scheme 1

2.4 Spectral data of representative compounds

2-phenyl-1H-benzo[d]imidazole 3a: IR (KBr): 1615 (C=N), 3565 (NH) cm-1. 1H NMR (400 MHz, DMSO-d6): δ 7.20-7.23 (m, 2H), 7.50-7.53 (m, 1H), 7.54-7.61 (m, 4H), 8.20 (d, J=8.0 Hz, 2H), 12.93 (bs, 1H).

2-p-tolyl-1H-benzo[d]imidazole 3e: IR (KBr): 1622 (C=N), 3446 (NH) cm–1. 1H NMR (400 MHz, DMSO-d6) δ 2.38 (s, 3H), 7.18 (d, J = 7.2 Hz, 2H), 7.34-7.37 (m, 2H), 7.47-7.51 (m, 1H), 7.60-7.63 (m, 1H), 8.06 (d, J = 8.0 Hz, 2H), 12.80 (bs, 1H).

III.RESULTS AND DISCUSSION

To examine the effect of catalytic activity of homogenous and heterogamous catalyst using summarized in (Table 1). When homogenous catalyst aluminium sulphate gave good to well yield but catalyst cannot be reused in model reaction of benzaldehyde and o-phenylenediamines was refluxed in ethanol. Using heterogeneous catalyst zinc dust exhibits poor catalytic activity in term of reaction time and product. In the presence of natural silica contain poor catalytic activity in term of reaction time and yield. With the catalytic activity of modified naturally occurring silica gave excellent yield of the desired product in short reaction time and catalyst can be reused at least two times.

Table 1 catalytic activity of homogenous and heterogonous catalyst[a]

Entry	Catalyst	Time (h)	Yield (%)[b]
1	$(NH_4)Al(SO_4)_2.12H_2O$	3	75
2	Zinc dust	3.5	45
3	Natural silica	4.5	45
4	Modified natural silica	2	93

[a]**Reaction condition:** benzaldehyde (1 mmol), o-phenylenediamines (1 mmol) catalyst (0.1g) and ethanol 15 ml; [b]Isolated yield.

After conformation of catalytic materials to optimized the effect of various solvents such as acetonitrile, di-chloro methane (DCM), methanol, acetone and ethanol with modified natural silica as catalytic materials. When di-chloro methane (DCM) gave moderate amount yield and no reaction was found in acetonitrile as a solvent, methanol and acetone gave less amount of yields (Table 2). The best result was found in ethanol as a solvent in term of reaction time and yield of the product hence we have chosen ethanol as a solvent for the synthesis of benzimidazole derivatives.

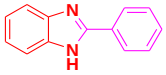
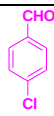
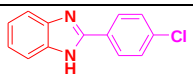
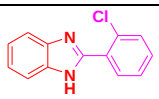
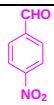
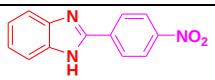
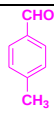
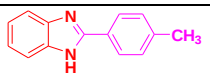
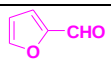
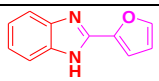
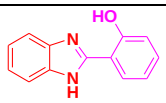
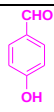
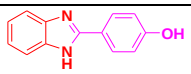
Table 2 Solvent stability of catalyst[a]

Entry	Solvent	Time (h)	Yield (%)[b]
1	Di-chloro methane (DCM)	4	60
2	Acetonitrile	4	No product
3	Methanol	4	75
4	Acetone	4	78
5	Ethanol	2	93

[a]**Reaction condition:** benzaldehyde (1 mmol), o-phenylenediamines (1 mmol) catalyst (0.1g) and ethanol 15 ml; [b]Isolated yield.

Table 3 shows the generality of the present protocol for variety of different substituted aromatic aldehyde possessing electron rich and electron deficient groups gave good to excellent yields (90-93%) of the respective product and reaction were completed within 2-3 h was refluxed in ethanol.

Table 3 Synthesis of Benzimidazole derivative[a]

Entry	Aldehyde	Product	Time (h)	Yield (%)[b]	M.P. (˚C)
3a			2	93	292
3b			2.5	91	295
3c			2.7	90	231
3d			2.5	91	310
3e			2.5	92	263
3f			3	90	285
3g			2.5	91	236
3h			3	90	256

[a]**Reaction condition:** benzaldehyde (1 mmol), o-phenylenediamines (1 mmol) catalyst (0.1g) and ethanol 15 ml; [b]Isolated yield.

One of the significant advantages of heterogeneous catalyst is the possible recovery and reusability of catalyst as this is important from an industrial and an economic point of view. After the completion of the reaction the catalyst was separated by filtration, washed with n-hexane and dried at 80˚C for 1 h before next catalytic run. Reusability of the catalyst was investigated for three times and it was found to retain almost consistent activity (Table 4) Figure 3.

Table 4 Reusability of Modified natural Silica catalyzed synthesis of Benzimidazole[a]

Run	Fresh	1	2	3
Yields (%)[b]	93	92	91	91

[a]**Reaction condition:** benzaldehyde (1 mmol), o-phenylenediamines (1 mmol) catalyst (0.1g) and ethanol 15 ml; [b]Yields after consecutive cycles.

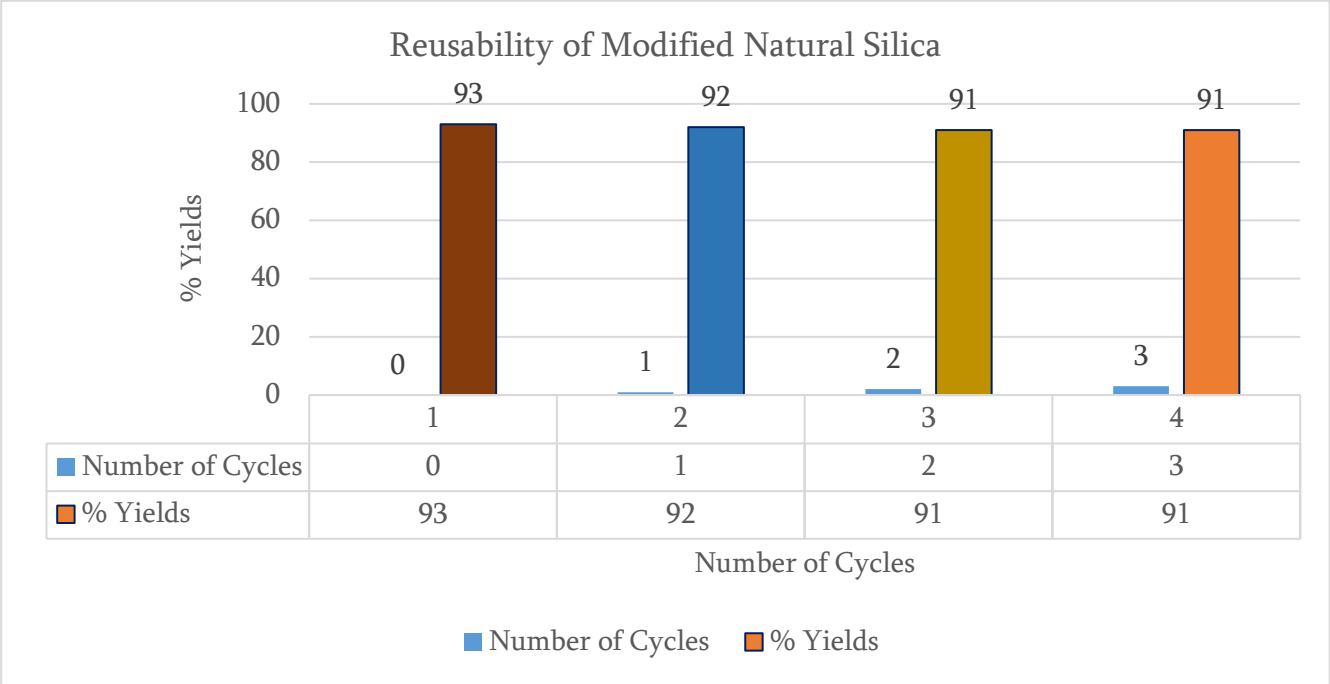


Figure 3 Recyclability of Modified Natural Silica in the synthesis of Benzimidazole

IV.CONCLUSION

In summary, an efficient catalytic system has been developed for the synthesis benzimidazole compounds derivatives from one-pot two component condensation of benzaldehydes, o-phenylenediamine refluxed in ethanol. Present method offers remarkable advantages such as non-toxic, non-corrosive more thermally stable and an inexpensive reaction condition. Simply recovery and reusability of the catalyst makes the reaction successful under environmental benign conditions.

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A Review on Integration of Analytical Chemistry Techniques in Forensic Science: Advancements and Applications

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ABSTRACT

Analytical chemistry plays an important role in scientific research, industry, and environmental monitoring by providing precise and accurate information about the composition of substances. This review paper aims to review recent advances in analytical chemistry techniques that have enhanced our ability to perform comprehensive chemical analysis in research areas. The paper covers recent developments in instrumentation, methods and applications, highlighting their impact on diverse fields such as environmental science, pharmaceuticals, food safety and materials science. Forensic science relies on analytical chemistry techniques to provide accurate and reliable evidence for legal investigations. This review of article explores the relationship between analytical chemistry and forensic science, highlighting recent advancements in instrumentation, methods, and applications. This Review Article covers the role of analytical chemistry in forensic toxicology, trace evidence analysis, and the detection of illicit substances, emphasizing the crucial contribution of these techniques to the criminal justice system.

Keywords: Analytical chemistry, Forensic science, Mass spectrometry, Chromatography, DNA analysis.

I. INTRODUCTION

Forensic science the multidisciplinary field dedicated to the application of scientific principles to criminal investigations, has witnessed a remarkable transformation in recent years, thanks to the integration of advanced analytical chemistry techniques. The synergy between analytical chemistry and forensic science has enhanced the accuracy and reliability of investigations and expanded the scope of forensic analyses to unprecedented levels. This integration plays a pivotal role in unravelling complex criminal cases, identifying perpetrators, and ensuring justice is served.

Analytical chemistry, as a cornerstone of forensic science, provides the tools and methodologies necessary for the detection, identification, and quantification of trace substances within diverse forensic samples. The convergence of traditional forensic methods with cutting-edge analytical techniques has propelled forensic

science into a new era, enabling investigators to extract invaluable information from minute quantities of evidence.

Forensic science plays a pivotal role in the legal system by providing scientific evidence to support criminal investigations and court proceedings. Analytical chemistry is a key component of forensic science, enabling the identification and quantification of substances crucial for establishing facts in legal cases. This section provides an overview of the importance of analytical chemistry in forensic science and the specific challenges addressed by these techniques.

II. INSTRUMENTATION IN FORENSIC ANALYTICAL CHEMISTRY

2.1. Mass Spectrometry in Forensic Toxicology: Advances in mass spectrometry have significantly enhanced forensic toxicology, allowing for the detection and quantification of drugs, poisons, and metabolites in various biological samples. This section explores how techniques like liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) contribute to the accurate analysis of forensic samples.

2.2 Chromatographic Techniques in Trace Evidence Analysis:

Analytical chemistry methods such as gas chromatography (GC) and liquid chromatography (LC) are crucial for analyzing trace evidence found at crime scenes. The paper discusses how these techniques aid in the separation and identification of complex mixtures, including fibers, paints, and gunshot residue.

2.3 Spectroscopic Techniques for Substance Identification:

Spectroscopic methods, including infrared spectroscopy and Raman spectroscopy play a vital role in the rapid and non-destructive identification of substances in forensic analysis. This section explores their applications in identifying drugs, explosives, and other materials encountered in criminal investigations.

III.METHODOLOGIES IN FORENSIC ANALYTICAL CHEMISTRY

3.1 DNA Analysis:

While not a traditional analytical chemistry technique, DNA analysis is an essential forensic tool. This section discusses the integration of analytical methods in DNA profiling, including polymerase chain reaction (PCR) and capillary electrophoresis, highlighting their role in establishing identity and relationships in criminal cases.

3.2 Forensic Imaging Techniques:

Analytical chemistry contributes to forensic imaging through technologies like mass spectrometry imaging (MSI) and nuclear magnetic resonance imaging (MRI). These methods aid in visualizing the distribution of substances within forensic samples, providing valuable spatial information.

IV.APPLICATIONS IN FORENSIC SCIENCE

4.1 Forensic Toxicology: Analytical chemistry techniques are integral in identifying and quantifying drugs, poisons, and alcohol in biological samples, contributing to determining the cause of death and evaluating impairment levels.

4.2 Trace Evidence Analysis: The paper explores how analytical chemistry assists in the analysis of microscopic traces found at crime scenes, including fibers, hair, and gunshot residue, aiding in establishing connections between individuals and locations.

4.3 Detection of Illicit Substances: Analytical chemistry methods are crucial in the identification and analysis of illicit substances such as drugs, explosives, and chemical warfare agents, providing essential evidence in criminal investigations.

V. CHALLENGES AND FUTURE DIRECTIONS

The paper concludes with a discussion of the challenges faced by forensic analytical chemistry, including sample complexity, legal admissibility, and the need for standardization. Future directions highlight potential advancements in technology and methodologies, emphasizing the continuous improvement of forensic analytical techniques.

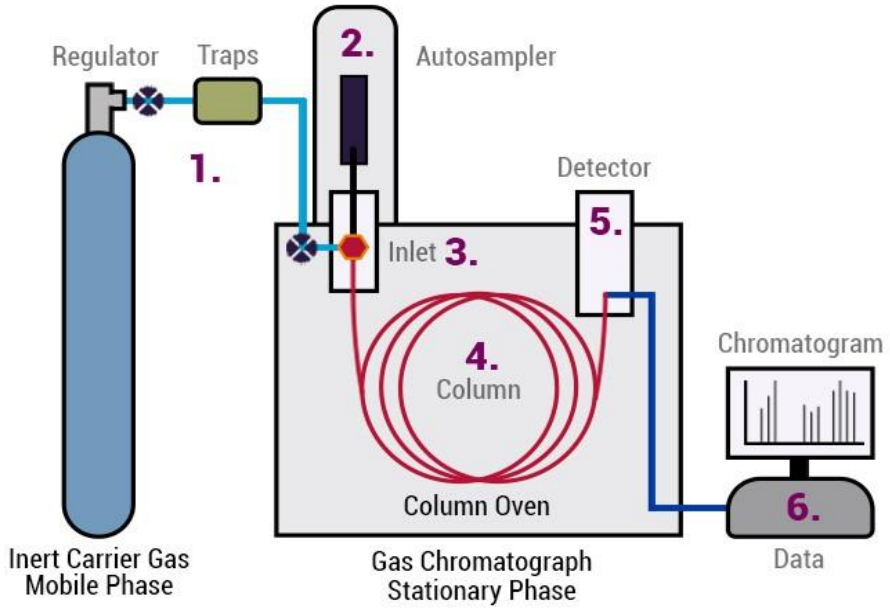

Fig. Gas chromatography instrumentation

VI.CONCLUSION

The integration of analytical chemistry techniques into forensic science has yielded significant advancements and applications across various domains. These advancements are evident in the increased precision, sensitivity, and speed of forensic analyses. Mass spectrometry, chromatography, spectroscopy, and other analytical methods have played crucial roles in the successful detection, identification, and quantification of trace substances in forensic samples. The following key results highlight the impact of this integration:

Furthermore, the review likely emphasizes the role of technology in driving these advancements, such as the development of more sophisticated instrumentation and data analysis tools. This integration has not only improved the speed and efficiency of forensic investigations but has also expanded the range of analytes that can

be detected and quantified. From drug analysis to DNA profiling, the integration of analytical chemistry techniques has broadened the scope of forensic applications.

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Synthesis, Characterization and Antimicrobial Analysis of Various Substituted 3-(3-(3-bromothiophen-2-yl)-1-(2,4-difluorophenyl)-1H-pyrazol-4-yl)-1-(2-hydroxyphenyl) prop-2-en-1-one

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ABSTRACT

Synthesis and biological activities of 3-(3-(3-bromothiophen-2-yl)-1-(2,4-difluorophenyl)-1H-pyrazol-4-yl)-1-(2-hydroxyphenyl) prop-2-en-1-one derivatives are described. The derivatives of novel chalcone were prepared by condensation of pyrazole aldehydes and various substituted aromatic ketones, in the presence of potassium hydroxide in ethanol. By using physical characteristics like melting point and TLC, followed by spectroscopic screenings to determine the molecular structure of the synthesized compound.

KEYWORDS: Pyrazole aldehyde, Chalcone, antimicrobial, Gram+ve and Gram–ve microorganisms.

I. INTRODUCTION

Chalcones are the aromatic ketones that belong to 1, 3-diaryl-2-propen-1-ones, chalcones form the central core for the synthesis of a variety of significant biologically active compounds. The compounds which are formed from chalcone have been reported to show a broad-spectrum variety of pharmacological activity such as antibacterial[i], anti-inflammatory[ii], antimalarial[iii], antifungal[iv], antituberculosis[v], antioxidant[vi], anticancer[vii], antileishmanial[viii]. Chalcone's novelty is that they serve as good precursors for the synthesis of numerous heterocyclic compounds like flavones, pyrazolines, aurones, flavanones, flavonols, pyrimidines, benzoylcoumarones as well as certain compounds like hydantions and deoxybenzoins which are few therapeutic importance[ix]. Due to the presence of an active α,β-unsatutated keto function in chalcones which is found to be responsible for its antimicrobial activity. Claisen–Schmidt condensation between benzaldehyde and acetophenone results in the formation of chalcone[x]. This reaction is both acids and bases catalyzed reaction under heterogeneous or homogeneous conditions. A lot of researchers have been yet reported the synthesis ofchalcone by using diverse catalysts like hydrotalcites and zeolites[xi], KF–Al2O3[xii], organolithium[xiii], zinc oxide[xiv], modified phosphates[xv] to get a chalcone with fewer by-products and higher yield. Due to numerous pharmacological activities and their synthetic utility, chalcones have attracted chemists to develop a lot of synthetic methodologies for their synthesis around the world.

II. MATERIALS AND METHODS

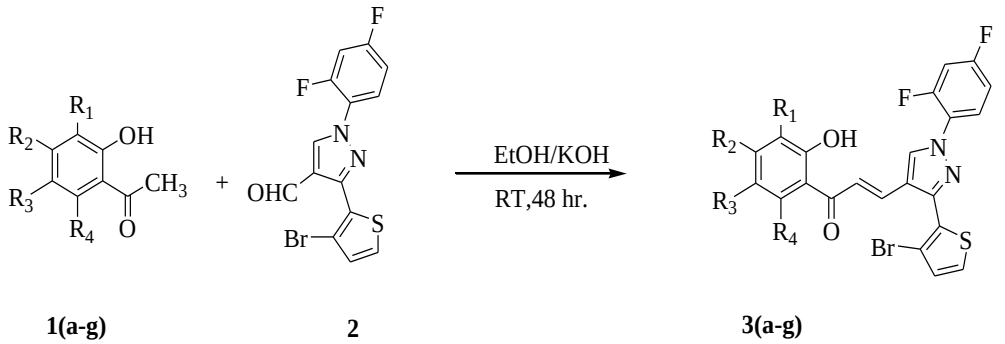
All starting materials and solvents which are used for each reaction are of the synthetic grade was obtained from S D Fine chemicals, and the obtained products checked for purity by melting point(physical constant) in open capillaries and which are uncorrected, and Thin Layer Chromatography (TLC).All the reactions were monitored by using thin layer chromatographyon pre-coated TLC plate which were obtained from Merck as stationary phase and a solvent mixture of hexane and ethyl acetate (80:20) as mobile phase. The ^{1}H NMR spectra were taken on Bruker Avance II 400 MHz NMR Spectrophotometer by using DMSO-d_6 and Tetra Methyl Silane as internal standards. The infra-red spectra were recorded by using FT-IR Spectrophotometer Model RZX (Perkin Elmer). Mass spectra of synthesized compounds were recorded on Macromass mass spectrophotometer (Waters) by using the electro-spray method (ES).

III.GENERAL PROCEDURE

A mixture of compound **1** (0.01 mole) and compound **2** (0.01 mole) was dissolved in 40 ml ethanol as solvent and contents were cooled in an ice bath up to 0^{o}C. In to this reacting mixture, 2g potassium hydroxide (KOH) pellets were added. The reacting mixture was stirred at RT (Room Temperature) for forty-eight hours. Then the reaction mixture was poured into the crushed ice and the contents were acidified by using 2M HCl which Resulted into yellow solid which was separated by filtration and washed using cold water. Using ethanol as a solvent product was crystallized. The same procedure was followed to prepare other analogs of this series. The physical data of the synthesized compounds **3(a-g)** were recorded in **Table 1**. The structures of synthesized compounds have been confirmed by ^{1}HNMR, IR and Mass spectra.

IR (3c) (cm^{-1}):1061(C-Cl), 1145(C-F), 1221(C-O),1535(C=C), 1579(C=N), 1643(C=O), 3179(O-H).
^{1}H NMR (3c) (DMSO-d_6)δ ppm: 6.9987-7.0105(d, 1H, Ar-H), 7.1344-7.1415(d, 1H,Ar-H), 7.2567-7.4571(m, 1H, Ar-H), 7.5123-7.6152(m, 2H, Ar-H), 7.6341-7.7006(d, 1H, CH=C-) 7.8570-7.8798(m, 2H, Ar-H), 7.9032-7.9061(d, 1H, Ar-H), 8.0457-8.0491(d, 1H,Ar-H),9.2468(s, 1H, pyrazole-H), 11.9687(s, 1H, Ar–OH).
ES-MS (3c) (m/z):521(M+1), 523(M+3).

IR (3f) (cm^{-1}):1064 (C-Cl),1107(C-F), 1202(C-O),1534(C=C), 1598(C=N), 1654(C=O), 3234(O-H).
^{1}H NMR (3f) (DMSO-d_6) δ ppm: 2.3159 (s, 3H, -CH3), 6.9781(s, 1H, Ar-H), 7.1984-7.2012(d, 1H, Ar-H), 7.3515-7.4541(m, 1H, Ar-H), 7.5136-7.5726(m, 1H, Ar-H), 7.7132-7.7164(d, 1H, CH=C-), 7.8024-7.8614(m, 1H, Ar-Hz), 7.9196-7.9664(m, 2H,Ar-H), 8.0127(s, 1H,Ar-H), 9.1941(s, 1H, pyrazole-H), 12.1468(s, 1H, Ar–OH).
ES-MS (3f) (m/z):535(M+1), 537(M+3).



1(a-g) **2** **3(a-g)**

- **Scheme 1: Synthesis of various 3-(3-(3-bromothiophen-2-yl)-1-(2,4-difluorophenyl)-1H-pyrazol-4-yl)-1-(2-hydroxyphenyl) prop-2-en-1-one**

Table 1: Physical data of compounds 3(a-g)

Comp.	R_1	R_2	R_3	M.P. (°C)	Yield (%)
3a	H	H	H	132-134	74
3b	H	H	CH_3	176-178	79
3c	H	H	Cl	156-158	81
3d	Cl	H	Cl	202-204	69
3e	H	H	F	196-198	72
3f	H	CH_3	Cl	138-140	70
3g	H	H	Br	162-164	82

IV.RESULT AND DISCUSSION

The synthesized derivatives of chalcones were synthesized successfully in moderate to good yields. These newly synthesized derivatives were characterized by ^{1}H NMR spectral analysis, melting point range, IR, and Mass spectral analysis. All the newly synthesized compounds were screened for their antimicrobial activity using the disc diffusion method.

Antimicrobial activity: By using the paper disc diffusion method, the synthesized derivatives of chalcones **3(a-g)** were screened for their in vitro antimicrobial activity against *Pseudomonas aeruginosa (ATCC 27853),Staphylococcus aureus (ATCC 25923),Escherichia coli (ATCC 25922),* A reference standard drug is used as Gentamycin. Also, antifungal activity was screened against *Candida sp.*, Nystatin is used as a standard drug. At 100 µg/ml concentration, all the tests were evaluated. The culture media used was Muller Hinton agar. At about 37°C, the region of inhibition was measured in a milimeter after 24 hr of incubation. Microbial data for compounds 3(a-g) are summarized below in **Table 2.**

Table 2: Antimicrobial Analysis Data

Sr. No.	Comp. No.	*Escherichia coli (ATCC 25922)*	*Pseudomonas aeruginosa (ATCC 27853)*	*Staphylococcus aureus (ATCC 25923)*	*Candida sp.*
1	3a	7	4.1	3.9	4.1
2	3b	7.9	5.6	7.1	7.6
3	3c	-	3.1	-	6.4
4	3d	5.2	5.1	1.5	8.2
5	3e	6.1	-	1.8	3.3
6	3f	5.6	7.4	4.0	1.8
7	3g	7.4	8.1	3.4	7.6
8	*Gentamycin*	28 mm	23 mm	32 mm	--
9	*Nystatin*	--	--	--	23 mm

V. CONCLUSION

In conclusion, starting from the pyrazole aldehyde and o-hydroxy ketone, we have successfully synthesized chalcones and their derivatives, these newly synthesized compounds were screened for their in vitro antimicrobial activity as well as antifungal activity. Most of the compounds shows moderate antimicrobial activity as compared to standard drug and Most of the compounds shows good antifungal activities.

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A Review on Pyrazole & Its Biological Activities

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ABSTRACT

In this review, we focussed on pyrazole & its biological activities, Pyrazole shows a wide array of biological activities, contributing to their prominence in medicinal chemistry. From anti-inflammatory pyrazalone's to triazoles with potent antifungal properties, the biological significance of these compounds spans pharmaceuticals, agrochemicals, and beyond. Notably, pyrazole derivatives have found application as building blocks in the synthesis of nonsteroidal anti-inflammatory drugs (NSAIDs), showcasing their pivotal role in drug discovery.

The synthesis of pyrazole derivatives has evolved through various methodologies, including classical approaches, cyclization reactions, and modern synthetic strategies. The discussion encompasses the structural diversity achievable through different substitution patterns, facilitating the fine-tuning of properties and activities of pyrazole-based compounds.

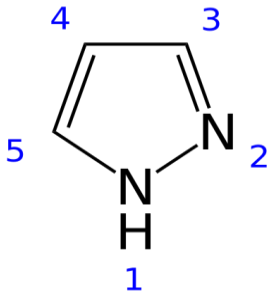
Keywords: Pyrazole, analgesic agent, anticancer agent, antifungal agent.

I. INTRODUCTION

A five-membered heterocyclic compound featuring a unique arrangement of three carbon atoms and two nitrogen atoms in its aromatic ring, has garnered significant attention in the realm of organic chemistry and medicinal science. This review provides a comprehensive examination of pyrazole and its derivatives, emphasizing their synthesis [1], physicochemical properties, and versatile applications.

Pyrazole is the organic compound containing heterocyclic ring consist of carbon atom in adjacent position of its structure. It is a compound with molecular formula $C_3H_4N_2$.

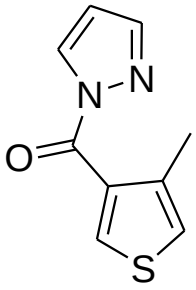
Pyrazole as an aromatic heterocycle with pi-electrons shows different reactivity patterns in organic chemistry. Nucleophilic substitution reactions take place at 3 and 5 positions while electrophilic substitution reactions at 4 positions. The N- atom at position 2 having two electrons is basic in nature and therefore reacts electrophiles. The N- atom at position 1 is unreactive and loses its proton in the presence of base.



Different biological activities shown by pyrazole.

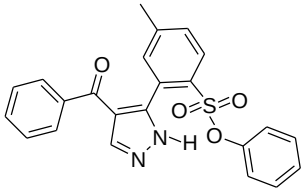
Pyrazole as analgesic agent

L. R. S. Dias et al. [1] were synthesized (4-methylthiophen-3-yl) (1H-pyrazol-1-yl) methanone (compound-1) and shows good analgesic activity.



Compound-1

Kendre et al. [2] synthesized various heterocyclic compound with pyrazole moiety exhibiting a good analgesic activity. Among these compounds, compound-2 shows highest analgesic action.

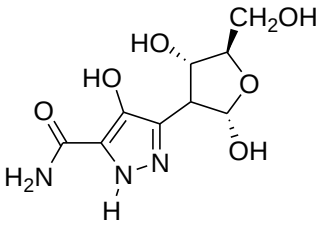


Compound-2

Pyrazole as an anticancer agent

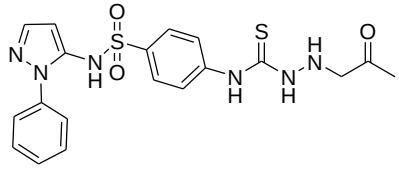
Cancer is a disease caused by uncontrolled growth of cells. This is a serious life threating health problem in the world. There are different types of cancers.

Pyrazole derivatives synthesized by Nitulescu et al. [3] shows anticancer activity. From these compound, compound-3 shows good anticancer activity.



Compound-3

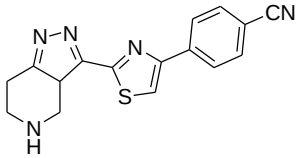
El Gaby et al. (4) have synthesized pyrazole derivatives by using 4-isothiocynato-(1-phenyl-1H-Pyrazole-5-yl) benzene sulfonamide and estimate their biological activity. Out of these synthesized derivatives 2-acetyl-N-(4-(N-(1-phenyl-1H-pyrazol-5-yl) sulfamoyl) phenyl) hydrazinecarbothioamide (compound-4) exhibit high anticancer activity compare with doxorubicin.



Compound-4

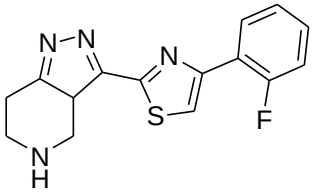
Pyrazole as antifungal agent

Most of new pyrazole-thiazole compounds synthesized by Sivagurunathan et al. [5a,5b &5c] mainly showed antibacterial activity and hence used in treatment of Candida albicans.



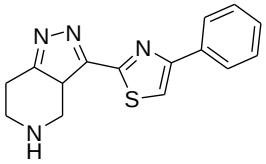
C-5a

4-(2,4,5,6,7-terahydro-1-methyl-1-pyrazole[3,4-C]pyridine-3-yl-thiazole-4-yl) benznitrile



C-5b

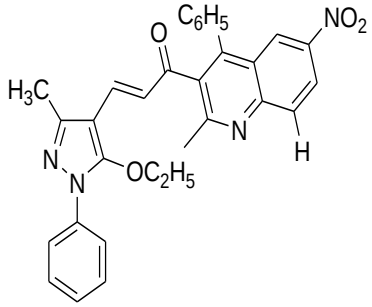
3-(4-(2-fluprophenyl)thiazole-2-yl)4,5,6,7-tetrahyro-1-methyl-1-H-pyrazole[4,3-C] pyridine



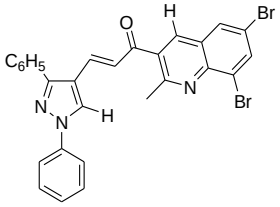
C-5c

4,5,6,7- tetrahydro-1-mthyl-3-(4-phenylthiazole-2-yl) 1-H-pyrazole [4, 4-C] pyridine.

Prasath et al. [6] synthesized various pyrazole-based compound and these compound shows antibacterial and antifungal activities.



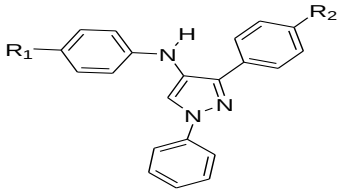
Compound-6



Compound-7

Pyrazole as an antiviral agent

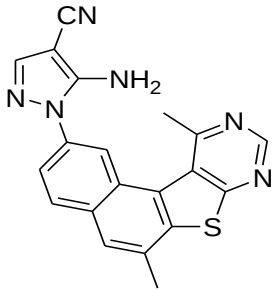
Fioravanti et al. [7] synthesized a series of N-(1,3-diphenyl-1H-pyrazol-4-yl) methylanilines and evaluated in vitro for cytotoxicity for antiviral activity against different types of viruses.



Compound-8

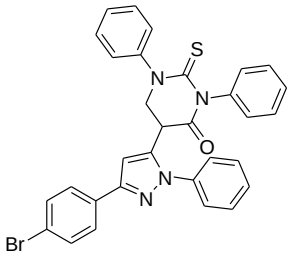
R_1= H, Br, Cl, CF_3, CH_3 R =CH_3, CH_3, CF_3, Br, H

Aymn E. Rashad, et al. [8 synthesized substituted pyrazole derivatives. These derivatives show encouraging antiviral activity against hepatitis A virus.



Compound-9

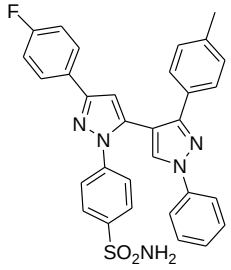
Kumar et al. [9] were developed several pyrimidine-pyrazoles and they shows good antimicrobial activity with MIC of 31.2544 µg/ml against S. aureus and Bacillus cereus.



Compound-10

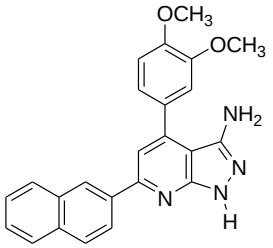
Pyrazole as an anti-inflammatory agent

Sharma et al. [10] synthesized and estimated pyrazolyl-pyrazoline derivatives for their anti-inflammatory activity. Among these compounds, compound 11 shows promising promising anti-inflammatory activity. It was compared with nimesulide.



Compound-11

Russo et al. [11] synthesized Pyrazolotriazolopyrimidine derivatives screened for anti-inflammatory activity and shows promising activity. Compound 12 shows good results.



Compound-12

II. CONCLUSION

Pyrazoles and its derivatives have various biological activities in different medicinal field. It is a distinct compound showing various useful activities. By studying literature of this compound, we can synthesize more compounds. Biological activities of different pyrazole derivatives can be considered for further research.

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Antibacterial and Antifungal Study of Schiff Base Rare Earth Complexes Derived from 4-Amino Benzoic Acid

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ABSTRACT

Antimicrobial activity of rare earth Schiff base complexes were studied in-vitro. Schiff base prepared from 4-amino benzoic acid and ortho-vanillin and rare earth complexes were prepared by using Lanthanum, Cerium, Praseodymium, Neodymium, Gadolinium and Dysprosium. Synthesized compounds were characterized using sophisticated instrumental technique, magnetic moment and molar conductance. The disc diffusion method and Minimum Inhibitory Concentration (MIC) studies using the double dilution method were employed to assess antibacterial and antifungal activities. Assay carried out by taking concentration 100 microgram per disk and compared with Chloramphenicol and Amphotericin B standard drug. Antibacterial activity studied in-vitro against Gram-positive bacteria Bacillus subtilis and with Gram-negative bacteria Pseudomonas aeruginosa. Antifungal activity studied in-vitro against Saccharomyces cerevisiae. Ligand and Ce(III) complex shows comparable activity against Saccharomyces cerevisiae.

Keywords: Antibacterial, Antifungal, Complex, Rare Earth.

I. INTRODUCTION

Amino acid Schiff bases are important biological ligands and their metal complex studies are limited to transition elements. Rare earth complexes have applications in fertilizer, medicine, antiseptic and feedstuff etc. and also have some interesting biological properties, such as less toxicity and anticancer activities [1]. Rare earth complexes with Schiff bases are flexible compounds and extensively used for commercial application. These complexes have comprehensive range of biological applications such as antifungal, anti-bacterial, anti-malarial, anti-proliferative, anti-pyretic, anti-inflammatory and anti-viral characteristics [2]. It is believed that the chelated complexes inhibit several cellular enzymes that are important in the metabolism of many of the microorganisms [3]. The rare earth elements can improve antibacterial properties when they are combined

with organic ligands. The antibacterial properties of rare earths-containing antibacterial materials have been shown to release large quantities of free hydride radicals [4]. Rare earth ions prevent the growth of bacteria, fungus, and soil nematodes [5]. Rare earths have been utilized as anticoagulants, anti-atherosclerotic drugs, and tuberculosis therapies with differing degrees of success [6]. The use of lanthanum carbonate or Fosrenol as a phosphate binder in the treatment of hyperphosphatemia in renal dialysis patients in the USA and Europe has been a success story for rare earths as therapeutic metals [7]. Several studies have been revealed that the C=N linkage in azomethine derivatives is important for biological activity and these types of compounds exhibit significant anticancer, antifungal, and antibacterial properties [8,9,10]. In recent years, there has been an increased focus on the synthesis of Schiff base complexes with rare earth elements due to their numerous applications, including their antibacterial and anticancer properties [11,12]. Due to their applications in diagnostic medicine, such as magnetic resonance imaging contrast agents, rare earth complexes have drawn attention for long period of time [13]. High biological activity is observed in the rare earth complexes, and the sensitivity and neutrality of rare earth ions are enhanced by a carboxylic acid ligand containing N and O atoms, which acts as an antenna [14]. Keeping this in view, preparations were made for Schiff base and its rare earth complexes, and their antibacterial and antifungal properties were studied.

II. MATERIALS AND METHODS

Chemicals used in the experiments were bought from S.D. Fine and Alfa aesar. In the antimicrobial activity microorganism used, its strain name and reference are [Bacillus subtilis NCIM 2250], [Pseudomonas aeruginosa (NCIM 2036)] and [Fungi (yeast) Saccharomyces cerevisiae (NCIM 3050)]. [NCIM: National Collection of Industrial Microorganisms, National Chemical Laboratory (NCL), Pune 411008 (India)]

Experimental

Synthesis of rare earth complexes:

Rare earth complexes with a Schiff base ligand were prepared using lanthanum, cerium, praseodymium, neodymium, gadolinium, and dysprosium [15]. Schiff base [L] (E)-4-((2-hydroxy-3-methoxybenzylidene)amino)benzoic acid synthesized by using ethanolic solution of 4-amino benzoic acid (0.002m) mixed with ortho-vanillin (0.002m) dissolved in ethanol, mixed solution stirred for 15 minutes at 60℃. An orange solid product was obtained and washed with methanol. Obtained product was filtered, dried and melting point was taken. To an ethanolic solution of Schiff base (0.004 mol) containing equimolar NaOH, lanthanide nitrate (0.002 mol) in 10 mL ethanol was added drop wise with constant stirring for half an hour on hot plate at 60℃, in the solution metal to ligand ratio is 1:2. A solid product was obtained, filtered off, and washed with ethanol.

Characterization:

Schiff base ligand and its rare earth complexes were characterized by different analytical sophisticated instrument techniques. UV, IR, NMR, HRMS, TGA, magnetic moment and molar conductance were used for Characterization. All synthesized Ln(III) complexes were correspond to the formula $[LnL_2(H_2O)_2]2H_2O$. All prepared complexes were stable in air and non-hygroscopic in nature.

Formation of Schiff base ligand was confirmed by NMR, a singlet pick observed at 9.00δ assigned to Schiff base proton [16]. HRMS for Schiff base calculated [M+H] is 72.0923 and in the spectra found at 272.0916 which confirms the proposed structure. A strong absorption band at 1619 cm^{-1}, which may be attributed to the azomethine group [HC=N], carbonyl[C=O] of COOH group observed at 1692 cm^{-1} [17]. As per differences in symmetric and asymmetric stretching frequencies, carboxylate group shows bidentate coordination to metal ion [18]. Metal-oxygen band found at 447 cm^{-1} and 453 cm^{-1} [19]. UV–Vis spectra of Complexes differ from the free Schiff base, supports the formation of new complexes. Blue shift observed in the electronic spectra of complexes [20]. Coordinated water molecules and lattice water molecules found in thermo gram. The TGA results showed that the Schiff base and its rare earth complexes are thermally stable at room temperature [21]. When rare earth coordinated with Schiff base ligands, the complexes exhibit unchanged magnetic moments, suggesting that the 4f electrons are not involved in bond formation [22]. Molar conductance studies suggest non-electrolytic nature of the complexes.

Antimicrobial studies:

The disc diffusion method was used to examine the antibacterial and antifungal properties of Schiff base and its rare earth complexes of Lanthanum, Cerium, Praseodymium, Neodymium, Gadolinium and Dysprosium. In the antibacterial activities, compounds were tested at 1000 ppm concentration against Pseudomonas aeruginosa and Bacillus subtilis and compared with chloramphenicol standard. Synthesized compounds were further tested for their antifungal efficacy against Saccharomyces cerevisiae at a concentration of 1000 ppm and compared with Amphotericin B standard [23,24]. Disc diffusion was used to monitor the antibacterial and antifungal activity in vitro using disc size 6 mm. For the stock solution compounds were dissolved in DMSO. The Whatman No. 42 paper discs of 6 mm in diameter were cut and sterilized in an autoclave and soaked with solution. Paper discs soaked in desired concentration of the compounds were placed aseptically in the plates containing media. The nutrient agar medium was used for screening the antibacterial activity and the potato dextrose agar and MGYP medium was used for screening the antifungal activity. The plates were incubated at 37°C for 24 hours, and the diameter of the inhibition zones (zones where bacterial growth is inhibited) was measured [25,26].

Table 1. Antimicrobial activity of Schiff base and its rare earth complexes.

Test Compound	Bacillus subtilis	Pseudomonas aeruginosa	Saccharomyces cerevisiae
Schiff base ligand	10.02	10.09	27.12
La(III) complex	00.00	13.12	00.00
Ce(III) complex	13.12	10.11	25.22
Pr(III) complex	13.02	13.33	00.00
Nd(III) complex	12.14	10.14	00.00
Gd(III) complex	6.56	00.00	00.00
Dy (III) complex	10.11	00.00	00.00
Chloramphenicol	26.12	24.53	NA
Amphotericin B	NA	NA	28.19

Zone of inhibition = Diameter in mm calculated by Vernier Caliper,

NA = Not applicable

Minimum inhibitory concentration (MIC) studies:

Minimum Inhibitory concentration (MIC) of Schiff base and its rare earth complexes was tested in-vitro using double dilution method at the different concentration. Stock solution 10.24 mg per 5 ml [equivalents to 2048 microgram per ml] of each compound was prepared in DMF. Further dilutions were prepared in water. In this double dilution method various concentrations Viz.1024, 512, 256, 128, 64, 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.125 microgram/mL were used. The incubation of tubes placed for 24 h at 37 °C and minimum inhibitory concentration (MIC) of each tube was measured. The results obtained were compared with known standard drug. Obtained data is presented in table 2 [25,26].

Table 2. Minimum inhibitory concentration (MIC) of Schiff base and its rare earth complexes.

Test Compound	Bacillus subtilis	Pseudomonas aeruginosa	Saccharomyces cerevisiae
Schiff base ligand	512	512	8
La(III) complex	>1024	256	>1024
Ce(III) complex	256	256	>1024
Pr(III) complex	256	256	>1024
Nd(III) complex	256	512	>1024
Gd(III) complex	>1024	>1024	>1024
Dy (III) complex	256	>1024	4
Chloramphenicol	0.125	4.0	NA
Amphotericin B	NA	NA	0.2

Minimum inhibitory concentration (MIC) microgram per ml (μg/ml)

III.RESULTS AND DISCUSSION

Testing was carried out against Gram positive strains Bacillus subtilis and Gram negative strains Pseudomonas aeruginosa and antifungal activity against fungi Saccharomyces cerevisiae by disc diffusion method. Schiff base ligand shows comparable zone of inhibition with standard against fungi Saccharomyces cerevisiae. The Ce(III) complex shows zone of inhibition close to standard. The data from the inhibitory zone shows that strains of bacteria and fungus, Schiff base and its metal complexes were moderate active or inactive. The impermeability of microbe cells or differences in ribosomes in microbial cells affects the toxicity of various complexes against various species [27-29].

The findings of the minimum inhibitory concentration (MIC) test show that the majority of the tested compounds required higher concentrations than the standard. Schiff base ligand required lowest 8 microgram/mL concentration against Saccharomyces cerevisiae among studied compounds. Dy(III) complex required lowest 4 microgram/mL concentration against Saccharomyces cerevisiae and shows good results of MIC compare to other complexes. In addition to being a requirement for antibacterial activity some factors are also responsible, such as steric hindrance, electronic and pharmacokinetic variables working along with the mechanistic pathway. It has also been observed that solubility, conductivity, dipole moment, size of the metal ion, stability constants of the complexes and their magnetic moments affect the activity of compounds against

microbes [30-32]. The inhibitory zone data reveals that both Schiff base and its complexes showed good to moderate activity against strain Saccharomyces cerevisiae than the other compounds.

IV.CONCLUSION

The disc diffusion method and double dilution method were used to investigate the antibacterial activity of the Schiff base and its rare earth complexes against the Gram positive strains Bacillus subtilis as well as the Gram negative strains Pseudomonas aeruginosa. According to the findings Schiff base and its complexes shows no zone to moderate inhibition. Although the majority of the tested compounds were determined to be modestly active compared to the standard. In minimum inhibitory concentration (MIC) studies show that the majority of the tested compounds need higher concentrations than the standard. Amongst all strains compounds good activity against strain Saccharomyces cerevisiae compared to others.

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Preparation, Characterization and Biological Relevance of Cr, Mn and Cu Complexes Synthesized from 2, 2'-(1,3phenylenebis(methylene)) bis (azanylylidene)) bis(methanylylidene)) bis(4chlorophenol)

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ABSTRACT

A synthesis of transition metal complexes of Cr (III),Mn (II) and Cu (II) from: 2, 2'-(((1,3phenylenebis(methylene))bis (azanylylidene))bis(methanylylidene))bis(4-chlorophenol) have been synthesized and characterized by 1H NMR, IR spectral studies. FTIR spectra confirms that the ligand co-ordinates metal ion to form complex via oxygen and nitrogen atom of the phenolic group and azomethine group respectively. The spectroscopic studies suggested the octahedral structure of Cr (III) , Mn (II),and Copper (II) Complexes. The spectroscopic data of complexes is in agreement with their structure in which N2O2 group act as tetra-dentate ligand and two chlorides as a mono-dentate ligands.

Keyword: Transition metal complex, Schiff base ligand, Characterization.

I. INTRODUCTION

More than 150 years ago Hugo Schiff prepared compounds with azomethine group by condensation of primary amine and carbonyl compound which are now a days commonly referred as Schiff bases.[1] The azomethine group of schiff bases contain a lone pair of electrons in the sp^2 hybridized orbital of nitrogen atom. Schiff bases on combination with one or more donor atoms close azomethine group have good chelating ability. Schiff bases are proven as interesting ligands in coordination chemistry[2].

The Schiff bases are the important compounds owing to their wide range of biological activities and industrial applications. They have been found to possess pharmacological activities such as antibacterial,[3-6] antifungal,[7] anticancer,[8] anti-HIV,[9] antitubercular,[10] antiviral,[11] antiinflammetry,[12] anticonvulsant[13] and antimalarial.[14] The metal complexes of Schiff bases are used as catalyst in various organic transformations.[15]

The presence of various substituents in the phenyl rings of aromatic Schiff bases are responsible for antifungal activity, which changes depending upon the type of substituent present on the aromatic rings.

In view of these above biological importance of Schiff bases, we have synthesized some new Schiff bases and metal complexes of these novel Schiff bases and evaluated their bioactivity. New Schiff bases were synthesized by refluxing the reaction mixture of m-xylylene diamine with halogen substituted salicylaldehyde in ethanol in the presence of glacial acetic acid.

The entire synthesized compounds were characterized on the basis of their IR, ^{1}H NMR spectra and halogen, nitrogen analysis. The antibacterial activity of compound was evaluated by Agar cup method respectively. In this study Schiff base metal complexes are widely studied subject due to their industrial and biological applications. Literature reports suggest that some drugs show enhanced activity when administrated as a metal complex rather than as an organic compound. The synthesis of novel schiff bases complex becomes wide spread due to their potential application in chemistry, biochemistry, medicine.

II. EXPERIMENTAL

Materials and reagents

Chemicals like m-xylylene diamine purchased from sigma Aldrich, salicylaldehyde from SD Fine and Cobalt salt from were used to prepare metal salt and other reagents were of analytical grade.

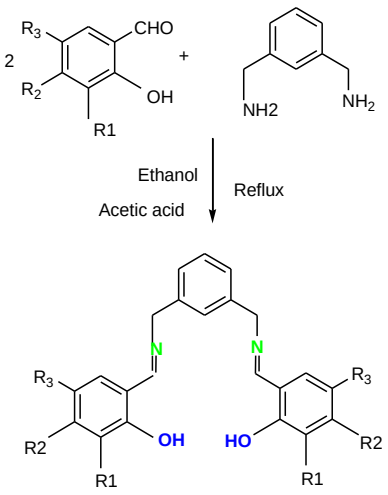
Physical measurements

The melting points were taken in open capillary tube and were uncorrected. The IR spectra of the compounds were recorded on a Bruket IFS 66V spectrometer with KBr pellets. ^{1}H NMR spectrums were recorded on a Gemini 200 MHz spectrometer using TMS as an internal standard and Mass spectra of ligand were recorded on VG 7070H mass spectrometer. The purity of the compounds was checked by TLC on silica gel plates and the spots were developed in iodine chamber.

Synthesis of Schiff base

The new Schiff bases were synthesized by condensing the substituted salicylaldehyde and m-xylylene diamine in a 2:1 proportion. The mixture was dissolved in 15-20 ml ethanol with the addition of 2-3 drops of acetic acid and heated under reflux condition for 3h. The yellow colour precipitate obtained was filtered. The yellow product was purified by recrystallization from hot ethanol.

Scheme: Synthesis of Schiff bases.



Spectral analysis of Schiff base

2,2'(((1,3phenylenebis(methylene))bis(azanylylidene))bis(methanylylidene))bis(4chlorophenol).

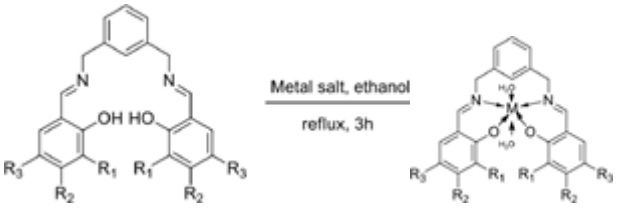
Yield 75%, mp 130 °C; IR (KBr) cm^{-1}: 3062(OH), 1635 (HC=N), 1569(C = C), 1208 (H_2C – N); ^1H NMR ($CDCl_3$) δ: 13.33 (2H, s, Ar – OH), 6.91- 7.40 (10H, m, Ar-H), 8.38 (s, 2H, -CH=N), 4.83(s, 2H, - CH_2-N). ^{13}C NMR ($CDCl_3$) δ ppm: 63.02 (-CH_2-N), 118.63-132.37 (phenyl), 164.61 (-CH=N). EIMS: m/z $[M]^+$ calculated for $C_{22}H_{18}Cl_2N_2O_2$: 413calcd.C63.93 H-4.39 Cl-17-48 N 6.65

Synthesis of metal complex

Synthesis of Schiff base metal complexes were carried out by the process as described below.

The Schiff base ligand (10 mmol) was dissolved in 20 ml absolute ethanol. A solution metal salt (10 mmol) in 30 ml absolute ethanol was added in to the above Schiff base ligand solution under constant stirring. In all the cases the reaction metal ligand molar ratio was 1:1. The resultant reaction mixture was refluxed for 3h and obtained precipitated product. The precipitate of product was filtered. The red brown coloured filtered product was dried at room temperature.

Scheme: Synthesis of metal complex Scheme



Where- M = Metal (Cr,Mn,Cu), R^1 = H, R^2 = H, R^3 = Cl

Spectral analysis of metal complex of Chromium

Yield 68%, mp 180 °C; IR (KBr) cm^{-1}: 3410 (OH), 2360(HC=N), 1635-1479 (C=C), 1184 (H_2C–N), 559 (Cr-N); MF $C_{22}H_{20}O_2N_2Cl_2Cr$

Spectral analysis of metal complex of Manganese

Yield 72%, mp 168 °C; IR (KBr) cm^{-1}: 3455 (OH), 2426(HC=N), 1635-1479(C=C), 1221.51 (H_2C–N), 644 (Mn-N); MF $C_{22}H_{20}O_2N_2Cl_2Mn$

Spectral Analysis of metal complex of Copper

Yield 68%, mp 250 °C; IR (KBR) cm^{-1}: 3421(OH), 2352(HC=N), 1618-1460 (C=C), 1280, (CH_2-N), 660 Cu-N); MF $C_{22}H_{20}O_2N_2Cl_2Cu$.

Antibacterial activity

Antibacterial (E. coli, B. subtilis, S. typhi and S. aureus) activity were evaluated by agar cup method. Diameter zone of inhibition in mm for antibacterial activity datagiven table 1.

Table- 1: Antibacterial activity of synthesized compound.

Sr. No	Name of compound	E. coli	B. subtilis	S. typhi	S. aureus
1	Schiff base	13	14	16	-
2	Metal complex of Chromium	10	04	02	01
3	Metal complex of Magnese	11	04	01	01
4	Metal complex of Copper	12	02	02	02
5	Standard	08	25	21	30

Ligands: -ve, no antibacterial activity

Zone of Inhibition: --mm

Antioxidant (DPPH radical scavenging activity)

The molecule 1,1-diphenyl-2-picrylhydrazyl (α, α-diphenyl-β-picrylhydrazyl; DPPH) is characterized as a stable free radical by virtue of the delocalization of the spare electron over the molecule as a whole, so that the molecule does not dimerize, as would be the case with most other free radicals. The delocalization of electron also gives rise to the deep violet colour, characterized by an absorption band in ethanol solution centred at about 517 nm. When a solution of DPPH is mixed with that of a substrate (AH) that can donate a hydrogen atom, then this gives to the reduced form with the loss of this violet colour.

The ability of compounds to scavenge DPPH radical was assessed using Sambath Kumar and co-worker's method and Manzocco and co-workers method[16] with modification. Briefly, 1 ml of synthesized compounds as 1 mM was mixed with 3.0 mM DPPH (0.5 mmol/L in methanol), the resultant absorbance was recorded at 517 nm after 30 min incubation at 37 ^{o}C. The percentage antioxidant or radical scavenging activity was calculated by using the following formula.[17-18] Antioxidant activity (%) = [(AC–AS) / AC] x 100 where AC is absorbance of DPPH and AS is absorbance reaction mixture (DPPH with sample).

The antioxidant activities of the Schiff bases are expressed in comparison with ascorbic acid as standard. Antioxidant activity of Schiff base showed poor activity compound as compared to that of standard (ascorbic acid) The results are reported in Table 2.

Table 2: Antioxidant activity of Synthesized compounds of Schiff base and metal complex

Sr. No.	Sample Code	ABS at 517 nm	Activity (%)
1	Blank	1.43	-
2	Standards	0.13	90.90
3	Schiff base	0.39	09.79
4	LM6	0.368	09.80
5	L1M5	0.376	07.84
6	L1M4	0.331	18.87

III.RESULT AND DISCUSSION

The Schiff bases were obtained in good yields from condensation reaction of halo substituted salicyaldehyde and m- xylylene diamine (**Scheme 1**) and purified by hot ethanol. The purity of the compound was checked by TLC. The compounds were characterized by elemental n structures of the Schiff bases were elucidated on the bases of spectroscopic data. The molecular ion peaks in the mass spectra of Schiff bases conformed to the calculated molecular masses.

In IR spectra of the compounds revels the disappearance of the band about 1700 cm^{-1} attributed to the carbonyl group (C=O) and appearance of a band in the region 1659-1607 cm^{-1} assigned to the azomethine (HC=N) band thereby indicating formation of the Schiff bases. The characteristic band in the region 3082-2979 cm^{-1} are assigned to phenolic (OH) with intermolecular N---HO hydrogen bonding. The H_2C-N bands are observed in the region at 1285-1208 cm^{-1}.

The IR spectrum of Schiff base shows OH stretching at 3036 cm^{-1} whereas complex molecules show it around 3400-3480 cm^{-1}. In IR spectra of Schiff base-metal complex molecule shows new metal-N coordinate bond stretching at 657 cm^{-1}. Therefore, the Schiff base-metal complex structure is confirmed.

The results show that Schiff base compound shows significant activity against B. subtilis, S. typhi, S. aureus and E. coli as compared with standard and metal complexes shows moderate activity as compared with standard.
All the synthesized Schiff bases were screened for their antioxidant activity. DPPH assay was performed to measure the ability of the Schiff bases to scavenge the DPPH free radicals. The colour change produced by free radical scavenging, result a change in absorbance among these compounds Schiff base have moderate Antioxidant activity as comparatively prepared metal complexes.. Table 2.

IV.CONCLUSION

In the present study, we synthesized new Schiff base and their metal complex with cobalt and they were characterized through elemental analysis, melting point, IR, ^{1}H NMR and ^{13}C NMR spectroscopic technique. From this data, structures of Schiff base have been confirmed. The results indicate mild to moderate antibacterial activity. The Schiff base compounds showed significant activity & metal complex showed poor activity as compared to Schiff base. Synthesized Schiff base & metal complex were screened for their antioxidant activity. The result was not good for metal complex of copper complex shows good antioxidant activity and Schiff base ligand and Cr (III) and Mn (II) moderate activity as compared to standard.

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Evaluation of LC-MS/MS Based Phytochemical Profiling and Antioxidant Activity of Argemone Mexicana L. Leaf Extract

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ABSTRACT

The medicinal plant Argemone mexicana L. belongs to Papaveraceae family shows potential ethnopharmacological activities. In Ayurveda, Homeopathy, Siddha and Unani system, its various parts are widely used as traditional medicine to treat various ailments. The present study was designed to evaluate LC-MS/MS based phytochemical profiling of different phytochemical constituents present in aqua-ethanolic extract of Argemone mexicana L. leaf and antioxidant activity. In the phytochemical evaluation of leaf aqua-ethanol extract obtained from Argemone mexicana L. demonstrated the presence of alkaloids, protein, glycoside, tannins, flavonoids, steroids and phenolic compounds, while it explants through LC-MS/MS profiling showed richness of about 11 chemical constituents. These bioactive phytocompounds may be utilized in treating various ailments.The antioxidant activity of Argemone mexicana L. plant was evaluated using its leaf aqua-ethanol extract by free radical scavenging DPPH assay study and has been found that effective free radical scavenging potential with IC50 value 43.38 ± 0.02 µg/mL. Therefore, the evaluation study clearly indicates that medicinal plant Argemone mexicana L. leaf aqua-ethanol extract was rich in phenols, flavonoids and other active phytochemical components. The antioxidant activity depends on polyphenolic content and other phytochemical constituents present in leaf aqua-ethanol extract. It could be a potential source of natural free radical scavenger and have greater importance as therapeutic agent in preventing or slowing oxidative stress related degenerative diseases. Therefore, aqua-ethanol extract of Argemone mexicana L. leaf reported rich source of phytochemical constituents with potential antioxidant activity.

Keywords: Argemone mexicana L., aqua-ethanol extract, LC-MS/MS, DPPH, antioxidant activity.

I. INTRODUCTION

Oxygen is essential for the survival of life on earth; a small amount of oxygen is converted to numerous free radicals as it is utilized in various living metabolic processes. The several biochemical reactions occurs in

human body generate reactive oxygen species and these are capable of damaging crucial biomolecules. They are not effectively scavenged by cellular constituents produce by living body, they lead to disease conditions. The use of local traditional medicine from plant sources present in a large scale contains natural antioxidant, which has been showing effective free radical scavenging activity that might serve as leads for development of more active drugs. Antioxidants are the chemical constituents that neutralize free radicals, otherwise which damages the crucial bio-molecules present in body. Free radicals are chemically active product of metabolism and include reactive oxygen species or reactive nitrogen species. Appearance of radicals originates a number of human neurologic and other metabolic disorders [1]. These different type of pathological disorders believed to the associated with oxidative stress [2,3]. Synthesized antioxidants have been widely used for treatment the pathological conditions. The continuous use of these antioxidants in food preparations have been introduces to potential health risks, toxicity and carcinogenicity [4,5]. Majority of the diseases today are due to the shift imbalance of the pro-oxidant and the antioxidant homeostatic phenomenon in the body. Pro-oxidant conditions dominate either due to the increased generation of the free radicals or due to the excessive oxidative stress of the depletion of the dietary antioxidant [6]. Many plants exhaustively studied in the last few years for their antioxidant and radical scavenging activities [7]. The different parts of the Argemone mexicana L. plant is extensively used as traditional medicine for the treatment of numerous diseases. Its chemical investigations reported to have the presence of active phyto constituent's [8]. The aerial parts of Argemone mexicana L. showed DPPH scavenging activity [9]. This activity reported by extract is due to the presence of flavonoids, phenolic and other various constituents in its parts [10]. The literature reviewed survey of Argemone mexicana L. were summarised for their some important medicinal and pharmacological activities. There is a scope to identify new bioactive compounds and check their claimed pharmacological activities [11]. Therefore, taking into consideration the vast potentiality of Argemone mexicana L. plant as source of antioxidants, a systematic investigation of leaf was undertaken to study.

II. METHODS AND MATERIAL

Collection of Plant material

Leaf of Argemone mexicana L. plant were collected from local area identified and authenticate with the help of our institute botanists. The collected leaf is cleaned with distilled water to remove dirt and air dried in shade.

Preparation of Extract

The Argemone mexicana L. dried leaf were rushed and powdered with the help of grinder. 20 g of powdered plant material was macerated in 100 mL of aqua-ethanol and kept on a magnetic stirrer for stirring and extracted using a soxhlet apparatus sequentially in aqua-ethanol solvent. The fraction of extract was collected and solvent was evaporated out to dryness. The extracted material was stored in airtight bottles for further investigation studies.

Phytochemical analysis

The leaf aqua-ethanol extract was qualitatively evaluated for the bioactive phytochemical contents reporting such as alkaloids, carbohydrate, protein, amino acids, glycoside, tannins, saponin, flavonoids, steroids, terpenoids and phenolic compounds etc. by the help of standard protocol [12,13,14] used for qualitative analysis.

LC-MS/MS analysis

LC-MS/MS analysis technique was used for identification of phytochemical ingredients separated by liquid chromatography. It provides separation of ingredients and detection by MS provides molecular weight of compounds. LC-MS/MS analysis of aqueous solvent extracted material was carried out on Waters UPLC-TQD Mass spectrometer. The ingredients were identified by comparison of mass spectra with the inbuilt Metlin, Lipid and Mass Bank databases.

In vitro antioxidant activity

The in vitro antioxidant activity was evaluated by using stable free radical DPPH (2, 2-diphenyl-1-picrylhydrazyl) with the help of UV-spectrophotometer [15,16,17]. 0.1 mM DPPH stock solution was prepared in ethanol solvent. 1.0 mL of this stock solution was added to 1.0 mL of extract solution in water at different concentrations (5-50 µg/mL) and final volumes were made to 3 mL by adding distilled water. After 20 minutes, the absorbance of each concentrations of test solution was measured at 517 nm. Ascorbic acid was used as standard. The absorbance of the test solutions were decreases with increase in concentration of leaf extract, which confirms presence of free radical scavengers in extracts. Percentage of DPPH free radical scavenges by test solution were measured as

$$\% \text{ Free Radical Scavenged} = (A_{Control} - A_{Test} / A_{Control}) \times 100$$

IC_{50} values were determined by using graphical method.

Statistical analysis

The tests were carried out in triplicate and its results expressed in mean ± SD. Values of $P < 0.05$ were considered as statistically significant.

III.RESULTS AND DISCUSSION

In the present evaluation study, LC-MS/MS based phytochemical profiling and antioxidant activity of Argemone mexicana L. leaf aqua-ethanol extract was carried out as follows

Phytochemical analysis

The phytochemical analysis of the leaf ethanol extract shows the presence of alkaloids, protein, amino acid, glycoside, tannins,flavonoids, steroids and phenols as shown in Table 1 [18].

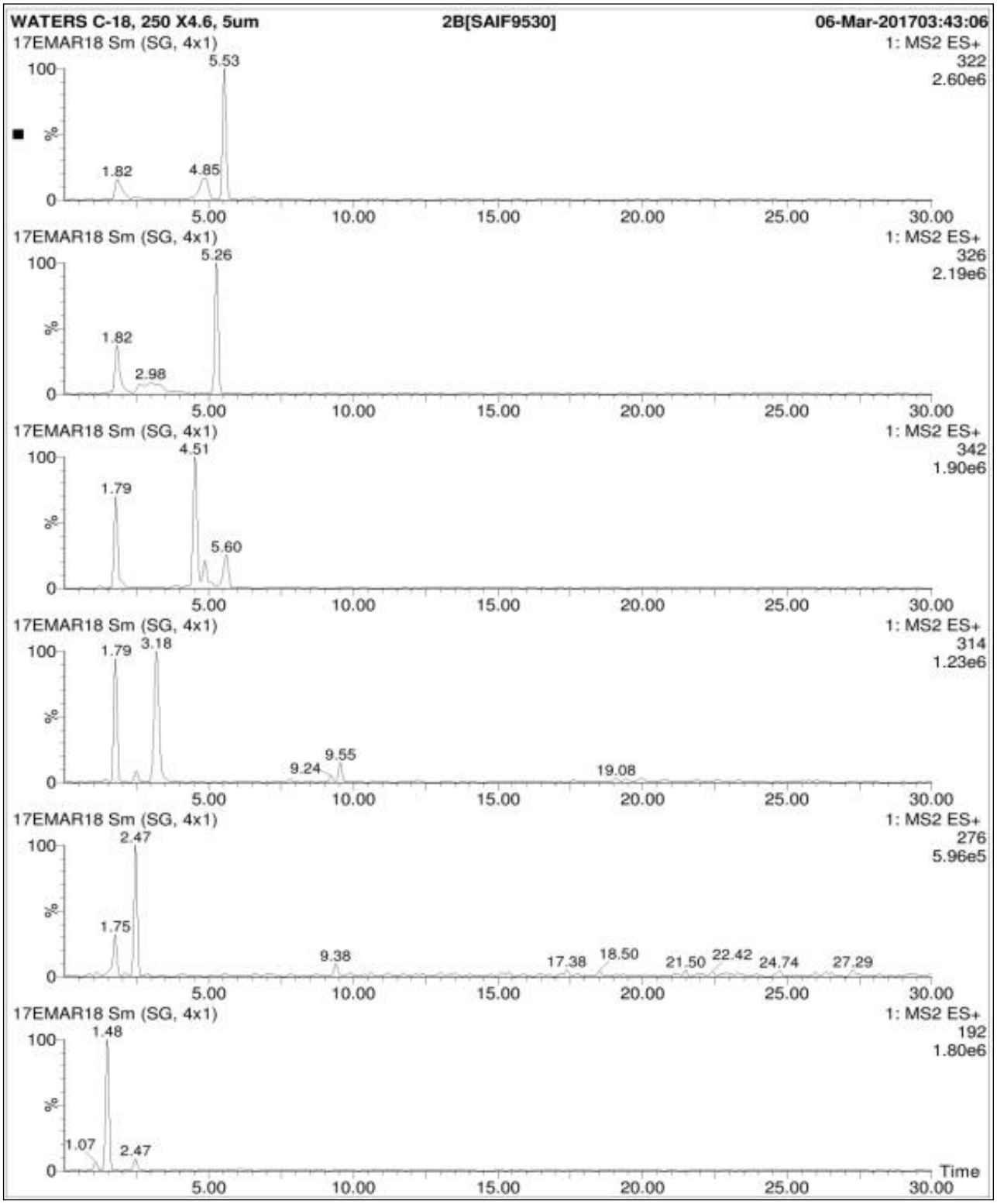
Table 1. Phytochemical analysis of leaf aqua-ethanol extract

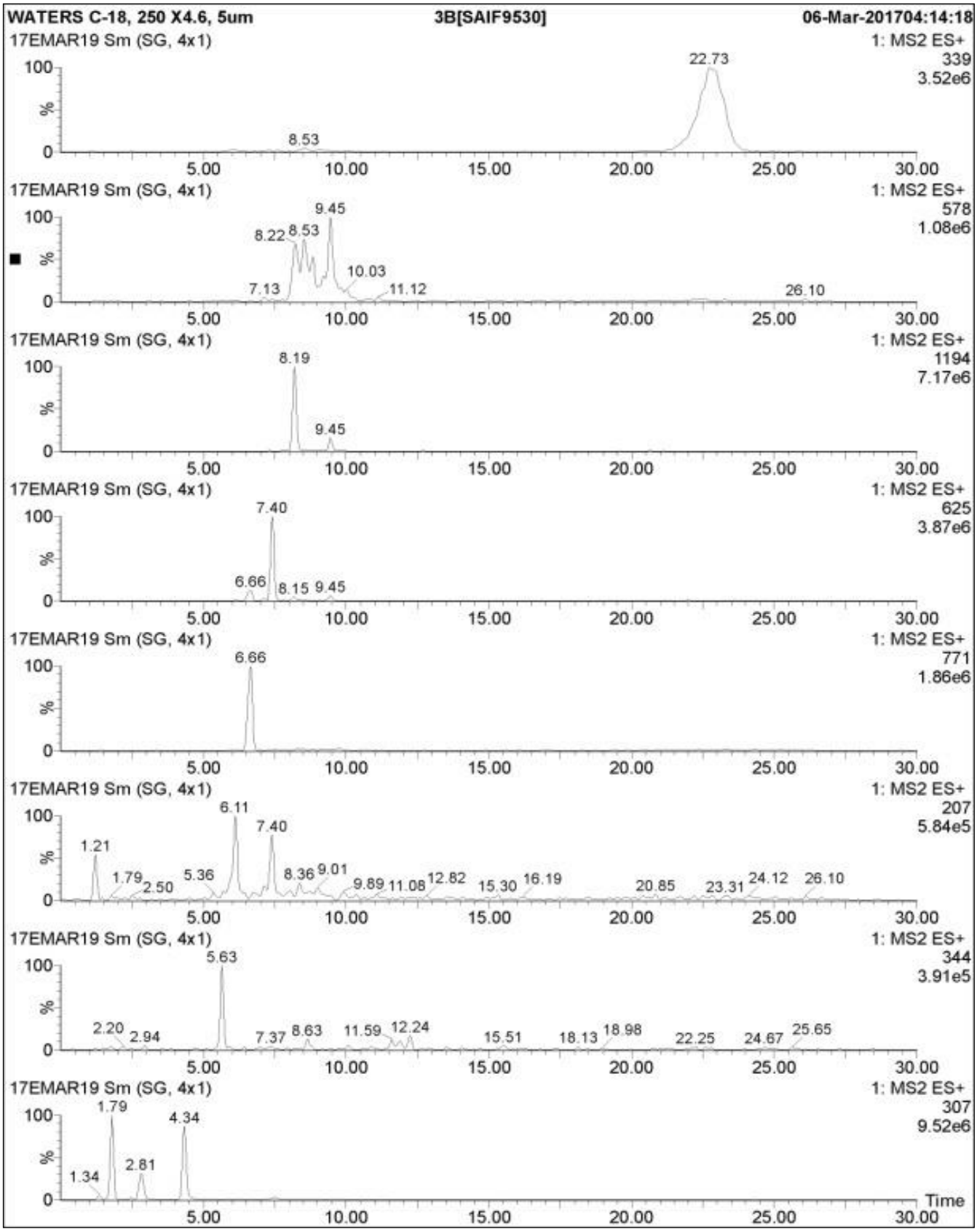
Sr. No.	Phytochemical Tests	Result
1	Alkaloid	+
2	Carbohydrate	-
3	Protein and amino acids	+
4	Glycoside	+
5	Tannin	+
6	Saponin	-
7	Flavonoids	+
8	Steroids	+
9	Triterpenoids	-
10	Phenolic compounds	+

(+) for present and (-) for absent

LC-MS/MS analysis of aqua-ethanol extract

The effective bioactive phytochemical ingredients in Argemone mexicana L. leaf are responsible for potency of antioxidant activity were screened by LC-MS/MS analysis spectral technique. The LC-MS/MS analysis of Argemone mexicana L. leaf aqua-ethanol extract was detected phytocompounds intensity peaks chromatogram (TIC and EIC) as shown in fig. 1.

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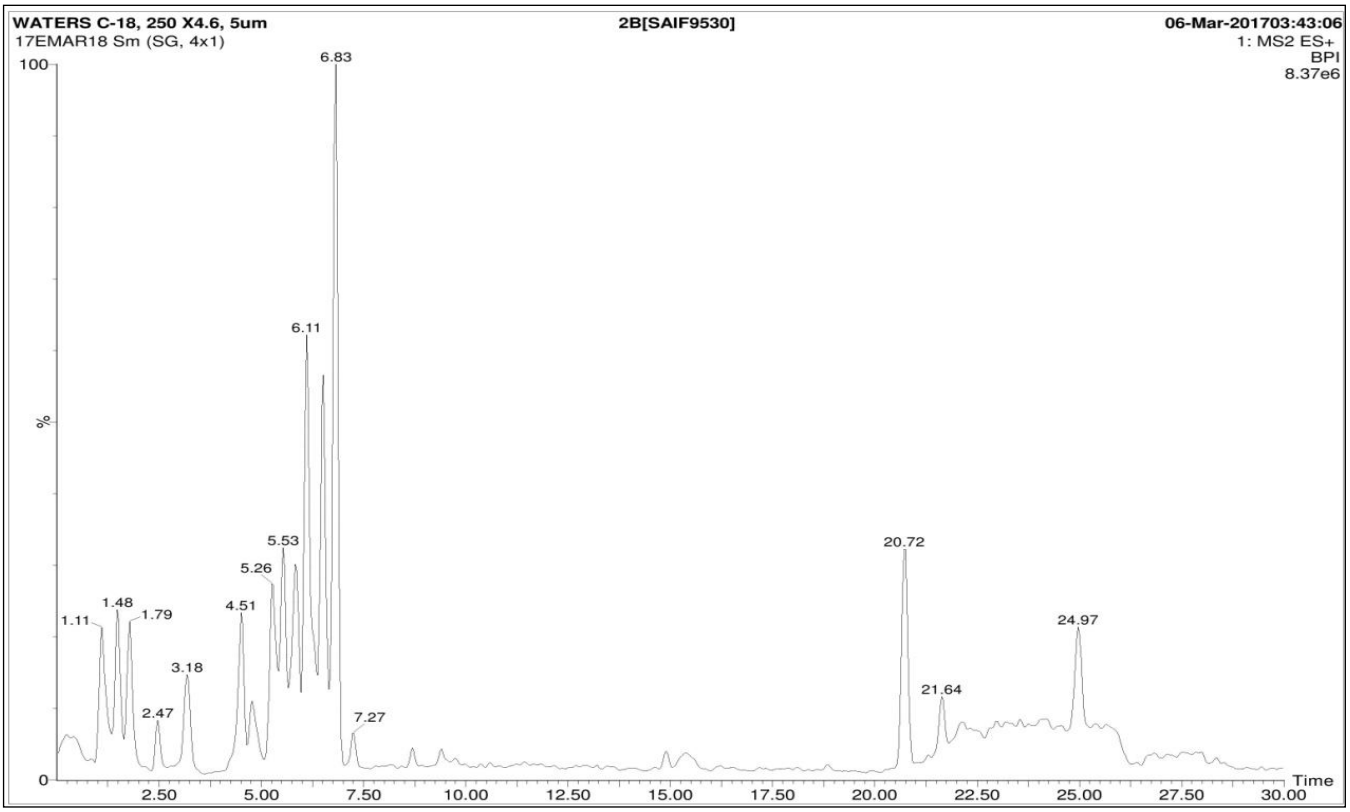

Fig. 1 LC-MS/MS chromatogram (TIC and EIC) of aqua-ethanol extract

Table 2. Phytochemical ingredients detected in leaf aqua-ethanol extract

Peak	R. Time	Name	Base m/z
1	1.48	2-amino-2,3,7-trideoxy-D-lyxo-hept-6-ulosonic acid	192
2	2.47	Glutarylcarnitine/(3S)-3-[(4-carboxybutanoyl)oxy]-4-(trimethyl azaniumyl)butanoate	276
3	3.18	1-methyl-2-acetyl-sn-glycero-3-phosphocholine	314
4	4.51	1,2-diacetyl-sn-glycero-3-phosphocholine	342
5	5.26	Ifenprodil	326
6	5.53	Clopidogrel / methyl 2-(2-chlorophenyl)-2-(6,7-dihydro-4H-thieno[3,2-c]pyridin-5-yl)acetate	322
7	6.11	1,2-dipropionyl-sn-glycero-3-phosphocholine	370
8	6.83	9,10-dimethoxy-5,6-dihydro[1,3] dioxolo[4,5-g]isoquino[3,2-a]isoquinolin-7-ium / Berberine	336
9	20.72	Seneciphylline	334
10	21.64	Chlorpyrifos / diethoxy-sulfanylidene-(3,5,6-trichloropyridin-2-yl)oxy-{5}-phosphane	350
11	24.97	Thiamine pyrophosphate	425

Phytochemical screening and LC-MS/MS analysis (Fig. 1) of Argemone mexicana L. leafs extract revealed the presence of 11 different bioactive phytocomponents [19]. The different parts of plant are used in the world for the treatment of several ailments. Chemical constituents isolated from this plant are mostly belong to the class of alkaloids, besides, terpenoids, flavonoids, phenolics, long chain aliphatic compounds and few aromatic

compounds [21,22]. Therefore Argemone mexicana L. is an important source of various types of phytocompounds, which are responsible for many pharmacological activities [23,24].

In vitro antioxidant activity

The antioxidant activity and phytochemical ingredients content in Argemone mexicana L. leaf aqua-ethanol extract was carried out. The experimental data and results of leaves aqua-ethanol extract and ascorbic acid as a standard were represents in Table 3.

Table 3. % Free radical scavenged activity of standard and leaf extract

Sr. No.	Concentration in (µg/mL)	% Free radical scavenged of standard	% Free radical scavenged of leaves extract
1	5	41.08 ± 0.02	32.09 ± 0.01
2	10	43.91 ± 0.04	35.17 ± 0.03
3	20	52.15 ± 0.05	39.88 ± 0.02
4	30	56.45 ± 0.05	43.46 ± 0.04
5	40	60.68 ± 0.02	47.98 ± 0.02
6	50	63.77 ± 0.03	54.27 ± 0.03
IC_{50} value (µg/mL)		17.42 ± 0.03	43.38 ± 0.02

The above, result table-3 shows the percentage of DPPH free radical scavenged activity by leaf aqua-ethanol extract and ascorbic acid at different concentrations tested. Leaf extract of Argemone mexicana L. exhibited potential scavenging activity [20] by IC_{50} value 43.38 ± 0.02 µg/mL and ascorbic acid as a standard 17.42 ± 0.03 µg/mL at concentrations ranging from 5µg/mL to 50µg/mL as shown in fig.2.

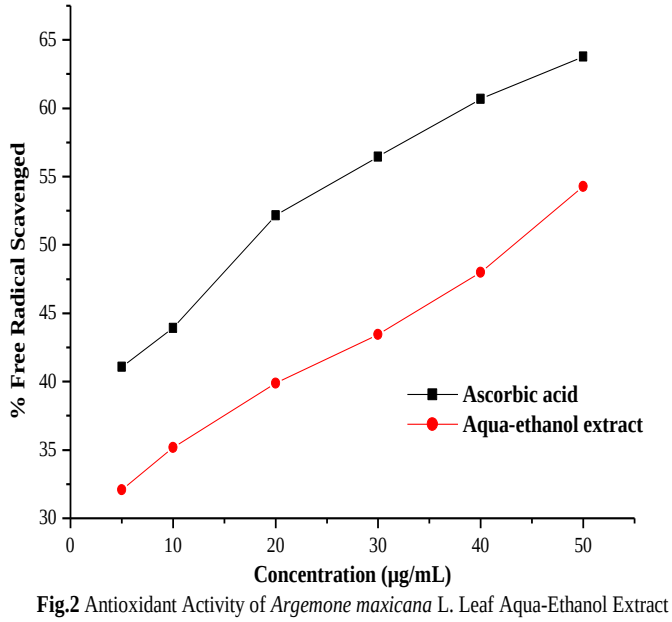

Fig.2 Antioxidant Activity of *Argemone maxicana* L. Leaf Aqua-Ethanol Extract

In all concentrations of both samples shows DPPH radical scavenging activity. Ascorbic acid scavenging activity was found to be higher than leaf aqua-ethanol extract of Argemone mexicana L. at all concentrations.

From the current result it may be suggested that the leaf extract of Argemone mexicana L. reduces the DPPH free radical and significantly noted antioxidant activity.

Different extracts of Argemone mexicana L. leaf were also reported to exhibit superoxide anion scavenging activity [25]. This activity is due to the presence of total Phenolic and flavonoidal content in different parts of plant [26]. As comparable with ascorbic acid used as a standard the ethanol extract exhibit significant antioxidant activity [27]. Phenolic compounds are responsible for antioxidant activity, because they are effective hydrogen donors, which make them antioxidant [28,29]. This overall discussion of results indicates that leafs of Argemone mexicana L. have potent antioxidant activity [30].

IV.CONCLUSION

These evaluation study suggest that Argemone mexicana L. leaf aqua-ethanol extract has acceptable antioxidant activity, but it has less efficiency than standard ascorbic acid. This indicates that this plant can have great scope of important bioactive antioxidant phytochemical ingredients, which can be formulated to make antioxidant dosage forms. The bioactive phytochemicals were content in the extract reveals important role in potent antioxidant activity. A leaf of Argemone mexicana L. plant could be become a source of natural antioxidant agents responsible for prevent and management of oxidative stress cause complications in humankind. Therefore, these screening studies concluded that Argemone mexicana L. leaf aqua-ethanol extract shows in vitro potential antioxidant activity in reducing role of oxidative stress related problems.

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Pyrimidine a Pharmaceutical Significant Molecule : A Review

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ABSTRACT

Pyrimidine and its derivatives are bioactive compounds having anticonvulsant, antibacterial, antifungal, antiviral and anticancer properties. Pyrimidine derivatives attract researchers due to their versatile scaffold & their medicinal significance. This broad spectrum of biochemical targets has been facilitated by the synthetic versatility of pyrimidine. Pyrimidines are synthetically versatile substrates, where they can be used for the synthesis of a large variety of heterocyclic compounds and as raw material for drug synthesis. In this review article, the recent new structural design and development of active agent studies and biological approaches are highlighted. In addition, the biological potency and the structure-activity relationship of pyrimidines such as antimicrobial, anticancer, anti-inflammatory, analgesic, anti-diabetic, anti-HIV, CNS depressants, and cardiac agents are discussed.

Keywords: Pyrimidine derivatives, bioactive, medicinal significance, Pharmaceutical Significant etc

I. INTRODUCTION

Pyrimidine and its derivatives exhibited several therapeutic applications [1] which include antimicrobial [2] , anticancer [3], anti-inflammatory [4], anti-malarial [5] , anti-diabetic [6] , anti- HIV [7], anthelmintic [8], CNS depressants [9], cardiac agents [10] and the thiouracil derivatives possess anti-thyroid activity [11]. In addition, fused pyrimidines have inhibitor activity against protein kinase [12]. Pyrimidines are the heterocyclic aromatic compounds similar to benzene and pyridine containing two nitrogen atoms at positions 1 and 3 of the six membered rings. Heterocycles containing pyrimidine moiety are of great interest because they constitute an important class of natural and nonnatural products, many of which exhibit useful biological activities and clinical applications [13,14] fig (1) pyrimidine and different isomeric forms.

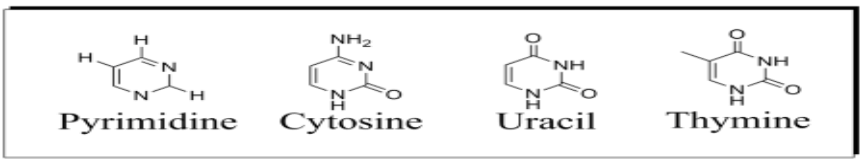

fig (1) pyrimidine and different isomeric forms

Many natural drugs such as quinine, papaverine, emetine, theophylline, atropine, procaine, codeine, morphine and reserpine are heterocycles. Almost all the compounds we know as synthetic drugs such as diazepam,

chlorpromazine, isoniazid, metronidazole, azidothymidine, barbiturates, antipyrine, captopril and methotrexate are also heterocycles. Some dyes, luminophores, pesticides and herbicides are also heterocyclic in nature.

II. METHODS AND MATERIAL

Pharmaceutical Significant:-

1. **As anti-cancer Agent:** -Pyrimidine and its derivatives majorly contributed to the process of prevention and treatment of cancer. Cancer treatments (Chemotherapy and radiotherapy) have been associated with many side effects which affect the healthy human life and some therapies give even serious problems. According to a WHO report eighteen million people are presently affected with cancer and nine million people died from cancer in 2018 mainly due to less effective treatments [15]. Zuhal Kilic Kurt et al. 2020. developed new pyrimidine containing aryl urea analogs & evaluated for anticancer potential. Among all the compounds (9) and (10) exhibited satisfactory anticancer potency against colon and prostate cancer cell lines (IC50: 11.08 μM, SW480). The enhanced activity is due to the presence of CF3, Cl, and amino-pyrimidine scaffold [16]. Huang T et al. 2019 synthesized novel pyrimidine analogs & tested for anticancer activity. Among the compounds (11) and (12) exhibits good anticancer potency against cancer cell lines (Inhibition rates: HeLa & A549: 45.08% & 41.69%) & (HeLa, HepG-2 & MCF7, IC50: 20.30, 12.37 & 13.18 μM). The observed activity may be due to the presence of ethanolamine and pyrimidine moiety (Fig 2) [17].

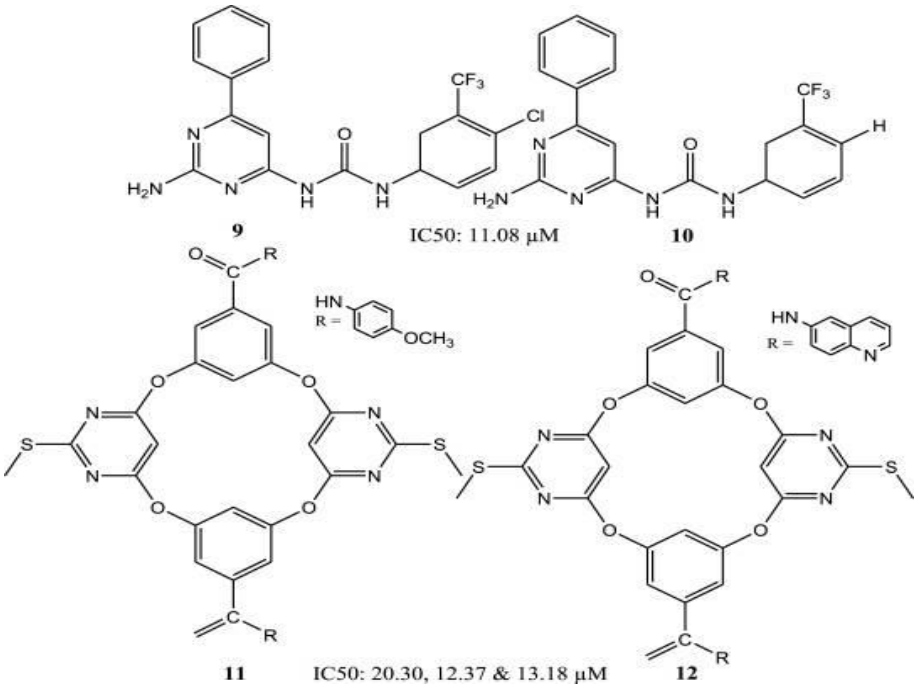

Fig (2) Pyrimidines nucleus as an anti-cancer Agent.

2. **Antibacterial and Antifungal Activities:** -Tetrasubstituted Pyrimidine Derivatives of Antibacterial and Antifungal Activities. A variety of pyrimidines derivatives were synthesized by Aly and Nassar by utilizing N (dicyclomethylazo) phenyl]-2-saccharin-2-ylacetamide and evaluated the derivatives for in vitro antibacterial activity and results revealed that compounds showed promising activity towards bacteria [18].

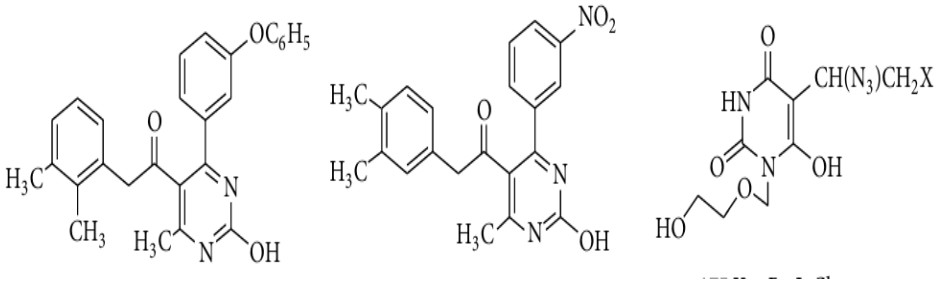

Fig 3:- Tetrasubstituted Pyrimidine Derivatives of Antibacterial and Antifungal Activities

Some novel series of pyrimidines derivatives were also reported by Waheed et al. and screened for their in vitro antibacterial activity. It is found that all the compounds were effective against Gram-negative test and compound having bromo substituent on the meta position of aminopyrimidines showed appreciable activity against E. coli [19]. Parmar and Parikh reported the synthesis of some novel derivatives of pyrimidine Thiones [20].

3. **Medicinal Properties of Pyrimidines: -** The presence of pyrimidine base in thymine, cytosine, and uracil, which are the essential building blocks of nucleic acids DNA and RNA, is one possible reason for their widespread therapeutic applications. The pyrimidines represent one of the most active classes of compounds possessing wide spectrum of biological activities like significant in vitro activity against unrelated DNA and RNA, viruses including polioherpes viruses, diuretic, antitumour, antiHIV, and cardiovascular [21]. The literature survey indicated that a wide range of pharmacological activities are exhibited by the compounds encompassing pyrimidines nucleus. In addition to this, various analogs of pyrimidines have been found to posses antileishmanial [22], anti-inflammatory [23], analgesic [24], antihypertensive [25], antipyretic [26], antiviral [27], antidiabetic [28], antiallergic [29], anticonvulsant [30]. and many of pyrimidines derivatives are reported to possess potential central nervous system (CNS) depressant properties [31] and also act as calcium channel blockers [32].

4. **Clinical and Pharmacological Applications of Pyrimidine in the Microbial World: -** Marketed Drugs During the last two decades several pyrimidine derivatives have been developed which are found to have wideclinical and pharmacological applications [33]. Antibacterial Agents. Drugs which are included in this category are antifolates possessing antagonistic activity against folic acid and sulfa drugs which are sulphur containing pyrimidine derivative drugs. 4.1.1. Antifolates. 2-Amino-4-hydroxypyrimidines are found to be antagonists of folic acid ; hence, a large number of 2,4-diaminopyrimidines have been synthesized as antifolates and it was eventually proved that these pyrimidines are inhibitors dihydrofolate reductase (DHFR) [34]. Notable amongst the 2,4-diaminopyrimidine drugs are the following. Trisubstituted Pyrimidine Containing Drugs. Brodiprim (11) is found to be an effective antibacterial compound . Iclaprim (12) which is a new selective dihydrofolate inhibitor was synthesized based on rational drug design and this drug is found to be active against methicillin-, TMP-, and vancomycin-resistant strains . Trimethoprim (13) is an antibacterial drug which selectively inhibits bacterial DHFR .

5. **As an anti- HIV agent:-** HAART-Highly Active Antiretroviral Therapy showed positive benefits in treating AIDS patients with HIV-1 infection. The use of different screening tests for the severe infection with human immunodeficiency virus (HIV) and based on the experimental test results we can understand the immune system response to HIV infection. HIV can be cured with medications, which slow down or stop the virus replication. Further, the body's immunity starts repairing it and also stops further severe damage. A different combination of HIV drugs is used for the treatment because HIV may get quickly resistant [35,36].6. As central nervous system depressant

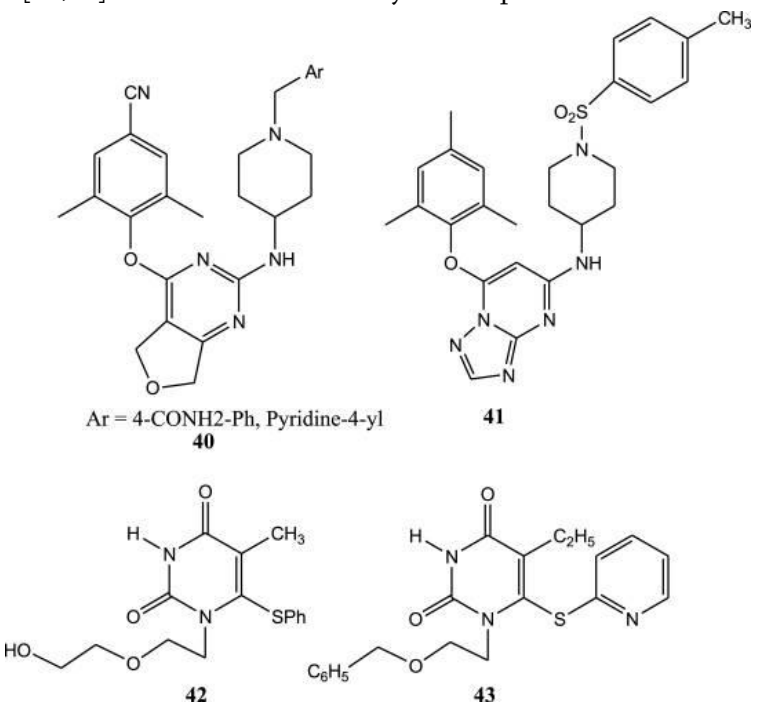

Fig 4:- anti- HIV agent

Barbiturates are a class of drugs derived from pyrimidinetriones and are commonly called barbituric acids which slow down the brain activity and relax the muscles and especially these may be used before surgery. The phenobarbital, meberal, seconal, nembutal, amytal, and pentothal are closely similar to barbiturates. Based on the above applications our group has been synthesized and found to be clinically useful as sedative and hypnotic drugs. N M Goudgaon et al. 2011 synthesized novel 5-substituted pyrimidin-triones & tested for CNS depressant activity [37.38]

III.CONCLUSIONS

The article has outlined the biological activities of the pyrimidine scaffold. The biological activities of the pyrimidine indicates the maneuverability and versatility, which offer the medicinal chemist a continued interest in the pyrimidine skeleton in medicinal chemistry and drug development, the development of efficient and reliable methods for the construction of these molecules will ensure that this is an active and important area of research in heterocyclic chemistry.

IV.ACKNOWLEDGMENT

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Synthesis and Characterization of Benzofuran Derivatives having Pyrimidine Moiety as Antimicrobial Agents

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ABSTRACT

A series of benzofuran Chalcones were synthesized by condensation of 2-acetyl-5-substituted benzofuran and pyrrole-2-carboxaldehyde in presence of base. These Chalcones further on reaction with urea and thiourea gives hydroxyl pyrimidines and thiopyrimidines having benzofuran scaffold. The structures of all synthesized compounds were established on the basis of analytical and spectral data. The synthesized compounds were screened for antimicrobial activity.

Keywords: Benzofuran Chalcones, Hydroxypyrimidines, Thiopyrimidines, Antimicrobial activity.

I. INTRODUCTION

Benzofurans are one of the heterocyclic compound types with strong biological properties. Benzofuran derivatives are pivotal biodynamic agents from both synthetic and natural sources.[1].Chalcones(1,3-diaryl-2-propen-1-ones) are an important class of plant secondary metabolites and possess a wide range of biological activities.[2] It has been reported that chalcone derivatives are able to directly scavenge a variety of reactive oxygen species (ROS) and possess strong antioxidant properties.[3] Recent evidence has suggested that chalcone derivatives have the capacity to inhibit Aβ fibril formation and exert neuro protection.[4] Interestingly, curcuminoids, a class of chalcone, have been shown to exhibit potent inhibitory effects on oxidative stress.[5] Therefore, introducing a chalcone pharmacophore into a hybrid molecule could impart it with neuro protective effects and the capacity to decrease oxidative stress [6].

Ailanthoidol, obtained by isolating from the Chinese herbal medicine Zanthoxylum ailanthoides, is a neol-ignan bearing a 2-arylbenzofuran ring. Studies show that neolignans have properties including antioxidant, antiviral, anticancer, antifungal, and immune suppressive activities [7]. Benzofuran-chalcone hybrids shows potential multifunctional agents against Alzheimer's disease.[8].Chalcones bearing benzofuran scaffolds shows anticancer [9] ,anti-Alzheimer's, Anti-Leishmanial [10],anti-cancer activity for human lung and breast [11],cytotoxic effect [12],antimicrobial [13] activity.

The role of pyrimidine entity is shown to attract essentiality in several biological processes, such as nucleoside antibiotics, multivitamin synthesis and functional activity maintenance of coenzymes [14]. Nevertheless, much

interest has been concentrated on the synthesis of pyrimidine possessing fungicidal, herbicidal, anti-depressant [15, 16], anti-infective [17], anti-convulsant [18], anti-viral [19], antiprotozoal [20], anti-hypertensive [21], anthelmintic [22], anti-tubercular [23], anticancer [24, 28] and anti-HIV [26] properties. The benzofuran having pyrimidine ring was screened in vitro anticancer activity using human lung cancer cell line A549 cells and human leukemia cell line K562 cells.[29].

In the present work, we have decided to synthesize some new chalcones containing benzofuran moiety; in addition, a novel series of fused pyrimidine with a potential to act as antibacterial and antifungal agents.

II. METHODS AND MATERIAL

Reagents and solvents were used as obtained from the supplier without further purification. All melting points reported are uncorrected and were determined on a Stuart electric melting point apparatus. TLC was performed on Merk TLC aluminium sheets silica gel. Column chromatography was performed on silica gel 90,200–300 mesh and then used for spectral analysis. IR spectra (in KBr, cm^{-1}) were recorded on Shimadzu spectrophotometer in the range of 400-4000 cm^{-1}. ^{1}H-NMR spectra were recorded on a Varian 300 MHz with deuterated solvent ($CDCl_3$). Tetramethylsilane (TMS) was used as an internal standard with chemical shifts δ in ppm. LC-MS were obtained using QP 2010 mass spectrometer using EIMS techniques at 70eV.

Experimental:

A) Typical experimental procedure for synthesis of (5-substituted benzofuran-2-yl)-3-(5-substituted-1H-pyrrol-2-yl)prop-2-en-1-one. (3a-d).

Flask was charged with mixture 2-acetyl 5-substituted benzofuran (I) (0.011 mole) and 5-substituted -1H-pyrrole-2-carbaldehyde (II) (0.011 mole). It was stirred in ethanol (25 mL) and then potassium hydroxide (50%) (10 ml) was added portion wise, keeping the temperature below the 10^0C throughout the Addition.

The mixture was kept for 36 hrs at room temp., after completion of reaction, reaction mixture was poured into crushed ice and the solid obtained was filtered under vacuum. It was washed firstly with sodium carbonate solution and then with water, dried and the product was recrystallized from ethanol to afford the pure product in 78-86 % yield (3a-d). Same procedure is extended for other compounds of this series.

B) Typical experimental procedure for synthesis of 4-(5-substituted-1H-pyrrol-2-yl)-6-(5-substituted benzofuran-2-yl)pyrimidin-2-ol (4a-d).

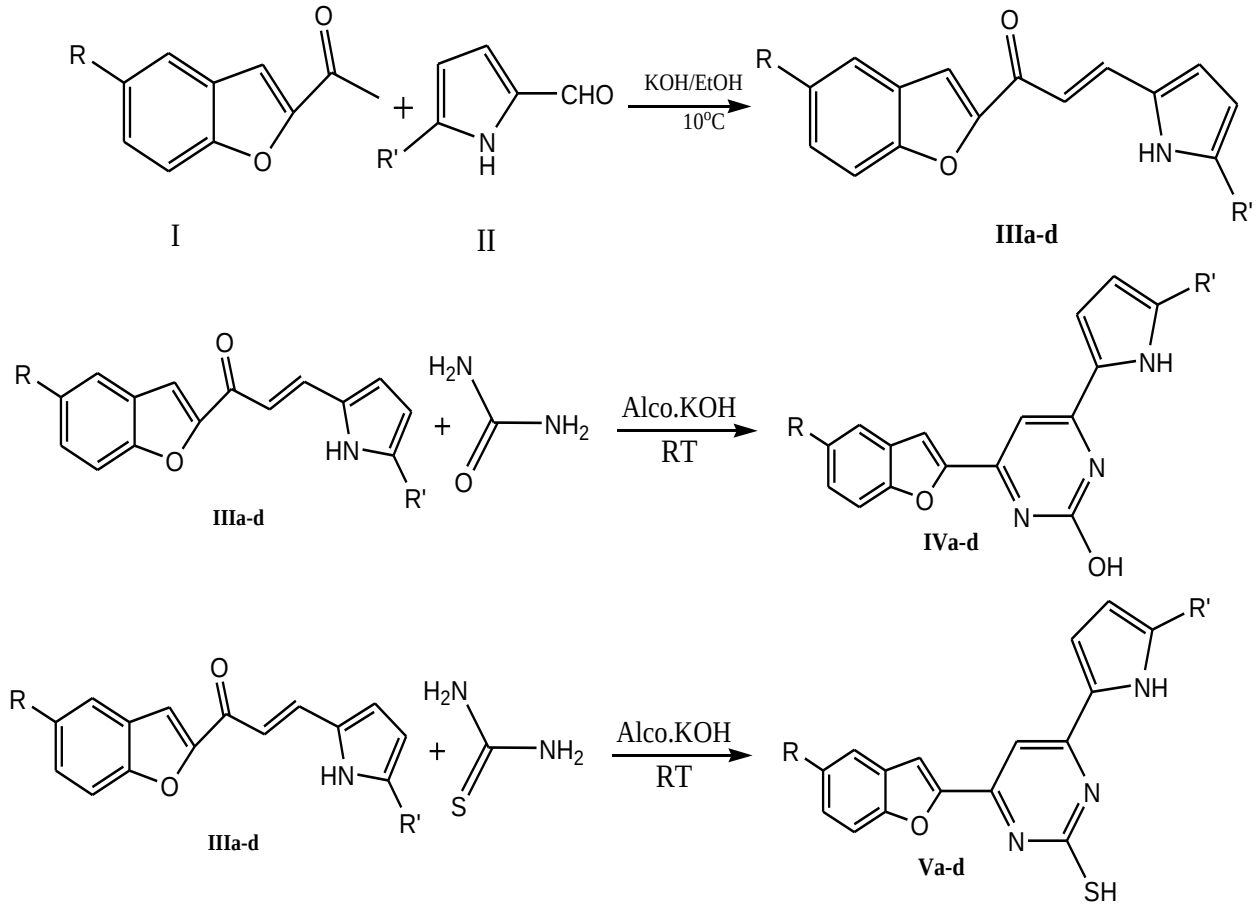
Benzofuran chalcones (2 mmol) (3a-d) were condensed with urea(2 mmol) in alcoholic KOH in a round bottom flask and the reaction mixture was continuously stirred for about 5-6 hr at room temperature.The progress of the reaction was monitoredby TLC and spots were observed by iodine vapor and/or UV light. After completion of reaction, the reaction mixture was cooled, poured into crushed ice with constant stirring and neutralized using 10% $NaHCO_3$.The precipitated product was filtered, dried and recrystallized using ethanol.(4a-d) Yield 71-74 %

C) Typical experimental procedure for synthesis of 4-(5-substituted-1H-pyrrol-2-yl)-6-(5 substituted benzofuran-2-yl)pyrimidine-2-thiol (5a-d).

Benzofuran chalcones (2 mmol) (3a-d) were condensed with thiourea (2 mmol) in alcoholic KOH in a round bottom flask and the reaction mixture was continuously stirred for about 5-6 hr at room temperature.The progress of the reaction was monitoredby TLC and spots were observed by iodine vapor and/or UV light. After

completion of reaction, the reaction mixture was cooled, poured into crushed ice with constant stirring and neutralized using 10% $NaHCO_3$.The precipitated product was filtered, dried and recrystallized using ethanol.(5a-d) Yield 68-71 %

Reaction Scheme:



Where R= -Cl and $-CH_3$ R'= -H and $-CH_3$

III.RESULTS AND DISCUSSION

Spectral discussion:

1) (5-chlorobenzofuran-2-yl)-3-(5-methyl-1H-pyrrol-2-yl)prop-2-en-1-one. (3b)

Yield 78 %, Yellow solid (EtOH) , M.P. 187°C;

IR (KBr, vcm^{-1}): 3067 cm^{-1} (-CH str. of. Ar), 1635 cm^{-1}(C=O str.in ketone), 1578 cm-^{1}(C=C str.) 1509 cm^{-1} (C=C str. in Ar), 1148 and 1178 cm^{-1} (C-O-C str) 832 cm^{-1}(-CH str.) 757 cm^{-1}(Ar-H-opb).

^{1}H NMR ($CDCl_3$ in δ ppm): 2.12 (s, 3H, 5-methyl protons on pyrrole ring) ,5.02(s, 1H, pyrrole N-H),6.86-7.02 (dd, 2H, Ar-protons of pyrrole), 6.31 (d,1H, Trans proton of alkene-CH=CH, J= 16.2 Hz),7.51 (d,1H, Trans proton of alkene-CH=CH-, J= 16.4 Hz) 7.26-7.42 (Complex multiplet , 3H, benzofuran protons), 7.49 (singlet, 1H, Aromatic proton of Furan ring)

Mass (m/z):285[M]$^+$

2) 4-(5-methylbenzofuran-2-yl)-6-(1H-pyrrol-2 yl)pyrimidin-2-ol (4c)

Yield 71 %, faint brown solid (EtOH) , M.P. 136°C;
IR (KBr, vcm^{-1}): 3467 cm^{-1} (-OH str.) ,1625 cm^{-1}(C=N str.in pyrimidine), 1518 cm^{-1} (C=C str. in Ar) ,1133 and 1158 cm^{-1} (C-O-C str.), 838 cm^{-1}(-CH str.),767 cm^{-1} (Ar-H-opb).
^{1}H NMR (CDCl$_3$ in δ ppm): 2.39(s, 3H, 5-methyl protons on benzofuran ring),7.31(d,1H,pyrrole N-H), 7.41-7.52 (dd,2H,pyrrole protons),8.86 (s, 1H, pyrimidine), 10.31 (s,1H,OH proton) , 7.38-7.58 (Complex multiplet , 3H, benzofuran protons), 7.52 (singlet, 1H, Aromatic proton of Furan ring).
Mass (m/z):291[M]$^+$

3) 4-(5-substituted-1H-pyrrol-2-yl)-6-(5 methylbenzofuran-2-yl)pyrimidine-2-thiol (5d).
Yield 68 %, brown solid (EtOH) , M.P. 168°C;
IR (KBr, vcm^{-1}): 2567 cm^{-1} (-SH str.), 1612 cm^{-1}(C=N str.in pyrimidine), 1522 cm^{-1} (C=C str. in Ar), 1386 cm^{-1} (C-H str.in –CH$_3$), 1121 and 1167 cm^{-1} (C-O-C str.) 828 cm^{-1}(-CH str.) 758 cm^{-1}(Ar-H-opb).
^{1}H NMR (CDCl$_3$ in δ ppm): 2.11 (s, 3H, 2-methyl protons on pyrrole ring), 2.22 (s, 3H, 5-methyl protons on benzofuran ring),7.11 (d,1H,pyrrole N-H), 7.52-7.72 (dd,2H,pyrrole protons), 8.74 (s, 1H, pyrimidine),10.37 (s,1H,SH proton),7.42-7.63 (Complex multiplet , 3H, benzofuran protons), 7.63 (singlet, 1H, Aromatic proton of Furan ring),
Mass (m/z):321[M]$^+$

Evaluation of anti-microbial activity;
All synthesized compounds were evaluated in-vitro for their antibacterial activity against gram positive bacteria Bacillus subtilis ,gram negative bacteria Escherichia coli and Pseudomonas aeruginosa.The antifungal activity against Alternaria alternate , Aspergillus niger and Candida albicans. Agar well diffusion technique was used for the determination of preliminary antibacterial and antifungal activities (37). Streptomycin and fluconazole were used as reference drugs for comparison. The tested compounds were dissolved in DMSO to get a concentration of 100% and 50%. The samples were loaded into wells of agar plates directly. Plates inoculated with the bacteria were incubated at 38 °C for 24 hr and the fungal culture was incubated at 25 °C for 72 hr.The results were recorded for each tested compound as average diameter of inhibition zones around the well in mm have been depicted in Tables-II and Table-III.

Experimental analysis
Synthesis of the various pyrimidine derivatives were achieved according to the reactions illustrated in the Scheme.
Chalcone intermediates were obtained by Aldol condensation of corresponding 2-acetyl -5 substituted benzofuran (I) with different pyrrole carbaldehydes (II) according to the reported procedure (30). The condensed heterocyclic compounds 4-(5-substituted-1H-pyrrol-2-yl)-6-(5-substituted benzofuran-2-yl) pyrimidin-2-ol (4a-d) and 4-(5-substituted-1H-pyrrol-2-yl)-6-(5 substituted benzofuran-2-yl)pyrimidine-2-thiol (5a-d) were synthesized by treating (2E)-(5-substituted benzofuran-2-yl)-3-(5-substituted-1H-pyrrol-2-yl)prop-2-en-1-one.(3a-d) with urea and thiourea respectively in ethanoic KOH. The structure of desired pyrimidine analogs (4a-d) and (5a-d) were confirmed using IR, NMR and Mass spectral data. The IR spectrum of compounds 4a-d exhibited a broad absorption band at 3454-3472 cm $^{-1}$which confirms the presence of hydroxyl group. Another peak in the region of 1607-1633 cm^{-1}which suggests presence of C=N stretching vibration. The ^{1}HNMR spectrum of compound 4a-d exhibited a broad singlet at δ 10.31-10.48 ppm due to

hydroxyl proton and multiplet between δ 7.21-7.59 ppm for aromatic protons. The mass spectrum of the compound 4c showed molecular ion peak at m/z 291.30 [M+] which corresponds to molecular weight of the compound. The physical and analytical data of the newly synthesized compounds (3a-d), (4a-d) and (5a-d) are tabulated in Table-1

Table-I Characterization data of synthesized compounds

Compound	R	R'	Yield %	Mol.Wt.
3a	Cl	H	78	$C_{15}H_{10}ClNO_2$
3b	Cl	CH_3	79	$C_{16}H_{12}ClNO_2$
3c	CH_3	H	86	$C_{16}H_{13}NO_2$
3d	CH_3	CH_3	74	$C_{17}H_{15}NO_2$
4a	Cl	H	73	$C_{16}H_{10}ClN_3O_2$
4b	Cl	CH_3	71	$C_{17}H_{12}ClN_3O_2$
4c	CH_3	H	74	$C_{17}H_{13}N_3O_2$
4d	CH_3	CH_3	72	$C_{18}H_{15}N_3O_2$
5a	Cl	H	69	$C_{16}H_{10}ClN_3OS$
5b	Cl	CH_3	71	$C_{17}H_{12}ClN_3OS$
5c	CH_3	H	68	$C_{18}H_{15}N_3OS$
5d	CH_3	CH_3	70	$C_{18}H_{15}N_3OS$

Table II. Anti-bacterial activity data of synthesized compounds.

Compd.	Zone of inhibition (in mm)					
	B. subtilis		E. coli		P. aeruginosa	
	100 (mg)	50 (mg)	100 (mg)	50 (mg)	100 (mg)	50 (mg)
3a	20.02	9.84	18.21	9.21	11.20	5.20
3b	19.35	7.95	17.89	8.95	18.32	9.65
3c	17.21	8.36	12.30	6.15	15.20	7.51
3d	16.68	7.56	15.20	7.14	18.32	9.31
4a	15.89	7.65	9.51	4.24	15.24	7.89
4b	18.23	8.21	17.20	8.85	14.21	7.41
4c	22.37	11.0	18.36	9.32	17.89	9.21
4d	19.36	9.50	20.41	10.21	16.66	8.21
5a	20.47	10.20	18.62	9.21	17.30	9.21
5b	21.22	10.43	17.88	8.97	17.21	8.91
5c	18.14	9.21	19.21	9.98	18.21	9.34
5d	19.18	8.99	21.21	10.22	14.54	7.41
Penicillin	24.32		22.04		19.09	

Table-III Antifungal activity of synthesised compounds

Comp.	B. subtilis	E. coli	P. aeruginosa	A. niger	C. albicans
3a	-ve	+ve	-ve	+ve	-ve

3b	+ve	- ve	+ve	+ve	-ve
3c	-ve	+ve	+ve	+ve	+ve
3d	+ve	+ve	+ve	-ve	-ve
4a	+ve	+ve	+ve	-ve	+ve
4b	--	+ve	+ve	+ve	+ve
4c	+ve	+ve	+ve	-ve	+ve
4d	-ve	+ve	-ve	-ve	+ve
5a	+ve	+ve	-ve	+ve	+ve
5b	-ve	+ve	+ve	-ve	-ve
5c	+ve	-ve	-ve	+ve	+ve
5d	+ve	-ve	+ve	+ve	+ve
Griseoful- vin	+ve	+ve	+ve	+ve	+ve

Biological activity

Many of the literature data suggests that the structural parameters of synthesized compounds may have better impact on changing the efficacy of antimicrobial activity (31). A study shows that all the compounds displayed a varied degree of MIC (22.37 to 4.24 μg/mL) against all the tested bacterial strains. The compound 4c, 5a and 5b exhibited excellent antibacterial activity against bacterial strain Bacillus subtilis. The compound 5a,5c and 5b exhibit good antibacterial activity against E. coli. Compounds 3b,3c,3d and 5c showed excellent effect against P. aeruginosa. Nevertheless, the remaining compounds showed negligible antibacterial activity.

The antifungal effect of newly synthesized compounds also indicate that mmajority of thhe compounds exhibited antifungal activity against all tested pathogens. All the antifngal and antibacterial study shows that presence of benzofuran scaffold incorporated with thiol and phenolic group moiety enhances the antimicrobial activity

IV.CONCLUSION

In present work, biologically active derivatives of benzofuran that is 4-(5-substituted-1H-pyrrol-2-yl)-6-(5-substituted benzofuran-2-yl) pyrimidin-2-ol and -2 thiols were synthesized from benzofuran chalcones having high chemical reactivity and diverse synthetic and biological applications. From antimicrobial activity results, it is also found that, the presence of hydroxyl and thiol groups in the pyrimidine ring displayed promising antimicrobial activity. Henceforth it can serve as pyrimidines have engendered long considerable interest which makes new building blocks for synthesis and design of broad spectrum antimicrobial compounds and needs medicinal chemist to be continued interest in pyrimidine moiety in drug development against microbes. It will also ensure the development of reliable methods for the construction of important area of research in heterocyclic chemistry.

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Studies of Some Metal Ion Chelates with 3- [3-(3,4-Dimeth Oxyphenyl) Acryloyl]-4-Hydroxy-6-Methyl-2h-Pyran-2-One

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ABSTRACT

Some First transition series metal chelates containing bidentate organic ligand, 3-(3-(3,4-dimethoxyphenyl) acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one derived from 3-acetyl-6-methyl-pyran-2,4(3H)-dione (dehydroacetic acid) and 3,4-dimethoxy benzaldehyde, have been synthesized and analysed by new modern spectroscopic techniques. Analytical & Spectral data, the complexes was found to be 1:2 (metal: ligand). The heterocyclic Chalcone forms transition metal chelates using metal ion viz. Fe(III), Mn(II), Co(II), Ni(II) and Cu(II) coordination number six. Chalcone works as uninegative bidentate in nature. The transition metal chelates of Chlcone decay are comparatively at high temperature signifying its great thermal stability. Metal chelates having dissimilar colours, they are insoluble in water, but soluble in organic solvent like chloroform, methanol, dimethylsulphoxide and dimethylformamide. Magnetic susceptibility measurements showed diamagnetic environment and existence of paired electrons in chelates. Ultraviolet-visible spectral records of complexes are helpful signs to charge transfer band. Powder XRD investigation of the chelates shown that some are monoclinic crystal arrangement, whereas other are Hexagonal crystal arrangement for with P type lattice.

I. INTRODUCTION

The chalcones having poly-functional groups deals a lot of practical advances besides distinctive structural atmosphere for chelation. They are as well identified for their biotic, manufacturing and analytical reputation. Chalcones are connected through several biotic actions due to the existence of α, β unsaturated carbonyl moiety[42]. A number of chalcones have shown insecticidal[22], tuberculostatic[31], germicidal[21,29,31], bacteriostatic[22], fungicidal[19], antileishmanial[14], antiplasmodial[1], antiviral[3] and oncogenic[17] actions.

3-acetyl-6-methyl-(2H)pyran-2,4-(3H)dione (DHA) is an main biotic lively organic materials. Investigations have exposed that the mutually antibacterial as well as antifungal properties of DHA organic material[11]. This organic material is commonly used in food processing. It is used to enrich vitamin-C strength in vegetables processing[41] and as a preserving[32]. In hydrous solution, even at moderate concentration (0.02–0.2%), 3-acetyl-6-

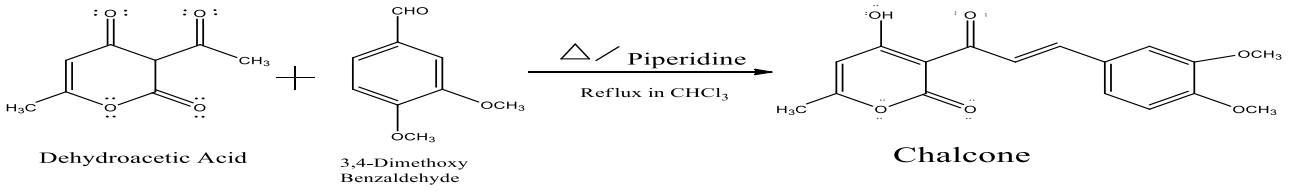
methyl-(2H)pyran-2,4-(3H)dione (DHA) appearances an excellent antibacterial actions[43]. Chelation of such organic material through transition metal ions such as Ni(II), Cu(II) and Fe(III) frequently increases its effects[16] as described for pathogenic moulds[13].

It is healthy recognized commencing the collected works that 3-acetyl-6-methyl-(2H)pyran-2,4-(3H)dione (DHA) compound have a strong capability to form metal complexes. Also their complexing capability, it moreover displays favourable fungicidal, antiseptic and antiprotozoal effects[4,7,36].

A exploration of the collected works shown that no research work has been completed on transition metal chelates of the 3-(3-(3,4-dimethoxyphenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one chalcone resulting as of 3-acetyl-6-methyl-(2H)pyran-2,4-(3H)dione (DHA) and 3,4-dimethoxy benzaldehyde (Veratraldehyde). The chelates of Nickel(II), Copper(II), Manganese(II), Cobalt(II) and Iron(III) through chalcone were as well synthesized in the solid form and analysed by various physical, analytical and spectral techniques.

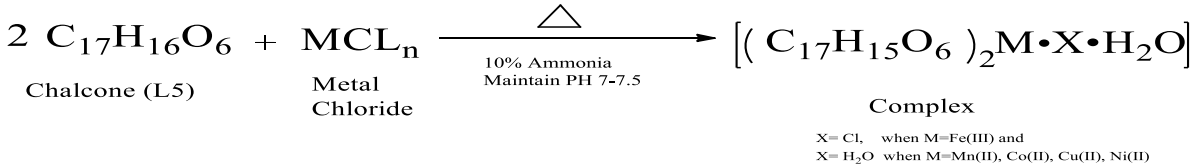
Experimental

A solution of 0.01 mol of 3-acetyl-6-methyl-(2H)pyran-2,4-(3H)dione (DHA), 8-10 drops of piperidine base and 0.01 mole of 3,4-dimethoxy benzaldehyde (Veratraldehyde) in 25 ml chloroform were refluxed for 6-8 hrs, numerous quantity of the $CHCL_3$-H_2O azeotrope mixture was separated by purification[2,37]. Crystal of chalcone 3-(3-(3,4-dimethoxyphenyl) acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one product separated on sluggish vanishing of the residual solvent. The resultant precipitate was filtered, washed many times with ethyl alcohol and recrystallized from chloroform[37,18].



PREPARATION OF METAL COMPLEXES

A 0.2mmol of 3-(3-(3,4-dimethoxyphenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one chalcone was taken in round bottomed flask containing 30 ml of chloroform and 0.01 mole of transition metal chloride in 20 ml of anhydrous methanol was added with constant stirring. The PH of the reaction mixture was maintained around 7.0-7.5 by adding 10% methanolic solution of ammonia. It was then refluxed for 2-3hr. the subsequent metal chelate was filtered in hot form and washed with ethyl alcohol, then dried over $CaCl_2$ in vacuum desiccator [2,37].



II. RESULTS AND DISCUSSION

I) PHYSICOCHEMICAL INVESTIGATION

The physical appearances as well as micro analytical records of the 3-(3-(3,4-dimethoxyphenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one Chalcone and their transition metal chelates are given in Table I. Elemental investigation indicates 1:2 (M:L) stoichiometry for every chelates[2,37]. The analytical records of the

Chalcone and its transition metal chelates matched healthy by the common formula [$M(L)_2(H_2O)_2$], where M= Co(II), Mn (II), Cu (II), Ni(II), and [$M(L)_2(H_2O)(CL)$], where M=Fe(III), L=$C_{17}H_{15}O_6$. The non-appearance of chloride ion except in the Fe(III) chelate was marked from the Vol-hard experiment[33] and existence of chelated water molecules was definite by TG/DT analysis. Meanwhile a particular crystal of the chelates could not be isolated after any common solvent, the probable structure was anticipated based on physicochemical, spectral, magnetic susceptibility and thermal results.

Table I: Physicochemical Results of Chalcone and their metal chelates

Compound	M_r gmol^{-1}	Colour	Yield %	M.P. in (ºC)	Found (Calcd.), %			
					M	C	H	O
Ligand HL $C_{17}H_{16}O_6$	316	Orange Yellow	62	162	-	64.09 (64.55)	5.05 (5.10)	30.06 (30.35)
$C_{34}H_{30}FeO_{12}$	686	Golden	30	276	8.08 (8.14)	59.39 (59.49)	4.35 (4.41)	27.90 (27.97)
$C_{34}H_{30}CuO_{12}$	694	Celadon	72	260	9.09 (9.15)	58.25 (58.83)	4.25 (4.36)	27.52 (27.66)
$C_{34}H_{30}CoO_{12}$	689	Orange	82	252	8.51 (8.55)	59.20 (59.22)	4.30 (4.39)	27.68 (27.84)
$C_{34}H_{30}MnO_{12}$	685	Brown	80	212	8.00 (8.01)	59.40 (59.57)	4.40 (4.41)	27.55 (28.01)
$C_{34}H_{30}$ NiO_{12}	689	Green Yellow	70	218	8.42 (8.52)	59.10 (59.24)	4.31 (4.39)	27.05 (27.85)

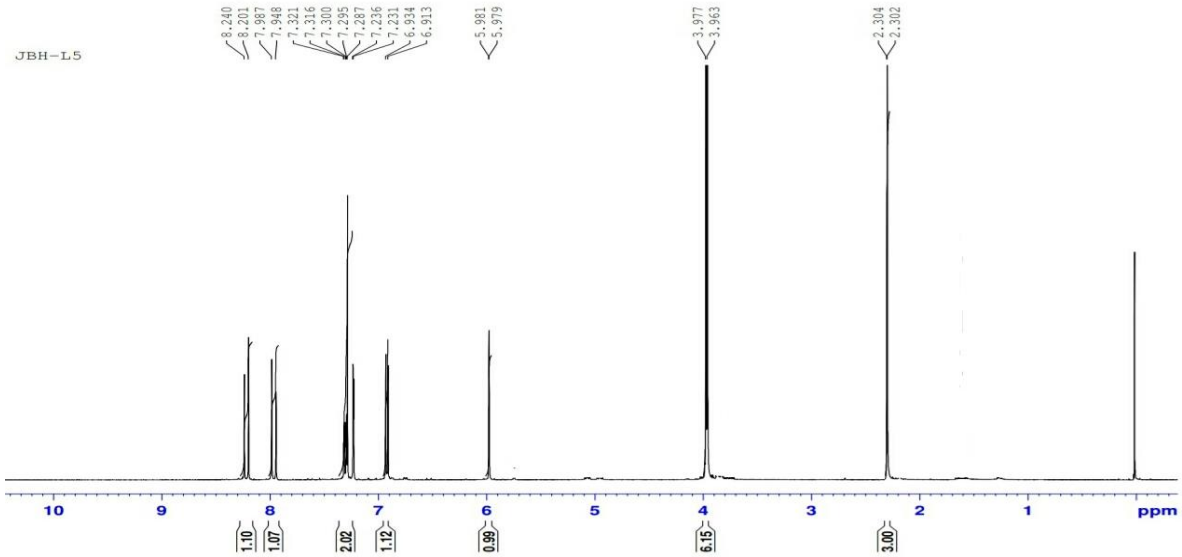
II) MASS SPECTRA OF CHALCONE

The mass spectrum of the 3-(3-(3,4-dimethoxyphenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one Chalcone displayed molecular ion peak at m/z=317 , which supports the molecular weight of the Chalcone .

III) ^{1}H-NMR SPECTRUM OF CHALCONE

The ^{1}H NMR spectrum of 3-(3-(3,4-dimethoxyphenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one Chalcone in deuterated chloroform at normal temperature appearances the resulting signals. δ 2.30 (singlet, 3H, -CH_3 group for DHA moiety), 3.97 (singlet, 6H, two -OCH_3 group associated with side chain aryl moiety), 5.98 (singlet, 1H, C_5-hydrogen of dehydroacetic acid moiety), 6.93-7.32 (multiplet, 3H, for Ar-H in side chain aryl moiety), 7.98 (doublet, 1H, β proton of α β unsaturated moiety on chalcone), 8.24 (doublet, 1H, α proton of α β unsaturated moiety on chalcone) and 14.82 (singlet, 1H, phenolic -OH of DHA moiety)[26,30,35] are shown in following fig.I.

Fig.I :- ^{1}H NMR Spectrum of Chalcone



IV) FTIR SPECTRA OF CHALCONE AND ITS COMPLEXES

Applicable FTIR bands that offer great structural confirmation for the formation of 3-(3-(3,4-dimethoxyphenyl)acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one Chalcone and their transition metal chelates are assumed. The FTIR spectrum of free Chalcone displays bands at 3093 cm^{-1} ν (OH) stretching of the intramolecular phenolic moiety of the 3-acetyl-4-hydroxy-6-methyl-2H-pyran-2-one DHA moiety, 1714 cm^{-1} ν (C=O) stretching of the lactone carbonyl on dehydroacetic acid ring, 1642 cm^{-1} ν(C=O) stretching of α β unsaturated carbonyl group, 1260 cm^{-1} ν (C-O) stretching of phenolic moiety on DHA and 996 cm^{-1} ν (C=C) stretching of α β unsaturated double bond[2,37,27,5]. In the Infrared spectra of Nickel(II), Copper(II), Manganese(II), Cobalt(II) and Iron(III) transition metal complexes, no band was found in between the area of 3165 and 3100cm^{-1}. As a replacement for, a wide-ranging band representative of ν (OH) of chelation water molecules was saw in between the area of 3548 and 3200cm^{-1}. The attendance of chelated water molecules was additionally definite by the attendance of a non-ligand band in between the area 825 and 845cm^{-1}. This was again evidences by thermal investigations. In case of complexes nonappearance of ν (OH) stretching of the intramolecular phenolic moiety at 3100cm^{-1} recommends successive deprotonation of the phenolic –OH group and chelation of phenoxide ion to the transition metal ion. This was also reinforced by a rising shift in ν (C-O) stretching of phenolic moiety on DHA[2,37,28] by 10-50cm^{-1}. The ν (C=O) stretching of α β unsaturated carbonyl group was moved to lesser energy with respect to the Chalcone, proposing the involvement of the α β unsaturated carbonyl group in the chelation[27,5]. The FTIR spectrum of Chalcone and their transition metal complexes exhibited a noticeable band at ≈1339 and ≈956cm^{-1}, representative of ν (C-O-C) and *trans* –CH=CH- absorption. The occurrence of new bands in between the region 600 and 450cm^{-1} can be allocated to ν (Metal-Oxygen) vibration[20].

Affording to the exceeding stated records, the Chalcone performed as mono-deprotonated bi-dentate and the chelation happens through the α β unsaturated carbonyl group and phenolic oxygen of 3-acetyl-4-hydroxy-6-methyl-2H-pyran-2-one DHA moiety.

Table II: Important IR spectral band of Chalcone and its metal chelates

Ligand & Complex	ν (OH) (dehydroacetic acid moiety)	ν (C=O) (lactone)	ν (C=O) (acetyl carbonyl)	ν (C-O) (phenolic)	ν (C=C) (trans)	ν (M-O)
Ligand HL $C_{17}H_{16}O_6$	3093(s)	1714(s)	1642(m)	1260(s)	996(m)	-
$C_{34}H_{30}FeO_{12}$	-	1710(s)	1644(s)	1306(w)	1002(w)	536(w) 486(m)
$C_{34}H_{30}CuO_{12}$	-	1705(m)	1656(s)	1311(m)	979(m)	562(m) 478(m)
$C_{34}H_{30}CoO_{12}$	-	1682(s)	1665(m)	1303(s)	984(s)	529(s) 478(s)
$C_{34}H_{30}MnO_{12}$	-	1676(m)	1641(w)	1303(w)	983(m)	550(w) 442(s)
$C_{34}H_{30}NiO_{12}$	-	1689(s)	1637(s)	1303(s)	981(s)	547(m) 526(s)

V) MAGNETIC MEASUREMENTS AND ELECTRONIC ABSORPTION SPECTRA

The Magnetic susceptibility as well as electronic absorption spectral information are assumed in Table III. The records are of bearing for the suggested structure of the chelates. The electronic absorption spectrum of the Copper(II) chelates in dimethylformamide exposed one comprehensive band at 15128 and 25126 cm^{-1} for Chalcone, predictable to a $^2E_g \rightarrow {}^2T_{2g}$ electronic transition also charge transfer. The detected magnetic measurement value for the Copper(II) chelate are 2.09μ_B[2,37]. The ultraviolet spectral records[8] attached through the magnetic measurement value propose a distorted octahedral configuration for the Copper(II) chelate[9]. The UV spectrum of Nickel(II) chelate found three bands at 9372, 15625 and 24213 cm^{-1} for Chalcone, predictable to $^3A_{2g} \rightarrow {}^3T_{2g}(F)$ (ν1), $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ (ν2) and $^3A_{2g} \rightarrow {}^3T_{1g}(P)$ (ν3) electronic transitions. This is in keeping through formerly described values for octahedral Nickel(II) chelates[15,34]. The considered value the range stated for octahedral configuration. The magnetic moment value of Nickel(II) 3.03μ_B checks the suggested geometry[2,37]. The UV spectral investigation of Cobalt(II) chelates appearance three electronic transitions at 9569, 18348 and 22675 cm^{-1} for Chalcone predictable to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ (ν1), $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ (ν2) and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (ν3) electronic transitions[9,15,34,10]. The magnetic susceptibility value of the Cobalt(II) chelate are 4.66μ_B, it indicates Cobalt(II) chelate shows octahedral geometry.

Table III: Magnetic Susceptibility and UV data of Chalcone and its Chelates.

Chalcone and Complex	ν /cm^{-1}	Band assignment	μ_{eff}/ μ_B	Geometry
Ligand HL $C_{17}H_{16}O_6$	32442 40545	INCT[a] INCT	-	-
$C_{34}H_{30}FeO_{12}$	14556 21692 24450	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)(\nu_1)$ $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)(\nu_2)$ $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)(\nu_3)$	8.93	Octahedral
$C_{34}H_{30}CuO_{12}$	15128 25126	$^2E_g \rightarrow {}^2T_{2g}$ INCT	2.09	Distorted Octahedral

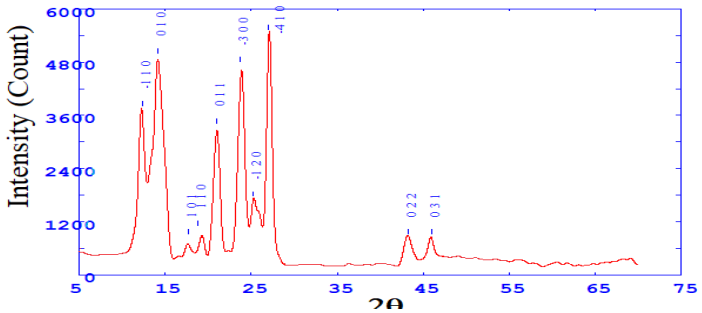
$C_{34}H_{30}CoO_{12}$	9569 18348 22675	$^6A_1 \rightarrow {}^4T_1(G)$ $^6A_1 \rightarrow {}^4T_2(G)$ $^6A_1 \rightarrow {}^4E(G)$	4.66	Octahedral
$C_{34}H_{30}MnO_{12}$	17794 19569 31056	Laporte and Spin Forbidden	5.77	Distorted Octahedral
$C_{34}H_{30}NiO_{12}$	9372 15625 24213	$^3A_{2g} \rightarrow {}^3T_{2g}(F)(\nu_1)$ $^3A_{2g} \rightarrow {}^3T_{1g}(F)(\nu_2)$ $^3A_{2g} \rightarrow {}^3T_{1g}(P)(\nu_3)$	3.03	Octahedral

The Iron(III) chelate of Chalcone display three electronic transition at 14556, 21692, 24450 cm^{-1} predictable to $^6A_1 \rightarrow {}^4T_1(G)$, $^6A_1 \rightarrow {}^4T_2(G)$ and $^6A_1 \rightarrow {}^4E$ (G) transitions. These values suggest octahedral confirmation for Iron(III) Chelate[9,15,25]. The magnetic moment value of Fe(III) 8.93μ_B checks the suggested geometry[2,17]. The electronic absorption spectrum of Manganese(II) chelate of Chalcone shows feeble bands at 17794, 19569 and 31056 cm^{-1}. These bands remain together Laporte and Spin-forbidden. However, due to sudden distortion of the octahedral configuration nearby the Manganese(II) metal cation, feeble bands sometimes do seem[9,15].

VI) POWDER X-RAY DIFFRACTION ANALYSIS

The powder XRD of prepared chelates was received from Department of Instrumentation Centre, Solapur University, Solapur. The Iron(III), Manganese(II) and Copper(II) chelates of 3-(3-(3,4-dimethoxyphenyl) acryloyl)-4-hydroxy-6-methyl-2H-pyran-2-one Chalcone were scanned in the varies 3–75° at a λ (wavelength) of 1.540598 A^0 to XRD studies. Powder X-ray records of every important peaks intense comparative intensity more than 10% have been indexed through using Powder-X Computer Software programme separately by trial and error procedure[2,17,6].

Fig. II: X-ray Diffractogram of Co(II) Complex of Chalcone



CRYSTAL SYSTEM : Monoclinic LATTICE TYPE : P 2/m
RADIATION : Cu WAVELENGTH : 1.540598 A^0
VOLUME : 467.19A^3 LAMBDA : 1.54060 A^0
RECIP. LATTICE : 0.08757 0.15783 0.17883 90.000 90.319 60.000
LATTICE PARAMETER :
a= 4.9168 α= 90
b= 4.9168 β= 90
c= 5.4089 γ=120
2Theta Start= 5 2Theta End= 70

Table. IV: X-ray Diffractogram data of Co(II) Complex of Chalcone

H	K	L	TH(OBS)	TH-ZERO	TH(CALC)	D(OBS)	D(CALC)	RI%
-1	1	0	6.20775	6.17148	6.05586	7.16527	7.30155	62.9
0	1	0	7.06602	7.02976	6.98302	6.29407	6.33599	81.1
1	0	1	8.83979	8.80352	8.80352	5.03310	5.03310	10.4
1	1	0	9.41197	9.37571	9.55101	4.72844	4.64244	12.9
0	1	1	10.49912	10.46285	10.58716	4.24178	4.19253	53.4
-3	0	0	11.87236	11.83609	11.67510	3.75549	3.80654	76.3
-1	2	0	12.61620	12.57993	12.55744	3.53670	3.54294	29.6
-4	1	0	13.47447	13.43821	13.53547	3.31459	3.29121	91.8
0	2	2	21.65669	21.62042	21.55919	2.09061	2.09627	12.2
0	3	1	22.97271	22.93645	22.94663	1.97660	1.97577	11.9

Commencing the Powder XRD spectral parameters formulated in above Table IV exposes that Cobalt(II) chelate have monoclinic crystal arrangement[17]. From the Powder XRD scale of Manganese(II) chelate cell data as well as crystal lattice parameters of considered and charted, specifies that chelate has Hexagonal crystal arrangement[24]. On the XRD studies of Nickel(II) complex Cell data as well as crystal lattice parameters point out that Nickel(II) complex have monoclinic crystal arrangement[2] with lattice type-P.

III.CONCLUSION

The heterocyclic Chalcone forms transition metal chelates using metal ion viz. Fe(III), Mn(II), Co(II), Ni(II) and Cu(II) coordination number six. Chalcone works as uninegative bidentate in nature. Magnetic susceptibility measurements showed diamagnetic environment and existence of paired electrons in chelates. Ultraviolet-visible spectral records of complexes are helpful signs to charge transfer band. FTIR spectra of the Chalcone and their metal chelates exposes that the Chalcone chelated to the transition metal ions through phenolic oxygen and α β unsaturated carbonyl oxygen atom and also coordinated water molecules. Existence of Metal-Oxygen feeble stretching vibrations in low wavelength area confirm contribution of α β unsaturated carbonyl group and phenolic oxygen in chelation. Powder XRD investigation of the chelates shown that $[Fe(C_{17}H_{15}O_6)_2H_2O.CL]$ and $[Cu(C_{17}H_{15}O_6)_2(H_2O)_2]$ with monoclinic crystal arrangement, whereas Hexagonal crystal arrangement for $[Mn(C_{17}H_{15}O_6)_2(H_2O)_2]$ with P type lattice.

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Complexation of Gadolinium with Novel Schiff Bases: Thermodynamic Study

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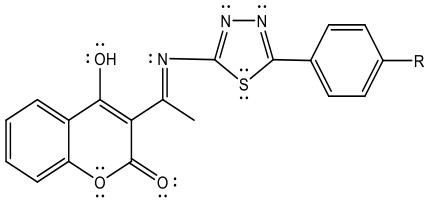
ABSTRACT
We have investigated the stability constant of seven Schiff bases with trivalent rare earth metal ion Gadolinium using a pH metric titration technique in 80%(v/v) ethanol-water mixture at three different temperatures 298K, 308K & 318K at an ionic strength of 0.1M NaClO4. The Calvin-Bjerrum method as adopted by Irving-Rossotti has been employed to determine metal-ligand stability constant logK values. The thermodynamic parameters such as, Gibb's free energy change (ΔG), entropy change (ΔS) and enthalpy change (ΔH) associated with the complexation reactions were calculated.
Keywords: Rare earth metal ion, Schiff bases, stability constant, pH metry, thermodynamic parameter etc.

I. INTRODUCTION

Metal complexes of Schiff bases play a central role in the development of coordination chemistry. Proton transfer also plays an important role in the reactions such as complexation, acid-base catalyzing, enzymatic reaction etc in aqueous solution. The stability constants can be of significance in order to predict different chemical processes such as isolation, extraction methods. The accurate determination of acidity and stability constants values are fundamental to understanding the behavior of ligands, their interaction with metal ions in aqueous solution. pH metric titration technique is a powerful, simple electro analytical technique for determination of stability constants. For the present investigation, we have selected a series of seven Schiff bases. Synthesis of all seven Schiff bases was done by reported methods.
In continuation of our earlier work with complexation of Schiff bases1-4 and after review of literature5-9, it was thought of interest to study the effect of temperature on thermodynamic parameters



R= -H, -CH3, NO2, -F, -Cl, -Br, -I

Figure: Schiff base ligand (Molecular formula C19H12 O3N3SR)

such as Gibb's free energy change ΔG, enthalpy change ΔH and entropy change ΔS of complexes of seven Schiff bases with rare earth metal ion Gd3+ pH metrically in 80% (v/v) ethanol-water mixture.

II. EXPERIMENTAL

2.1. Materials and Solution: Gadolinium metal salt, NaOH, NaClO4, HClO4 used were of AR grade. The solutions used in the pH metric titration were prepared in CO2 free double distilled water. The NaOH solution was standardized against oxalic acid solution, standard alkali solution was again used for standardization of HClO4. The measurements were made at temperatures 298K, 308K and 318K in 80% (v/v) ethanol-water mixture at constant ionic strength (0.1M NaClO4). The thermostat model SL-131 [Adar dutt and Co. India Pvt. Ltd. Mumbai] Narang Scientific Works Pvt. Ltd., New Delhi is used to maintain the temperature constant and the solutions were equilibrated in the thermostat for about 10-15 minutes before titration. The pH measurement was made using a digital Spectra lab potentiometric titrator AT 38 C with combined glass electrode consisting of glass and reference electrodes in the single entity. This digital potentiometric titrator has built in voltage stabilizer for ± 10% fluctuations in voltage supply. The instrument has built in temperature compensator having range 0-99 °C. The instrument could read pH in the range 0.001-14.000 with an accuracy of 0.0017 pH unit and (0.1mV). Provision of in built three way valves and gas tight burette with Teflon piston with an accuracy of 0.001 mL enabled the required precision during the titration particularly near the equivalence point. The instrument was calibrated at pH 4.00, 7.00 and 9.18 using the standard buffer solutions.

2.2. pH metric procedures: For evaluating the protonation constant of the ligand and the formation constant of the complexes with Gadolinium metal ion, the following sets of solutions were prepared in 80% (v/v) ethanol-water mixture (total volume 50 ml) and titrated pH metrically against standard NaOH solution at three different temperatures 298K, 308K and 318K.

i. HClO4 (A)
ii. HClO4 + Schiff base (A+L)
iii. HClO4 + Schiff base + Metal (A+L+M)

The above mentioned sets were prepared by keeping M: L ratio, the concentration of perchloric acid and sodium perchlorate (0.1M) were kept constant for all sets.

2.3. Determination of the thermodynamic parameters: Thermodynamic parameters such as Gibb's free energy change (ΔG), entropy change (ΔS) and enthalpy change (ΔH) for formation of complexes were determined. The change in Gibb's free energy (ΔG) of the ligands was calculated by using the equation. $\Delta G = -2.303RT \log K$

Where R (ideal gas constant) = 8.314 JK-1mol-1,

K is the dissociation constant for the ligand or the stability constant of the complex and

T is absolute temperature in Kelvin.

The change in enthalpy (ΔH) is calculated by plotting logK vs 1/T

The equation utilized for the calculation of changes in enthalpy is as $\text{Slope} = -\Delta H/2.303R$

The evaluation of changes in entropy (ΔS) is done by the equation: $\Delta S = ((\Delta H - \Delta G))/T$

Table 1: Proton-ligand stability constant of Schiff bases

		Schiff bases						
Temperature	Proton-ligand stability constant	S1	S2	S3	S4	S5	S6	S7
298K	pK1	3.2234	3.3961	3.0385	2.9744	3.6355	3.4792	--
	pK2	4.4968	5.1755	4.7142	3.6138	4.8790	5.3457	4.0972
308K	pK1	3.0782	3.2750	2.9374	2.8893	3.4614	3.3438	--
	pK2	4.3749	5.0532	4.5991	3.487	4.7013	5.1946	3.9860
318K	pK1	2.9303	3.1228	2.826	2.8061	3.3052	3.1451	--
	pK2	4.2027	4.8810	4.4339	3.3352	4.5062	5.0035	3.8637

Table 2: Gd(III)-ligand stability constant of Schiff bases

Temperature	298K			308K			318K		
Gd(III)-ligand stability constant → Schiff Bases↓	$logK_1$	$logK_2$	$log\beta$	$logK_1$	$logK_2$	$log\beta$	$logK_1$	$logK_2$	$log\beta$
S_1	3.5492	3.3382	6.8874	3.4654	3.2581	6.7235	3.3885	3.1798	6.5683
S_2	3.9597	3.6472	7.6069	3.8312	3.5224	7.3536	3.6970	3.4058	7.1028
S_3	4.0111	3.6280	7.6391	3.9308	3.5287	7.4595	3.8400	3.4357	7.2757
S_4	3.3484	3.0498	6.3982	3.2755	3.0042	6.2797	3.2059	2.9610	6.1669
S_5	4.6810	3.9812	8.6622	4.4966	3.8312	8.3278	4.3204	3.6914	8.0118
S_6	5.1956	5.0378	10.2334	4.9672	4.8452	9.8124	4.7624	4.6528	9.4152
S_7	3.5095	3.2910	6.8005	3.4345	3.2310	6.6655	3.3654	3.1712	6.5366

Table 3: Thermodynamic parameters of Schiff base complex formation with Gd(III) at 298K

Schiff Bases	$-\Delta G_1$	$-\Delta G_2$	$-\Delta H_1$	$-\Delta H_2$	ΔS_1	ΔS_2
	(KJmol^{-1})		*(KJmol^{-1})*		*(KJK^{-1}mol^{-1})*	
S_1	20.251	19.047	14.584	14.371	19.00	15.70
S_2	22.593	20.810	25.240	19.252	-8.90	5.20
S_3	22.887	20.701	15.510	17.450	24.80	10.90
S_4	19.105	17.402	12.930	8.058	20.70	31.40
S_5	26.709	22.716	32.719	26.298	-20.20	-12.00
S_6	29.645	28.745	39.320	34.924	-32.50	-20.70
S_7	20.025	18.778	13.039	10.867	23.40	26.50

Table 4: Thermodynamic parameters of Schiff base complex formation with Gd(III) at 308K

Schiff Bases	$-\Delta G_1$	$-\Delta G_2$	$-\Delta H_1$	$-\Delta H_2$	ΔS_1	ΔS_2
	(KJmol^{-1})		*(KJmol^{-1})*		*(KJK^{-1}mol^{-1})*	
S_1	20.437	19.214	14.584	14.371	19.00	15.70
S_2	22.594	20.773	25.240	19.252	-8.60	4.90

S_3	22.429	20.134	15.510	17.450	23.20	9.00
S_4	18.690	17.142	12.930	8.058	19.30	30.50
S_5	25.657	21.810	32.719	26.298	-23.70	-14.90
S_6	28.342	27.646	39.320	34.924	-36.80	-24.40
S_7	19.597	18.436	13.039	10.867	22.00	25.40

Table 5: Thermodynamic parameters of Schiff base complex formation with Gd(III) at 318K

Schiff Bases	$-\Delta G_1$	$-\Delta G_2$	$-\Delta H_1$	$-\Delta H_2$	ΔS_1	ΔS_2
	(KJmol^{-1})		*(KJmol^{-1})*		*(KJK^{-1}mol^{-1})*	
S_1	20.632	19.361	14.584	14.371	19.00	15.70
S_2	22.510	20.737	25.240	19.252	-8.60	4.70
S_3	21.910	19.604	15.510	17.450	21.50	7.20
S_4	18.292	16.895	12.930	8.058	18.00	29.70
S_5	26.709	22.716	32.719	26.298	-20.20	-12.00
S_6	27.174	36.548	39.320	34.924	-40.80	-28.10
S_7	19.202	18.094	13.039	10.867	20.70	24.30

III.RESULTS AND DISCUSSION

The results obtained are analyzed by computer programme and stability constant values were calculated. The proton-ligand stability constant was determined by point wise calculation method as suggested by Irving and Rossoti. The proton ligand stability constant pKa of all seven Schiff bases were determined in aqueous medium at three different temperatures 298K, 308K, 318K at 0.1M NaClO4 ionic strength. The proton- ligand stability constants of all the Schiff bases are presented in Table 1. The Schiff base S7 has only one pK value where as S1, S2, S3, S4, S5 and S6 have two pK values. The $\bar{n}$_A value ranges between 0.2 to 1.8 indicates the presence of two pK values whereas the range of $\bar{n}$_A is in between 0.2 to 0.8 shows only one pK value. In the present investigation Schiff base selected contains hydroxyl group and azomethine nitrogen as bonding sites. The order of pKa values of seven ligands is as:

S6 > S2 > S5 > S3 > S1 > S4 > S7

The above order indicates that S7 has lowest basicity whereas S6 has highest basicity Metal ligand stability constant logK of Gd(III) metal ion with Schiff bases are calculated by point wise and half integral method of Calvin-Bjerrum as adopted by Irving-Rossotti. The logK1 values calculated by point wise calculation method and half integral method, indicates simultaneous formation of 1:1 complex. we got values of proton-ligand formation number ($\bar{n}$_A) between 0.2 to 0.8 and 1.2 to 1.8 indicating 1:1 and 1:2 complex formations. The proton-ligand stability constant pKa values decrease with increase in temperature i.e. the acidity of the ligands increases12, it suggests that the liberation of proton becomes easier at higher temperature. Order of stability constants for Gd(III) complexes with Schiff bases (Table 2) found to be as follows:

S6 > S5 > S3 > S2 > S1 > S7 > S4

The metal-ligand stability of bromo (Br) substituted Schiff base was found higher, while fluro (F) substituted Schiff base lower {S6 > S5 > S7 > S4} and the metal-ligand stability of nitro substituted Schiff base was found higher, while unsubstituted Schiff base lower. {S3 > S2 > S1}

The negative ΔG values indicates that both dissociation of the ligand and the complexation process are spontaneous12. A decrease in metal-ligand stability constant logK with an increase in temperature and the negative values of enthalpy change ΔH for the complexation suggests that all the complexation reactions are exothermic, favorable at lower temperature and the metal-ligand binding process is enthalpy driven11 and metal-ligand bonds are fairly strong.

The positive entropy changes ΔS accompanying a given reaction are due to the release of bound water molecules from the metal chelates. The positive value of ΔS is considered to be the principal driving force for the formation of respective complex species. According to Martell -Calvin positive entropy effects was predicted towards an increase in the number of particles after the reaction and positive ΔS is responsible to give more negative ΔG. The positive values of ΔS in some cases indicate that the entropy effect is predominant over enthalpy effect. The positive ΔS values for metal complexes indicated that the formation of these complexes was entropy favored, while negative ΔS values (Table 3 - 5) for metal complexes suggesting a highly solvated metal complexes12.

IV.CONCLUSIONS

Gadolinium metal ion forms 1:1 and 1:2 complexes with all Schiff Bases. The metal-ligand stability constant logK decreases with an increase in temperature. The negative values of change in enthalpy ΔH for the complexation suggest that all the complexation reactions are exothermic, favorable at lower temperature. The negative change in free energy ΔG values indicates that both dissociation of the ligand and the complexation process are spontaneous. The positive ΔS values for some metal complexes indicated that the formation of these complexes was entropy favored, while negative ΔS values indicated a highly solvated metal complex.

V. ACKNOWLEDGMENT

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Amoxicillin : An Important Bioactive Molecule

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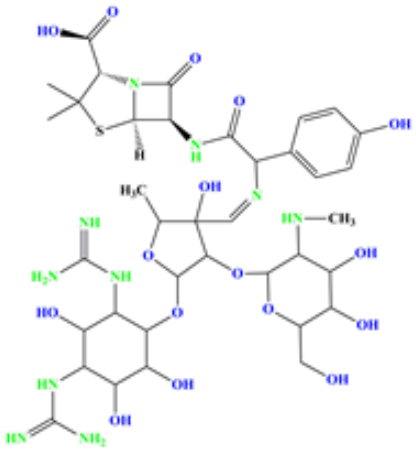
ABSTRACT
Amoxicillin is a compound containing Nitrogen and Oxygen known to exhibit a broad spectrum of various biological activities like: anticancer, antifungal, antibacterial etc. when this amoxicillin is reacted with aldehyde and converted to Schiff base ligand it enhances the biological activities. Also, if this Schiff base ligand coordinated with the transition metals (Mn, Fe, Co, Ni, Cu, Zn etc) the activity ratio get considerably increases. Recently various types of Schiff base ligand and metal complexes of amoxicillin were synthesized and evaluated against some biological activities, the observations suggest positive result of these biological activities. In this review article we have presented an overview on synthesis methods and biological activities of amoxicillin and its metal complexes. The comparison between the Schiff base ligand and its metal complexes is given.

I. INTRODUCTION

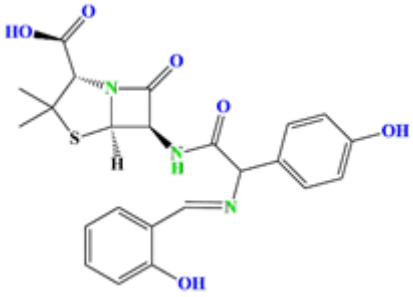
Amoxicillin is a widely prescribed antibiotic belonging to the beta-lactam class, specifically categorized as a penicillin derivative. Now a days, in the pharmaceutical industry it's a challenging job to resist an unbelievable adaptability and flexible metabolic power developed by various diseases so the synthesis of antibiotic-based Schiff base metal complexes with different modes of action is important for designing derivatives with greater anticancer, antifungal, antibacterial activity to face such type of problems.[1-2] In the last decade compound containing Schiff base ligand are much focused and documented in various literature because of their studies related to biological activities of Schiff base and their metal complexes including antimicrobial, antifungal, antioxidant and anticancer[5-10].

II. APPLICATIONS

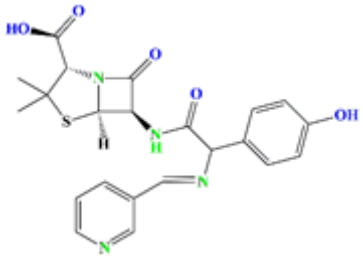
A. The metal complexes of Ni(II), Cu(II) and Zn(II) with Schiff base ligand derived from streptomycin sulphate with amoxicillin trihydrate[11]. They show antimicrobial activities against *E. coli, B. subtilis, S. aureus* and *K. pneumonia.* Metal complexes show higher activity than ligand. The structure of metal complexes shown in **scheme 1**.



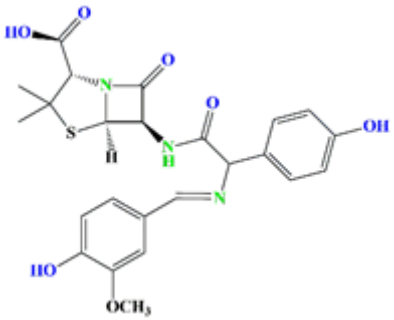
B. The metal complexes of Mn(II), Ni(II), Cu(II), Zn(II) and Ag(II) with Schiff base ligand derived from condensation reaction of salicylaldehyde with amoxicillin trihydrate[12]. The antibacterial activity of Schiff base ligand and metal complexes shows significant activity shown in **scheme 2.**



C. The metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) with schiff base ligand prepared from Nicotinaldehyde with amoxicillin trihydrate[13].The in vitro antibacterial activity of all the compounds at their two different concentrations, was screened against four bacterial pathogens namely, E.coli, P. vulgaris, K. pneumoniae and S. aureus, and showed better activity compared to parent drug Amoxicillin and control drug Amikacin shown in **scheme 3.**



D. The condensation reaction of 4-Hydroxy-3-methoxy benzaldehyde with amoxicillin trihydrate [14]. Prepared ligand shows antibacterial activity. The synthesized compound was investigated in vivo the toxic effects via the measurement of toxic dose (LD50) which was moderate shown in **scheme 4.**



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Synthesis of Substituted N-Phenyl Pyrazoles Using Natural Catalyst

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ABSTRACT
Considering the economic and environmental point of view, now a days more study has been focused on the synthesis of organic compounds using natural catalysts. These catalyst have advantages like safe, economical, easily accessible and environmental friendly nature. Green chemistry focussed on use of less toxic solvents or solvent free synthesis according to environmental point of view. Substituted N-Phenyl Pyrazoles scaffold is a cyclic compound having two nitrogen atoms at adjacent position in a ring. It is an important pharmacophore and privileged structure in medicinal chemistry. One pot two component synthesis of Substituted N-Phenyl Pyrazoles obtained by the reaction of mixture of propane 1,3-dial and phenyl hydrazine under ultrasonication using a natural catalyst.The products were obtained in good yields with simple experimental work up procedure.

Keywords: Substituted N-Phenyl Pyrazoles synthesis, propane 1,3-dial, phenyl hydrazine, ultrasonication.

I. INTRODUCTION

Pyrazole it is a heterocyclic compound. It is aromatic ring compound containing two nitrogen atoms adjacent to each other. In natural products pyrazoles were rarely found . As literature survey revealed that pyrazoles shows great biological activity [1]. It can act as a essential building blocks unit of ligands[2-4]. for transition metals, supermolecules, and liquid crystals.[5]. Pyrazole ring is very important to develop a new class of drugs and present in large number of medicinal compounds .[6].Among heterocyclic compounds nitrogen containing heteroclyclic compounds are found as a core framework for building block of library of heterocycles.[7]. Recent study focus on synthesis of heterocyclic compounds by following green chemistry principles. Hence ultimately we need to find green solvent. As water is the safest and abundant substance in nature and almost all compounds are sparingly soluble in water. Hence it is referred as a benign 'Universal Solvent'. The search for alternative reaction media to replace volatile, flammable and often toxic organic solvents is an important objective in the development of green chemical process.[8] Hence organic synthesis in an aqueous medium is preferred from environmental as well as from economical point of view.Pyrazole a regioselective ring core structure and has great impact in synthetic chemistry[9-13].

In continuation of our efforts to the ecofriendly synthetic approach towards synthesis of bioactive heterocyclic compounds, here in we wish to report one pot two component synthesis of Substituted N-Phenyl Pyrazoles by the reaction of mixture of propane 1,3-dial and phenyl hydrazine under ultrasonication using a natural catalyst in aqueous medium.

II. EXPERIMENTAL

All reagents and chemicals were of analytical grade and used without further purification. Sonication was performed in ultrasonic cleaner with a frequency of 25 KHz and nominal power 250 W. The reaction temperature was controlled by addition or removal of water from ultrasonic bath.

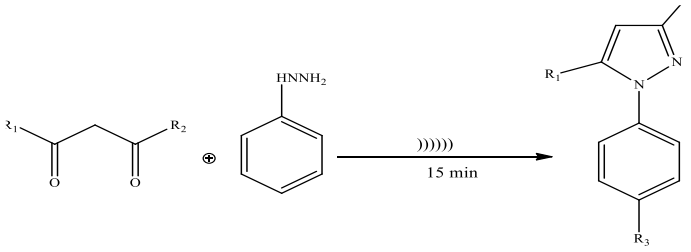
General procedure for the synthesis of substituted N-Phenyl pyrazole.

In 100 mL round bottom flask A mixture of propan-1, 3-dial (1) (13.8 mmol) and phenyl hydrazine (2) (13.8 mmol) was dissolved separately and lemon peel powder (10 % mol) were taken in 40 mL water as a green solvent. The resulting reaction mixture was sonicated for a period as indicated in **Table-1**. the progress of the reaction was monitored by using TLC. After the completion of reaction, the the reaction mixtures were poured on crushed ice, solid product obtained was filtered, washed with water and recrystallized from ethanol to afford the pure product. All the products were confirmed by comparing their melting points, IR and ^{1}H NMR data with literature data.

Table 1: Optimisation of lemon peel catalyst for one pot synthesis of substituted N-phenyl pyrazoles

Sr.No	Lemon peel Catalyst in wt%	Time(min.)	Yield
1	10	**15**	**85 %**
2	20	**15**	**95 %**

Compound 3c: Yield 89%; bp 143-145.IR (KBr) cm^{-1}: 1520 (C=N str., Pyrazolyl); 1196 (C-N str.); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.12 (t, 1H, Pyrazolyl), 7.65 (d, 1H, Pyrazolyl), 7.74 (d, 1H, Pyrazolyl), 7.57-7.60 (m, 5H, Ar-H) ppm.



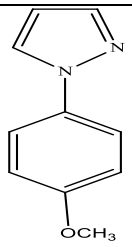
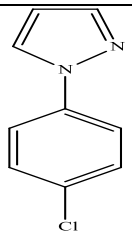
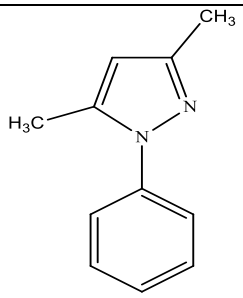
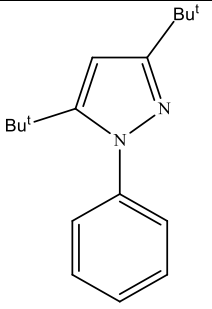
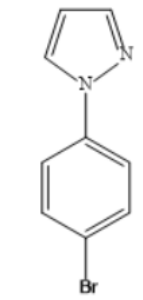
Where R1 & R2 =-H, -CH3, tBu
R3=-H, -Cl, Br, -I, -OCH3

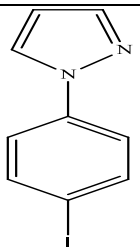
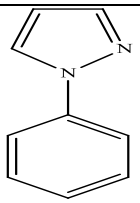
Scheme 1: One pot synthesis of substituted N-phenyl pyrazoles (3a-g) using lemon peel powder as a catalyst.

III.RESULTS AND DISCUSSION

N-Phenyl Pyrazoles have been synthesized by one pot synthesis by using different 1,3-dicarbonyls (1a-g) and phenyl hydrazine (2). And lemon peel powder as a catalyst. The reactions were carried out at ultrasonication for 15 min. and the progress of the reaction was monitored by TLC. Various 1,3-dicarbonyls (1a-g) could give desired pyrazoles (3a- g) through the same experimental procedure with good yields.

Table 2: One pot synthesis of substituted N-phenyl pyrazoles (3a-g)

OMPOUND	R'	R1	R2	PRODUCT	Yield	M.P./ B.P.(C)
3a	p-OMe	H	H		64	B.P.; 282
3b	p-Cl	H	H		86	M.P.;87-90
3c	H	Me	Me		89	B.P.; 143-145
3d	H	Bu^t	Bu^t		90	M.P.;105-107
3e	p-Br	H	H		91	M.P.;68-70

3f	P-I	H	H		89	M.P.;89-91
3g	H	H	H		92	B.P.; 140-142

IV.CONCLUSION

In conclusion, we have developed a simple, highly efficient, and environmentally friendly green method for the synthesis of substituted N-phenyl pyrazoles under ultrasonication using lemon peel powder as a natural catalyst. It was found observed that lemon peel powder found to be good catalyst for rapid conversion and giving good yields. Further studies on the biological activities of the products and application of this methodology to other interesting pyrazole derivatives are underway in our laboratory.

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Supramolecular Assemblies and Their Diversified Applications

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ABSTRACT

The synthesis and construction of synthetic self-assembled systems, inspired by biological features, rely on sophisticated components utilizing supramolecular interactions to achieve advanced structural and functional complexity. Nucleobase interactions, crucial in various biological processes, serve as a motivation for researchers exploring nucleobase synthons to generate diverse functional systems. This review focuses on the progress made in the last decade concerning naphthalene diimides (NDIs) and their versatile applications. The utilization of NDIs spans various domains, including supramolecular chemistry, sensors, host–guest complexes for molecular switching devices, ion-channels employing ligand gating, gelators for sensing aromatic systems, catalysis facilitated by anion–π interactions, and NDI intercalations with DNA for medicinal purposes. Special attention is given to core-substituted naphthalene diimides (cNDIs), highlighting their relevance in artificial photosynthesis and solar cell technology.

The review provides insight into single-component and multicomponent co-assembly techniques, emphasizing the significance of assemblies in drug delivery systems, pollutants capture, materials synthesis, and beyond. Novel synthetic routes and methodologies are introduced, contributing to the ongoing development of NDI-based compounds for prospective applications.

In Conclusion, the review offers perspectives on NDI chemistry for future research initiatives and outlines key challenges that must be addressed for NDIs to find practical applications. This comprehensive examination facilitates a qualitative leap in understanding natural products, progressing from monomolecular to supramolecular structures and multi-component interactions. The insights provided are valuable for both intensive research and practical applications in various fields.

Keywords: Supramolecular Self-assembly, Naphthalene diimides (NDI's), Drug Delivery, Sensing, and Solar Cell Technology.

I. INTRODUCTION

The promising field of synthetic self-assembled systems, drawing inspiration from the intricacies of biological structures, relies on sophisticated components that leverage supramolecular interactions to achieve heightened structural and functional complexity. Among the myriad of interactions crucial in biological processes, nucleobase interactions stand out, serving as a key motivation for researchers exploring nucleobase synthons to

craft diverse functional systems. Over the past decade, remarkable strides have been made in understanding and harnessing the potential of naphthalene diimides (NDIs) and their versatile applications across various domains. NDIs have proven to be invaluable in supramolecular chemistry, acting as foundational elements in the development of sensors, host–guest complexes for molecular switching devices, and ion-channels employing ligand gating. Furthermore, NDIs have found utility as gelators for sensing aromatic systems, catalysts facilitated by anion–π interactions, and as agents for NDI intercalations with DNA for medicinal purposes. This review aims to provide a comprehensive overview of the progress made in the utilization of NDIs, with special attention directed towards core-substituted naphthalene diimides (cNDIs) and their pivotal role in artificial photosynthesis and solar cell technology.

In addition to surveying the diverse applications of NDIs, this review delves into the intricacies of single-component and multicomponent co-assembly techniques. Emphasis is placed on the significance of these assemblies in drug delivery systems, pollutants capture, and materials synthesis, showcasing the expansive reach of NDI-based compounds. Novel synthetic routes and methodologies are introduced, contributing to the ongoing development of NDI-based compounds for prospective applications in various scientific and technological realms.

As we navigate the promising landscape of NDI chemistry, this review also illuminates future research initiatives. By delineating key challenges that must be addressed for NDIs to find practical applications, the review aims to guide researchers and practitioners in navigating the evolving landscape of synthetic self-assembled systems. This qualitative leap in understanding, transitioning from monomolecular to supramolecular structures and multi-component interactions, is poised to unlock new frontiers in the realms of natural product exploration, intensive research, and practical applications across diverse fields. The insights provided herein aspire to serve as a valuable resource, development in both scientific investigation and real-world applications.

II. SUPRAMOLECULAR SELF-ASSEMBLY IN NATURE

Recognition of two molecules results to aggregation of two or more distinct unit which forms structurally constant well defined aggregates due to non-covalent interactions called self-assembly. Hydrogen bonding in DNA is on of the best example of supramecular self assembly. (Fig. 1) Double helical form in DNA due to hydrogen bonding between nitrogenous bases pairing of purinese (adenine and thymine) and pyrimidines (cytosine, gyanine) *via* triple and double hydrogen bonding.[1]

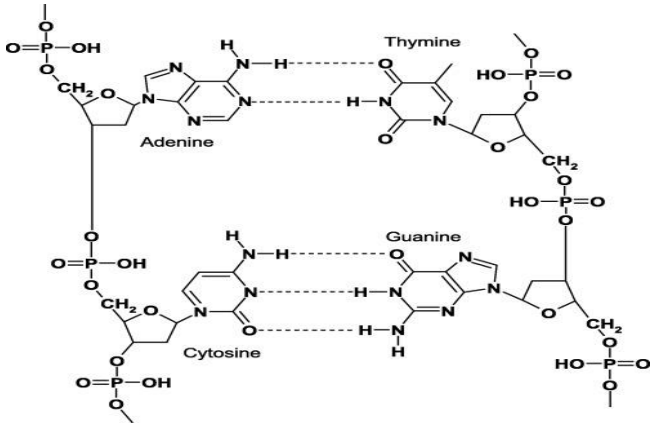


Figure 1: Chemical structure of DNA.

A fibrous protein i.e. Collagen, is an vital structural component of all connective tissues such as bones, cartilage, ligaments, and skin.[2] Naturally occurred collagens form triple helices consist of all identical homotrimer (AAA), two different heterotrimer (AAB), or three different heterotrimer (ABC) polypeptides.[3] The form of a right-handed super helix of collagen has triple helical assembly in which three left-handed poly-proline helices twist around one another.[4] Peptide series in Collagen includes a middle core of proline-hydroxyprolin and Glycine (Pro-Hyp-Gly) repeat sequences flanked by distinct sets of peptide repeats containing either negatively (Glu) or positively (Arg) charged amino acid residues showed in (Fig. 2). The Pro-Hyp-Gly peptide sequence forms the structurally essential hydrophobic core of the assembly, which is responsible for maintaining the thermodynamic stability of the collagen triple-helical structure.[5] It observed that electrostatic, hydrophobic, and hydrogen-bonding interactions plays a major role in collagen self assembly.

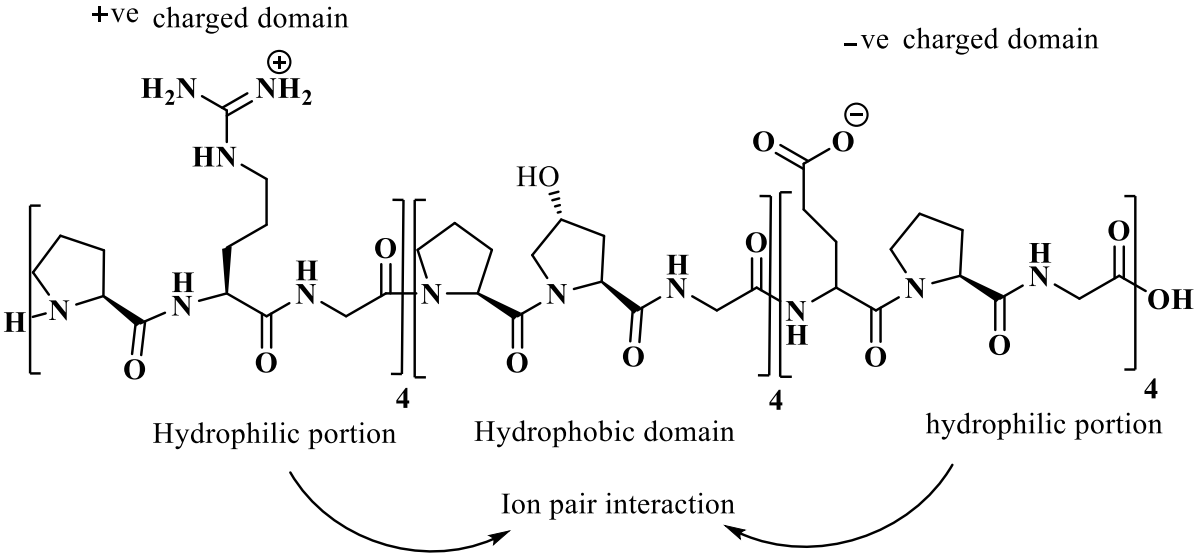


Figure 2: Amino acid sequence of synthetic collagen-mimetic peptide indicating the distinct domain structure of collagen triads.

III.SYNTHETIC SUPRAMOLECULAR SELF ASSEMBLY

The term synthesis has suggested that, the construction of molecular systems as a result of in order to formation covalent bond. Synthetic chemist can build nano-systems which are common in the natural world; chemist must have idea to control a different type of bonds such as the intermolecular and noncovalent bonds. The synthetic chemist's move toward the synthesis of nanoscale composites, employing the noncovalent bond leads to the birth of a highly interdisciplinary field of chemical research called supramolecular chemistry. There are two particular modern-day chemical syntheses which are influenced by supramolecular chemistry. These are (1) the synthesis of multicomponent supramolecular architectures utilizing non-covalent bonding interactions, i.e., supramolecular synthesis and (2) the synthesis of discrete molecular entities held together using completely covalent and mechanical bonds supported and assisted by intermolecular, non-covalent interactions, i.e., supramolecular assistance to molecular synthesis. The development of both of these aspects of synthetic supramolecular chemistry based on as been self-assembly, the spontaneous generation of well-defined supramolecular architectures from specifically "engineered" building blocks.[6]

The self-assembly process driven by non-covalent interactions crucial in the abundance of all biological organisms, offers stepwise bond formation in the construction of large supramolecular assemblies. These

include (1) a highly convergent synthetic protocol based on the simultaneous assembly of the programmed building blocks. The preparation predetermined building blocks significantly fewer steps than the comparable covalent synthesis. The fast and facile formation of the final product since non-covalent interactions are usually established very rapidly, and (2) natural defect-free assembly as the equilibrium between the constituents and the final product contribute to the self-rearrangement of the component within the assembled structure and thus to the self-correction of defects.[7]

J. Williams *et al* demonstrate the spatial distribution of structures formed *via* the mechanisms of molecular self-assembly. They choose a small organic, amphiphilic Fluorenylmethoxycarbonyl (Fmoc) pentapeptide that contains the biochemically useful peptide sequence Arginine-Glycine-Aspartic acid (RGD). (Fig.3)They finally observed the influence of the fucoidan on the assembly process and supramolecular ordering; finally we explored the effect of this process on the mechanical properties of the resultant hydrogel matrix.

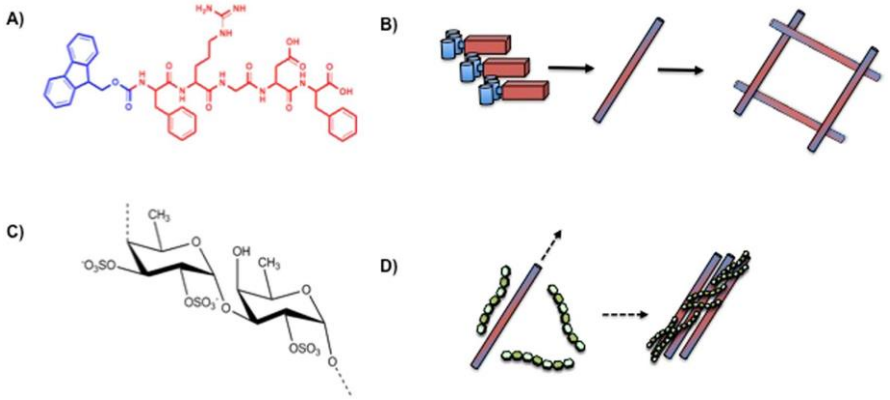


Figure 3: Peptide self-assembly: (**A**) structure of Fmoc-FRGDF. (**B**) Schematic of the assembly process where individual peptides form fibrils which become entangled to form the hydrogel matrix. (**C**) Repeating unit of fucoidan (**D**) Schematic of proposed induction of supramolecular ordering by interaction between fucoidan and individual fibrils to yield thicker bundles.

A very different approach for the formation of supramolecular species *via* spontaneous self-assembly of precursor building blocks is the use of metals and dative bonding *via* coordination (Fig. 4). Although this methodology has been successfully employed in the formation of infinite networks and grids as well as the template-based synthesis of catenanes and molecular knots and discrete helical species.[8]

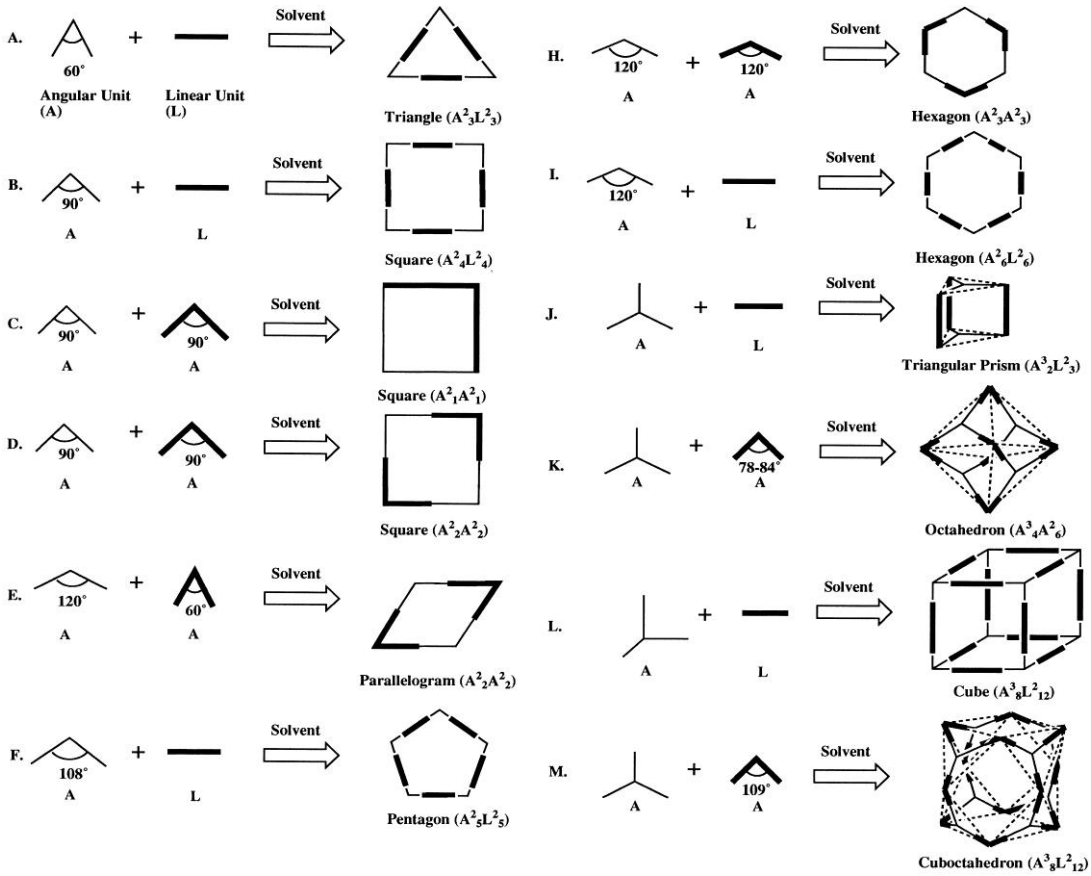


Figure 4: Self-assembly, symmetry, and molecular architecture: coordination as the motif in the rational design of supramolecular metallacyclic polygons and polyhedra.

IV.AMPHIPHILES

Amphiphiles are compounds possessing both hydrophilic (water-loving) and lipophilic (fat-loving) or water-hating components. Amphiphiles are synthetic or natural molecules with the ability to self-assemble into a wide variety of structures. Most of bio-materials are amphiphilic in nature and are usually consist of carbohydrates, peptides, and fatty acids whose aggregation is driven by soft interactions such as hydrogen bonds and steric effects and hydrophobic and electrostatic interaction. Amphiphilic molecules self-assemble in water or in an organic phase to form various kinds of ordered structures including micelles, vesicles, microemulsions, and liquid-crystalline mesomorphic phases. In addition, chiral self-assembly can hierarchically lead to a rich variety of more organized nanostructures such as fibers, ribbons, helices, “superhelices”, and tubes when the amphiphiles are capable with chiral elements. In conventional head/tail(s) amphiphiles the lipophilic part consists generally of a long (saturated or unsaturated) hydrocarbon chain, while the hydrophilic head can be either non-ionic or ionic. Non-ionic surfactants have either polyether or polyhydroxyl units as the hydrophilic group. The large no of conventional non-ionic surfactants consist of hydrophilic poly (ethylene oxide) chain connected with hydrophobic alkyl chain. [9]

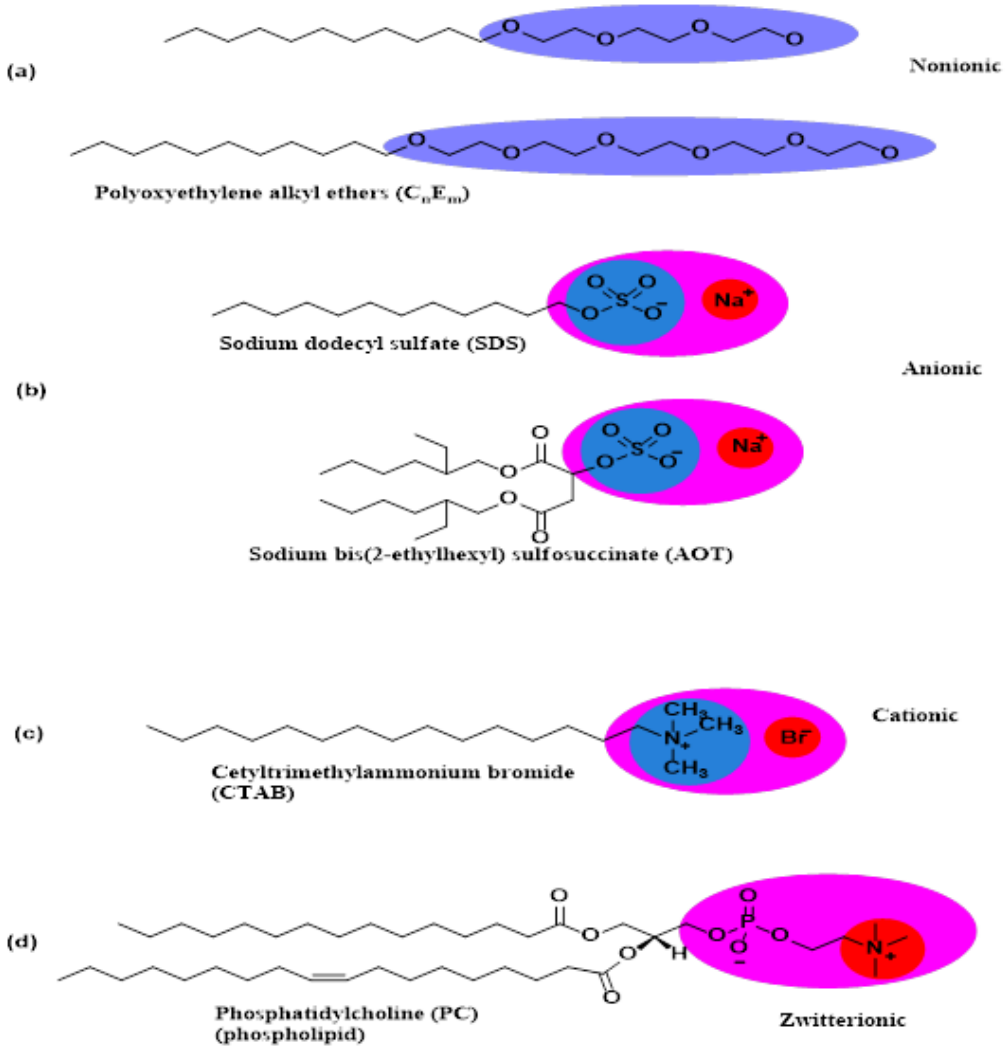


Figure 5: Example of most common (a) non-ionic, (b) anionic, (c) cationic and (d) zwitterionic amphiphilic molecule.

In above figure polyoxyethylene alkyl ethers, C*n*E*m*, are non-ionic surfactants made of *m* hydrophilic oxyethylene units and an alkyl chain with *n* methylene groups (Fig. 5 a). Anionic surfactants, which are commonly used as detergents and soap for cleaning processes, consist generally of negatively charged head groups and positively charged counter ions such as sodium, potassium, or ammonium ions, sulfate, sulphonate, Carboxylate and phosphate are the commonly used polar groups (Fig. 5b). Cationic surfactants consist of positively charged head groups such as a quaternary ammonium and a halide ion as a counter ion. Cetyltrimethylammoniumbromide (CTAB) and sodium bis (2ethylhexyl) sulfosuccinate (AOT) are the most engaged cationic amphiphiles (Fig 5b and 5c). Finally in zwitterionic amphiphiles the head groups possess both a positive and negative charge, for example, in the vesicle forming phospholipid phosphatidylcholine (Fig. 16d). If zwitterions contain a carboxylate and a protonated ammonium ion, it may behave as an anion (at high pH) or a cation (at low pH) assuming then an amphoteric character.[10]

4.1. Peptide amphiphiles:

Peptide amphiphiles (PAs) were first described by the group of Matthew Tirrell in 1995. The Peptide amphiphiles (PAs) are an important family of peptides with huge potential to create biological functionality and

structure. Hartgerink *et al.* in the early 2000s demonstrated a peptide amphiphile which has three regions, a hydrophobic tail, a region of beta-sheet forming amino acids and a peptide epitope designed to allow solubility of the molecule in water perform a biological function by interacting with living systems. Peptide supramolecular assemblies can participate with designed proteins in their capacity to offer useful biological functions and structural diversity to synthetic soft matter. Figure 6 explains structural variations in Peptide amphiphiles; peptide assemblies can generate filaments, 2D-sheets, spheres, networks, tubes, helices and more complex shapes. In aqueous environment self-assembly is driven by the non-covalent interaction forces to form ordered structures ranging from monomer to micron size self-assembled materials. In addition self-assembly can be influenced temperature, pH and concentration. [11-15]

Stupp *et al* reported on a method to form nanofibers from two oppositely charged PAs (Fig. 7) carrying different biological signals at neutral pH. They demonstrated nanofiber formation by these peptide-amphiphiles over a large pH range. Together these new mechanisms of self-assembly may become important in the biomedical application of these materials for either in vitro or in vivo cell therapies.[16]

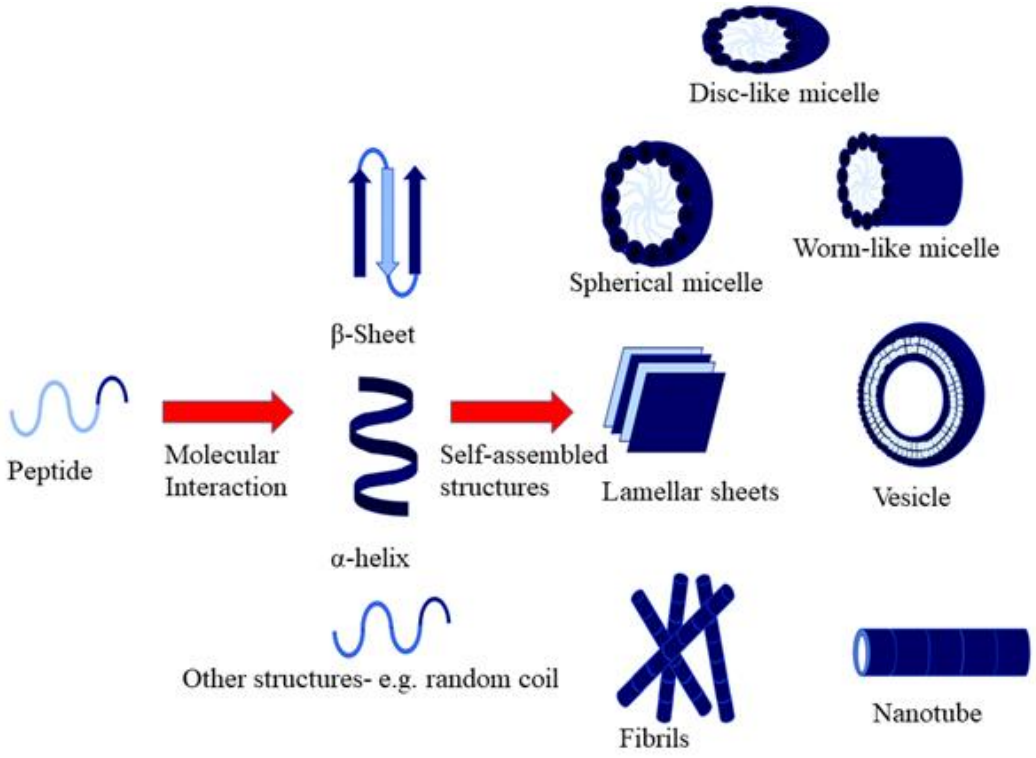


Figure 6: Possible self-assembled structures of peptide amphiphiles. Amphiphilic peptides may assemble into secondary structure through inter and intramolecular interactions (*e.g.* electrostatic interactions and hydrogen bonding), and continue to aggregate into larger self-assembled structures.

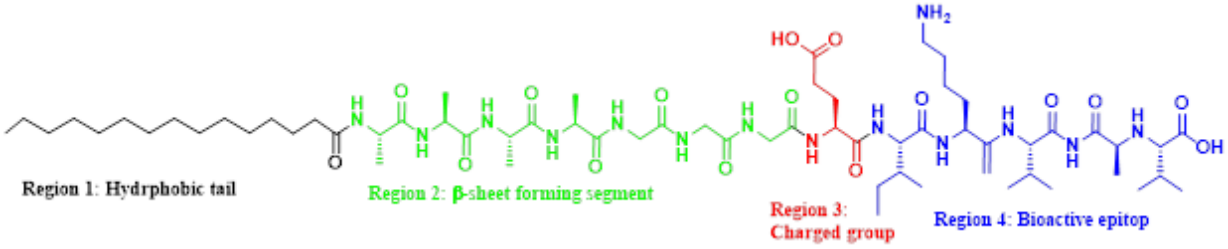


Figure 7: Molecular structure of a representative PA with four rationally designed chemical entities.

Stupp *et al.* studied twelve derivatives of peptide amphiphile (Fig. 8) molecules by changing alkyl tail and amino acid in the peptide amphiphile molecule. The yielded nanofibers change in morphology, surface chemistry, and potential bioactivity. These results revealed the chemically versatile nature of this supramolecular system and its high potential for manufacturing nanomaterials. In addition, three different modes of self-assembly resulting in nano- fibers are described, including pH control, divalent ion induction, and concentration.[17]

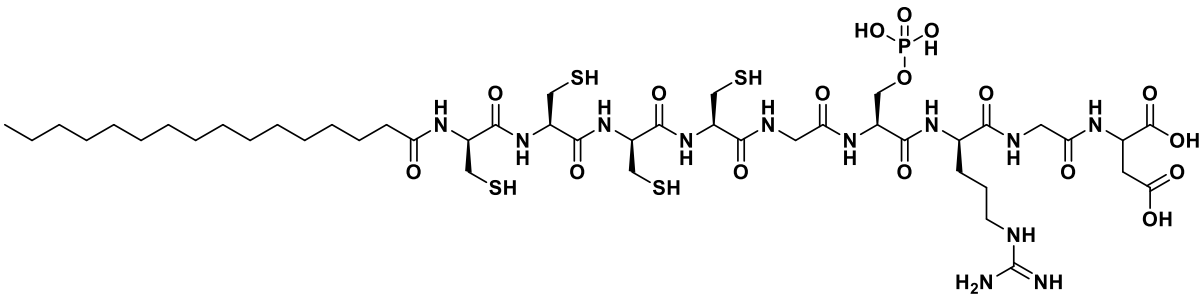


Figure 8: Chemical structure of peptide amphiphile having various polar groups.

Recent years, many groups have been focusing to make different self-assemblies and applying wide range of applications. In this scenario, the core moiety plays an important role to form stable self-assemblies. Majorly aromatic diimides are promising in this area because of their excellent properties, among naphthalenediimides (NDI) is come under first, due to having unusual properties such as good charge mobility, high electron affinity, easy to functionalize with different groups and excellent thermal oxidative stability.[18, 19] These properties open wide range of applications such as organic electronics, self-cleaning, tissue engineering and so on. The NDIs chromophore functionalizes through the core-substitution and the imide nitrogen atoms.[20]

4.2. Naphthalenediimide (NDI) amphiphiles:

Naphthalenediimide (NDI) is an attractive molecular unit due to their n-type semiconducting property and air stability. Recently, NDI molecules have been studied as key components in several systems, including light-emitting diodes, solar cells, field effect transistors and ion sensors as well as in cell imaging and photodynamic therapy. In addition, NDI used as components in various supramolecular nanostructures, including barrels, catenanes, rotaxanes, and vesicles as well as one dimensional nanostructures which can be utilized to construct more promising three-dimensional materials such as organogels and hydrogels because of their desired electronic and spectroscopic properties.[21]

Das *et al.* studied the self-assembly and application of a naphthalenediimide (NDI)-appended peptide amphiphile (PA). H-bonding among the peptide moiety in conjunction with π-stacking between NDI and hydrophobic interactions within the alkyl chain are the major driving forces behind the stepwise aggregation of the PA to form hydrogels. The PA produced efficient self-assemblies in water, forming a nanofibrous network that further formed a self-supportive hydrogel. This water soluble conjugate was found to be nontoxic and cell permeable, was used for cell imaging, and has an extended biological application to assess intracellular pH.[22]

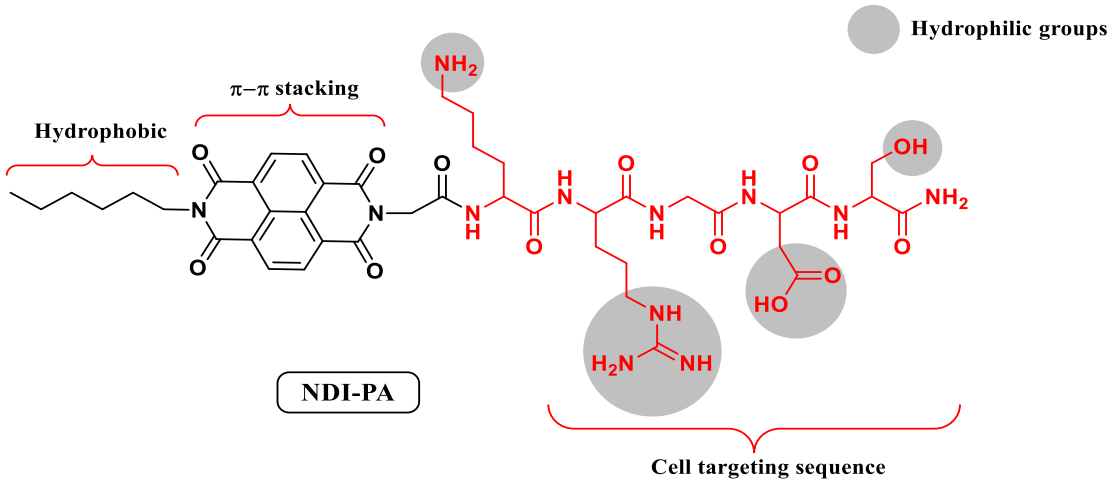
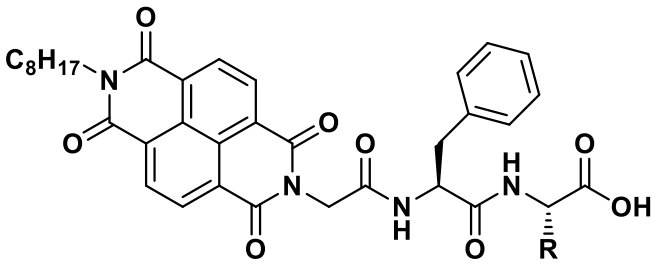


Figure 9: NDI peptide amphiphile

Lin *et al.* studied self-assembly of dipeptide conjugated electron deficient NDI. The presence of the NDI group at the N-terminus of Phe-Phe and Phe-Gly (Fig. 10) support the formation of one-dimensional (1-D) nanostructures and three dimensional (3-D) colored hydrogels under both acidic and physiological conditions. These gels were stabilised by π-π interaction of conjugated system and hydrogen bonding. [23]



R= CH_2Ph (Phe) or H (Gly)

Figure 10: NDI- peptide conjugate.

Parquette *et al.* reported the formation of n-type 1D nanostructure from the β-sheet assembly of dipeptide (Fig. 11) in which NDI as side chain. Depending upon placement of NDI side chain leads into either helical nanofibers or twisted nanoribbons in aqueous solution. B-Sheet-type hydrogen bonding and π-π association play important roles in directing the assembly process. A slight balance between electrostatic repulsion and hydrophobic interactions is critical for the self-assembly. Fluorescence lifetime and anisotropy experiments indicate nature of the intermolecular organisation and packing of the nanostructure.[24]

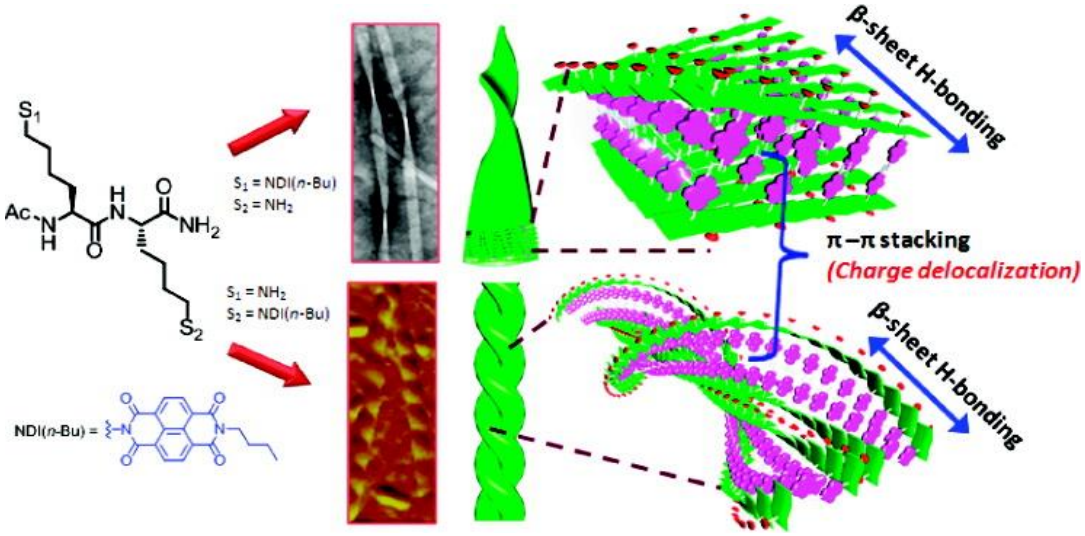


Figure 11: Assembly of dipeptide-NDI conjugates into left-handed fibers (Top) and ribbons (Bottom). Interstrand distances of β-sheets and plane-to-plane distance of NDIs showed determined by XRD.

V. BOLAAMPHIPHILES

Bolaamphiphiles are amphiphilic molecules that have hydrophilic groups at both ends of a sufficiently long hydrophobic (e.g., one, two, or three alkyl chains, a steroid or a porphyrin) hydrocarbon chain. Bolaamphiphiles are another interesting class of amphiphilic molecules which can self-assemble to form well-defined nanostructures. In the last two decades, various synthetic methods have been developed to produce functional bolaamphiphiles which mimic their natural counterparts. Bolaamphiphilic molecules as that have hydrophobic repeating units connecting hydrophilic head groups at the two ends of the molecule, symmetrically or asymmetrically. In Fig 12, asymmetric bolaamphiphile has two hydrophilic head groups: carboxylic acid and a glucose moiety. The hydrophobic connector consists of methylene repeating units which connects two hydrophilic groups.[25]

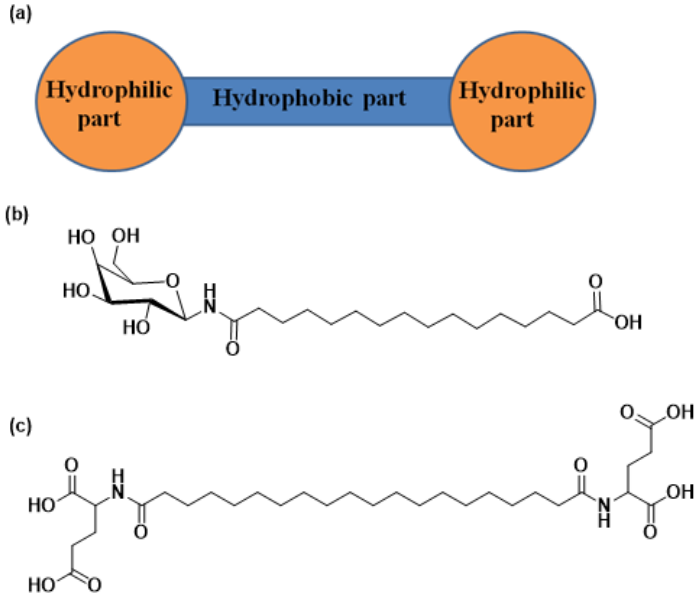


Figure 12: (a) Schematic drawing of defined bolaamphiphiles (b) unsymmetrical and (c) symmetrical bolaamphiphiles.

5.1. Peptide bolaamphiphiles:

Natural proteins and peptides implement well-defined secondary structures such as α-helices and *β*-sheets through interaction of hydrophobic collapse, hydrogen bonding and electrostatic and van der Waal interactions.[41] Peptide bolaamphiphiles are building blocks for structures such as membranes, fibers, tubes, ribbons, and ropes. Peptide bolaamphiphiles self-assembled in various solvent and forms hydrogels in aqueous medium and organogels in organic solvents.[26]

Das *et al.* studied peptide-based hydrogels which form through the self-assembly of small peptide molecules (Fig. 13). They designed peptide bolaamphiphile molecules with two different hydrophilic dipeptides, which are covalently connected by a succinic acid moiety. They studied stimuli responsive self-assembly and morphological changes of peptide bolaamphiphile. The tryptophan and phenylalanine containing peptide bolaamphiphile forms a hydrogel upon sonication under physiological conditions (Fig. 14). The disassembly and self-assembly processes are influenced by various stimuli, including heating-cooling and shaking-rest methods. The extensive hydrogen bonding and π-π stacking interactions are responsible for the self-assembly process, which is confirmed by FT-IR, temperature dependent NMR and fluorescence spectroscopy studies.[27]

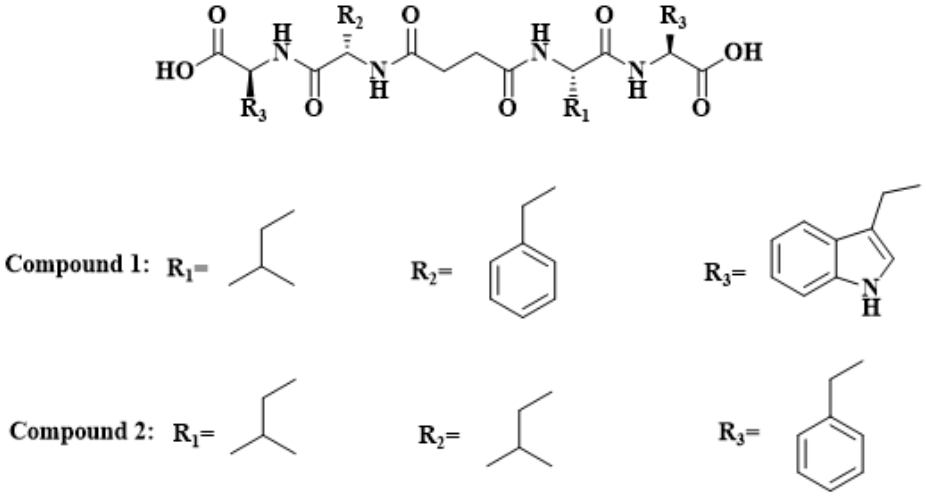


Figure 13: Structures of peptide bolaamphiphiles 1–2.

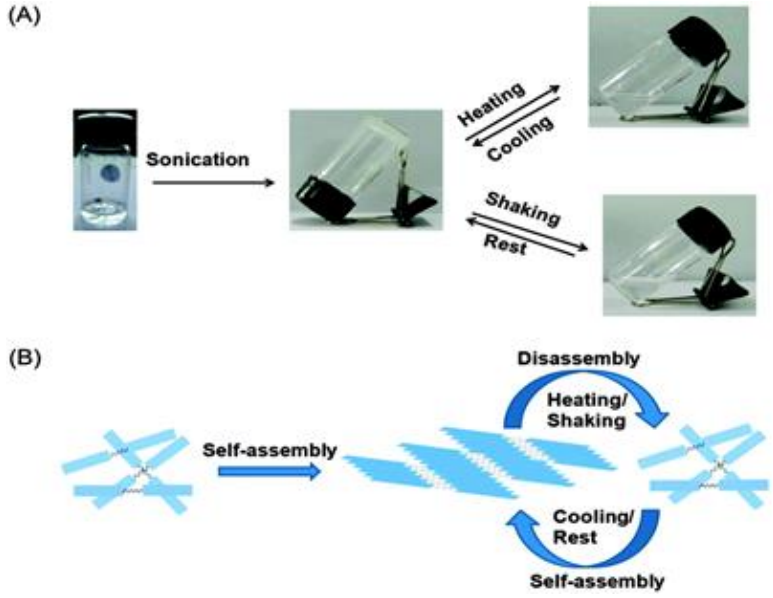


Figure 14: **(A) Stimuli responsive assembly–disassembly of peptide bolaamphiphile 1 and (B) a scheme of the assembly–disassembly of 1.**

D. Tovar *et al* demonstrated the macroscopic alignment of peptide nanostructures bearing π- conjugated functionality. The photophysical differences between the hydrogels derived from randomly oriented peptide nano structures are aligned *via* noodle producing method. The alignment of this π -electron oligomers within the noodle macrostructures leads to overall directionality among the internal π-stacked chromophores. The anisotropic electrical properties of the organic semiconductors hidden within this methods leads to an order-of-magnitude enhancement of hole mobilities along the length of the macrostructure. The anisotropic electronic properties of the resulting macrostructures will enable future studies of directional energy migration through aqueous and biological regimes.

In (Fig. 15) α-Quaterthiophene (OT4, a hole-transporting organic semiconductor) and 1,4-distyrylbenzene (OPV3, a fluorophore) were embedded into the backbones of two different linear peptide sequences (yielding HO-EAA-OT4-AAE-OH **1** and HO-VEVAG-OPV3- GAVEV-OH **2** , respectively) using an on-resin dimerization protocol that we developed previously that allows for rapid incorporation of several types of π -conjugated substructures into peptide backbones.[28]

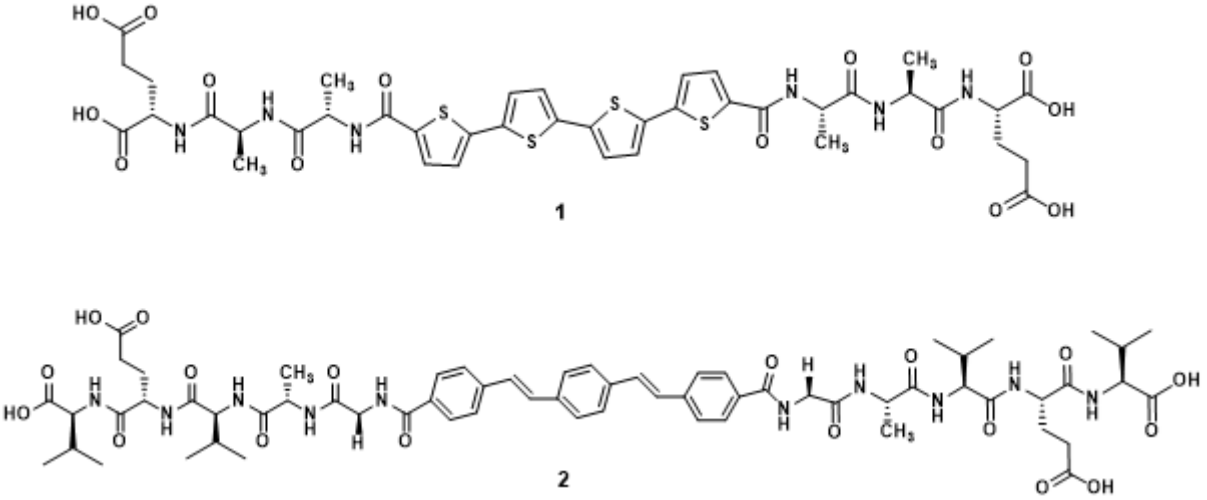


Figure 15: Structures of peptide- π -peptide molecules incorporating (1) α-quaterthiophene OT4 and (2) 1, 4-distyrylbenzene OPV3.

5.2. Naphthalenediimide bolaamphiphiles:

Ghosh *et al.* studied the spontaneous vesicular assembly of a naphthalene–diimide (NDI)-based non-ionic bolaamphiphile in aqueous medium by using the synergistic effects of π-stacking and hydrogen bonding. In NDI-1 (Fig. 16), the peripheral hydrophilic wedge is attached to the NDI core by a hydrazide group, which is a very effective strategy for hydrogen-bonding-mediated self-assembly in non-polar organic media. In this system to protect these moieties from the bulk water so that the distinct role of hydrogen bonding in the self-assembly of hydrazide-functionalized NDI building blocks were studied, even in aqueous solution the electron deficient NDI could hold in donor–acceptor (D–A) charge-transfer (CT) interactions with a water-insoluble electron rich pyrene donor by good feature of intercalation. More interestingly even the Pyrene was hold in between two NDI molecules the intermolecular hydrogen bonding between hydrazide group remain same. The vesicular assembly of NDI-1 in aqueous medium and CT-interaction-mediated 2D-to-1D vesicle-to-hydrogel transformations in the presence of an electron-rich pyrene intercalator.[29]

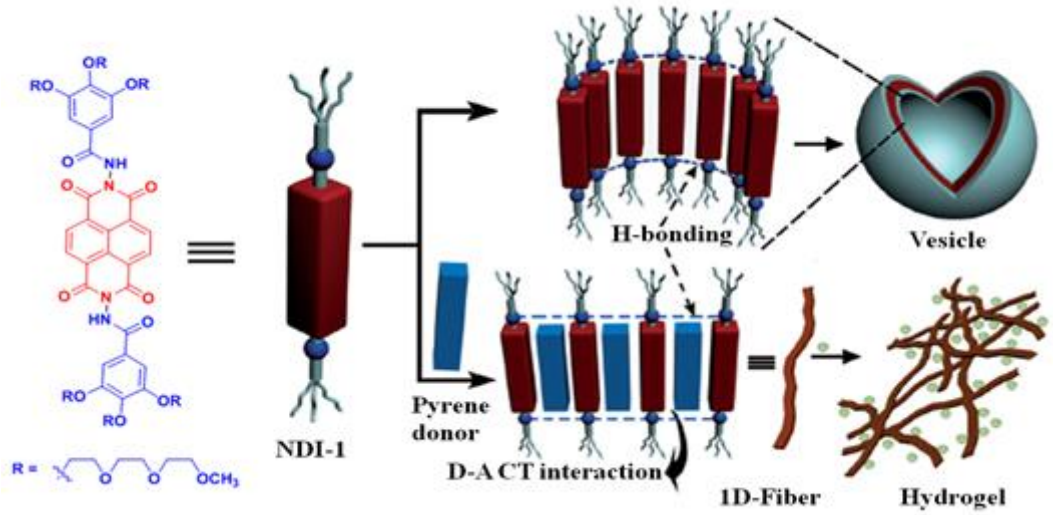


Figure 15: (Top) Structure and vesicular assembly of NDI-1. (Bottom) CT-interaction-mediated morphological transition (2D-to-1D vesicle-to-fibres) and gelation by Pyrene intercalation.

George *et al.* studied, NDI amphiphiles substituted with dipicolylethylenediamine –zinc complex (DPA–Zn) motifs (Fig. 17). DPA-Zn support guest induced self-assembly and chiral induction through specific binding interactions. They examine the adenosine phosphates (guests) induced one-dimensional (1-D) self-assembly and the resultant supramolecular chirality of naphthalenediimide (NDI) NDPA-Bola.[30]

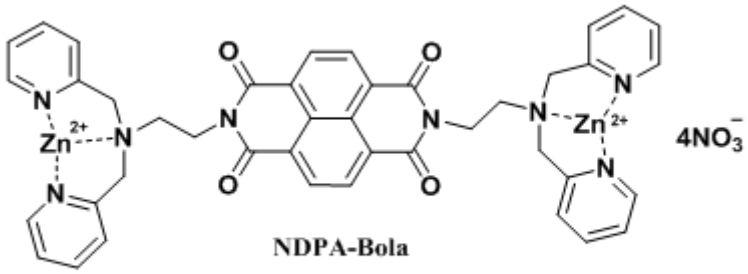


Figure 17: Molecular structures of NDPA-Bola.

In our group we reported the self assembly of phosphonic acid bolaamphiphile in presence of L- and D-arginine (Fig.18) through molecular recognition and leading to the formation of well-defined long nanobelts and particular aggregates in water at pH 9, respectively, *via* chirality induced molecular recognition.[31]

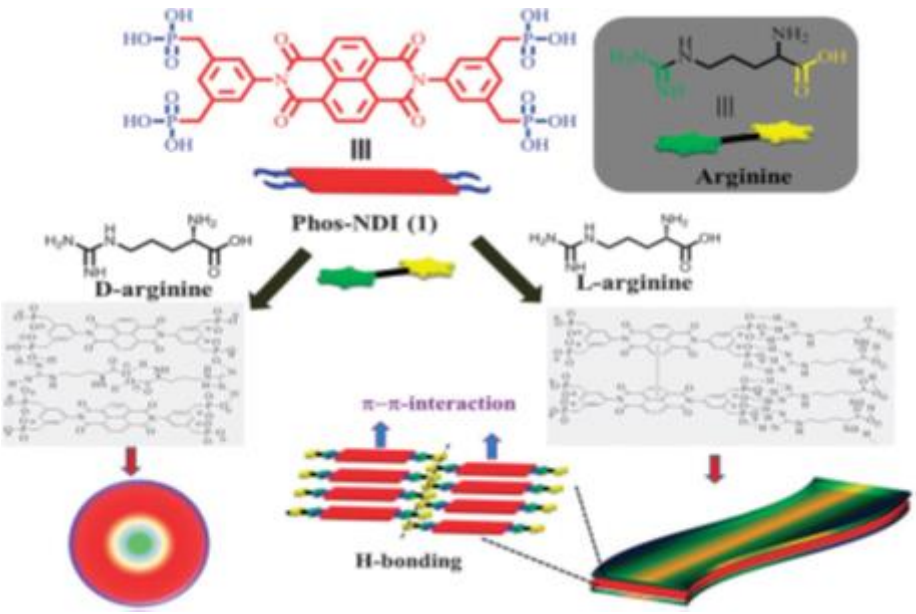


Figure 18: Schematic illustration of the proposed organized structure of Phos–NDI (1) with L- and D-arginine assembled into nanobelts and spherical aggregates, respectively.

Parquette *et al.* reported a one-dimensional n-type nanotube formation by stacking rings formed from the bolaamphiphilic self-assembly of naphthalenediimide (NDI) with L-lysine headgroups (Fig. 19). Solid-state NMR studies demonstrate the exceptional conformational homogeneity of the constituent molecules that make up the nanotubes.[32]

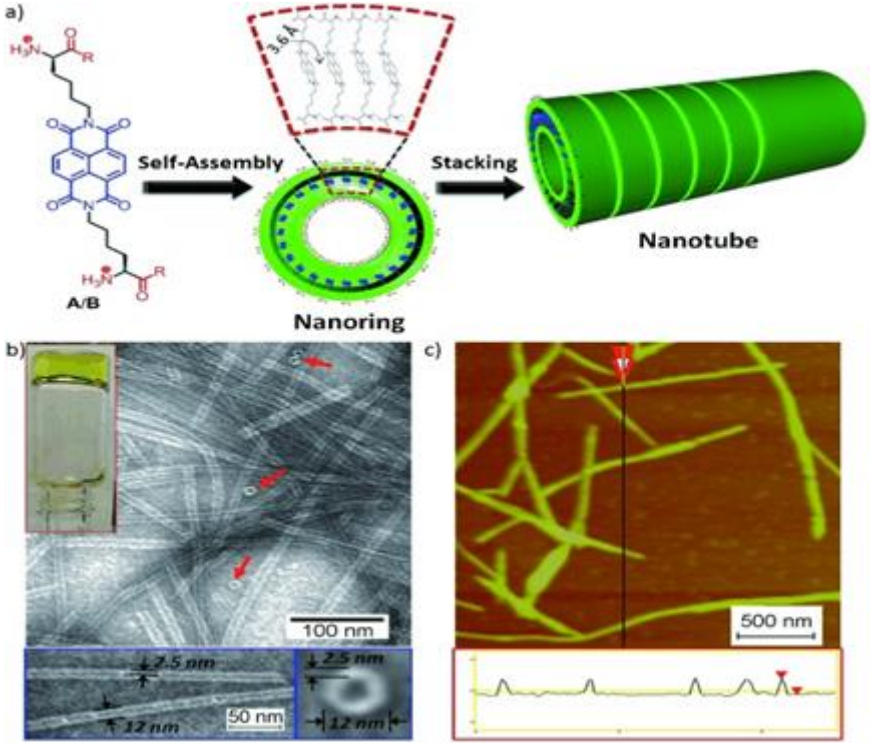


Figure 19: a) Structures of lysine-based bolaamphiphiles **A** (R=O) and **B** (R=OMe) and the assembly of **A** into rings, which stack to give tubes. The blue sections of **A** undergo hydrophobic π–π stacking interactions, and the red sections electrostatic interactions. b) TEM image of bolaamphiphile **A** in water (250 mm; carbon-coated copper grid); 2% (w/w) uranyl acetate as negative stain. Blue insets: Two nanotubes and one nanoring. c) Tapping-mode AFM images of bolaamphiphile **A** in water (250 mm) on freshly cleaved mica. Red inset: Section analysis showing uniform height of the assemblies.[33]

VI.FABRICATION OF FUNCTIONAL NANO MATERIALS USING SUPRAMOLECULAR ASSEMBLY AND THEIR APPLICATIONS

Molecular self-assembly is a powerful approach for fabricating novel supramolecular architectures. Govindaraju *et al.* explained how the self-assemble materials undergo well-ordered architectures and controlled configurations to develop advanced functional systems and biological applications comprise the field of molecular architectonics (Fig. 20). *Architectonics* designates the study and character of various types of structure.

Particularly ordered molecular assemblies can express remarkable developments in several areas such as energy, health and environment. For example, the well-defined nano, micro, and macroarchitectures of functional molecules with specific molecular ordering possess potential applications in flexible electronics, photovoltaics, photonic crystals, microreactors, sensors, drug delivery, biomedicine, and superhydrophobic coatings, among others. The functional molecular architectures having unparalleled properties are widely evident in various designs of nature. By drawing inspirations from nature, intended molecular architectures can be designed and developed to harvest various functions, as there is an infinite resource and scope.

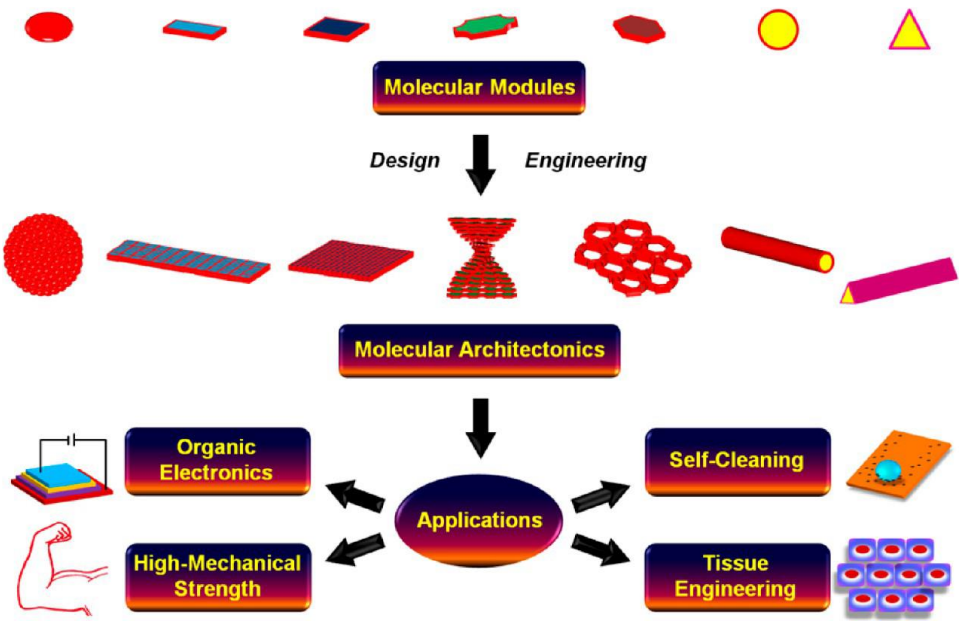


Figure 20: Molecular architectonics for functional applications.[34]

The stereochemistry and minute structural modifications in the molecular designs that effects in the supramolecular interactions and construction of self-assembled zero-dimensional (OD), one dimensional (1D), and two-dimensional (2D) nano- and micro architectures like particles, spheres, cups, bowls, fibers, belts, helical belts, supercoiled helices, sheets, fractals, and honeycomb-like arrays . They explains molecular systems that platform for the elegant designs of co-assembly, templated assembly, hierarchical assembly, transient self-assembly, chiral denaturation, retentive helical memory, self-replication, supramolecular regulation, supramolecular speciation, supernon linearity, dynamic pathway complexity, supramolecular heterojunction, living supramolecular polymerization, and molecular machines. They describe the molecular engineering

principles that have leads to several applications, namely, organic electronics, self-cleaning, high-mechanical strength, and tissue engineering.[34]

Arylenediimides (NDIs/PDIs) and few other molecular systems serve as functional modules that have applications ranging from electronics to biomedicine. The planarity and high π-acidity of the NDI system is ideal for face-to-face π-stacking, while their enhanced solubility offers better processability than other aromatic imides. Naphthalenediimides (NDIs) are among the most promising n-type semiconductors for electronic devices based on organic materials and they have potential applications in organic field effect transistors, supramolecular switches, fluorescent chemosensors, ion channel, catalysis and electron and energy transfer systems. NDIs possess excellent characteristics for the construction of artificial photosystems.[35]

6.1. Ion transportation:

The recently discovered anion-π interaction, the anion-π interactions are termed as favourable non-covalent contacts between an electron deficient aromatic system and an anion (Fig. 21).[36, 37]These interactions play a crucial role in various chemical, biological processes and ion channels. The *N*, *N*-naphthalenediimide (NDI) building unit has a highly positive global quadrupole moment (Q_{zz} = +19.4 B) and exhibits an electron deficient character at the centre of the molecule. S. Matile *et al.* reported the design, synthesis, and evaluation of π-acidic, shape-persistent oligo-(*p*-phenylene)-*N*, *N*-naphthalenediimide (O-NDI) rods that can transport anions across lipid bilayer membranes with a rare halide selectivity ($Cl^- > F^- > Br^- > I^-$). This process attributed to anion- π interactions with the π -slide which compensate for the cost of ion dehydration. Such synthetic channels are of great interest in light of the importance of anion channels in diseases such as cystic fibrosis and other anion channelopathies.[38]

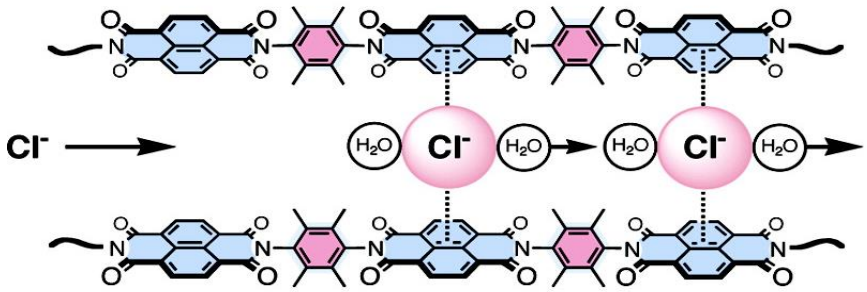


Figure 21: The concept of anion-π slide in lipid bilayer.[38]

6.2. Catalysis.

Kim *et al.* synthesise range of water soluble NDI derivatives (Fig. 22) having different chain length at imide position which used for variety of application from catalysis to optoelectronics. Substitution of chain length increases solubility of material in various polar and nonplar solvents. They design the molecular structure with positive charge centre located at different distance from NDI core. They studied the rate of base catalysed hydrolysis reaction of imide substituted NDI, the ethyl linker compound (1) hydrolysed 6.8 times faster than a compound with propyl linker (5), further investigate the equilibrium constant at pH 7.5 for compound 1 is less stable than 5 finally they conclude the rate of hydrolysis of the NDI increased when the cationic is closer to NDI core.[39]

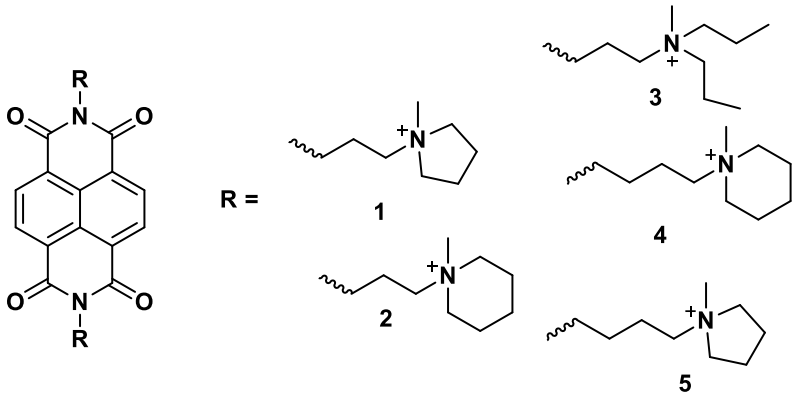


Figure 22: NDI derivatives for catalytic study.

Matile *et al.* demonstrated asymmetric anion–π catalysis of cascade reactions that afford bicyclic products with quaternary stereogenic centres. They focused on the addition of cyclohexanedione **1** to nitro olefin **2** (Fig. 23). In the presence of a base (catalyst), they engage in a domino (cascade) Michael–Henry reaction to afford bicyclo[3.2.1]octan-8-one 3, which is a bicyclic product with four chiral centres made from achiral substrates.[40, 41] The first step is the Michael addition of the conjugate enolate base of **1** to acceptor **2** (see transition state TS1, Fig. 23). The resulting nitronate engages in an intramolecular Henry reaction to close the second carbocycle (TS2, Fig. 23).[42]

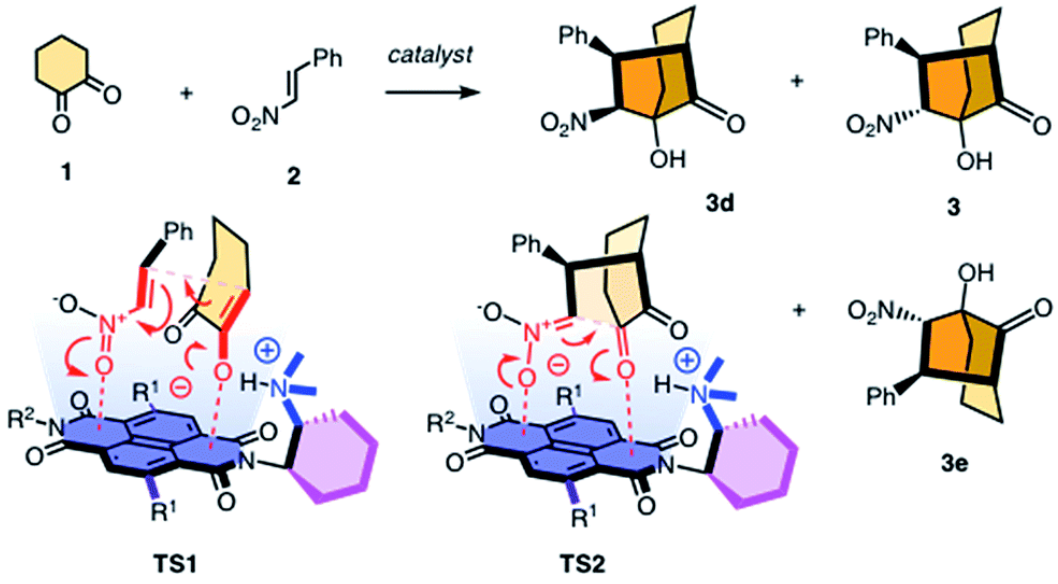


Figure 23: The reaction selected for anion–π catalysis of cascade reactions to bicyclic products, with speculative structures for the stabilization of the anionic transition state **TS1** and **TS2** on the π-acidic surface of naphthalenediimide.[42]

Similarly, Matile *et al.* successfully performed enamine addition to nitro-olefins, which occurs on the aromatic surface of π-acidic NDIs, by placing at one side a proline for enamine formation and at the other side a glutamic acid for nitronate protonation, where the active site is constructed by **6** and **7** (Fig. 24). According to molecular models, orthogonal orientation of the nitronate appears preferable to produce syn products (TS1) and is necessary for intramolecular protonation of the nitronate (TS2). Carboxylate-π interactions[43] in the resulting reactive intermediate will ensure the removal of the product from the aromatic surface.[44]

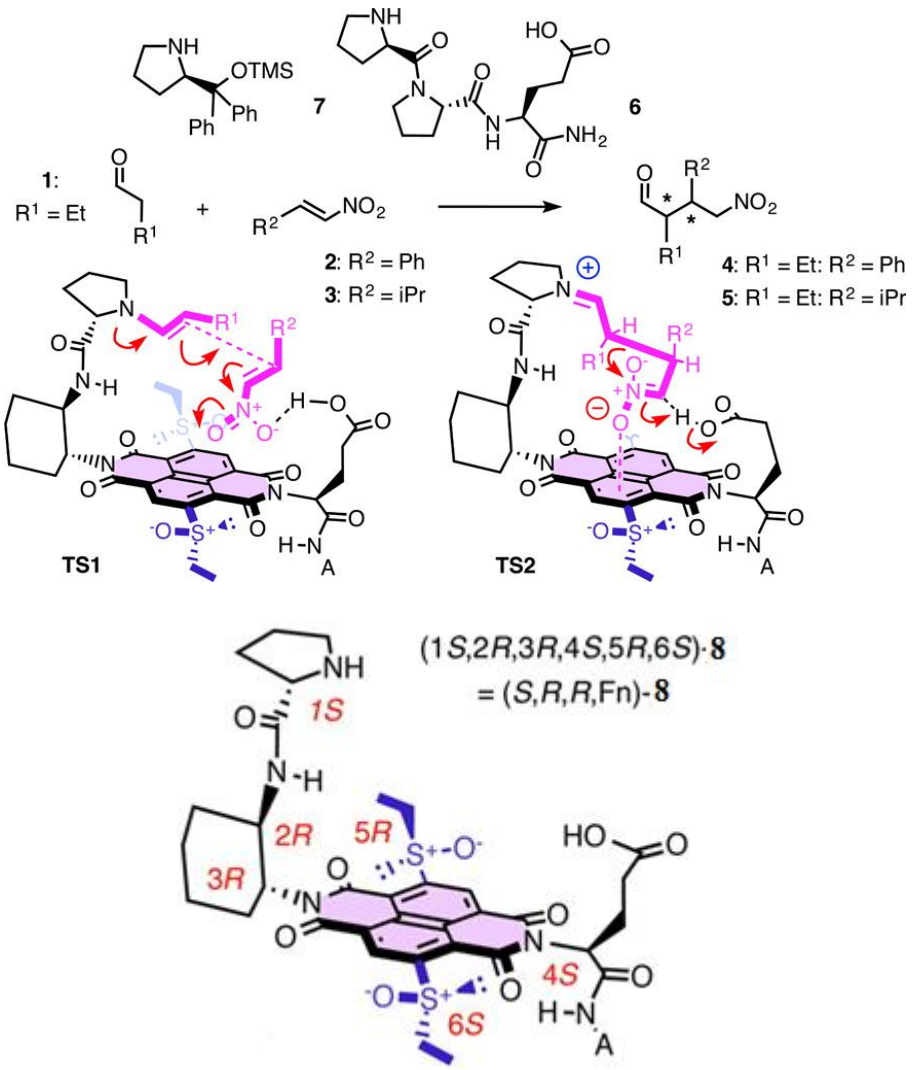


Figure 24: Structure of Wennemers and Jorgensen-Hayashi catalysts **6** and **7**, respectively and possible stabilization of adding enamines (formaldehyde **1**) to nitrolefins **2** or **3** (TS1) and nitronate protonation (TS2) on the π-acidic surface of anion-π catalyst **8**.[44]

6.3. Optoelectronics:

The electron deficient nature of NDI π-scaffold leads to several applications in organic electronic devices.[45, 46] The effect of substituent to form well-ordered self-assembly and solubility in common solvents has been major problem with NDI derivatives. Each of its sub-parts such as naphthalene unit, imide regions, imide carbonyls, and pendant axial groups has a precise role to perform to carry out the overall function and affects the semiconductor devices or photovoltaics as well as it improves stability and charge transport characteristics. Various NDI derivatives employed in Organic battery, anion transport and photosensitizers.[46]

Organic photovoltaics are made of electron donor and electron acceptor materials rather than semiconductor p-n junctions. NDI showed strong electron-withdrawing nature, high electron affinity and high LUMO value, therefore NDIs are mostly used as small organic molecules in fabrication of OPV devices. In organic solar cells (OSCs), the electron donor (D) and electron acceptor (A) blended active layer is the most crucial component for leading the power conversion efficiency (PCE).[47]

Russell *et al.* synthesized **BiNDI** by linking two NDI monomers *via* a vinyl conjugation. The device employing **BiNDI**: PTB7 blend exhibited a PCE of 2.31% due to the formation of a nano-fibrillar crystal in active blend

which increased the charge-transporting properties.[48] Later, several π-conjugation linkers were incorporated such as thiophene, thienothiophene, vinyl-thiophene, dibenzosilole and DBT flanked with two NDI units, resulting in different degrees of red-shifted absorption depending on the nature of electron rich central linker e.g. Bis **NDI-T-EG** show PCE of 1.31 %.[49]

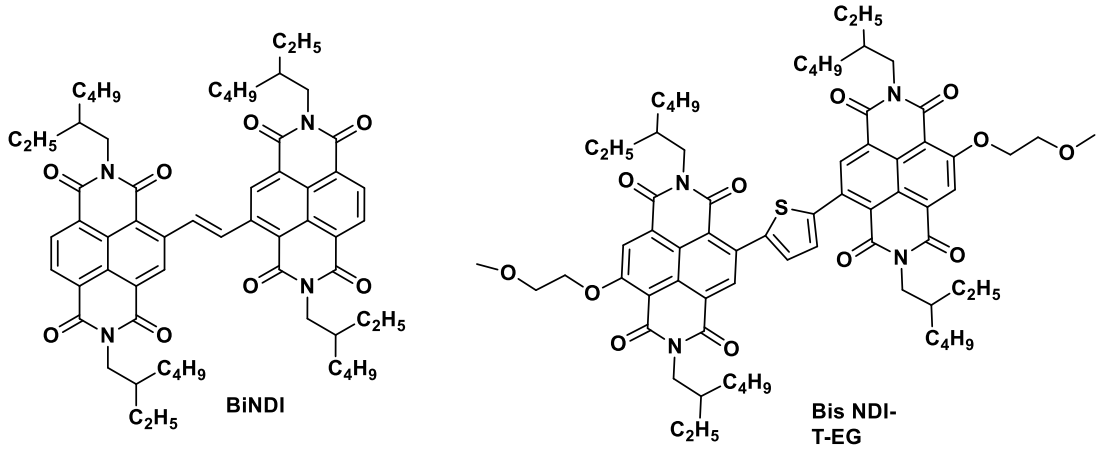


Figure 25: Molecular structures of the NDI dimers of **BiNDI** and **Bis-NDI-T-EG**.

In our group, we developed four novel naphthalenediimide (NDI) core-based non fullerene acceptors, N3, N4, N5 and N6 (Fig.26) having rhodanine, 1, 3-indanedione, 2-methoxyethyl-2-cyanoacetate and cyanopyridone acceptor functionalities at the terminals, respectively, along with central NDI block. The influence of terminal units on optoelectronic and photovoltaic properties was studied. The N3, N4, N5 and N6 (**Fig.** 37) shows PCE of 4.76%, 3.52%, 4.03%, 6.11% respectively.[50, 51]

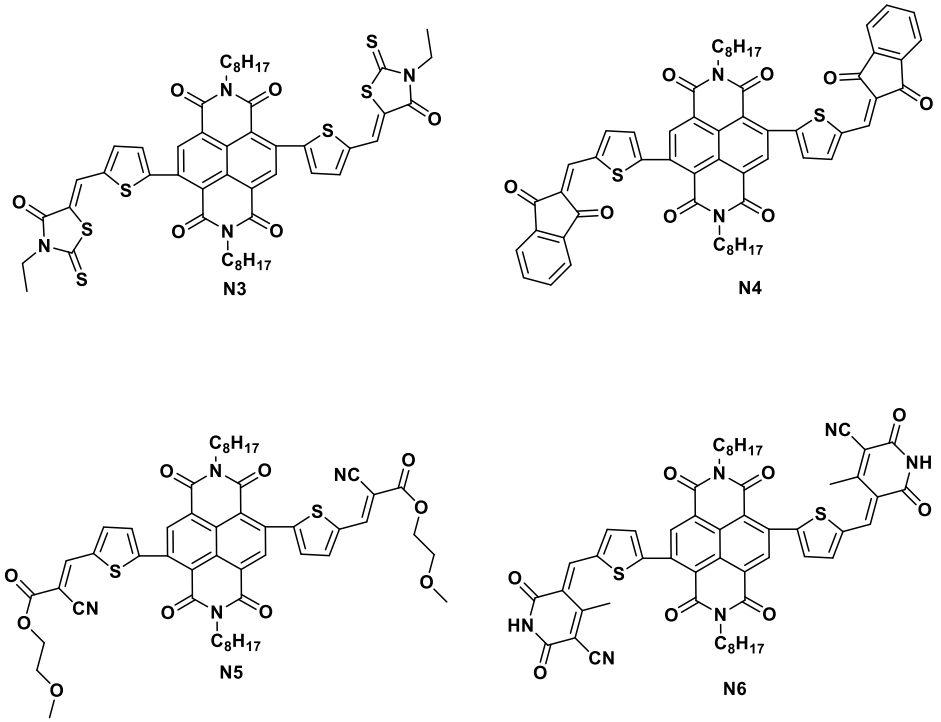


Figure 26: Chemical structures of the newly designed and synthesized NDI core-based acceptors, N3, N4, N5 and N6.

Recently, Ulijn *et al.* demonstrate the use of amino acids to actively decorate a self-assembling core molecule in situ, thereby controlling its amphiphilicity and resulting mode of assembly. The organic semiconductor

naphthalenediimide, functionalized with *D*- and *L*- tyrosine methyl esters (Fig. 27) as competing reactive sites. In the presence of α-chymotrypsin and a selected encoding amino acid, kinetic competition between ester hydrolysis and amidation results in covalent or non-covalent amino acid incorporation, variable supramolecular self-assembly pathways. Taking advantage of the semiconducting nature of the naphthalene diimide core, electronic wires could be formed and subsequently degraded, giving rise to temporally regulated electro-conductivity. These may use for biological such as neuronal cells or tissues, its electronic property used for therapeutic and diagnosis application.[51]

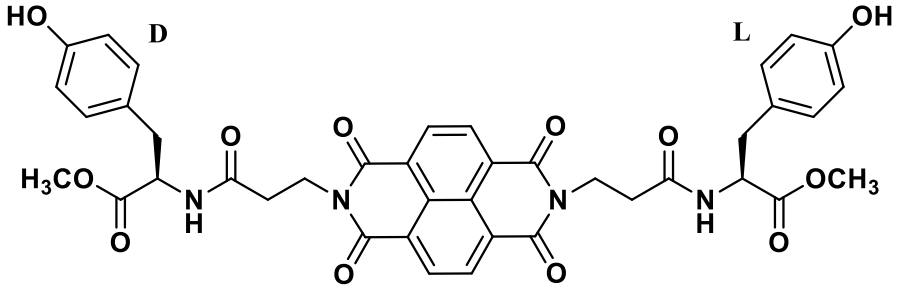


Figure 27: Chemical structure of *meso* molecule with *L*- and *D*- enantiomers of tyrosine methyl ester on two ends.

VII. CONCLUSIONS

In conclusion, this review article highlights on the supramolecular chemistry and self-assembly of organic small molecules. The author briefly discussed about non-covalent interactions and their role in formation of various supramolecular self-assembled structures. Design and synthesis supramolecular amphiphiles and bolaamphiphiles (peptide and NDI) can be used for realization of controlled self-assembly for functional supramolecular materials in various polar and non-polar solvents. The importance of controlling weak supramolecular interactions like π-stacking and H-bonding (through the π -scaffold and axial substituents) has also been well appreciated to realize molecular systems with high electron mobility and high-performance n-type semiconductors. Such noncovalent interactions also play key role in controlling anion- π interactions as well as in anion transport and anion catalysis. The self-assembled materials have been used in different potential applications and explained with suitable examples.

VIII. ACKNOWLEDGEMENT

I would also like to thank our Principal, Dr. Dinanath D. Patil, Sahakar Maharshi Bhausaheb Santuji Thorat College of Arts, Science and Commerce, Sangamner, for providing me with this wonderful opportunity to work on this review. The completion of the Review would not have been possible without their help and insights.

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A Short Overview on Synthesis and Biological Assay of Pyrazole Linked Benzothiazole

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ABSTRACT
Pyrazole and Benzothiazole are an important class of heterocyclic compounds. In recent years two or more heterocyclic compounds linked with each other have attracted strong interest due toenhance intheir biological and pharmacological properties. Pyrazole and Benzothiazole coupled nucleus containing compounds involved in research aimed at evaluating new products that possess more potent biological activities, such as antimicrobial, anticancer, antifungal, anthelmintic, anti-diabetic. In these present overview focus on the different methods of synthesis with potential activities that are now in developing phase.

Keywords: Pyrazole and Benzothiazole linked derivatives, Cytotoxicity, Antimicrobial, Anthelmintic, Antimalarial activity.

I. INTRODUCTION

Heterocyclic compounds are widely distributed in nature and are essential for life and in the field of medicinal chemistry.The attraction of heterocyclic compounds containing nitrogen and sulphur in medicinal chemistry has increased significantly in the past few decades as they have been proven to be highly active as a pharmaceutical scaffold. More specifically, the Pyrazole-benzothiazole linked heterocyclic compounds have shown great promise in the pharmaceutical industry.

Pyrazole is well well-knownnitrogen-containing heterocyclic component which finds prominent applications in the field of medicinal [1-3] and pesticide chemistry. Many of the pyrazole derivatives have obtained considerable attention of chemist due to its considerable application as main building blocks for drug discovery.

In the past few decades, there has been an increasing interest in the chemistry of Sulphur and nitrogen both containing ina heterocyclic compound.Thiazole and benzothiazole play an essential role in the development of tremendous derivatives of benzothiazole as both the heteroatoms are in one molecule and it was find different pharmacological activities. The derivatives of thiazole or benzothiazole are used in various disease treatments. [4]

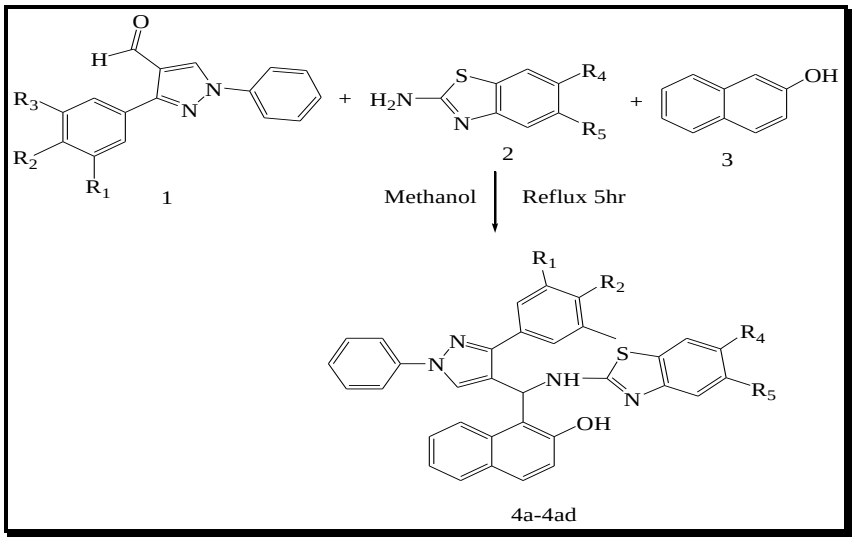
Pyrazole-benzothiazole linked heterocyclic structures are prominent throughout the literature and it is very important to acknowledge their efficacy and applicability. Herein, we review the recent developments covering

the past few years concerning the advancements in synthetic methodology for the preparation of medicinally relevant Pyrazole-benzothiazole linked heterocyclic structures.

II. SYNTHETIC STRATEGIES AND BIOLOGICAL ACTIVITIES

Scheme 1:

Pyrazole linked benzothiazole-β-naphthol derivatives were synthesized as shown in scheme 1. Condensation of the acetophenones with phenylhydrazinein ethanol produced the corresponding acetophenone phenylhydrazones. This was followed by cyclization of the acetophenone phenylhydrazones via the Vilsmeier-Haack reaction resulted in the formation of 1,3-biphenyl pyrazole carboxaldehydes (1). Finally, via a simple one pot condensations of subsequent aldehydes (1) with β-naphthol (3) and various 2-aminobenzothiazole (2) in the presence of methanol under reflex conditions afford the required pyrazole linked benzothiazole-β-naphthol derivatives (4a-ad) in good to excellent yields[5].



4a: R_1, R_4, R_5= H; R_3 = NO_2 **4k:** R_1, R_3, R_5 = H; R_4 = OCH_3; R_2 = NO_2 **4u:** R_1, R_3, R_5 = H; R_2, R_4 = Cl

4b: R_1, R_2, R_4, R_5 = H **4l:** R_1, R_3, R_5 = H; R_4 = OCH_3; R_2 = F **4v:** R_1, R_2, R_5 = H; R_3, R_4 = Cl

4c: R_1, R_2, R_4, R_5 = H; R_3 = OCH_3 **4m:** R_1, R_3, R_5 = H; R_2, R_4 = OCH_3 **4w:** R_1, R_2, R_3, R_5 = H; R_4 = Cl

4d: R_1, R_2, R_4, R_5 = H; R_3 = CH_3 **4n:** R_1, R_2, R_5 = H; R_4 = OCH_3; R_3 = NO_2 **4x:** R_1, R_3, R_5 = H; R_2 = I; R_4 = Cl

4e: R_1, R_3, R_4, R_5 = H; R_2 = OCH_3 **4o:** R_1, R_2, R_5 = H; R_4 = OCH_3; R_3 = I **4y:** R_1, R_3, R_5 = H; R_2 = NO_2; R_4 = Cl

4f: R_1, R_3, R_4, R_5 = H; R_2 = NO_2 **4p:** R_1, R_2, R_5 = H; R_4, R_3 = OCH_3 **4z:** R_1, R_3, R_5 = H; R_2 = NO_2; R_4 = CH_3

4g: R_1, R_2, R_4, R_5 = H; R_3 = Cl **4q:** R_1, R_2, R_3, R_5 = H; R_4 = OCH_3 **4aa:** R_1, R_2, R_5 = H; R_3 = Cl; R_4 = CH_3 **4h:** R_1, R_3, R_4, R_5 = H; R_2 = CH_3 **4r:** R_1, R_3, R_5 = H; R_2 = F; R_4 = Cl **4ab:** R_1, R_2, R_5 = H; R_3 = Cl; R_4 = CH_3

4i: R_1, R_3, R_4, R_5 = H; R_2 = I **4s:** R_1, R_2, R_4, R_5 = H; R_3 = NO_2; R_4 = Cl **4ac:** R_1, R_3 = H; R_2, R_4, R_5= CH_3

4j: R_1, R_3, R_5 = H; R_4 = OCH_3; R_2 = Cl **4t:** R_1, R_2, R_4, R_5 = H; R_3 = OCH_3; R_4 = Cl **4ad:** R_1, R_3= H; R_2 = NO_2; R_5, R_4 = CH_3

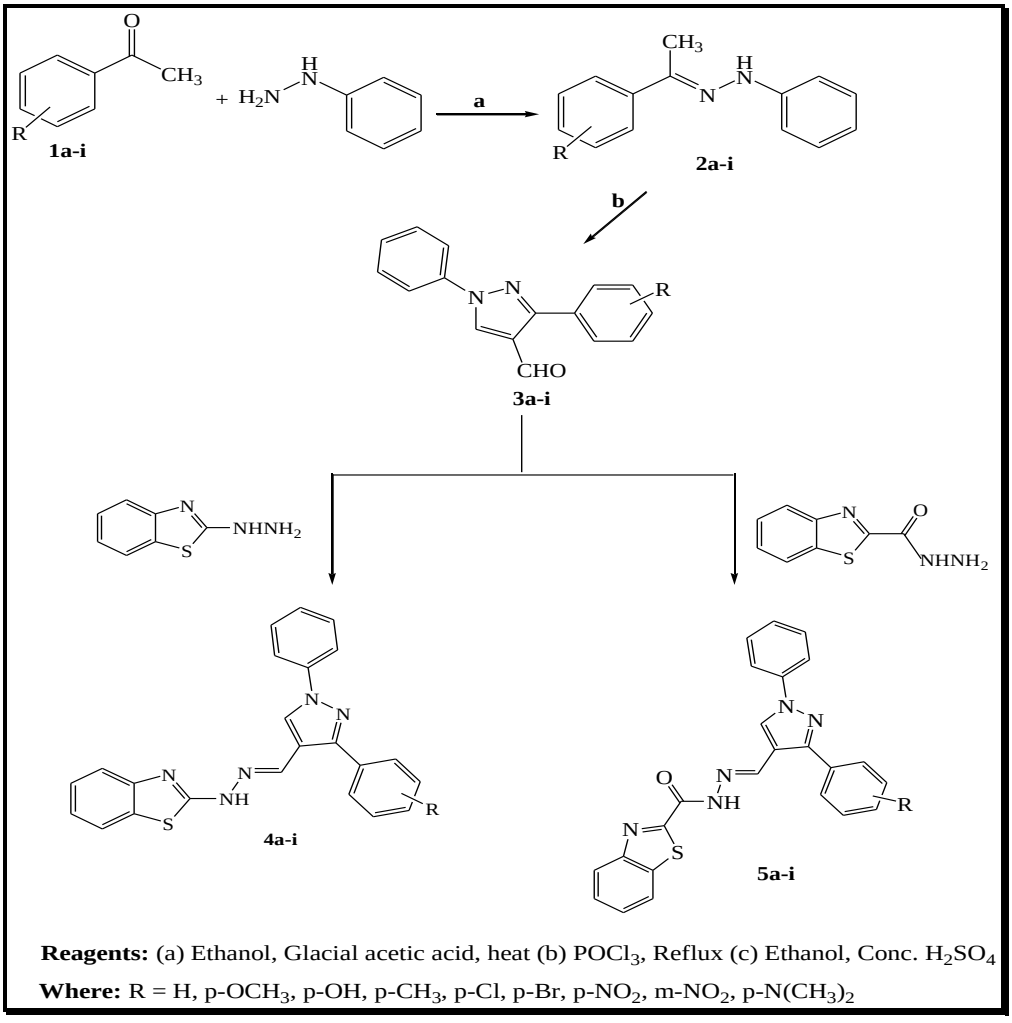
Biological assay:

Cytotoxicity: All the synthesized compounds (4a-4ad) were evaluated for their cytotoxicity against selected human cancer cell lines such as A549 (lung cancer), HeLa (cervical cancer) and MCF-7 (breast cancer) using MTT assay. The cytotoxicity results in comparison to the positive control doxorubicin and Hoechst 33258 are

expressed in IC50 values and are tabulated in Table 1. Most of the derivatives exhibited considerable cytotoxicity values against the tested cancer cell lines.

Scheme 2:

Pyrazole-conjugated benzothiazole derivatives was synthesised byMahesh Bhat&ShiddappaLagamappaBelagali [6]Starting fromdifferent substituted acetophenones were condensed with phenyl hydrazine followed by the Vilsmeier–Haack cyclization reaction. The obtained intermediates were condensed with the 1,3-benzothiazole-2-carbohydrazide and 2-hydrazinyl-1,3- benzothiazole through azomethine linkage as shown in Figure 2.



Biological assay: The newly synthesized compounds were screened for the antibacterial, antioxidant and anti-TB activities. They showed moderate antibacterial and antioxidant activities. Compounds containing -OH, -CH_3 and -Cl groups exhibited the superior antibacterial activity in the series. Majority of the compounds exhibit excellent in vitro anti-TB activity, showed the MIC values up to 1.6 µg/ml and they are appeared nontoxic to the normal cell line in that concentration. The synthesized compounds with p-CH_3 and p-Cl showed superior activity.

Scheme 3:

A new series of (E)-6-methyl-N-((3-phenyl-1-(4-phenylthiazol-2-yl)-1H-pyrazol-4-yl)methylene)benzo[d]thiazol-2-amine derivatives was developed by Diksha Sharma and co-workers [7].

In the present protocol for the synthesis of Pyrazole-conjugated benzothiazole derivatives, freshly produced phenacyl bromide in ethanol yielded the chemical 2-(4-(aryl) thiazol-2-yl)-1-(1-arylethylidene) hydrazine (3) via Hantzschthiazole synthesis. Afterwards, a Vilsmeier-Haack cyclization reaction with a corresponding quantity of reagent Dimethylformamide/ Phosphorous oxychloride (DMF/$POCl_3$) at 80- 90^{o}C for 4-5 hours yielded thiazolyl-pyrazole-4-carbaldehydes (4). In final step, (E)-6-methyl-N-((3-phenyl-1-(4-phenylthiazol-2-yl)-1H-pyrazol-4-yl)methylene)benzo[d]thiazol-2-amine derivatives (5) were synthesized on refluxing thiazolyl-pyrazole-4-carbaldehydes (4) with suitable benzothiazole amine in ethanol as solvent and fused sodium acetate

Biological assay:

Antimicrobial Activity: All the synthesized analogues were examined for their antimicrobial activity. The majority of the derivatives were active against all the tested bacterial strains.

Anthelmintic Activity:

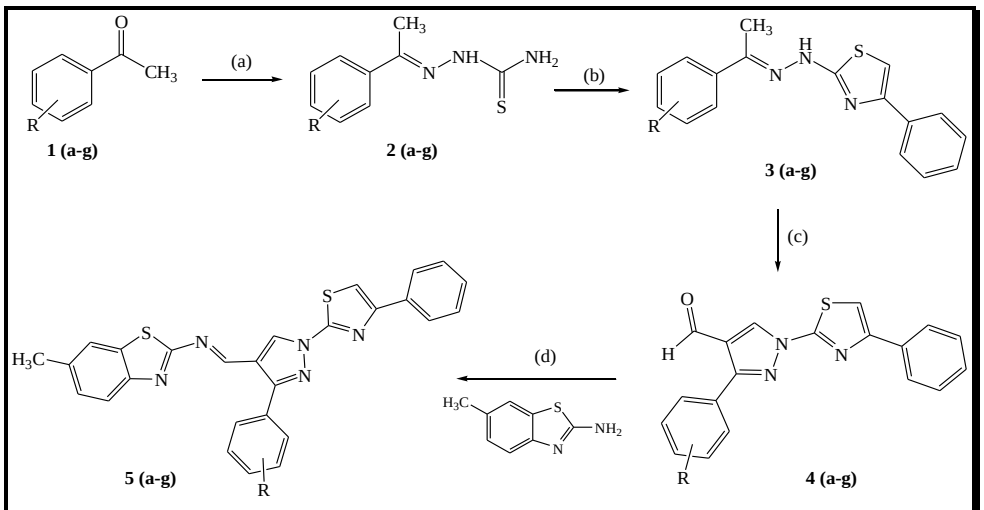
The anthelmintic data of derivatives 5a-5g and its comparison with standard drug albendazole. The biological data suggested that all the prepared analogues displayed moderate to excellent anthelmintic activity in contrast to reference compound (albendazole).

Antimalarial Activity:

The antimalarial action of all newly synthesized analogues was tested. The compounds were tested at the various concentrations to determine their MIC value toward Plasmodium falciparum and compared with standard drugs. It was noticed that the presence of an electron-donating group i.e. (Phenyl and OH groups) has a great influence on activity.

Cytotoxic Activity:

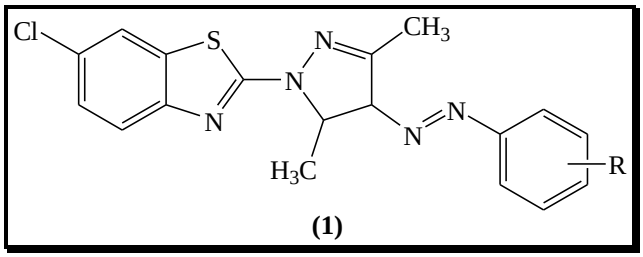
Newly synthesized derivatives 5a-5e was examined for their cytotoxic action towards two cell lines viz. MCF-7 and Hop-62. The SRB assay indicated that compound 5e (2, 4-diCl2, electron withdrawing group) has been identified as the moderate cytotoxic agent in response to MCF-7 cancer cells having GI50 65.4µg/mL than the reference drug adriamycin (GI50<100 µg/mL).



Reagents and conditions:
(a) Thiaosemicarbazide, ethanol, H_2SO_4, 3-4 drops, reflux 4h.
(b) $ArCOCH_2Br$, ethanol, reflux 3h.
(c) DMF, $POCl_3$, 70-80 ^{O}C, 5h.
(d) Ethanol, fused CH_3COONa, reflux 3-4h.

Scheme 4:

A novel class of 4-arylhydrazono-1-benzothiazolyl-3- methylpyrazolin-5-ones and 4-arylazo-1-benzothiazolyl-3,5- dimethylpyrazoles (1) were designed as pharmacophore hybrids between pyrazolinone/pyrazole and benzothiazole moiety and screened for antimicrobial activity.[8]



(1)

III.CONCLUSION

As discussed above Pyrazole linked benzothiazole scaffold have widespread medicinal applicability. The extensive literature presentations in the preceding sections show that thePyrazole linked benzothiazole moiety as a template for development of newer therapeutic agents. Biological properties of the nucleus include Cytotoxicity, Antimicrobial, Anthelmintic, Antimalarial activity.

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Physicochemical Properties for Binary Mixtures of 2-Butanone with Amides at Temperatures between 293.15 and 308.15 K

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ABSTRACT

Densities for the binary mixtures of 2-butanone with formamideN-methyl formamide and N,N-dimethyl formamide were measured over the entire mole fractions at 293.15, 298.15 and 303.15 K. and refractive indices nD for the binary mixtures of 2-butanone with formamide N-methyl formamide and N,N-dimethyl formamidewere measured over the entire mole fractions at 298.15, 303.15 and 308.15 K. Using the experimental values of densities and refractive indices nD, the excess molar volumes VE and excess refractive indices ΔnD were calculated. The values of excess molar volumes VE and excess refractive indices ΔnD were fitted to the Redlich-Kister polynomial. The results are discussed in the light of intermolecular interactions present amongst the components.

Keywords: Density; Refractive indices; Excess molar volume; Excess refractive indices; 2-Butanone.

I. INTRODUCTION

Thermodynamic and transport properties provides important information for the design of industrial processes, to improve our understanding of the molecular interaction existing the liquid mixtures, and to test the predictive capability of the models and methods developed to predict these properties **[1,2]**.Measurement of some of the bulk properties like density, refractive index have been widely used in the field of interactions and structural aspect evaluation studies**[3]**. Inotherward, these bulk properties have been adequately employed in understanding the nature ofmolecular systems and physicochemical behavior in liquid mixtures **[4,5].** In the foregoing study, we report excessmolar volumes (VE)and deviations in refractive index (ΔnD) for binary liquid mixtures of 2-Butanone with formamide N-methyl formamide and N,N-dimethyl formamide at 293.15,298.15 and 303.15 K.

II. MATERIALS

2-butanone (S.D. fine A.R.) was doubly distilled over anhydrous potassium carbonate/ sodium carbonate to eliminate trace of acids and to reduce further the water content[6].Formamide (Spectrochem Pvt. Ltd.), n-methyl formamide (S.D. fine Chem.) and n,n-dimethyl acetamide (Spectrochem Pvt. Ltd.) were distilled at atmospheric

pressure.The triple distilled liquids invariablywereused.The purity of purified solventswaschecked bycomparing themeasured densities and refractiveindiceswith those reported inthe literature.Themeasured values are included inTABLE1 along with the literature values.

III.MEASUREMENTS

The binary liquid mixtures were prepared by mixing known masses of pure liquids in airtight-stoppered bottles in order to minimize the evaporation losses. All measurements of mass were performed on a Mettler one-pan balance (E-METTLER,ZURICH),which allows reading up to fifth decimal digit, with a precision of ± 0.05mg.The uncertainty in the mole fractions of the mixtures was estimated to be ± 5 x 10^{-5} g.cm^{-3}. Densities of pure components and their mixtures were measured using the single arm capillary pycnometer having a bulb volume of approximately 5 cm^3 and a capillary bore with an internal diameter of 0.75mm. The uncertainty in the density measurements was found to be ± 3 x 10^{-5} g.cm-3. The pycnometer was calibrated using double distilled water at 298.15K. The refractometer was calibrated by means of aglass test piece of known refractive index supplied bythemanufacturer.At a level of confidence of 99.7%,theuncertaintyin the refractive indexmeasurementwas±3×10^{-4}.Calibrationwas performed bymeasuring therefractive indices of doubly distilledwater, ethanol atdefined temperature.The samplemixturewas directlyinjected intothe prismassemblyof the instrumentusingan airtight hypodermic syringe, and an average of fivemeasurements was taken for each mixture. For all themeasurements, temperature was controlled by circulatingthewater through an ultra-thermostat JULABOF-25which has an accuracy ±0.020C.

TABLE 1: Densities and refractive indices of pure componentsat 298.15 K

	ρ /g.cm-3		n_D	
Compounds	**Exptl.**	**Lit.**	**Exptl.**	**Lit**
2-Butanone	0.79970	0.7997	1.3768	1.3769
Formamide	1.12913	1.2910	1.4459	1.4468
N-Methyl formamide	0.99934	0.99930	1.4318	1.4319
N, N-Dimethyl acetamide	0.93649	0.93650	1.4363	1.4356

TABLE2: Measured density and refractive index values for 2-butanone +formamide, n-methyl formamide and n, n-dimethyl formamide at different temperature

2-butanone+formamide

x_1	ρ /g.cm-3			n_D		
	298.15K	303.15K	308.15 K	298.15K	303.15K	308.15 K
0.0000	1.12913	1.12471	1.12046	1.4459	1.4443	1.4425
0.0427	1.09777	1.09321	1.08901	1.4369	1.4358	1.4354
0.0877	1.06795	1.06348	1.05951	1.4285	1.4274	1.4282

0.1351	1.03962	1.03521	1.03111	1.4209	1.4208	1.4212
0.1851	1.01284	1.00858	1.00448	1.4141	1.4142	1.4148
0.2380	0.98766	0.98329	0.97934	1.4075	1.4081	1.4091
0.2940	0.96357	0.95939	0.95541	1.4015	1.4026	1.4037
0.3534	0.94083	0.93679	0.93273	1.3963	1.3977	1.3991
0.4165	0.91937	0.91541	0.91122	1.3918	1.3933	1.3947
0.4837	0.89901	0.89566	0.89086	1.3879	1.3897	1.3912
0.5540	0.87974	0.87581	0.87154	1.3849	1.3869	1.3878
0.6320	0.86161	0.85768	0.85324	1.3827	1.3844	1.3852
0.7142	0.84454	0.84051	0.83594	1.3806	1.3821	1.3827
0.8024	0.82851	0.82427	0.81961	1.3794	1.3801	1.3801
0.8474	0.81358	0.80905	0.80421	1.3781	1.3774	1.3767
1.0000	0.79970	0.79481	0.78978	1.3768	1.3743	1.3721

2-butanone+ n-methyl formamide

x_1	ρ /g.cm-3			n_D		
	298.15K	303.15K	308.15 K	298.15K	303.15K	308.15 K
0.0000	1.6810	1.5612	1.4489	1.4318	1.4301	1.4283
0.553	1.5286	1.4216	1.3252	1.4212	1.4201	1.4201
0.119	1.3775	1.2892	1.2068	1.4131	1.4121	1.4228
0.1700	1.2463	1.1721	1.0998	1.4058	1.4053	1.4068
0.2295	1.1278	1.0621	1.0000	1.3995	1.3993	1.4013
0.2906	1.0187	0.9620	0.9084	1.3944	1.3944	1.3967
0.3532	0.9231	0.8739	0.8280	1.3901	1.3904	1.3928
0.4175	0.8372	0.7937	0.7546	1.3867	1.3874	1.3895
0.4835	0.7579	0.7212	0.6871	1.3841	1.3851	1.3868
0.5513	0.6871	0.6524	0.6245	1.3823	1.3834	1.3845
0.6210	0.6217	0.5893	0.5667	1.3809	1.3821	1.3827
0.6926	0.5586	0.5325	0.5116	1.3803	1.3809	1.3809
0.7662	0.4977	0.4733	0.4550	1.3793	1.3798	1.3792
0.8419	0.4328	0.4133	0.3070	1.3788	1.3787	1.3773
0.9198	0.3629	0.3454	0.3344	1.3779	1.3769	1.3752
1.0000	0.2828	0.2666	0.2601	1.3768	1.3743	1.3721

2-butanone+ n, n - dimethyl acetamide

x_1	ρ /g.cm-3	n_D

	298.15K	303.15K	308.15 K	298.15K	303.15K	308.15 K
0.0000	0.9365	0.8760	0.8253	1.4363	1.4346	1.4319
0.0794	0.8636	0.8087	0.7646	1.4244	1.4235	1.4219
0.1567	0.7971	0.7476	0.7086	1.4144	1.4145	1.4137
0.2320	07372	0.6926	0.6579	1.4066	1.4072	1.4071
0.3052	0.6826	0.6423	0.6119	1.4006	1.4016	1.4018
0.3766	0.6323	0.5968	0.5696	1.3961	1.3971	1.3975
0.4461	0.5866	0.5547	0.5301	1.3922	1.3934	1.3938
0.5139	0.5443	0.5154	0.4940	1.3894	1.3905	1.3908
0.5800	0.5053	0.4789	0.4594	1.3872	1.3881	1.3882
0.6444	0.4686	0.4448	0.4275	1.3853	1.3861	1.3861
0.7073	0.4339	0.4122	0.3971	1.3841	1.3844	1.3838
0.7687	0.4014	0.3815	0.3681	1.3827	1.3827	1.3817
0.8286	0.3700	0.3520	0.3400	1.3814	1.3811	1.3795
0.8870	0.3400	0.3227	0.3130	1.3802	1.3789	1.3773
0.9442	0.3105	0.2948	0.2864	1.3886	1.3771	1.3747
1.0000	0.2828	0.2666	0.2601	1.3768	1.3743	1.3721

TABLE3: Coefficients, ai of eq. (4) and standard deviations, for the binary mixtures at 298.15K

Parameter	a_0	a_1	a_2	σ
2-butanone(1) + formamide				
$V^E/cm^3.mol^{-1}$	1.8422	0.5897	-0.0350	0.0031
Δn_D	0.0963	0.0460	-0.0058	0.0001
2-butanone(1) + n-methyl formamide				
$V^E/cm^3.mol^{-1}$	2.4451	0.3157	0.0177	0.0024
Δn_D	-0.0822	0.0506	-0.0074	0.0002
2-butanone(1) + n,n-dimethyl acetamide				
$V^E/cm^3.mol^{-1}$	2.8458	0.1432	-0.0093	0.0026
Δn_D	-0.0665	0.0412	0.0009	0.0001

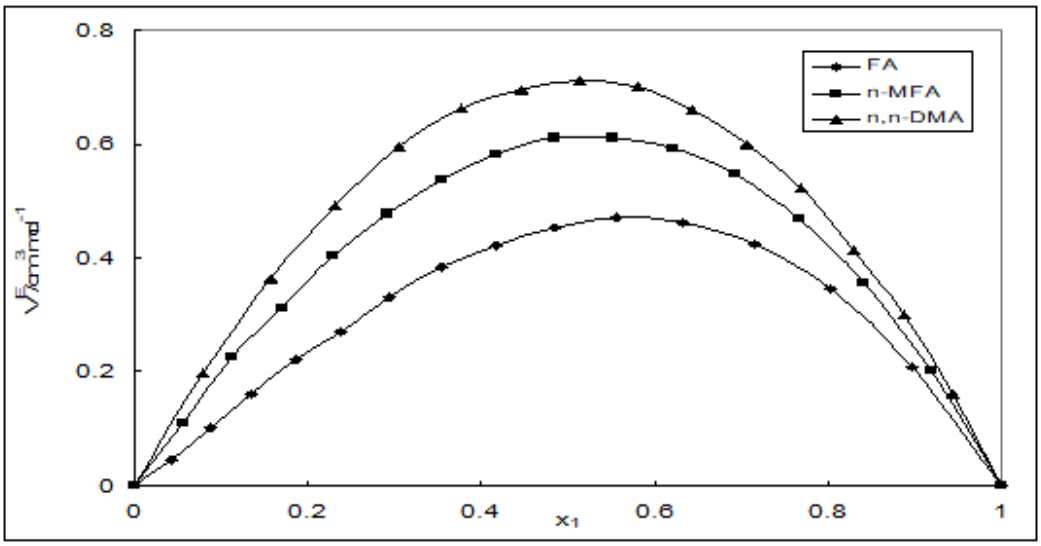

Figure 1: Variation of excess molar volume (V^E) against mole fraction (x1) of 2-butanone at 298.15K: (♦) formamide, (■) n-methyl formamide (▲) n,n-dimethyl acetamide

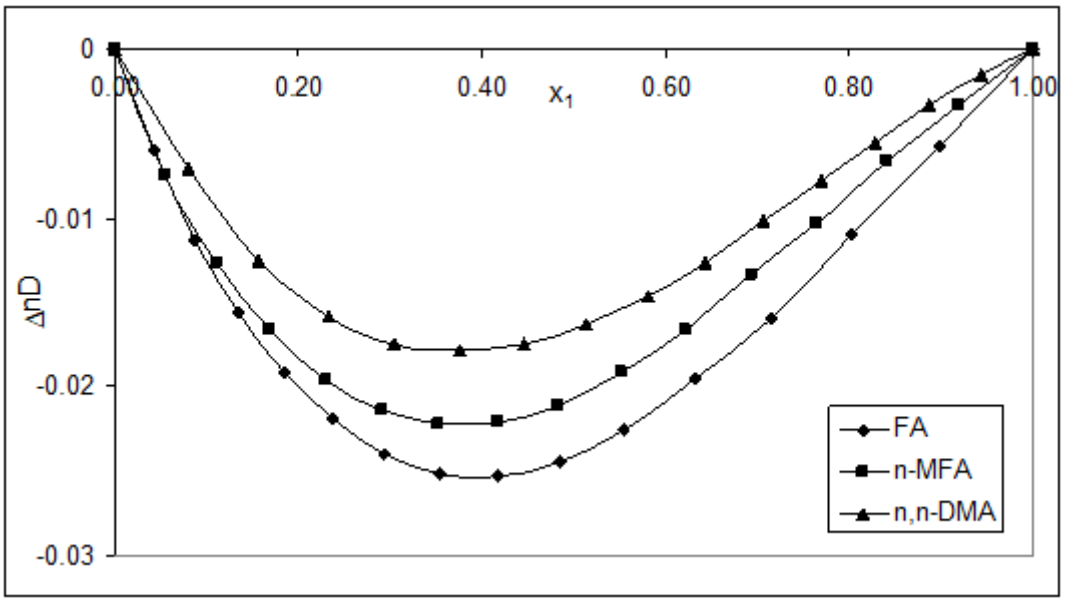

Figure 2:Variation of deviation in refractive index (Δn_D) against mole fraction (x_1) of 2-butanone at 298.15K: (♦)formamide, (■)n-methyl formamide, (▲)n,n-dimethyl acetamide

IV.RESULTS AND DISCUSSION

The experimentallydetermined values of densities (ρ) and refractive indices (n_D) for the binary liquid mixture of 2-Butanone with amides at 298.15, 303.15 & 308.15 K are summarized in TABLE 2. From the values of densities (ρ), refractive indices(n_D) Excess molar volume **[8]** (V^E) were calculated from the measured densities (ρ) by using equation

$$V^E = ((x_1M_1 + x_2M_2) / \rho). (x_1V_1 + x_2V_2) \quad (1)$$

Where ρ is the density of themixture andM_1, V_1, x_1 andM_2, $V_2x_2$are themolecularmass, molar volumes andmole fractions ofpure components 1 and 2 respectively.The deviation in refractive index (ΔnD) of binary mixtures were calculated **[9]** by using the simple additivity rule,

$$\Delta n_D = n_{Dm} - x_1n_{D1} - x_2n_{D2} \quad (2)$$

Where, n_{Dm}, n_{D1} and n_{D2} are the refractive index of liquid mixture,pure components 1 and 2 respectively. x_1 and x_2 are molefractions of pure components 1 and 2 respectively. Thecalculated valuesof excessmolarvolumes (V^E) and deviation in refractive indices (Δn_D)were correlated by Redlich .Kisterpolynomial [10] as shown inEq.:

$$\Delta Y = x_1x_2\Sigma a_i(x_1 - x_2)^I \quad (3)$$

The coefficients in equation (3) were estimated bythe least squares fit method and the standard deviationswere calculated by equation.

$$\sigma = [\Sigma (\Delta Y_{Exp.} - \Delta Y_{Cal.})^2 /(D - N)]^{0.5} \quad (4)$$

Where D and N are the number of data points and parameters,respectively.

Regression results for excess molar volumes and deviation in refractive indices of binary liquid mixture of 1,2-Ethanediol (1) and aliphatic alcohols as Methanol, Ethanol, 1-Propanol, and 1-Butanol (2) at 298.15 K are as shown in TABLE 3.

The graphical variation of V^E for the binary mixtures of 2-butanone with formamide, n-methyl formamide and n,n-dimethyl acetamide with increasing mole fractions of 2-butanone at 298.15Kis shown in figure 1. The values of excessmolar volume are found to be positive for all the systems,where dispersion, induction and dipolar forces are operating, the values of excessmolar volume are found to be positive,whereas the existence of specific interactionsbetween themixingcomponents of thevariousbinarysystems tends tomakeexcessmolar volume negative[11].Since,normallydispersive interactionbetween unlike molecules is weaker than those between likemolecules, it is reasonable that they contribute positively[12] toV^E. In these systems the excess molar volume values decreasewith increase in carbon atom of alcohol,which results solute-solvent interaction between mixing components.

Figure 2 shows the graphical variation of nD for the binary mixtures of 2- butanone with formamide, n-methyl formamide and n.n-dimethyl acetamide with increasing mole fractions of 2-butanone at 298.15K. In the present study, the values of Δn_D are found to be negative for the binary mixtures of 2-butanone with formamide, n-methyl formamide and n,n-dimethyl acetamide. Figure 2 shows graphical variation of excess refractive index, Δn_D for binary mixtures of 2-butanone with formamide, N-methyl formamide and N, N-dimethyl acetamide at 298.15 K. The Δn_Dvalues at equimolar concentrations follows the order N, N-dimethyl acetamide < N-methyl formamide < formamide. Hence in conclusion, we can say that even though some dispersion interaction is observed in case of all these binary mixtures or dominance of dispersion forces [13, 14] is observed.

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Biosynthesis of Nickel Nanoparticles by Using Water Extract of Banana Peels

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ABSTRACT

Nickel nanoparticles were biosynthesized by solution reduction process using banana peel extract method successfully. The properties of synthesized nickel nanoparticles were characterized by Scanning Electron Microscopy (SEM), Powder X-ray Diffraction (XRD), and FTIR spectroscopy. The formation of nickel nanoparticles, size, shape and nature of nickel nanoparticles have been confirmed by the spectroscopic methods. The results showed that Ni nanoparticles are amorphous in nature. The usage of plant extract for the biosynthesis of nickel nanoparticle makes the process cost effective, non-hazardous and green method.

Keywords: Nickel Nanoparticles, Biosynthesis, Banana Peels, Nickel Chloride.

I. INTRODUCTION

Metal nanoparticles have been attracting intensive interest because of their outstanding properties and potential applications in the areas of catalysis [1, 2], magnetism [3], electronics [4], biological activity [5, 6] etc. In recent years, scientists are taking continuous efforts to develop catalysts that exhibit 100% selectivity for desired products and eliminate waste generation. This kind of selective method is frequently called Green Chemistry or Green technology [7]. Nanoparticles are welldesigned materials with distinctive properties for a diversified chemical technology and applications. The improved surface area to volume ratio makes them superior for use as catalysts, in analytical assays and for antimicrobial evaluations. In particular, metal nanoparticles like nickel, silver, gold, ruthenium, platinum, palladium and rhodium nanoparticles are relevant in biomedical, antimicrobial, drug delivery, and sensing/bio sensing materials [8].

Nickel nanoparticles are widely used in various fields and are synthesized by various physicochemical methods including sol-gel [9], micro emulsion [10], hydrothermal [11], sonochemical [12] and vapor phase [13]. However, the physicochemical synthetic protocols are costly and produce toxic, reactive chemical that generate environmental dispute which is to be treated before being discharged into the environment [14]. Hence, there is scope to develop new processes for the synthesis of nickel nanoparticles.

The plant extracts are extensively used for preparation of metal nanoparticles as they are easily accessible, benign, nontoxic and have ample variety of metabolites (phytochemicals) that aid in the reduction of metal ions faster than the microbes mediated synthesis [15]. Biosynthesis of nickel nanoparticles were reported by using

Hordeum vulgare [16], *Cocos nucifera* [17],*Ocimum sanctum* leaf extract [18] and *Calotropis gigantean*[19]. However, the synthesis of nickel nanoparticles using banana peels is not reported in the literature. Bananas are a significant food crop that is extensively grown in tropical and subtropical regions [20,21]. The edible part of banana constitutes only 12 wt% of the plant; the remaining parts become agricultural waste and cause environmental problems [22]. The banana peel is a rich source of starch (3%), crude protein (6-9%), crude fat (3.8-11%) [23], total dietary fiber (43.2-49.7 %), and polyunsaturated fatty acids, particularly linoleic acid and α-linoleic acid, pectin and essential amino acids [24,25]. The essential amino acids found in banana peel were leucine, valine, phenylalanine and threonine. Here we use the banana peel extract for the preparation of nickel nanoparticle.

II. EXPERIMENTAL

We use banana peel. The peels was washed with distilled water and dried in oven at 60°C.The dried peels have been crushed. The 20 gm of crushed peels taken in 100 mL of distilled water in a 200 mL beaker. The resulting solution was heated at 100°C for 20 to 25 min. and filtered through Whattman filter No. 1. The resulting filtrate was kept at 4-5°Cup to further use.

In a 250 mL beaker 0.1M of 100 mL $Ni(NO_3)_2$ solution and 20 ml of peels extract were missed with constant stirring. The resulting solution was stirred for 1 to 2 hours and the solution kept for overnight. The settled Ni nanoparticles were centrifuged at 12500 rpm for 45 min at 26°.Centrifuged sample was collected in crucible and kept in hot air oven at 110° for 20 min. The powdered form of nanoparticles has been characterized with the help of UV,FTIR, XRD and SEM.

III.RESULTS AND DISCUSSION

X-Ray Diffraction:-Analysis through x-ray diffraction was carried out to confirm the crystalline/amorphous nature of nickel nanoparticles. The dry powder of nickel nanoparticles were used for XRD analysis. The X-ray diffraction pattern of the nickel nanoparticles synthesized with banana peels is shown in Fig.1. The average particle size of biosynthesized nickel nanoparticles obtained from the half width full maxima of the different peaks by using the Debye Scherrer formula which is about 16nm to 85nm; these results were matched with SEM data of the particle sizes. The XRD graph shows broad nature of peaks it means the prepared Ni nanoparticles are amorphous in nature.

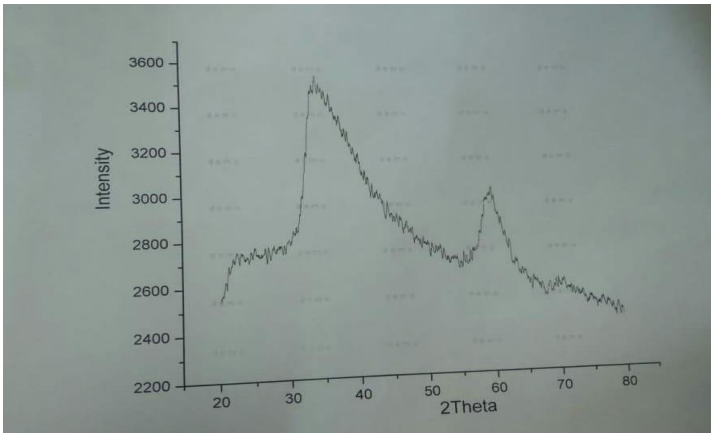

Fig.1:-XRD of Nickel nanoparticles

FTIR:- On the basis of the FTIR spectra we have obtained the results for the surface chemistry of the nanoparticles. The frequencies for the different functional groups have been reported [26-28]. The position and the presence of these functional groups can be detected by the FTIR technique. The Fig. 2 shows the IR spectrum of the as prepared sample of nickel nanoparticles. Peak at 3308 cm^{-1} corresponds to the O-H stretching band. Peak at 2921cm^{-1}correspond to the C-H stretching vibrations. The spectrum also contains bands at 516cm^{-1}, 453cm^{-1}, 407cm^{-1} and 540cm^{-1} are due to the nickel nanoparticles.

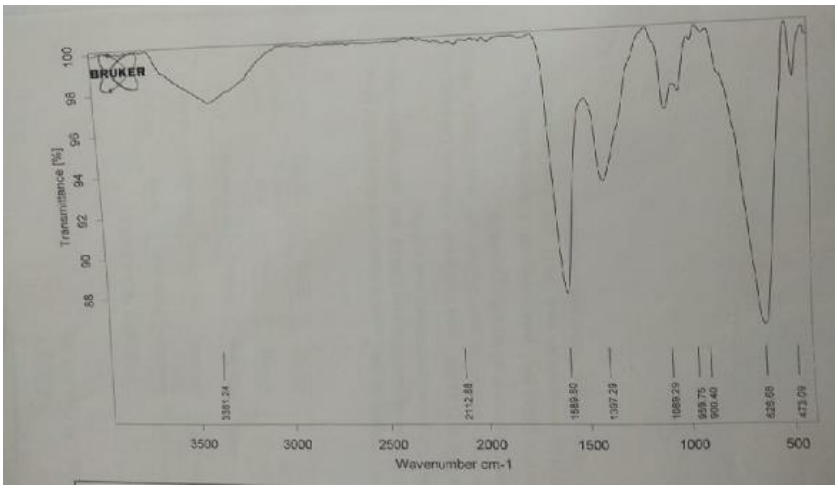

Fig.2:-FTIR of Nickel nanoparticles

Scanning Electron Microscopy: - SEM analysis provided the morphology and size details of the nanoparticles. Figure 4 a, b, and c shows that high density of nanoparticles synthesized by banana peels extract, the interaction such as hydrogen bonding and electrostatic interaction between the bioorganic capable to form molecular bond is a reason for synthesis of nickel nanoparticles using banana peels. The nickel nanoparticles are porous in nature and irregular in shape with uniform distribution. However the average size of an individual particle is estimated to be 15-100nm.

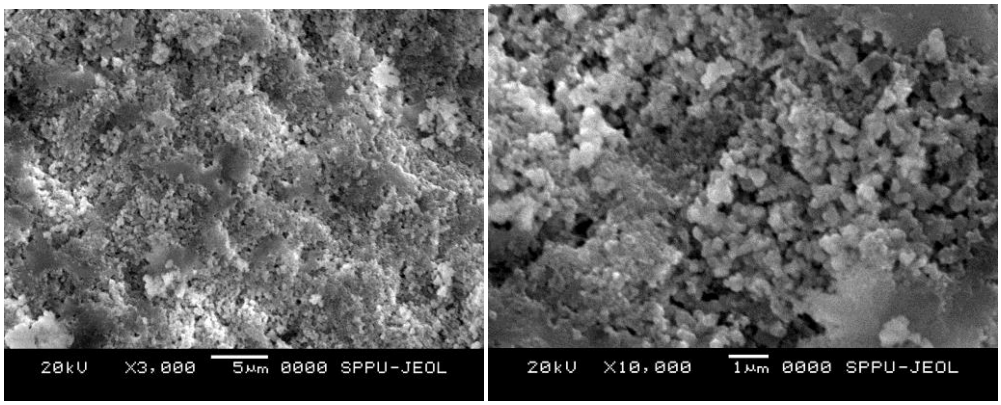

Fig.3:-SEM images of biosynthesized Nickel nanoparticles

IV.CONCLUSIONS

In this study simple approach was attempted to obtain a green eco-friendly, non-toxic way for synthesis of nickel nanoparticles. The primary confirmation for formation of nickel nanoparticles were due to colour changes of colloidal solution. The SEM study was identified that the shape of nickel nanoparticle appeared like

irregular spherical shape with porous surface. XRD results shows average particle size of biosynthesized nickel nanoparticlesare between 15nm-100nm in range. This green synthesis method is rapid, convenient and less time consuming.

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Synthesis, Characterization and Antimicrobial Activity of Novel Schiff Base of 3-Aminoquinoline and 6-Chloro-3-Formylchromone and Their Ni (II) and Fe (III) Complexes

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ABSTRACT

Coordination compounds of Ni(II) and Fe(III) with Schiff base obtained through the condensation of 6-chloro-3-formylchromone and 3-aminoquinoline were synthesized. The characterization of the newly formed from compounds was done by 1H NMR, UV-Visible, IR, elemental analysis and molar conductivity. The analytical data was studied which indicate that the metal to ligand molar ratio is 1:2 in all the complexes. Molar conductivity data have been shown that entire complexes are neutral in nature. The in vitro antibacterial activity of ligand and complexes was assessed against Klebsiella pneumoniae, Staphylococcus aureus and Proteus vulgaris and antifungal activity against Candida albicans and Aspergillus niger by MIC (minimum inhibitory concentration) method and compared with standard tetracycline.

Keywords: 6-chloro-3-formylchromone, 3-aminoquinoline, Schiff Base, Antimicrobial activity.

I. INTRODUCTION

The chemistry of coordination compounds is an intrinsic field and foundation of modern inorganic chemistry. Accretion of coordination chemistry revealed new way regarding the concept of chemical bonding. Coordination chemistry has variety of applications in many branches of sciences. The study of schiff bases and metal complexes is most focused and interested research area of inorganic chemistry. In modern coordination chemistry, the Schiff base and its metal complexes deal a vital role. The ability of Schiff base to link by coordinate bond with many metal ions through both azomethine group and phenolic group[1-4]. Chemists have attention for Schiff base and its metal complexes due to biological vitality including anti-tumor, antibacterial, fungicidal, and anti-carcinogenic properties[5-10] and catalytic activity[11-16]. The recent work in coordination chemistry has been shown almost all metals in periodic table have ability to form complexes with coordination number ranging from 2 to 12. In the last few decades, huge research has been done on metal complexes both in

solution and solid state. Literature findings indicate that many organic molecules acts as chelating ligands. These organic molecules contain aminoquinolines, thiosemicarbazones, chromones, amines, carboxylic acids and β-diketones etc. Chemists have developed their interest towards Schiff base and their metal complexes due to their chemical properties. Researchers have found that wide variety of structural configuration in Schiff base metal complexes.

However, researchers are always in seek for synthesis of new ligands with specific skeleton which can impact on the structural configuration of metal complexes. The stability of metal complexes judged on design and geometrical arrangement of ligands. Hence, scientists have always challenged for the structural investigation of new coordination compounds. Because of their excellent chelating properties, and diverse structural features, the ligands have been used extensively in the preparation of metal complexes and have enormous share in the development of coordination chemistry.

In the present work, the oxygen heterocyclic compound, 6-chloro-3-formylchromone condensed with 3-aminoquinoline to form novel Schiff base which form complexes with Ni(II) and Fe(III).

II. METHODS AND MATERIAL

A. Materials

3- aminoquinoline, 3-formyl chromone, Nickel chloride hexahydrate, ferric chloride hexehydrate and solvent used were AR grade.

B. Physical measurement

Molar conductance of the complexes was measured in DMF at 1×10^{-3} M using Elico CM-180 conductometer. Elemental analysis (CHN) was carried out using Thermo finnigan, Italy CHN analyzer. The IR spectra (4000-400 cm^{-1}) in KBr disc were recorded on Bruker, Germany spectrophotometer. The NMR spectra were carried out by mercury plus 300 MHz NMR spectrometer, using TMS as internal standard. The solvent used were chloroform-d_6 for Schiff base and DMSO-d_6 for metal complexes. Electronic spectra were measured by using Shimadzu UVmini-1240 spectrophotometer. The magnetic moment data obtained by Gouy-type magnetic balance at room temperature using $Hg[Co(NCS)_4]$ as calibrant.

C. In vitro antimicrobial studies

The antibacterial and antifungal activity of Schiff base ligand and its Ni(II), Cu(II), Co(II) and Fe(III) complexes towards the bacteria *Klebsiella pneumoniae, Staphylococcus aureus* and *Proteus vulgaris* and fungi *Candida albicans* and *Aspergillus niger* was carried out at different concentration by using minimum inhibitory concentration (MIC) method. The detailed description of MIC method were determined using literature method.

D. Synthesis of Schiff Base ligand and Metal complex

The synthesis of Schiff base ligand (L) was prepared by total amount of solution by 75-80 ml ethanol contain of 10 mmol (2.08 gm) of 6-chloro-3-formylchromone and 10 mmol (1.44 gm) of 3-aminoquinoline were refluxed for 3 hours. The progress of reaction was monitored by TLC. The resulting yellow coloured product precipitated, filtered off and washed with ether and stored in vacuum desiccators over anhydrous calcium chloride. The product was purified and recrystallized with hot ethanol. Yield obtained was 75%[17].

E. Materials

A hot ethanolic solution of ligand (10 mmol, 3.34 gm) was added to ethanolic solution of $NiCl_2 6H_2O$ (5mmol, 1.18 gm) and $FeCl_3 6H_2O$ (5mmol 1.35 gm). The resulting reaction mixture was refluxed for 4-5 hours. After cooling, coloured precipitate obtained was collected, filtered, washed with ether, recrystallized from ethanol and dried in vacuum [17].

III.RESULTS AND DISCUSSION

Ni(II) and Fe(III) complexes are coloured, non-hygroscopic and stable in air. The solubility of ligand is in chloroform solvent. The solubility of complexes are in DMF and DMSO solvent but are insoluble in many common organic solvent. The analytical and molar conductance data are given in table I . The analytical data predicted that the metal to ligand ratio is 1:2 in both the complexes. The molar conductance value of complexes has indicating non electrolytic natureparagraphs must be indented.

TABLE I ELEMENTAL ANALYSIS AND PHYSICAL PROPERTIES OF METAL COMPLEXES

Compound		Ligand (L)	$[Ni(L)_2(Cl)_2]$	$[Fe(L)_2(Cl)_2]$
Molecular formula		$C_{19}H_{11}O_2N_2Cl$	$C_{38}H_{22}O_4N_4Cl_4Ni$	$C_{38}H_{22}O_4N_4Cl_4Fe$
Colour(% yield)		Yellow (75)	Light Green (81)	Brown (82)
Molecular Weight		334.45	798.5	795.65
Melting point		303	314	295
% Found (caid)	C	68..65	57.55	57.51
		(68.17)	(57.10)	(57.31)
	H	3.8	2.43	2.29
		(3.28)	(2.75)	(2.76)
	N	8.72	7.41	7.34
		(8.37)	(7.01)	(7.03)
	M	-	7.83	7.25
			(7.35)	(7.01)
Molar Conductace		7	10	12

A. Electronic Absorption Spectral Studies of Metal complexes

UV spectrum data of Schiff base ligand in DMSO shown two maxima in absorption region one at 312 nm and another compare to more intense at 435 nm. These two absorption region may be assigned to azomethine group and aromatic ring respectively. The lower energy band is due to $n \rightarrow \pi^*$ of conjugation between lone pair of electrons of p orbital of N atom in azomethine group and conjugated π bond of the aromatic nucleus. The band at the λ_{max} = 314 nm attributed to $\pi \rightarrow \pi^*$ transition state of the azomethine group and λ_{max} = 439 nm corresponds to the $n \rightarrow \pi^*$ transition state associated with azomethine group with intermolecular charge transfer[18]. The Schiff base derived from 3-formylchromone and 2-aminopyridine have shown two maxima in its UV spectrum

assigned to the π →π* and n→π* transition at 295 nm and 370 nm respectively[19]. The ligand obtained from 6-hydroxy-3-carbaldehyde chromone and ethylenediamine showed two maxima in the region of 200 nm to 258 nm and other at 325 nm[20]. The UV spectrum of ligand were shown two band at 207 nm and 296 nm for π →π* and n→π* transition respectively[21]. The electronic spectra of Ni(II) complexes showed usual absorption pattern of three band which consistent for their octahedral geometry that is, 9512 cm^{-1} (υ_1), 13827 cm^{-1} (υ_2) and 22272 cm^{-1} (υ_3). These absorption band indicated their transition $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{2g}(P)$ respectively. These observed transitions may be assigned to the characteristic three spin allowed transitions of octahedral complexes[20-21]. The electronic spectra showed bands in the region 12327 cm^{-1} and 24498 cm^{-1} attributed to $^6A_1g \rightarrow {}^4T_2g$ (^4D) and LMCT transitions respectively assigned to octahedral structure. Electronic absorption data have mentioned in table II and figure 1 show UV-visible spectrum of ligand.

TABLE II ELECTRONIC ABSORPTION SPECTRA OF COMPLEXES

Compound	Band position (cm^{-1})	Assignments	μ_{eff} (B.M.)
$[Ni(L)_2(Cl)_2]$	9512 cm^{-1}	$^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ (υ_1)	3.17
	13827 cm^{-1}	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (υ_2)	
	22272 cm^{-1}	$^3A_{2g}(F) \rightarrow {}^3T_{2g}(P)$ (υ_3)	
$[Fe(L)_2(Cl)_2]$	12327	$^6A_1g \rightarrow {}^4T_2g$ (G)	3.83
	24498	LMCT transi	

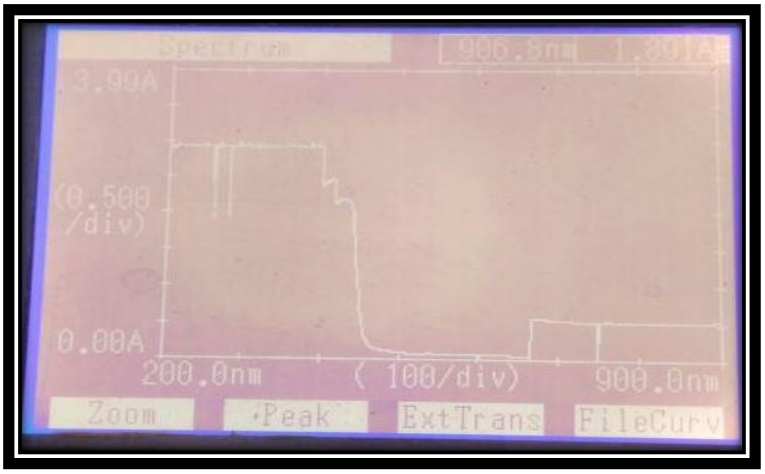

Figure 1: UV-Visible spectrum of Schiff base ligand

B. Infrared spectral studies of ligand

In the IR spectra of all the Schiff base ligand showed most characteristic band of azomethine group in the IR region of 1597 cm^{-1}. P. Kavitha et.al[19,22] revealed υ(C=N) azomethine vibrational stretching of ligand were exhibit the band in the region of 1600-1550 cm^{-1}. Yong Li & Zhengyin Yang[23] demonstrated the band for azomethine group at 1601 cm^{-1}. The IR spectra of Ni(II) and Fe(III) complexes have shown the band in the region 1573 cm^{-1} and 1572 cm^{-1} respectively are attributed to C=N stretching. In the free ligands, these bands are arrived at 1597 cm^{-1}. During complexation, these bands are shifted to lower wave number which indicated involvement of azomethine nitrogen bonding with the central Ni(II) and Fe(III) ion[23-24]. The band in the region of 1641 and 1642 cm^{-1} corresponds to carbonyl C=O stretching in the Ni(II) and Fe(III) complexes respectively while in their free ligand, these band are came in the region 1650 cm^{-1} respectively. In the complex formation these band are shifted to lower wave number by 4 to 40 cm^{-1}. This lowering of wave number have proved the

carbonyl oxygen involved in coordination with central Ni(II) and Fe(III) ion[24-25]. IR data was given in table III and figure 2 show IR spectrum of ligand.

TABLE III IR SPECTRAL DATA OF LIGAND AND THEIR NI(II) AND FE(III) COMPLEXES

Compound	Bond Vibrational modes (stretching-υ) Band position (cm^{-1})				
	Azomethine C=N	Carbonyl (C=O)	Aromatic (C=C)	υ(M—O)	υ(M—N)
Ligand (L)	1597	1650	1465	-	-
$[Ni(L)_2(Cl)_2]$	1573	1641	1562	470	552
$[Fe(L)_2(Cl)_2]$	1572	1642	1426	463	536

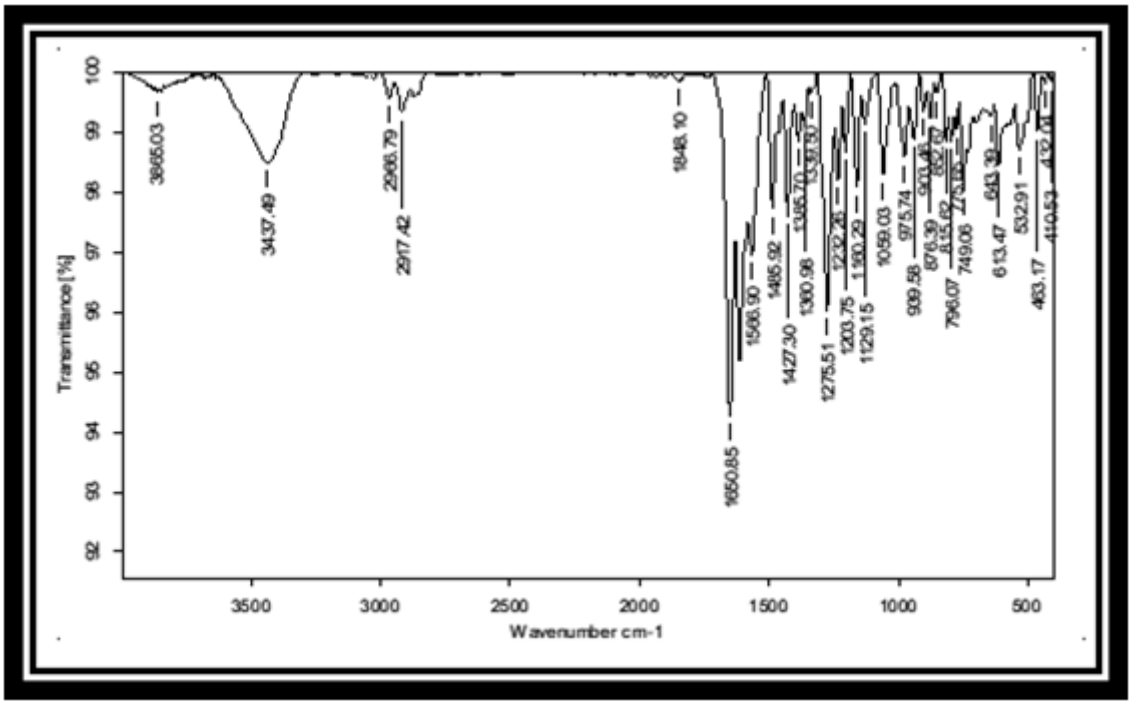

Figure 2: IR spectral data of ligand and their Ni(II) and Fe(III) complexes

C. ^{1}H NMR Studies of Metal Complexes

The ligand was shown signal at 8.06 ppm which confirmed that the formation of azomethine (CH=N–) group[26-27]. The multiplet signals in the range of 6.9 ppm to 7.6 ppm have revealed the protons of aromatic ring of chromone nucleus[28]. The protons of quinoline nucleus were shown multiplet signals in the range of 7.6 to 9.1 ppm[29]. The water impurity of the deuterated DMSO were shown a singlet of 3.7 ppm[30].

D. Antimicrobial activity

The minimum inhibitory concentration (MIC) of the complexes have compared with ligand and standard tetracycline are listed in table 4. The antimicrobial studies revealed that the metal complexes were shown more antibacterial and antifungal activity compared with parent ligand under similar experimental conditions on the same pathogens. The Ni(II) complex has shown significant antibacterial activity against K. pneumoniae and S. aureus and Fe(III) complex has shown significant antibacterial activity against P. vulgaris. Fe(III) complex has shown potent antifungal activity against C. albicans and A. niger compared to parent ligand and Ni(II) complex. On complexation, antibacterial and antifungal activity will increase can be explained according to chelation

theory[31-32]. According to overtone concept, lipid permeability is key factor to decide the antimicrobial activity because the cell is surrounded by lipid membrane and any molecule must have liposolubility nature for to enter into the cell[33]. The chelation process reduces polarity of metal ion due to extent of overlapping positive charge of metal ion with ligands. In complex compound, lipophilicity will increase due to the delocalization π electrons extended over chelate ring. This enhanced lipophilic nature will allow to penetrate the complex into the cell membrane and blocking the metal binding sites on the enzymes of microorganisms. The complexes also interfere the respiration process of the cell and thus block the protein synthesis which inhibit the growth of organism.

IV.CONCLUSION

In the present work, Ni(II) and Fe(III) complexes were prepared from 6-chloro-3-formylchromone and 3-aminoquinoline Schiff base and analyzed by various spectral technique. The analysis of IR spectral data revealed that the nature of ligand is bidentate, coordinating through azomethine nitrogen and carbonyl oxygen atoms. Magnetic and electronic spectral data indicate octahedral geometry for both the complexes. All the prepared compounds exhibited significant antibacterial and antifungal activity. Metal complexes have shown potent antimicrobial activity than the ligands.

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Eco-Friendly Sol-Gel Auto-Combustion Processing, Structural, Microstructural and Magnetic Characteristics of Nd^{3+} Incorporated Mixed $Ni_{0.5}Co_{0.3}Zn_{0.2}Fe_2O_4$ Nanocrystals

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ABSTRACT

In this effort, rare earth neodymium (Nd^{3+}) ions doped nanocrystalline nickel-cobalt-zinc mixed spinel ferrite chemically expressed as $Ni_{0.5}Co_{0.3}Zn_{0.2}Nd_{0.5}Fe_{1.5}O_4$ was synthesized via eco-friendly glycine supported sol-gel auto-combustion procedure. X-ray diffraction (XRD), transmission electron microscopy (TEM) and vibrating sample magnetometer (VSM) were used to illustrate the microstructural and magnetic characteristics of the produced nanocrystals. The examination of XRD diffractograms discloses the development of cubic spinel phase without any contamination peak. The average crystallite diameter was found to be in nano regime dimensions and well analogues by TEM outcomes (~ 45 nm). Magnetic characteristics of the sample was accomplished using VSM at 300 K. The magnetic quantities viz. saturation magnetization (*Ms* = 34.25 emu/g,), remanence magnetization (*Mr* = 19.73 emu/g) and coercivity (*Hc* = 886 Oe) were determined from M-H plot. The ideal ferromagnetic nature was obtained for the present mixed ferrite sample. The obtained mixed spinel ferrite nanocrystals can be utilized for multifunctional applications in biomedical as well as technological sector.

Keywords: Ni-Co-Zn ferrite, sol-gel, nanocrystal, rare earth, magnetic properties.

I. INTRODUCTION

In recent years, multifunctional materials have acknowledged more consideration by scientist and technologist owing to their potential applications in magneto-electric, magneto-optic and biomedical devices [1, 2]. In the group of ferrites, spinel ferrites are expansively investigated by a number of investigators due to their extraordinary magnetic, electrical and dielectric characteristics [3, 4]. Mixed spinel ferrites are widely used in microwave devices, water treatment, industrial electronic devices, magnetic cards, catalysis, power supplies, sensors, solar cells, and many more [5-7].

Spinel ferrites (XY_2O_4) shows a face centered cubic (fcc) ordered structure where both trivalent and divalent metal cations are lodging the tetrahedral (X) and octahedral [Y] sites in a cubic closed packing of oxygen (O^{2-}) [8].

The diverse characteristics of spinel ferrites can be transformed with approaches of synthesis routes, microstructural and chemical variation, types of substituents, etc. aspects. Currently, nanoferrites have established substantial consideration as probable candidates owing to their ability to express enhanced and exceptional characteristics in distinction with conventional bulk ferrites [9]. The nanocrystalline ferrites are produced by the several synthesis techniques viz. chemical co-precipitation, hydrothermal, microemulsion, citrate-gel etc. procedures [10]. The sol-gel route is the most adjustable technique to produce nanocrystals of spinel ferrites and it needs simple equipment, low temperature, most important eco-friendly, synthesis of chemically stable solids with skilful geomorphology via alteration of synthesis circumstances and parameters [11, 12].

Furthermore, Ni–Co–Zn mixed magnetic ceramics are considerable electronic materials, which are utilized in electronic applications suitable for high-frequency devices in the tele-communication sector and also for manufacture contaminant nano-adsorbent, chemical sensors, data storage devices, magnetic actuators, etc[13]. These solids are commercially used in antenna rods, radio-frequency circuits, high-quality filters, transformer cores and read or write memory heads. The excellent electro-magnetic properties of these solids make them appropriate for the miniaturization of devices. The rare earth incorporation in spinel ferrites is accountable for unusual alterations in micro-structural, optical, magnetic, electric and dielectric characteristics of the ferrites [14]. The structural disorder, lattice micro-strain and other physical characteristics of cobalt\nickel\zinc ferrite can be transformed by the incorporation of rare earth metal ions like Nd, Gd, Sm, Ho, etc. ions. Incorporation of rare earth cations into the mixed spinel ferrites can give outstanding magnetic properties. Rare-earth element (Re3+) has 4f unpaired electrons and iron has 3d unpaired electrons, consequently, the substitution of Re3+ induces Re3+-Fe3+ communication which turns out the magnetic, electrical and dielectrical characteristics [15]. On account of their numeral of applications and effectiveness in the diverse field there is a requirement to investigate the mixed nickel-cobalt-zinc (Ni-Co-Zn) nanoferrite materials with enhanced characteristics which can be achieved through different synthesis routes and using different rare earth dopants.

In this work, nanocrystalline rare earth neodymium (Nd^{3+}) doped Ni-Co-Zn nanocrystalline ferrite was produced using sol-gel auto combustion route and impact of Nd^{3+} incorporation on the structural, microstructural, and magnetic properties were scientifically explored.

II. METHODS AND MATERIAL

Materials: The analytical reagent grade (AR) nickel nitrate ($Ni(NO_3)_2.6H_2O$), cobalt nitrate ($Co(NO_3)_2.6H_2O$), zinc nitrate ($Zn(NO_3)_2.6H_2O$) neodymium nitrate (Nd(NO3)3.9H2O), ferric nitrate ($Fe(NO_3)_3.9H_2O$) and glycine (NH_2-CH_2-COOH) were utilized as source materials (99% pure) and used without additional distillation.

Synthesis: Nanocrystals of $Ni_{0.5}Co_{0.3}Zn_{0.2}Nd_{0.5}Fe_{1.5}O_4$ was effectively produced by means of sol-gel auto combustion route and glycine as a firing agent. The AR grade cobalt nitrate, zinc nitrate, nickel nitrate, neodymium nitrate, ferric nitrate and glycine were liquified in distilled water distinctly to get a consistent solution. The metal nitrates were liquified composed with a least quantity of distilled water required to attain a transparent solution. The ratio of metal nitrates to firing agent (i.e. glycine) was maintained as 1:4. Liquid ammonia solution was added to preserve the pH value 7 i.e. neutral. The temperature essential for the

formation of nanocrystals was low that is around 110 ˚C. The auto combustion reaction takes placed after continuous heating and stirring at about 5-6 hours. The as-synthesized powder is ground using a pestle mortar and then sintered at 750 ˚C for 5 hrs and afterward utilized for further examinations.

Characterizations

The room temperature X-ray diffraction patterns of the synthesized sample was observed through X-ray powder diffractometer PANalytical X'pert pro-diffractometer. The wavelength of the X-ray was 1.542 Å (Cu-Kα radiation, 40 kV and 100 mA), in the 2θ scale 20°- 80°and with the scanning rate of 0.02 ˚. The surface geomorphology and micro-structural inspections were supported using transmission electron microscopy (TEM, Philips) instrument. The magnetic measurement of synthesized sample was scrutinized with the help of a vibrating sample magnetometer (VSM) (Lakeshore model) technique with an applied magnetic field of 7 kOe.

III.RESULTS AND DISCUSSION

XRD patterns of the prepared nanocrystals recorded at room temperature are appeared in Fig. 1. The spinel cubic development without any impurity phases and nano-crystalline appearance of the prepared sample was inspected by the powder X-ray diffraction (P-XRD) data documented at room temperature in the 2θ angle range of 20° to 80°.

The observed Bragg's reflections are sharp and intense reflections with broader peaks confirming the nanocrystalline nature of the produced sample. The occurrence of planes (220), (311), (222), (400), (422), (511) and (440) in the XRD pattern reveals the cubic spinel structure of all the samples.

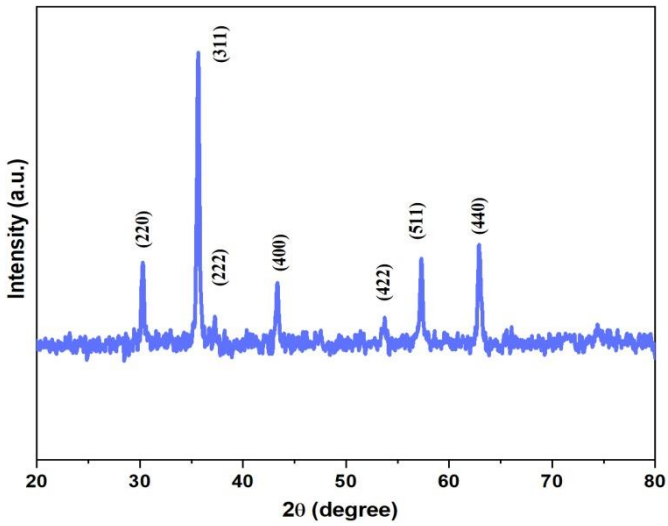

Figure 1: XRD diffractogram for $Ni_{0.5}Co_{0.3}Zn_{0.2}Nd_{0.5}Fe_{1.5}O_4$

The average crystallite size (d) of the produced powder was estimated with the most intense peak (311) and by means of the Debye-Scherer's formulation [16],

$$d = \frac{0.9\lambda}{\beta \cos\theta} \quad \text{nm} \qquad (1)$$

where, λ is wavelength of the Cu-Kα radiation, β is the full width of the half maximum, θ is Bragg's angle. The average crystallite diameter calculated by using Debye-Scherer's formula is of the order of 42 nm showing nano-regime dimension.

The values of the lattice constant (a) of the $Ni_{0.5}Co_{0.3}Zn_{0.2}Nd_{0.5}Fe_{1.5}O_4$ ferrite sample was calculated using the standard relation and found to be 8.3426 Å ,

$a = D\sqrt{(h^2 + k^2 + l^2)}$ (2)

where, D is interplanar spacing; (hkl) is Miller Indices. The unit cell volume (V) was calculated by using lattice constant. The unit cell volume was obtained to be 580.636 Å^3.

The X-ray density (d_x) value was assessed with the help of relation (3) and it if found to be 5.2435 g/cm^3 [17];

$$d_x = \frac{Z \times M}{V \times N_A} \quad (3)$$

where, Z is the number of molecules per formula unit (Z = 8 for spinels), M is molecular mass of the sample, V is the unit cell volume, N_A is the Avogadro's number.

The bulk density (d_B) of the pellets was measured using Archimedes method using water as solvent (ρ = 0.997 g/cm^3) using following equation [18]. The value of bulk density was found to be 4.3690 g/cm^3.

$$d_B = \frac{W_{dry}}{W_{wet} - W_{sus}} \times d_{H_2O} \quad (4)$$

where, W_{wet} and W_{dray} are wet and dry weights of the pellets subsequently measured in air before and after drying at 100 ˚C for 24 h, W_{sus} is the suspended weight in water of each pellet. The bulk density was lower as compared to X-ray density. The porosity ($\%P$) was obtained using dx and d_B values and found to be ~16 % suggesting the porous nature of the prepared sample due to progression of practical gases during the combustion reaction.

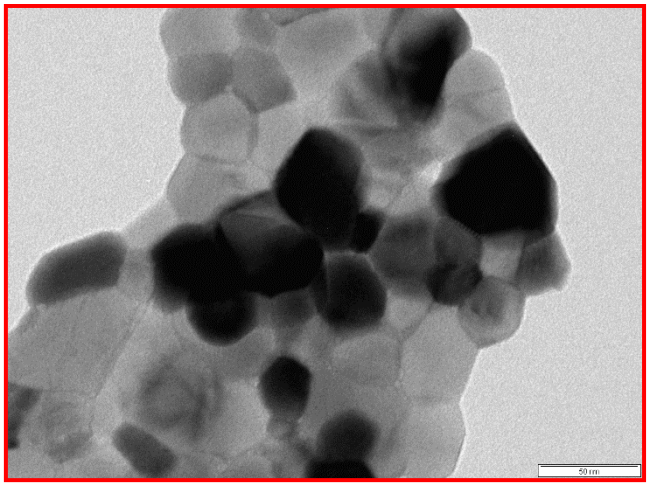

Figure 2: TEM picture of the $Ni_{0.5}Co_{0.3}Zn_{0.2}Nd_{0.5}Fe_{1.5}O_4$

TEM study demonstrated that spherical shaped, uniform nanocrystalline powder was successfully manufactured. The TEM picture is revealed in Fig. 2. The grains exhibit the agglomerate spherical and cubical shape morphology for the prepared samples. The attained average crystallite size (t) of the prepared nanocrystals from TEM was found to be ~45 nm.

TEM study demonstrated that spherical shaped, uniform nanocrystalline powder was successfully manufactured. The TEM picture is revealed in Fig. 2. The grains exhibit the agglomerate spherical and cubical shape morphology for the prepared samples. The attained average crystallite size (t) of the prepared nanocrystals from TEM was found to be ~45 nm.

In order to examine the magnetic response of the prepared samples to an external field, the field dependent magnetization of samples at normal room temperature was measured by means of VSM instrument. Fig. 3 displays the M-H plot of the prepared sample.

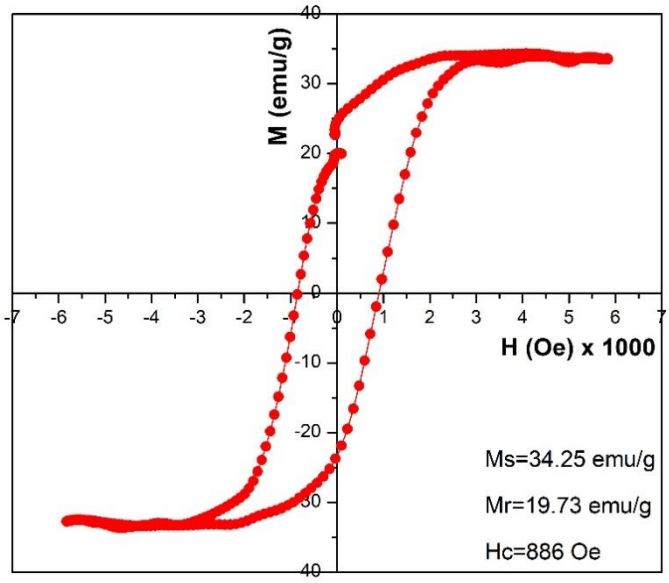

Figure 3: VSM plot for $Ni_{0.5}Co_{0.3}Zn_{0.2}Nd_{0.5}Fe_{1.5}O_4$ ferrite sample

The M-H plot viewing the banana shaped loop of ideal ferromagnetic behaviour for the prepared sample. The magnetic quantities viz. saturation magnetization (Ms), remanence magnetization (Mr) and coercivity (Hc) were determined from M-H plot. The ideal values of Ms = 34.25 emu/g, Mr=19.73 emu/g and Hc = 886 Oe were found for the present mixed ferrite sample. The values of magnetic parameters were slight lower as compared to pure spinel ferrite. In spinel ferrites, 3 kinds of super-exchange exchanges known as A-A, B-B and A-B exchanges are believable among the cations of (A) and [B]-site. The slight lesser values of remanence magnetization approve the produced sample is a soft ferrite solid, thus such nanoferrite was recommended for coils and cores of inductance applications. The magnetic properties of the spinel nanoferrite dependent on the cation distribution and these properties can be improved by substituting the numerous cations.

IV.CONCLUSION

In this paper, the eco-friendly and facile sol-gel auto combustion synthesis of (Nd^{3+}) ions incorporated nickel-cobalt-zinc mixed ferrite nanocrystalline chemically expressed as $Ni_{0.5}Co_{0.3}Zn_{0.2}Nd_{0.5}Fe_{1.5}O_4$ nanocrystals at 750˚C is presented. The influence of Nd^{3+} doping has been explored about a remarkable variation in the structural, microstructural, and magnetic characteristics of diverse Ni-Co-Zn nano-ferrite. The XRD investigation approved the development of nanocrystals of cubic spinel structure with space group *Fd-3m* lacking any contamination peak. The average crystallite diameter of synthesized nanocrystals was calculated by the Debye-Scherer formulation which obtained to be ~ 42 nm. The lattice constant was in reported range. A TEM examination verified that sphere-shaped, unchanging nanocrystals was effectively produced. The TEM outcomes analogous to the XRD data. The M-H plots evidenced a characteristic ferromagnetic nature of the produced nanocrystals. The obtained mixed spinel nanocrystals probably used for multifunctional applications in biomedical as well as technological field.

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An Overview of the Use of Electricity as a Reagent in Chemical Reactions

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ABSTRACT

In general, the circumstance of a chemical reaction is accompanied by the emancipation or immersion of heat and not of any other form of energy; but there are numerous chemical responses that when allowed to do in contact with two electronic operators, separated by conducting cables liberate what's called electrical energy, and an electric current is generated. Again, the energy of an electric current can be used to bring about numerous chemical responses that don't do spontaneously. Over the once decade, organic electrochemistry has endured a belle époque in the field of preliminary organic styles. Electro-organic conflation is the synthetic organic chemistry discipline that enables the direct use of electricity to induce precious composites. Hence, it's possible to transfer green aspects of sustainable energy sources to the whole product process. This research paper highlights the uses of electricity as a reagent in organic reactions.

Keywords: Use of Electricity, Reagent in Organic Reactions, Organic Reactions and Use of Electricity

I. INTRODUCTION

The advancement of environmentally friendly artificial processes is becoming more significant and needs undisputed energy supplies. In contemporary years, there has been a noteworthy enhancement in the use of renewable energy sources worldwide to mitigate pollution, carbon dioxide emissions, and waste production. Although these energy sources contribute to making artificial processes more environmentally friendly in terms of energy use, it is also valuable to apply this approach to chemical emulsion. Electro-organic emulsion is a branch of synthetic organic chemistry that allows for the direct use of electricity to trigger valuable combinations. Therefore, it is feasible to include environmentally friendly elements from sustainable energy sources throughout the whole product manufacturing process.

II. REAGENT

The introduction of reagents, which can be either single compounds or mixtures of substances, initiates or verifies chemical reactions. The term reagent describes an element that is consumed in a chemical process,

although it may mean the same thing as a reactant. Cleansers, although part of the reaction medium, are not typically referred to as reactants. Furthermore, catalysts retain their activity throughout the process as they are not consumed. In biochemistry, substrates describe the substances involved in enzyme-catalyzed reactions.

Chemicals meeting rigorous purity criteria are described as "reagent-grade" in commercial or laboratory contexts, ensuring their suitability for precise and dependable chemical analysis, chemical reactions, or physical testing. Organizations such as ASTM International or the American Chemical Society define the criteria for purity requirements in chemicals. Reagent-quality water must include minimal quantities of impurities, including salt and chloride ions, silica, and microorganisms. Additionally, it should have a high electrical resistivity. To distinguish them from reagent-grade goods, categorize items in the laboratory that are not completely pure but useful for basic tasks as a specialized, practical, or crude grade.

III.PROCESS OF ELECTROLYSIS

Electrolysis is a vital process in which particles and ions undergo electron transfer, either acquiring or losing electrons, due to the influence of an applied electric current. The products formed during electrolysis often have a distinct physical state from the electrolyte and can be separated using mechanical methods. The current directly determines the volume of the products, and when two or more electrolytic cells are connected in series to the same power source, the products formed in the cells are directly proportional to their original weight. These ideas are known as Faraday's laws of electrolysis.

Each electrode exhibits electrostatic attraction towards ions that possess an opposing charge. Cations move towards the cathode, which acts as an electron source. Anions go towards the cathode, which is the electrode that accepts electrons. The cathode introduces electrons as a reactant and extracts them at the anode as a product. Oxidation is the denotation for the phenomenon of electron loss in the realm of chemistry, while reduction is the recognition for the gain of electrons.

Neutral particles or molecules, present on the surface of an electrode, undergo ionization upon gaining or losing electrons. Subsequently, these ions have the potential to dissolve in the electrolyte and engage in interactions with other ions. When ions experience electron gain or loss, leading to a neutral state, they will join to form mixes that separate from the electrolyte. Positively charged cations, such as Cu_2, are solidly deposited on the cathode. Electroplating, electrowinning, and electrorefining designate these operations. An ion's electrical charge is altered when it undergoes electron gain or loss without achieving neutrality. Specifically, the phenomenon of electrolysis occurring in Neptune leads to the generation of hydrogen and chlorine gasses. The gases undergo bubble formation inside the electrolyte and then gather together. The first response is as follows:

$2NaCl + 2H_2O \rightarrow 2NaOH + H_2 + Cl_2$

The process taking place at the anode results in the generation of chlorine gas from chlorine ions. The process entails the transformation of two chloride ions (Cl^-) into a single chlorine molecule (Cl_2) while simultaneously releasing two electrons ($2e^-$).

At the cathode, the process produces hydrogen gas and hydroxide ions.

$2\ H_2O + 2\ e^- \rightarrow H_2 + 2\ ^-OH$

Without a barrier between the electrodes, the OH ions produced at the cathode can freely spread out inside the electrolyte towards the anode. As the proportion of hydroxide (OH) ions in the electrolyte rises, the production of chlorine gas (Cl_2) decreases. Instead, the chlorine gas combines with hydroxide ions to generate hypochlorite

ions (ClO) at the anode. The combination of chlorine gas (Cl_2) with sodium hydroxide (NaOH) results in the formation of sodium chloride (NaCl), sodium hypochlorite (NaClO), and water (H_2O). As the interaction between Cl_2 and NaOH increases in the reaction, the quantity of Cl2 that occurs on the reaction surface decreases, and the synthesis of hypochlorite proceeds more quickly. This is dependent on parameters such as the temperature of the solution, the time of contact between the Cl_2 patch and the solution, and the concentration of NaOH.

IV.ELECTROLYSIS-INDUCED ALTERATIONS IN ENERGY

The required input of electrical energy is equal to the difference in Gibbs free energy of the reaction plus the energy losses inside the system. The losses may approach zero to a high degree, therefore resulting in the maximum thermodynamic effectiveness being equal to the ratio of the enthalpy change to the free energy change of the response. Typically, the electrical input exceeds the enthalpy change of the reaction, resulting in the release of energy in the form of heat. In some instances, such as during the electrolysis of water into hydrogen and oxygen at high temperatures, the opposite holds and heat energy is taken in. The heat is extracted from the surroundings, and the heating value of the generated hydrogen exceeds the electrical input.

V. ELECTRICITY ASSISTANCE

Applying an electric current to a solution of blue vitriol results in the deposition of metallic copper at the electrode, where the current departs the solution. The opposite electrode generates sulfuric acid as the current enters the solution. The process in which electric current breaks down chemical compounds into their constituent parts is called electrolysis. This process forms the basis for several important businesses. Electrolysis of salt. Sodium chloride, often referred to as table salt, is a cost-effective and essential component of our inventory of chemical raw materials. Throughout history, individuals have used intricate and very beneficial methods to manufacture two significant substances: sodium hydroxide and sodium carbonate. These compounds are extensively used in several sectors, including glassmaking, cleaning, and textile production. A swab was used to extract the bleaching grease paint used in commercial applications, employing an elaborate technique. The field of electrochemistry has brought about a significant transformation in these situations.

VI.CONCLUSION

Electric current may be used to induce several non-spontaneous chemical reactions. During the process of electrolysis, electrical energy is immediately turned into chemical energy, which is then stored in the resulting products of the reaction. Typically, electrochemical reactions might be difficult to borrow or replicate due to their reliance on non-standardized response containers. Typically, when discussing synthetic electrochemistry, the primary focus is on the sustainability of oxidation-reduction reactions. This involves substituting chemical oxidants or reductants with an electrode. The use of electric current eliminates the production of chemical waste and enhances resource efficiency, since it just requires the manipulation of electrons for reactivity.

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The Synthesis of Xanthene Derivatives Catalyzed by Mixed Tartrate as an Efficient Catalyst

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ABSTRACT
Mangenese doped iron tartrate is a very efficient, water soluble and reusable catalyst for synthesis of 3,3,6,6-tetramethyl-9-aryl-1,8-dioxooctahydro xanthene derivatives through a one-pot condensation with various aromatic aldehydes. Catalyst used under solvent-free conditions and can be recovered by simply evaporation. Compared with other synthetic methods, this new method has advantages such as milder reaction conditions, good to excellent yields, short reaction times, and environmentally benign procedure.
Keywords: Solvent-free,3,3,6,6-tetramethyl-9-aryl-1,8-dioxooctahydro xanthene derivatives,mangenese doped iron tartrate, reusable catalyst, water soluble catalyst.

I. INTRODUCTION

Multicomponent reactions (MCRs) are very important and attractive subjects in organic synthesis due to formation of carbon–carbon and carbon–hetero atom bonds in one pot.Research is changing to most efficient and atom economic tool in synthesis, due to their inherent simple experimental procedure, structural diversity etc. Herein the proposed research work plans to develop new synthetic methodologies for several heterocyclic compounds. Simple and flexible building blocks will combined with other structurally active units together.
The procedures for its synthesis have been extensively studied and such studies have been stimulated by various promising applications, especially in the case of highly substituted 4-hydroxycoumarin derivatives. In fact, certain substituted chromene are used as antimicrobial, anticancer, anti-inflammatory, antidepressant, anticonvulsant, antihyperglycemic, antipyretic, antibacterial, antifungal activities, fungicidal, anti-arthritic activities [1-4].The knowledge of such applications has pointed out that substituted 4-hydroxycoumarin are important target to be prepared to our interest on synthesis and molecular structure determination of some types of 4-hydroxycoumarin [5].
Amongst the heterocyclic compounds Triazoles, thiadiazoles, pyrazoles, oxadiazoles, Xanthene, coumarinattracted a tremendous attention, as they are full of many ramifications especially in the biological and industrial applications. In this chapter we have given a short introduction of these compounds. In view of the general observation that the biological activities are invariably associated with a large variety of

heterocyclic systems such as 1,8-dioxooctahydroxanthene a large number of their new derivatives have been synthesized and extensively studied for various pharmacological properties .

II. METHOD AND MATERIAL

A) Experimental

The melting points were determined on an electrothermal apparatus and the temperature was not calibrated. IR spectra were recorded as thin films on KBr using the Spectrum 400 spectrophotometer. The 13CNMR spectra were recorded on a Bruker AVANCE NEO 500 MHz NMR spectrometer. The sample solution was prepared in DMSO containing tetramethylsilane (TMS) as an internal reference. Mass spectra were recorded on a Water S, Q-TOF MICROMASS (ESI-MS) at 70 eV. All chemical reagents were commercially available and purified with standard methods before use. Solvents were dried in routine ways and redistilled.

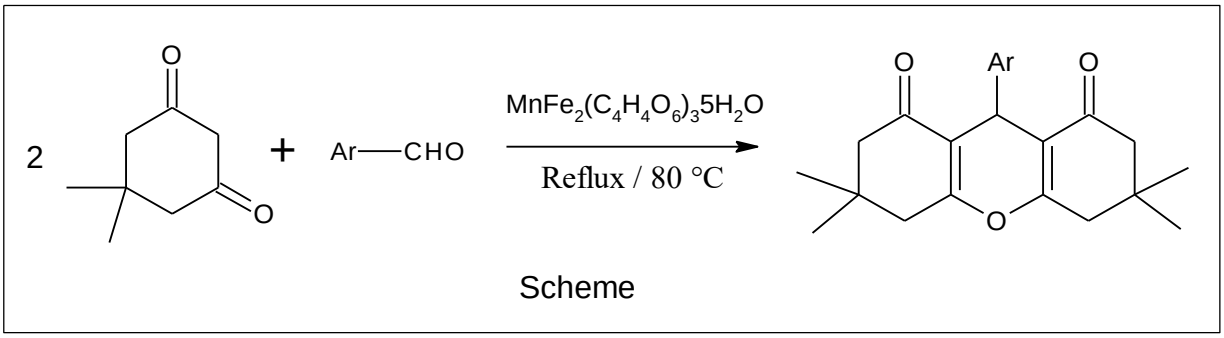
B) General Procedure for the Synthesis of 1,8-dioxooctahydroxanthene Derivatives:

The 5,5-dimethyl-1,3-cyclohexanedione (2mmol), an aromatic aldehyde (1mmol) and $MnFe_2(C_4H_4O_6)_3.5H_2O$ (10 mol %) was heated in the oil bath at 110°C for the appropriate time. The progress of reaction was monitored by thin layer chromatography (TLC). Upon completion, the reaction mixture was cooled to room temperature and ethanol (10 ml) was added. The catalyst was recovered from filtrate. The residue was washed with ethanol (95%) to give compounds 3a-l in high yields. Recovered catalyst was washed with diethyl ether (10 ml) and calcined at 120°C for 1h, before reusing.

III.RESULT AND DISCUSSION

We have reported that mangenese doped iron tartrate ($MnFe_2(C_4H_4O_6)_3.5H_2O$) is an efficient and reusable catalyst for the synthesis of 3,3,6,6-tetramethyl-9-aryl-1,8-dioxooctahydro xanthene derivatives. The main characteristic of this method include the use of a catalytic amount of the $MnFe_2(C_4H_4O_6)_3.5H_2O$, good yields, operational simplicity, short reaction times, catalyst separation from the reaction medium and catalyst reusability. Moreover, the use of environmentally benign catalyst and avoidance of hazardous organic solvents are important features ofthis protocol.

To optimize the reaction conditions, the reaction of 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) and benzaldehyde (1 mmol) under solvent-free conditions was selected as a model. After many studies on the above model reaction, we found that when less than 10 mol % of $MnFe_2(C_4H_4O_6)_3.5H_2O$ was applied, the corresponding products obtained in lower yields and require more time , whereas use of more than 10 mol % catalyst did not improve the yield and require same time. This was due to the fact that beyond a certain concentration, there exist an excess of catalyst sites over what is actually required by the reactant molecules and hence, the additional catalyst does not increase the rate of reaction. Therefore, in all further reactions 10 mol % of $MnFe_2(C_4H_4O_6)_3.5H_2O$ catalyst was used.



Scheme

In order to evaluate the generality of the process, we next carried out a series of reactions using 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) and various aromatic aldehydes (1 mmol) in presence of $MnFe_2(C_4H_4O_6)_3.5H_2O$ (10 mol%) at 110°C under solvent-free conditions. Most importantly, aromatic aldehydes with substituent's bearing either electron-donating or electron-withdrawing groups as well as heterocyclicaldehydes reacted successfully in the presence of $MnFe_2(C_4H_4O_6)_3.5H_2O$ as a catalyst. In all these reactions expected products were obtained in good to excellent yields. The results are shown in Table. The suggested mechanism for the $MnFe_2(C_4H_4O_6)_3.5H_2O$ catalyzed synthesis of 3,3,6,6-tetramethyl-9-aryl-1,8-dioxooctahydro xanthene is shown in Scheme. Concerning the reaction mechanism, we suggest that, initially activation of the carbonyl group of aldehyde by $MnFe_2(C_4H_4O_6)_3.5H_2O$ catalyst facilitates nucleophilic attack of dimedone in its enol form and form corresponding carbocation. This carbocation was then reacts with the second activated dimedone to give intermediate, which then undergo dehydration to give the final product.

Many procedures for the synthesis of xanthenes and benzoxanthenes have been reported in the literature, including the reaction of cyclodehydration[6] trapping of benzynes by phenols, cyclocondensation of 2-hydroxy aromatic aldehydes and 2-tetralone, aryloxymagnesium halides with triethylorthoformate, intermolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones , and cyclization of polycyclic aryltriflate esters . Recently, the preparation of xanthene derivatives has been achieved by the condensation of aldehydes with 2-naphthol by cyclodehydration in the presence of diverse catalysts, such as *p*-toluenesulfonic acid , *p*-dodecylbenzenesulphonic acid, triethyl-benzylammonium chloride, diammoniumhydrogen phosphate under various conditions , I_2 , $K_5CoW_{12}O_{40}\cdot3H_2O$/silicagel/ MW, LiBr/MW , and isonitriles . However, some of these methods have some drawbacks, such as hazardous organic solvents, unsatisfactory yields, and use of expensive catalysts, longer reaction time and tedious workup [7].

TABLE 1.**SYNTHESIS OF 1,8-DIOXOOCTAHYDROXANTHENE BY CONDENSATION OF ALDEHYDES AND 5,5-DIMETHYL-1,3-CYCLOHXANEDIONE USING $MNFE_2(C_4H_4O_6)_3.5H_2O$ AS CATALYST.**

Entry	R	Product	Time(min)	% Yield	M.P(^{0}C)	
					Found	Reported
1	H	1a	45	90	203-204	204-205[8]
2	3-Cl	1b	45	95	180-182	182-184[8]
3	4-Cl	1c	60	92	225-227	226-228[8]
4	4-NO_2	1d	50	94	223-225	224-225[8]
5	4-OH	1e	60	92	245-246	247-248[8]
6	3-OMe	1f	60	90	235-238	238-240[8]

IV.CONCLUSION

In conclusion, $MnFe_2(C_4H_4O_6)_3.5H_2O$was demonstrated a new efficient catalyst for the synthesis of 1,8-dioxooctahydroxanthene using $MnFe_2(C_4H_4O_6)_3.5H_2O$as a homogeneous catalyst under aqueous media. These conditions had advantages such as shorter reaction time,simpler work-up, inexpensive and non-toxic catalysis, environmental benignity and excellent yields. The protocol described herein is advantageous in terms of preclusion of hazardous organic solvents, catalytic amount of reagents, shorter reaction time, good yields, recovery and reusability of catalyst.

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Green Synthesis, Spectral, Thermal Characterization, Antimicrobial Screening Of Schiff Base Ligand and their Transition Metal Complexes Derived From (8E)-N'-((6,8-Dichloro-4-Oxo-4H-Chromen-3-Yl)Methylene)-4-Methyl-1,2,3-Thiadiazole-5-Carbohydrazide

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ABSTRACT

This work reports synthesis Of novel Schiff base ligand of (8E)-N'-((6,8-dichloro-4-oxo-4H-chromen-3-yl)methylene)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide and its transition metal complexes of Fe(III), Co(II), Ni(II), Cu(II), And Zn(II) were prepared under microwave irradiation as a green approach compared to the conventional method. The structures of these Schiff base and its metal complexes were confirmed by different spectroscopic tools. i.e, UV, IR, 1H-NMR, LC-MS, IR, and Powder XRD and electronic spectra of the synthesized complexes explained their geometrical structures. The thermal stability of metal complexes was studied by thermo-gravimetric analyses (TGA). The elemental analysis revealed metal to ligand stoichiometry was 1:2 molar ratio and screened for biological activities (antimicrobial)

Keywords: microwave synthesis; NO,ONO donor Schiff base; thermal study; biological activity.

I. INTRODUCTION

Schiff bases are important special and effective multi-dentate Schiff bases are widely studied in coordination chemistry, especially those that possess compounds containing heterocyclic compounds with the azomethene group, as they have basic properties due to the presence of a pair of electron on the azomethene nitrogen atom (-C = N) and often they are pentagonal or hexagonal rings with the metallic ion [1-4]. The Schiff bases heterocyclic metals complexation have been intensively investigated in recent years in many applications such as in antibiotics and medicine.

Coordination complexes are formed by ligands that have various donor sites generally heterocyclic rings, for example: -ONO, - NNO or NNS and NO. Among the ligands hydrazone playing a significant role since coordination complexes of these compounds are at present extensively used for the treatment of numerous

diseases, in analytical and synthetic chemistry as heterogeneous catalysts in the oxidation-reduction reaction process and a variety of chemical, photochemical reactions as well as different industrial significance in the field of science and technology [5-8].

II. EXPERIMENTAL

2.1 Materials

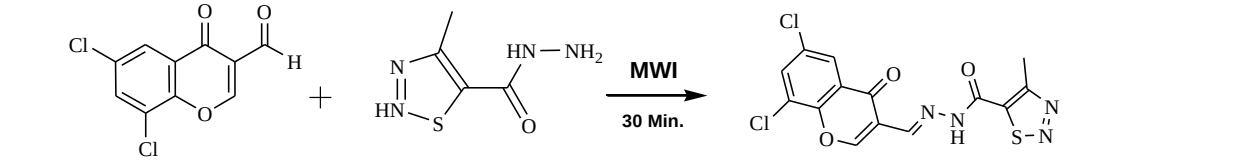
All chemicals and solvents employed in synthesis were of extra-pure grade and used as received without anyfurther purification. Solvents were purified and dried according to literature method [9-11]. All chemicals were obtained from Sigma–Aldrich chemical used without purification. They 6,8-Dichloro-4-oxo-4H-chromene-3-carbaldehyde and 4–Methyl-1,2,3,-thiadiazole-5-carbohydrazide, remaining all chemical solvents were purchased from spectrochem ltd.

2.2 Physical measurements

Elemental analysis (C, H, N,) was performed using Perkin Elmer CHN analyzer. TLC was visualized by VL-6-LC, UVlamp.IR spectra of the ligands and their metal complexes were recorded on Bruker spectrometer within the range of 4000–400 cm^{-1}. The UV spectra of compounds were recorded by UV-Vis. Spectrophotometer (UV-1700, Shimadzu). Thermal studies of the complexes were carried out on a Perkin Elmer diamond TGA instrument. ^{1}H-NMR and ^{13}C-NMR spectra of the ligands were recorded on Bruker spectrometer using DMSO-d6 as a solvent and TMS as internal standard. Mass spectra were recorded on water, Qt of micromass (ESI-MS).

2.3 Synthesis of the Schiff base ligand

The Schiff base has been synthesized by reacting 6-mercapto-4-oxo-4H-chromene-3-carbaldehyde (1.00 mmole) and 4–Methyl-1,2,3,-thiadiazole-5-carbohydrazide (1.00 mmole).The reaction was carried out in a microwave oven for 30 minutes. The irradiated product was washed with dry ether and filtered. The final product was recrystallized from ethanol to give pale yellow crystals. The purity of the product was monitored by the use of TLC, using n-hexane and ethyl acetate (7:3) ratio.



6,8-Dichloro-4-oxo-4H-chromene-3-carbaldehyde

4-methyl-1,2,3-thiadiazole-5-carbohydrazide

(8*E*)-*N*'-((6,8-dichloro-4-oxo-4*H*-chromen-3-yl)methylene)-4-methyl-1,2,3-thiadiazole-5-carbohydrazide

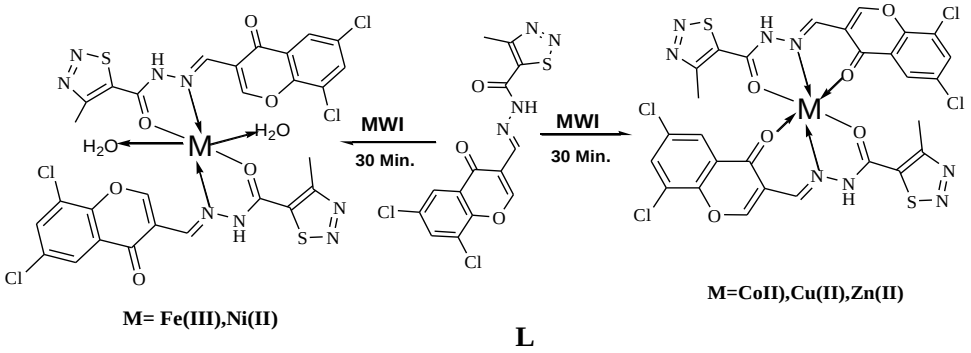
Scheme: The schematic route for synthesis of Schiff base (L)

2.4 Spectral data of ligand:

Color: Yellow , Yield: 78%, M.P.: 256°C, Selected FT-IR bands (KBr, cm^{-1}) : 3163 ν (NH), 1680 ν(C=O chromone), 1624 ν (C=O hydrazonic), 1596 ν(C=N); ^{1}H- NMR (DMSO-d6, δ ppm) 12.26 (1H,s, iminolic -OH); 8.48 (S, 1H, HC=N), 6.94-8.26 (m, 4H, Ar-H); 2.98 (S, 3H, $-CH_3$); ^{13}C NMR (DMSO-d6, δ ppm) 168.01 (C=O chromone), 158.66 (C=O hydrazone), 156.94 (-HC=N), 15.33($-CH_3$- chromone)12.44($-CH_3$- hydrazone);

2.5 Synthesis of metal complexes

The Schiff base ligand and metal salts were mixed in a grinder 1:1 (metal: ligand) ratio. The reaction mixture was then irradiated in a microwave oven. The reaction was completed in a short time, between 60-180 sec. The progress of the reaction and purity of the product was monitored by TLC plate. Each product was recrystallized from ethanol and ether, and finally, different colored crystals were obtained. (Yield: 70-75 %)



Scheme: The schematic route for synthesis of metal complexes

III.RESULTS AND DISCUSSION

In the present study of the microwave-assisted synthesis, it was observed that the reaction time had been drastically reduced with a better yield of the products. The difference was observed probably due to the strong microwave effect and the high enhancement of reaction rate. The conformation of results was also checked by repeating the synthesis process [12-14]. The microwave irradiation technique was completed with 60-180 Sec. and yield 70-75%. All the metal complexes are colored, solid and stable towards air and moisture at room temperature. They possess a sharp melting point. The complexes are soluble in dimethylformamide and dimethyl sulfoxide but insoluble in common organic solvents 3.1.Elemental analysis.

Table-1: Physical and analytical data of L and its metal complexes.

Compound	Mol. Formulae (F.W.)	M.P.°C	Colour	Elemental analysis found (calculated.)%			
				% C (cal.)	% H (cal.)	% N (cal.)	% M (cal.)
Ligand (L)	$C_{14}H_8Cl_2N_4O_3S$ (383)	256°C	Brown	42.70 (43.88)	2.06 (2.10)	13.76 (14.62)	-
$[Ni(L)_2(H_2O)_2]$	$C_{28}H_{16}Cl_4N_8NiO_6S_2$ (821)	>280°C	Red	39.88 (40.76)	1.72 (1.95)	12.90 (13.58)	7.34 (7.11)
$[Cu(L)_2]$	$C_{28}H_{16}Cl_4CuN_8O_6S_2$ (826)	>280°C	Violet	38.99 (40.52)	1.77 (1.94)	12.54 (13.50)	6.44 (7.66)

3.1 FT-Infrared spectra

The characteristic IR bands of the chromone hydrazones give important information about the various functional groups present in it .The ligands showed a Strong band at 1680cm^{-1} which is due to ν (C=O) group of the chromone moiety. This Strong band was shifted to lower wave number region 10–35 cm^{-1} in their corresponding metal complexes, indicating the coordination of oxygen atom of carbonyl group of the chromone moiety. The stretching vibration of the azomethine group (C=N) was observed at 1596 cm^{-1} in the ligand. This band was shifted to lower wave number region 20-40 cm^{-1} in their metal complexes, indicating the participation of nitrogen atom of azomethine group in coordination to the metal ion. An appearance of new broad band in the region 3234-3409 cm^{-1} indicates the presence of coordinated water in Fe(III),Ni(II), metal complexes. The coordination of nitrogen and oxygen atoms was supported by the appearance of a non-ligand bands in the range 522-542 cm^{-1} and 426-460 cm^{-1} region due to the ν(M–O) and ν(M–N), respectively. From the above spectral data, it was concluded that schiff base ligand acts as bidentate with coordinate two water moleculs in Fe(III) and Ni(II), metal complexes and tridentate ligands in Co(II), Cu(II) and Zn(II)The FT-IR spectral data containing relevant vibrational bands of the ligands and their metal complexes are listed in Table 2.

Table-2: The selective Infrared frequencies of ligand (L) and its metal complexes

Compound Name	ν(C=O) Chromone	ν(C=O) hydrozonic	ν(C=N)	ν(M-O)	ν(M-N)
L	1680	1640	1596	-	
$[Fe(L)_2 (H_2O)_2]$	1666	1610	1533	522	426
$[Co(L)_2]$	1643	1620	1530	516	410
$[Ni(L)_2 (H_2O)_2]$	1656	1610	1545	512	414
$[Cu(L)_2]$	1685	1630	1586	542	420
$[Zn(L)_2$	1670	1638	1590	542	460

3.2 Electronic spectra

In UV-Visible spectra the intra ligand transitions of copper (II) complexes are assigned to bands in the range λ_{max} (DMF) **logε (L mol^{-1} cm^{-1})** 280 -366 nm (35844 -27398 cm^{-1}) and 426-482 nm (23532-15420 cm^{-1}) It is due to the Intra ligand transition, $^2B_1 \rightarrow {}^2E(dx^2\text{-}y^2 \rightarrow dxz, dyz)$, $^2B_1 \rightarrow {}^2B_2$ $(dx^2\text{-}y^2 \rightarrow dxy)$, $^2B_1 \rightarrow {}^2A_1$ $(dx^2\text{-}y^2 \rightarrow dz^2)$ and $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ transitions of hydrazone ligands suffered a marginal shift up on complexation. The shift of the bands may be caused by intra ligand transitions which weakening of the C=N bond and extension of conjugation upon complexation.

In UV-Visible spectra the intra ligand transitions of Ni(II) complexes are assigned to bands in the range λ_{max} (DMF) **logε (L mol^{-1} cm^{-1})** 284 nm (35211 cm^{-1}) 325-305,650 (30769 -19801,15420 cm^{-1}) It is due to the Intra ligand transition, $^3A_{2g}(F)\rightarrow{}^3T_{1g}(F)$, and $^3A_{2g}(F)\rightarrow{}^3T_{1g}(F)$ and $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ transitions of hydrazone ligands suffered a marginal shift up on complexation. The shift of the bands may be caused by intra ligand transitions which weakening of the C=N bond and extension of conjugation upon complexation.

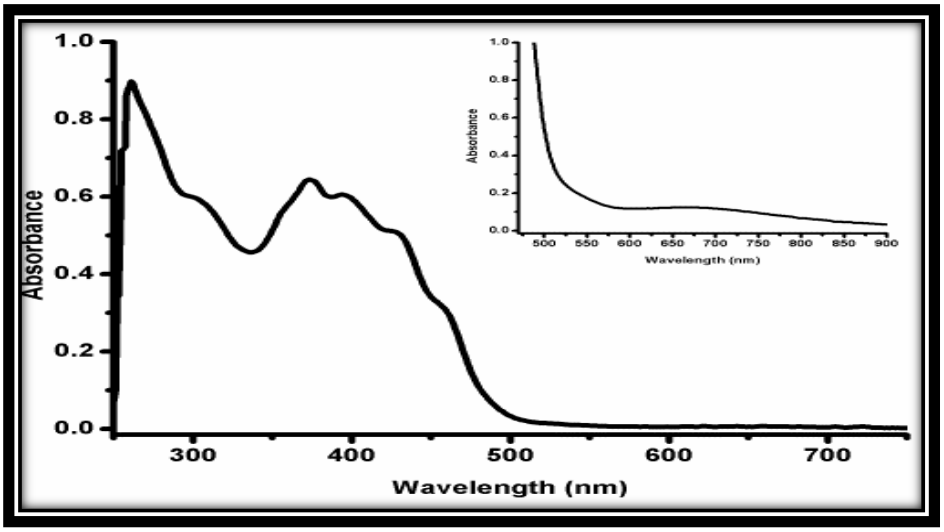


Figure 3.33 UV-visible spectrum of $[Cu(L)_2]$

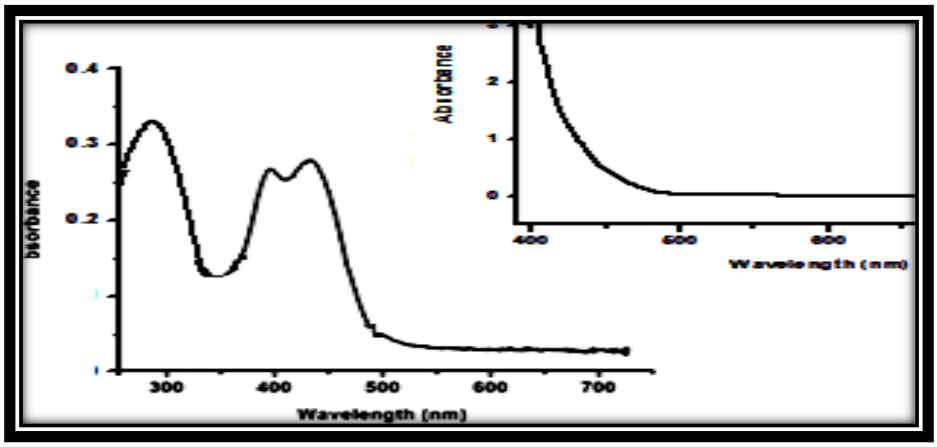


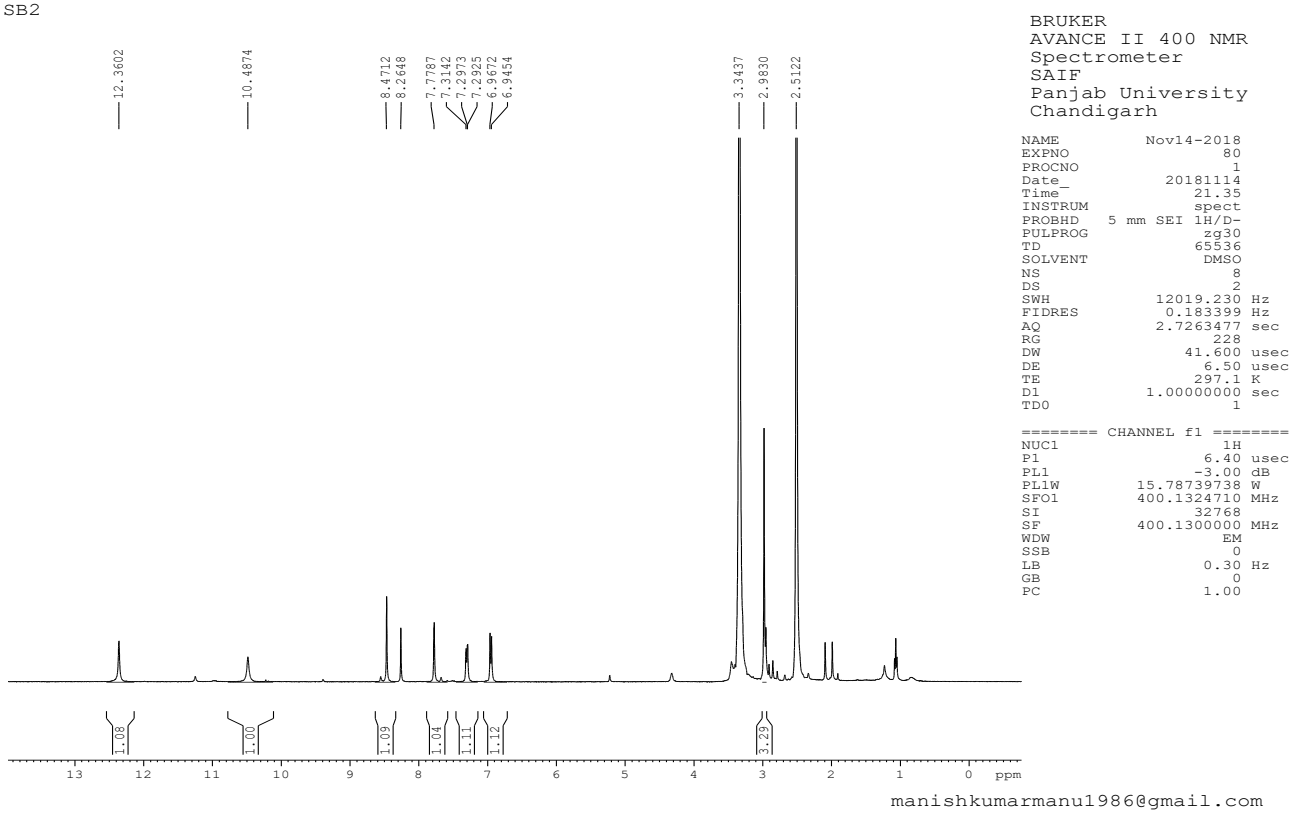
Figure 3.25 UV-vis. spectrum of $[[Ni(L)_2 (H_2O)_2]$

Table 2.3 Electronic spectral assignments for $[Cu(L)_2]$ and $[Ni(L)_2 (H_2O)_2]$

Compounds	Electronic spectral bands :nm (cm^{-1})	logε (L mol^{-1} cm^{-1})	Band assignment
	280 (35844)	3.95	Intra ligand transition
	366 (27398)	2.79	Intra ligand transition
$[Cu(L)_2]$	426 (23532)	1.69	$^2B_1 \rightarrow {}^2E(dx^2\text{-}y^2 \rightarrow dxz, dyz)$
	482 (20843)	1.54	$^2B_1 \rightarrow {}^2B_2 (dx^2\text{-}y^2 \rightarrow dxy)$
	650 (15420)	1.0	$^2B_1 \rightarrow {}^2A_1 (dx^2\text{-}y^2 \rightarrow dz^2)$
	294 (37460)	3.95	Intra ligand transition
	284 (35211)	3.77	Intra ligand transition
$[Ni(L)_2 (H_2O)_2]$	325 (30769) 505 (19801)	2.64 1.66	CT $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$
	510 (19607)	1.65	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$
	275 (36363)	3.47	Intra ligand transition

3.3 1H-NMR spectra

The ^{1}H-NMR spectrums of ligand and metal complexes were recorded in DMSO-d6. The spectrum of ligand shows following signals: ^{1}H- NMR (DMSO-d6, δ ppm) 12.26 (1H,s, iminolic -OH); 8.48 (S, 1H, HC=N), 6.94-8.26 (m, 4H, Ar-H); 2.98 (S, 3H, -CH_3);



3.4 Thermogravimetric analysis

Thermal analysis was used mainly for the confirmation of the water molecule or solvent associated with being in the sphere of coordination or in the outer sphere of the complex [15-18] and the information about its properties, the nature of the products intermediate and final thermal decomposition. From the TGA curves, the weight loss was calculated for the different steps and compared with the theoretically calculated weight for the suggested formulas based on the results obtained from the elemental analyzes. Thermal stability of the synthesized metal complexes was done up to 900 °C at a heating rate of 10 °C/min in nitrogen atmosphere. Metal complexes exhibit similar decomposition pattern as evident from their TGA graphs. The TGA graph shoes that decompose of Ni metal complex in Three steps with in temperature range of 10–700 °C. First step corresponds to the loss of two coordinated water molecules $(H_2O)_2$ (Found 04.10 %, calcd. 04.36 %)%) in temperature range of 10-170 ^{0}C. The second step corresponds to the loss of $(C_{11}H_6Cl_2N_2O_3)_2$ (Found 68.74 %, calcd. 69.43 %) in temperature range of 230–44735 °C. The third step corresponds to the loss of $(C_3H_4N_2S)_2$ (Found 21.88 %, calcd. 24.36 %) in temperature range of 435–600 °C. In the third step and as a final product, it leaves NiO as residue. The TGA graph shoes that decompose of Cu metal complex in three steps within temperature range of 10–700 °C. First step corresponds to the loss of $(C_{11}H_6Cl_2N_2O_3)_2$ (Found 67.96 %, calcd. 69.24 %) in temperature range of 210–420 °C. The second step corresponds to the loss of $C_3H_4N_2S)_2$ (Found 22.66 %, calcd. 24.21 %) in temperature range of 435–600 °C. The third step and as a final product, it leaves CuO as residue.

Table 4: Thermal analysis data of metal complexes

Comp.no.	Molecular formula	Stages	Temp(°C)	Possible evolved species	Residual species	Mass loss
						Found Calc.
1	$C_{28}H_{16}Cl_4N_8NiO_6S_2$ (821)	1st 2nd 3rd	10-170 ^{0}C 230-435 ^{0}C 435-600 ^{0}C	$2H_2O$ $(C_{11}H_6Cl_2N_2O_3)_2$ $(C_3H_4N_2S)_2$	NiO	04.10 04.36 68.74 69.43 21.88 24.36 08.74 09.01
2	$C_{28}H_{16}Cl_4CuN_8O_6S_2$ (826)	1st 2nd	210-420 ^{0}C 420-580 ^{0}C	$(C_{11}H_6Cl_2N_2O_3)_2$ $(C_3H_4N_2S)_2$	CuO	67.96 69.24 22.66. 24.21 08.22 09.55

3.5 Powder XRD studies

The X-ray diffractograms of Fe(III) and Zn(II) complexes were recorded in between the range 5-80° at wavelength 1.541551 Å. The unit cell parameters and calculation were performed using powder-X software. Average particle size was calculated using grain software. **Table- 4.3.3** gives the summary of unit cell parameters and average particle size. Miller's indices and the calculated lattice constants correspond to monoclinic system for Fe(III) and triclinic for Zn(II) complexes.

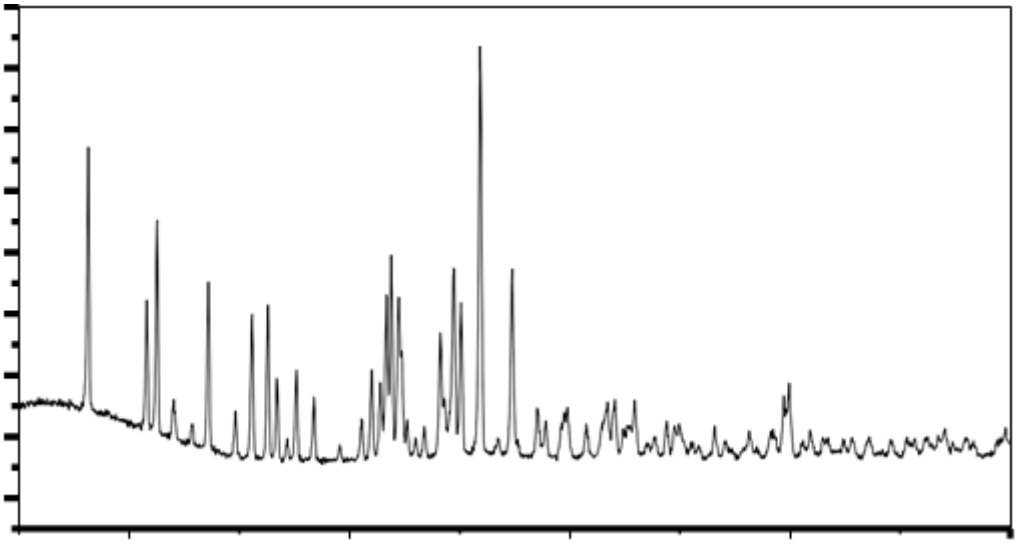


Figure-: Powder X-ray diffractogram pattern of $[Zn(L)_2]$

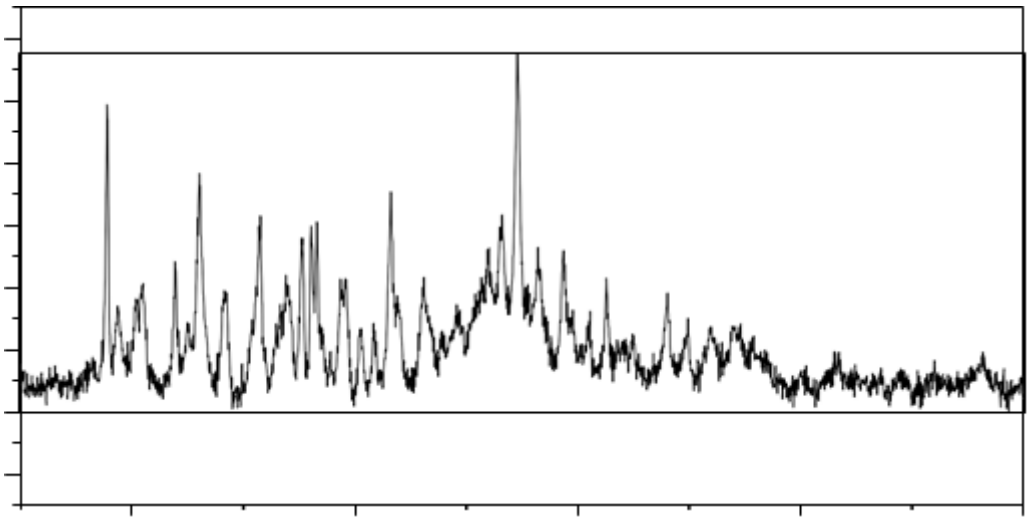


Figure-: Powder X-ray diffractogram pattern of $[Fe(L)_2 (H_2O)_2]$

Table-5: X-ray diffractogram data of Fe(III) and Zn (II) Complexes.

Parameters	$[Fe(L)_2 (H_2O)_2]$	$[Zn (L)_2$
Temperature	298K	298K
Wavelength (Å)	1.541551	1.541551
Radiation	CuKα	CuKα
Crystal system	Monoclinic	Triclinic
Unit Cell Dimension		
a(Å)	14.4858	9.6864656
b(Å)	16.9522	14.8052
c(Å)	19.4512	17.06102
α(°)	90	101.75
β(°)	106.21	100.29
γ (°)	90	100.873
Average particle size (nm)	14.923436	21.051432

3.6 Antimicrobial activity

The in vitro antimicrobial screening of synthesized ligand and metal complexes was tested against four bacteria (*S. Aureus, S. Pyogenes, E. Coli & S. Typhi*) and two fungi (*C. Albicans & T. Rubrum*) by petri-plate containing 30 ml potato dextrose agar and nutrient agar medium, the plates were incubated for 20-24 hr and 24-48 hr for bacteria and fungi stains, respectively. The activities were measured in terms of zone of inhibition in mm. Cefotaxime, Azithromycin and Clotrimazole were used as standard drugs for bacteria and fungi, respectively at 500 ppm concentration of sample as well as drugs. The results of antimicrobial activity of ligand and metal complexes are shown in Table 4.

The metal complexes exhibit higher inhibition against tested microorganism compared to the free ligand. [19-22]. The value in the above table indicates that the activity of the Schiff base ligand became more pronounced when coordinated with the metal ions. The presence of azomethine moiety and chelation effect with central

metal enhances the antibacterial activities. This enhancement in antibacterial activity of these metal complexes can be explained based on the chelation theory [23-26].

When a metal ion is chelated with a ligand, its polarity will be reduced to a greater extent due to the overlap of ligand orbital and the partial sharing of the positive charge of the metal ion with donor groups. Furthermore, the chelation process increases the delocalization of the π-electrons over the whole chelate ring, which results in an increase in the lipophilicity of the metal complexes. Consequently, the metal complexes can easily penetrate into the lipid membranes and block the metal binding sites of enzymes of the microorganisms [27-30]. These metal complexes also affect the respiration process of the cell and thus block the synthesis of proteins, which restrict further growth of the organism.

Table 6: Results of antimicrobial activity of synthesized compounds

Compounds	Zone of Inhibition in mm					
	Gm +ve bacteria		Gm -ve bacteria		Antifungal activity	
	S. Aureus	S. Pyogenes	E. Coli	S. Typhi	C. Albicans	T. Rubrum
Ligand (L)	06	08	08	09	08	10
$[Fe(L)_2 (H_2O)_2]$	08	08	08	09	08	09
$[Co(L)_2]$	10	09	11	10	11	10
$[Ni(L)_2(H_2O)_2]$	14	15	14	15	18	20
$[Cu(L)_2$	18	17	18	14	20	18
Cefotaxime	-	-	**24**	**22**	**-**	-
Azithromycin	**22**	**24**		-	**-**	-
Clotrimazole	-	-	-	-	**12**	**14**

Figure-: Selected images of antimicrobial activity of ligands L its metal complexes.

IV.CONCLUSION

The study of the reaction between the transition metal complexes (**Fe(III), Co(II), Ni(II), Cu(II), And Zn(II))** and the derived Schiff base indicates its high stability. This encourages the synthesis and careful investigation of the nature of bonding between the Schiff base and the transition metal cation of important biological role, using physicochemical method of analyses.

In the present work, **Fe(III), Co(II), Ni(II), Cu(II), And Zn(II)** complexes were prepared from 6,8-Dichloro-4-oxo-4H-chromene-3-carbaldehyde and 4- Methyl-1,2,3,-thiadiazole-5-carbohydrazide These Schiff base are characterized using various spectral techniques. IR spectra revealed coordination of Schiff base ligand with metal ion through azomethine nitrogen, carbonyl oxygen of chromone moiety and carbonyl oxygen of hydrazide moiety. The structural elucidation studies by various spectral techniques (IR, TGA and ^{1}H NMR) suggested the nature of ligand is tridentate and geometry of the metal complexes are octahedral. Thermogravimetric analysis studies demonstrate the stability of complexes as well as provided the number of coordinated water molecules.. Antimicrobial studies suggest that Schiff base and its complexes play a vital role in developing a new class of antibiotics.

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Design and Synthesis of 1, 3-Dipolar Cycloaddition Reaction by Using Huisgen's Approach and Their Antimicrobial Activity

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ABSTRACT
Synthesis of new 1, 2, 3 triazole some quinoline derivatives 3 and 4 using 1, 3-dipolar cycloaddition (click chemistry) reaction of 4-azidoquinoline with substituted alkynes (4) in the presence of Cu (I) catalyst has been achieved in very high yields. The some newly synthesized compounds were characterized by IR, NMR spectroscopy and evaluated for their antimicrobial activity. Among the synthesized compounds, the compounds 3c and 4d was found to be an excellent Compounds 3c have shown good antifungal activity as compared to standard drugs griseofluvin and compounds 4d have shown to be moderate antibacterial activity as compared to standard drugs Streptomycin.

Keywords: Click chemistry, Quinoline, Antibacterial and Antifungal etc.

I. INTRODUCTION

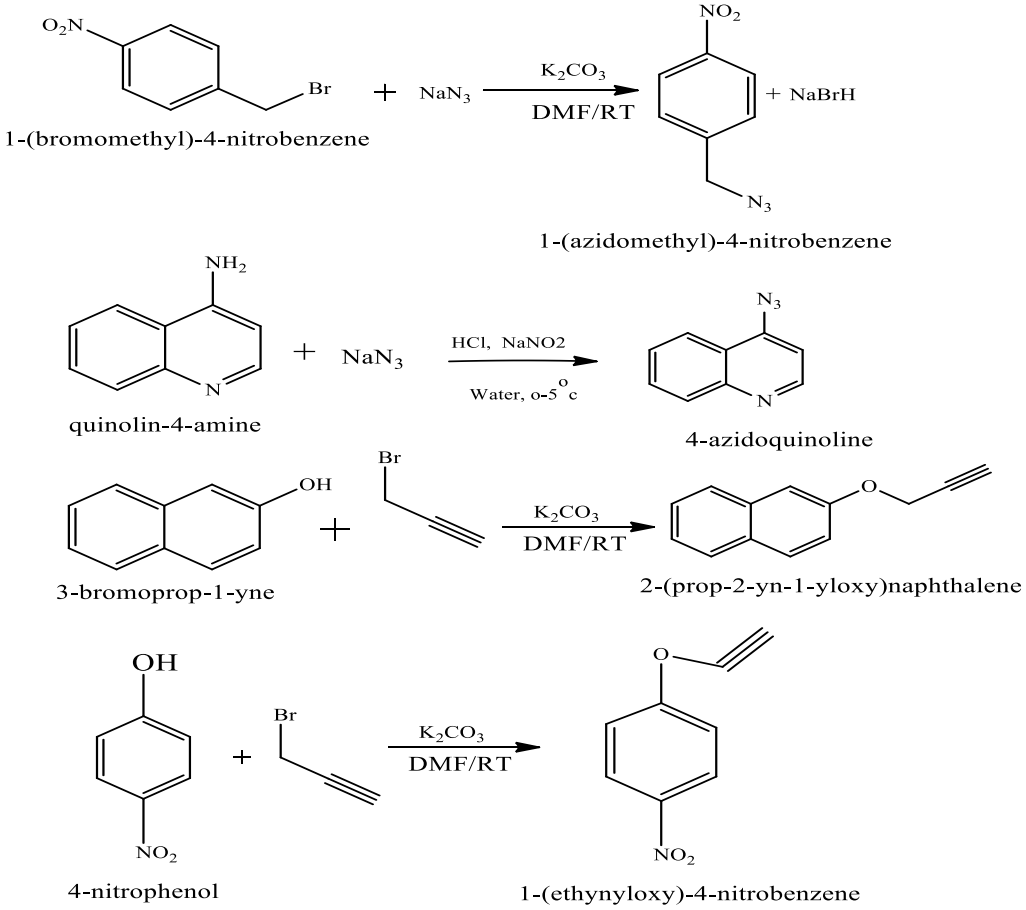
Click chemistry represents an ideal set of near perfect reactions (Nordell, P. *et, al.;* 2007 [1]). In recent years, click chemistry has emerged as a fast and powerful approach to the synthesis of novel compounds with desired properties. Among the various click reactions capable of producing wide range of functional organic molecules, the copper catalyzed [3+2] azide and alkyne cycloaddition (CuAAC) resulting in the formation of 1,2,3-triazoles has drawn considerable attention as an archetypical example of click chemistry (Barraja, p. *et al.*; 2006 [2]). [CuAAC] is particularly useful for the synthesis of a variety of molecules ranging from enzyme inhibitors to molecular materials [3].

1, 2, 3-Triazoles are important class of target molecules due to their interesting biological properties such as anti-allergic[4] anti- bacterial [5] and anti-HIV activity[6] some of these classes of drug molecules are now available in the market or in the final stage of clinical trials [7] additionally, due to the resemblance in physiochemical properties such as planarity, dipole moment, Ca distance and H-bond acceptor properties (of the lone pairs in nitrogen atoms), 1,2,3-triazoles are considered as peptide bond isosteres (Caturla, *et, al.*; 2003 [8]). In addition to this, 1,2,3-triazole ring is highly chemically stable under hydrolytic as well as reductive and oxidative conditions. Consequently, amide-to-triazole substitutions are now common in drug-like molecules whose amide bonds are known to be crucial for biological activity [9]. A recent trend in this field is the synthesis.

Quinolines have been the interest of research for many years as a large number of natural products contain these heterocyclic and they are found in numerous commercial products including pharmaceuticals, fragrances and dyes (Levy. S. et, al.;1994 [10]). Quinoline alkaloids such as quinine, chloroquine, mefloquine and amodiaquine are used as efficient drugs for the treatment of malaria (Wenekebach, *et,al.*;1923 [11]). The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmaceutical properties.

II. METHODOLOGY

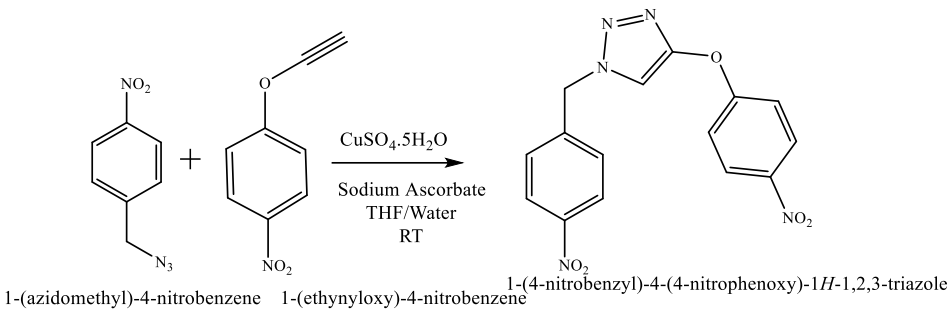
Azide & Alkyne Reaction



General procedure of 1, 2, 3-triazole derivatives

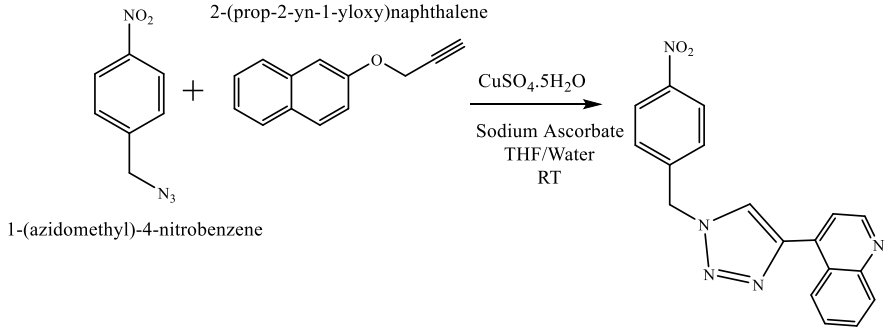
The azide compounds (2) (1.0 equiv) and substituted alkynes (2) (1.1 equiv) were dissolved in THF/H2O (9:1). To this solution CuSO4.5H2O (0.05 equiv) and sodium ascorbate (0.40 equiv) were added. The reaction mixture was stirred for 1-2 h at room temperature. After completion of reaction, reaction mixture was poured on crushed ice. The solid obtained was extracted with EtOAc (2*50 ml). The organic extract was washed with water and brine The organic extract was washed with water and sodium sulphate. The solvent was removed under sunlight to afford Crude product, which was purified by crystallization using ethanol to obtain pure products (4).

Click Reaction



1-(azidomethyl)-4-nitrobenzene 1-(ethynyloxy)-4-nitrobenzene 1-(4-nitrobenzyl)-4-(4-nitrophenoxy)-1*H*-1,2,3-triazole

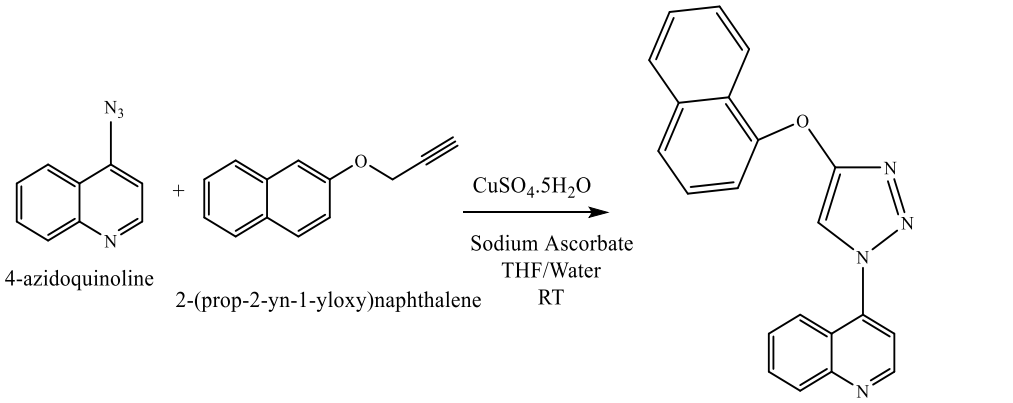
2-(prop-2-yn-1-yloxy)naphthalene



1-(azidomethyl)-4-nitrobenzene

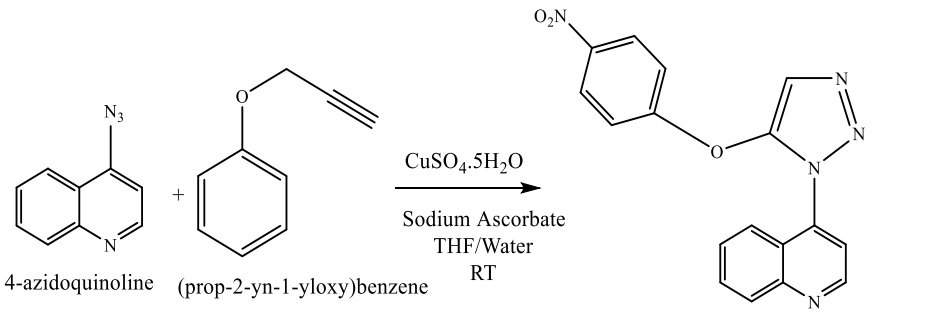
4-(1-(4-nitrobenzyl)-1*H*-1,2,3-triazol-4-yl)quinoline

Click Reaction



4-azidoquinoline 2-(prop-2-yn-1-yloxy)naphthalene

4-(4-(naphthalen-1-yloxy)-1*H*-1,2,3-triazol-1-yl)quinoline

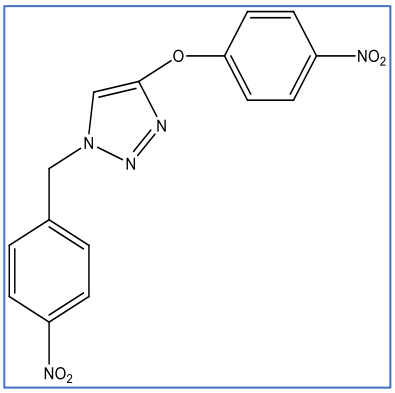


4-azidoquinoline (prop-2-yn-1-yloxy)benzene

4-(5-(4-nitrophenoxy)-1*H*-1,2,3-triazol-1-yl)quinoline

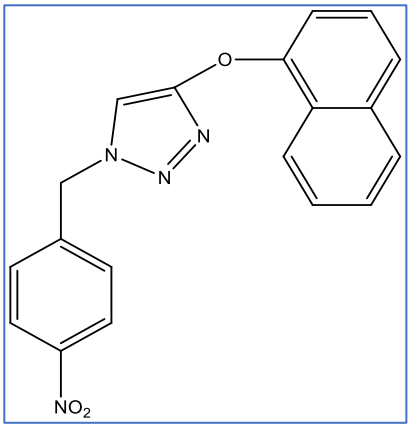
III.RESULT & DISCUSSION

1. 1-(4-nitrobenzyl)-4-(4-nitrophenoxy)-1H-1, 2, 3-triazole.(1a)



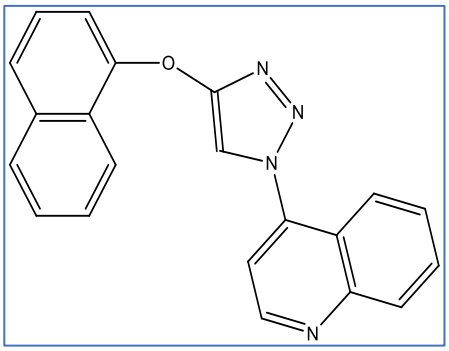
Yield: 85%, MF/FWt: $C_{15}H_{11}N_5O_5$ /341.28, MP: 130-132°C, IR (cm-1): 2981, 2889, 1595, 1335, 1107, 707:1H NMR (300 MHz, CDCl3, δ ppm): 8.14 (d, 2H J=3Hz, Ar-H), 7.32 (8, 1H, Ar-H), 7.48 (d, 2H, J=9Hz, Ar-H), 7.63(s, 1H, triazoles), 5.48 (s, 2H, CH2-).

2. 4-(naphtalen-1-yloxy)-1-4-nitrobenzyl)1H-1,2,3-triazole(2b)



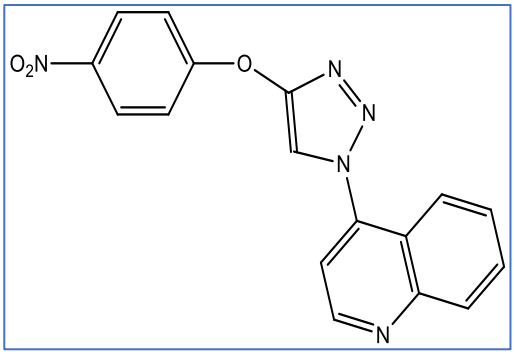
Yield: 80%, MF/FWt:$C_{19}H_{14}N_4O_3$ /346.34, MP: 110-113°C,:1H NMR (300 MHz, CDCl3, δ ppm): 8.14 (d, 1H J=3Hz, Ar-H,Nitrobenzene), 7.49 (d,1H, Ar-H), 6.65 (d, 1H, J=9Hz, Ar-H),8.22(d,1H,Ar-H),8.09(d,1H, Naphthalene),7.40(t,1H,Naphthalene), 7.61(t,1H,Naphthalene), 7.58(t,1H,Naphthalene), 9.05(s, 1H, triazoles), 5.48 (s, 2H, CH2-).

3. 4-(4-naphthalen-1-yl) 1H-1,2,3-triazol-1-yl) (3c)



Yield: 82%, MF/FWt: C21H14N4O/338.36, MP: 111-113°C,:1H NMR (300 MHz, DMSO, δ ppm): 8.83 (d, 1H J=3Hz, Ar-H,), 7.78(t,1H, Ar-H), 7.60(t, 1H, J=9Hz, Ar-H), 8.22(d,1H,Ar-H),7.46(d,1H,Quinoline), 7.61(t,1H,Naphthalene), 7.61(t,1H,Naphthalene), 7.58(t,1H,Naphthalene),8.09(d,1H,Naphtalene),7.72(d,1H, Naphthalene),7.40(t,1H, Naphthalene),6.65(d,1H,Naphtalene), 8.08(s, 1H, triazoles).

4. 4-(4-(4-nitrophenoxy)-1H-1, 2, 3-triazol-1-yl) quinolone (4d)



Yield: 84%, MF/FWt: C17H11N5O3 /333.30, MP: 122-123°C,:1H NMR (300 MHz, DMSO, δ ppm): 8.09 (dd, 2H,Ar-H,), 7.48(dd,2H,Ar-H), 7.46(d,1H,Ar-H), 8.83(d,1H,Ar-H,quinoline),7.98(d,1H,Quinoline),7.78(t,1H,Quinoline), 7.61(t,1H, Quinoline), 8.22(t,1H, Quinoline),8.08(s, 1H, triazoles).

IV.ANTIMICROBIAL ACTIVITY

All the synthesized compounds (1a-4d) were evaluated for antimicrobial activity against various bacterial strains such as Bacillus subtilis, Escherichia coli and Serretia macescens and fungal strains such as Aspergillus niger. Antimicrobial activity was determined by measuring the diameter of inhibition zone. Antibacterial activity of each compound was compared with Streptomycin as standard drug and the results are summarized in Table. Compounds **1a & 3c** showed potent antibacterial activity against all the selected strains as compared to the standard drug streptomycin and other compounds showed moderate activity. Antifungal activity of each compound was tested against Aspergillus Niger and compared with the standard Grisefulvin .The results are summarized in Table. Compounds **3c** shown significant zone of inhibition Against Aspergillus niger as compared to the standard Grisefulvin .Other compounds interpreted moderate antifungal activity.

Table No.1: Antimicrobial activities of 1, 2, 3-triazole derivatives (1a-4d)

Entry	Bacillus subtilis	Escherichia coli	Serretia macescens	Aspergillus niger
	ZI [a] (MIC)[b]	ZI[a] (MIC)[b]	ZI [a] (MIC)[b]	ZI [a] (MIC)[b]
1a	**18(30)**	10(25)	9(30)	10(30)
2b	13(25)	10(25)	-	12(25)
3c	10(20)	**20(25)**	10(30)	**14(20)**
4d	-	11(25)	15(25)	10(30)
Streptomycin	15(05)	16(05)	15(05)	-
Griseofulvin	-	-	-	15.5(05)

Where

ZI[a]: Zone of Inhibition

MIC[b]: Minimum inhibitory concentration

Antimicrobial Result Photos

Comp.3c Antibacterial Potent Activity

V. CONCLUSION

We concluded that the a series of 1,2,3-triazole heterocyclic compounds were successfully designed and synthesized by using click chemistry , described by Husign 1,3-dipolar cycloaddition that is green chemistry approach because of high yield , high purity , stereospecific , simple to perform and can be conducted in easily removable benign or green solvents which were confirmed by spectral analysis.

The importance of such work lies in the possibility that the new compounds might be more efficacious drugs against bacteria, fungi, activity which could be helpful in designing more potent antibacterial agents for therapeutic use.

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An Efficient Synthesis of 2,4,5-Trisubstituted Imidazole Derivatives by Using Taurine as an Efficient Organocatalyst

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ABSTRACT

In this study Taurine is utilized as an effective and environmentally friendly organocatalyst for one-pot multi component synthesis of 2,4,5-Triaryl-1H-imidazoles in an aqueous ethanol medium. The protocol is characterized by its cost-effectiveness, accessibility, safety of catalyst, environmentally friendly nature, rapid reaction times and higher yields.

Keywords: Imidazole, Multicomponent, Taurine.

I. INTRODUCTION

Multicomponent reactions (MCRs) emphasizes the ideal technique in creating adducts with diverse functional groups, which can subsequently undergo different cyclization processes to yield a varied array of products. The increasing focus on diversity-oriented synthesis has led to significant advancements in the design and application of MCRs for generating diverse heterocyclic scaffolds [1-4]. There is a growing trend in chemistry towards "green" or environmentally friendly processes, with focus on the use of efficient catalysts and other materials in organic transformations. Green chemistry also highlights the preference for using reaction medium free from the issues related to conventional volatile solvents in this context the suitability of water as a solvent from the perspective of green chemistry [5-7]. Taurine (2-aminoethanesulfonic acid) is a semi-essential amino acid found in the bodies of many living organisms, including humans. It is noted that taurine is one of the components of bile and is utilized to encourage the Knoevenagel reaction between malononitrile and aldehydes as a green bio-organic catalyst. The term "taurine" originates from its initial separation from ox bile, known as Bos Taurus [6-9]. Taurine can be used as an inexpensive, readily accessible commercial catalyst with several benefits, including low cost, safe and environmental friendliness. [10].

The multicomponent synthesis of Triaryl-1H-imidazoles involved the use of diverse conditions, including ultrasonic irradiation [11] microwave-assisted techniques [12] and various catalysts and reagents such as UO2(NO3)2.6H2O [13] [EMIm][BH3CN] Ionic Liquid [14] Pumice@SO3H [12] silica lanthanum trifluoroacetate and trichloroacetate [15], TiO2 nano particle based hybrid nano catalyst [16], barium chloride dispersed on silica gel nanoparticles (BaCl2-nano SiO2) [17], sulfuric acid immobilized on silica [18], silica

chloride [19], mandelic acid [20], different magnetic nanoparticle [21], sodium oxalate in aqueous medium [22], barium sulfate nano-particles [23], acetic acid [24], ceric ammonium nitrate [25], Syzygium cumini seed [26] and nano- TiCl4.SiO2 [27]. Some of the developed methods contain drawbacks such as increased temperatures, poor yields, use of toxic solvents, extended reaction times, and high catalytic loading. Therefore developing a practical, moderate, and more widespread approach to address these shortcomings continues to be a challenge for the multi componenet synthesis of 2,4,5-triarylsubstituted imidazoles.

II. METHODS AND MATERIAL

All of the chemicals and solvents used for present study were used of AR grade and used without further purification. The melting points were determined in open capillary tubes with no corrections. Formation of the compounds was checked by thin-layer chromatography (TLC) on aluminum sheets with silica gel 60 F254 plates 0.5 mm thick. Infrared (FT-IR) spectra were recorded on a Shimadzu FT-IR-8400 instrument using the KBr pellet method. NMR were recorded in CDCl3 solvent on a Bruker Avance Neo 500-MHz spectrometer.

Typical Procedure for the synthesis of 2,4,5-Triaryl-1H-imidazoles derivatives (4a-h)

In a 20 mL round bottom flask (RBF) a mixture of benzil (1.0 mmol), Aromatic aldehyde (1.0 mmol), ammonium acetate (4.0 mmol) and (20 mol%) of taurine in 5mL of EtOH : H_2O (1:1) was refluxed. With the use of TLC, the reaction's progress was tracked. After completion of the reaction, the reaction mixture was cooled to room temperature. Subsequently, ice water was incorporated and then stirred for three minutes. Afterward, the mixture underwent filtration and was subsequently washed with a combination of water and ethanol. Finally, it was subjected to the drying process followed by recrytallization by ethanol to afford the final products.

Spectra data

2-(4-Methoxy-phenyl)-4,5-diphenyl-1H-imidazole (4a)

M.p. 220-225 ^{o}C; **^{1}HNMR** (500MHz-$CDCl_3$) spectrum recorded at δ 3.80(s, 3H,OCH_3, Aliphatic hydrogen), 6.90 (d, 2H, J= 7.5Hz, Ar-H), 7.80 (d, 2 H, J= 7.4Hz, Ar-H), 7.24-7.50 (m, 10H, Ar-H), **^{13}C NMR**(500MHz-$CDCl_3$) spectrum recorded at 55.33, 114.27, 122.57, 126.89, 127.34, 127.84, 128.54, 132.79, 146.15, 160.20. **;Mass, m/z:** 327.15 [M+1].

III.RESULTS AND DISCUSSION

A green, environmentally friendly method was devised for producing 2,4,5-triaryl-1H-imidazole derivatives (4a–h). This involved reacting benzil (1.0 mmol), aromatic aldehydes (1.0 mmol), and ammonium acetate (4.0 mmol) using Ethanol : H_2O (1:1) as the solvent reaction medium, along with taurine (2-aminoethanesulfonic acid) as a green bio-organic catalyst at 20 mol% under reflux conditions. The approach was efficient, straightforward, and convenient.

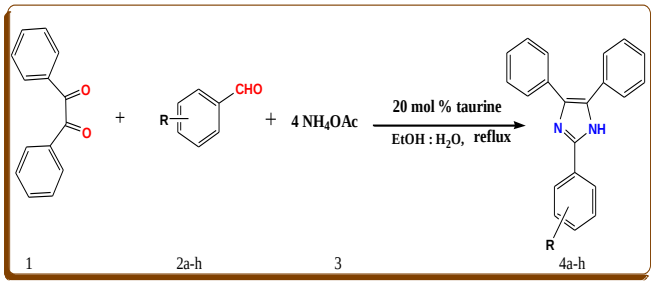

Figure: 1. Synthesis of 2,4,5-Triaryl-1*H*-imidazoles derivatives under different conditions

To establish the standard reaction conditions for the synthesis of 2,4,5-Triaryl-1H-imidazole, the reaction involving benzil, p-methoxy benzaldehyde, and ammonium acetate was chosen as a model reaction.

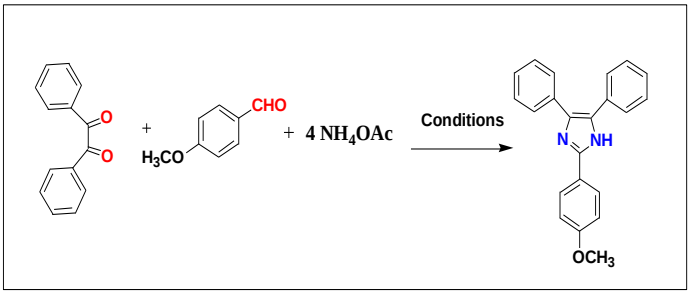

Figure 2. Optimization of reaction conditions

In our investigation, we explored the impact of solvents on the cyclization process by using various solvent ratios, such as acetonitrile, ethanol: water, dimethylformamide, methanol, and dichloromethane, in the presence of taurine (20 mol%) as a catalyst under reflux conditions (Table 1). Notably, we observed an 80% yield of the product (4a) within three hours when using methanol under reflux (Table 1, entry 1). However, the use of tetrahydrofuran as the solvent resulted in a lower yield of the product after three and a half hours (Table 1, entry 3). Additionally, the use of dimethylformamide, acetonitrile, and dichloromethane led to yields of 72%, 79%, and 76%, respectively (Table 1, entries 2, 4, and 5). Furthermore, conducting the reaction in ethanol yielded a favorable outcome for the product within three hours (Table 1, entry 6). Interestingly, when mixing ethanol with water in a 1:1 ratio, we observed an increase in the product yield (Table 1, entry 7, 90%). However, doubling the ratio of water to ethanol resulted in a decreased yield of the product (Table 1, entry 8), leading us to conclude that the 1:1 ratio of water to ethanol produced the best results (Table 1, entry 7)

TABLE I THE EFFECT OF THE SOLVENT ON THE SYNTHESIS OF 2,4,5-TRIARYL-1H-IMIDAZOLES

Entry	Solvent	Condition	Time (h)	Yield (%)[a]
1	Methanol	reflux	3	80
2	DMF	reflux	4	72
3	THF	reflux	3.5	48
4	Acetonitrile	reflux	3.5	79
5	DCM	reflux	3	76
6	Ethanol	reflux	3	88
7	Ethanol:Water(1:1)	reflux	3	**90**
8	Ethanol:Water(1:2)	reflux	3	87

[a]Isoated Yield

TABLE II EFFECT OF CATALYST LOADING FOR THE SYNTHESIS OF 4A

Entry	Taurine catalyst loading (mol%)	Temperature (^{0}C)	Time (hr)	Yield [b] (%)
1	5	reflux	6	57
2	10	reflux	4	72
3	15	reflux	3.5	90
4	**20**	reflux	3	**90**
5	25	reflux	3	90

[a]Isoated Yield

Similar investigation was conducted to establish the optimal volume of taurine (2-aminoethane sulfonic acid) to employ as a catalyst for product formation. For this conversion, it was found that 20 mol % of the catalyst was enough to produce the best yield with the shortest reaction time. Thus, we ultimately chose to employ this amount (20 mol%) of catalyst for best results (Table 2, entry 4).

Following the optimization of reaction conditions, we examined the generality of the newly developed taurine-catalyzed protocol in aqueous ethanol for the synthesis of 2,4,5-Triaryl-1H-imidazoles. This examination involved the use of different substituted aldehydes to produce the corresponding products (4a-h). Remarkably, it was found that all the aromatic aldehydes, regardless of the nature of the substituents, yielded the corresponding products in good to excellent yields (Table 3, entries 1-8)

TABLE 3 SYNTHESIS OF 2,4,5-TRIARYL-1 *H*-IMIDAZOLES (4A-H)

Entry	Product	R	Reaction time (h)	Temp. (ºC)	Melting point (mp, ºC)	Yield %[a]
1	4a	4-CH_3O	3	reflux	228-230	90
2	4b	4-CH3	4	reflux	226-229	89
3	4c	4-Cl	3.5	reflux	266-278	90
4	4d	2-Cl	4	reflux	196-198	79
5	4e	2-OH	5	reflux	259-262	77
6	4f	4-NO_2	4.5	reflux	306-308	83
7	4g	H	2.5	reflux	268-271	85
8	4h	4-OH	3	reflux	260-263	78

[a] Isolated Yields

IV. CONCLUSION

In conclusion, the one-pot multicomponent synthesis of 2,4,5-Triaryl-1H-imidazole derivatives (4a–h) has been successfully achieved using taurine (2-aminoethanesulfonic acid) as a stable, green organic catalyst in environmentally friendly conditions, utilizing an aqueous ethanol medium. This study presents several significant advantages over reported protocols, including the avoidance of dangerous organic solvents, the metal-free nature of the catalyst, short reaction times, high yields, benign reaction conditions, and easy workup.

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Synthesis of Alkoxy Derivatives of Benzothiazole and Their Screening Against MDR E. Colie

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ABSTRACT

A new series of benzothiazole compounds were synthesized and screened against multi drug resistant bacteria E. Colie. the starting molecule ethyl 2-(3-formyl-4-hydroxyphenyl)-4-methylthiazole-5-carboxylate was reacted with 2-amino thiophenol in presence acetic acid resulting in the formation of ethyl 2-(3-(benzo[d]thiazol-2-yl)-4-hydroxyphenyl)-4-methylthiazole-5-carboxylate. The obtained compound was further reacted with alkyl halides to get ethyl 2-(3-(benzo[d]thiazol-2-yl)-4-(alkyloxy)phenyl)-4-methylthiazole-5-carboxylate. The synthesized compounds were screened against MDR E. Colie and compare with Tetracycline as standard drug. The compound 11h was found to be moderately active at 25µL concentration while at 50 and 100µL concentration showed better results as compared to Tetracycline.

Keywords: Synthesis, benzothiazole, MDR, E. Colie, antibacterial.

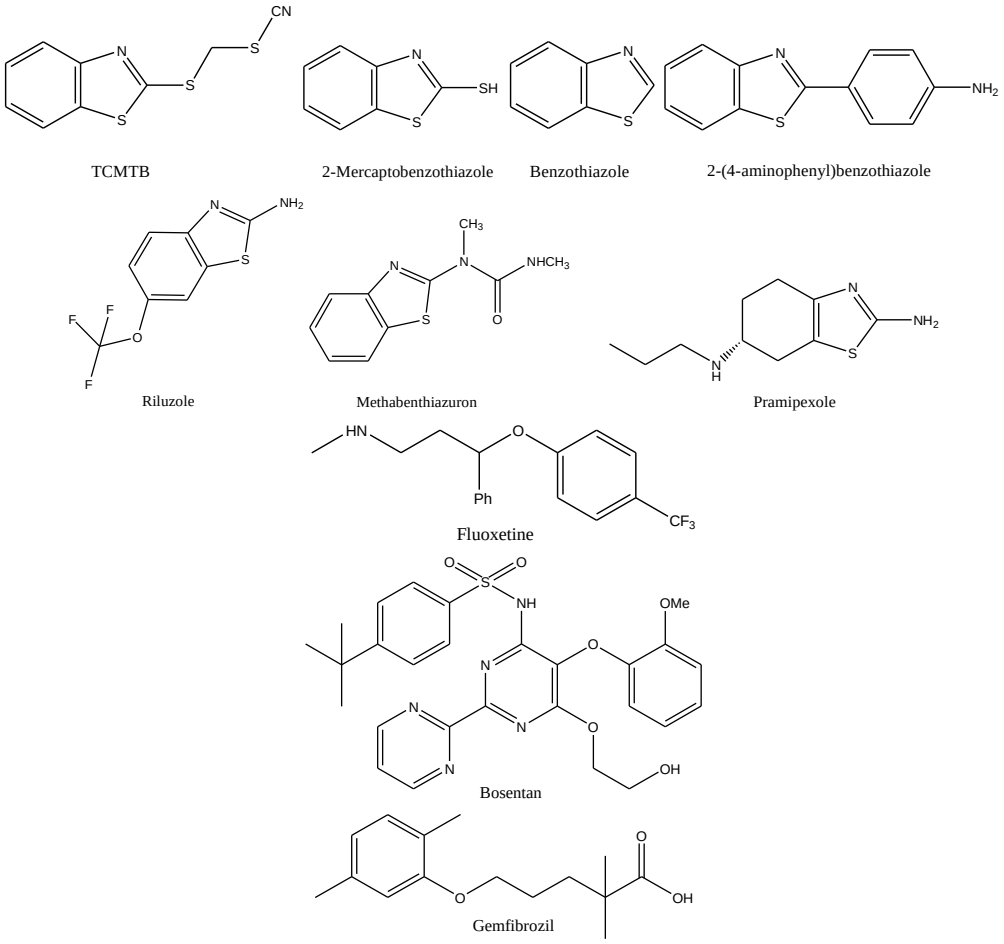
I. INTRODUCTION

Benzothiazole is an important core in the heterocyclic compounds. Benzothiazoles are the main core in not only in many marketed drugs but also found many other applications [1,2] such as TCMTB (antifungal), Benzothiazole (Antifungal), 2-(4-aminophenyl) benzothiazole (Anti-tumor), Riluzole (Anticonvulsant), Pramipexole (dopamine agonist), 2-Mercaptobenzothiazole (for acceleration of rubber vulcanization), Methabenthiazuron (Herbicide).

Along with these hypoglycemic[3] anticonvulsant [4], anticancer, [5] antimalarial, [6] antitubercular, [7] anti-inflammatory, [8] anti-helminthic,[9] anti-fungal activities [10] are also possessed by benzothiazole molecules.[2]

The phenyl ethers are also found to be biologically active. The compounds containing phenyl ether linkages are reported effective and currently are approved for treatment. e.g. a) For Neurological Disorder: Iloperidone, [11] Fluoxetine, [12] Atomoxetine, [13] b) For Viral Treatment: Lopinavir, [14] Doravirine [15] Etravirine [16] c) For Cardiac Treatment: Carvedilol,[17] Bosentan, [18] Ranolazine, [19] Mexiletine [20] d) In Pain Treatment: Nimesulide [21] e) For Microbial Treatment: Penicillin V [22] Pheneticillin, [23] Propicillin [24] e) For Cholesterol Treatment: Etofibrate, [25]

Gemfibrozil [26] f) For Blood Pressure Treatment: Bumetanide, [27] Piretanide [28] g) For Leukemia Treatment: Zanubrutinib, [29] Ibrutinib [30], etc. [31]



On considering the biological activities possessed by benzothiazole and phenyl ether moieties, we decided to synthesis the molecules containing both moieties and screened for antimicrobial activity.

II. RESULTS AND DISCUSSION

There are many bacteria which are harmful for humans. Among these E. Colie is common bacteria. Due to the excessive use of antibiotics, E. Coli is found to become resistant against many antibiotics. [32] Recent studies show that beta-lactam drugs are ineffective for the treatment of MDR E. Coli. Carbapenum is the only effective drug currently present to which E. Coli has 2% of drug resistance.[33] The infection can arise because of contaminated unpasteurized milk products, contaminated water, and fresh vegetables. The person infected by such pathogen shows typical symptoms like diarrhea, abdominal cramping, and hemorrhagic colitis. It is the main pathogen that causes intestinal and other infections such as Gram-negative pneumonia, mastitis, meningitis, and urinary tract infection. Currently, we have no treatment for MDR E. Coli other than supportive care.[34] The alkoxy derivatives of benzothiazole were screened against multidrug-resistant Escherichia Coli bacteria strain. These compounds were screened by the disc diffusion method. E. Coli bacteria were cultured over nutrient agar media. Inoculums suspension (100 CFU / µL) was prepared from a microorganism in broth media, nutrient broth inoculated with bacterial species was incubated for 24 hr at 37 °C. Sterile filter paper disks (4 mm in diameter) were impregnated with 10 µL, 25µl, 50 µl and 100 µl (stock concentration 10 µg/ml) of each

compound. The disks were allowed to dry at room temperature in a sterile airflow laminar chamber for one hour, and then they were placed in the center of fresh nutrient agar plates previously seeded with 100 µL of inoculum suspension of each bacterial. The cultures were incubated either at 37 °C for 24-48 hr for bacteria. Each experiment was replicated three times. Antibiotics were used as a positive control; tetracyclin was used as an antibacterial standard. The antimicrobial activities were evaluated by measuring the inhibition zone diameters (millimeters) surrounding each disk.[35]

TABLE I ANTIBACTERIAL ACTIVITIES OF BENZOTHIAZOLE DERIVATIVES [10-11(A-H)] AGAINST MDR E. COLI

Compound	Zone of inhibition in mm for given concentration (µL)				
	0	10	25	50	100
10	0	--	--	--	--
11a	0	--	--	--	--
11b	0	4	8	12	29
11c	0	--	--	--	--
11d	0	--	--	--	--
11e	0	--	--	--	--
11f	0	--	--	--	--
11g	0	--	12	19	27
11h	0	--	--	--	--
Tetracycline	0	7.9	11.7	14.1	15.9

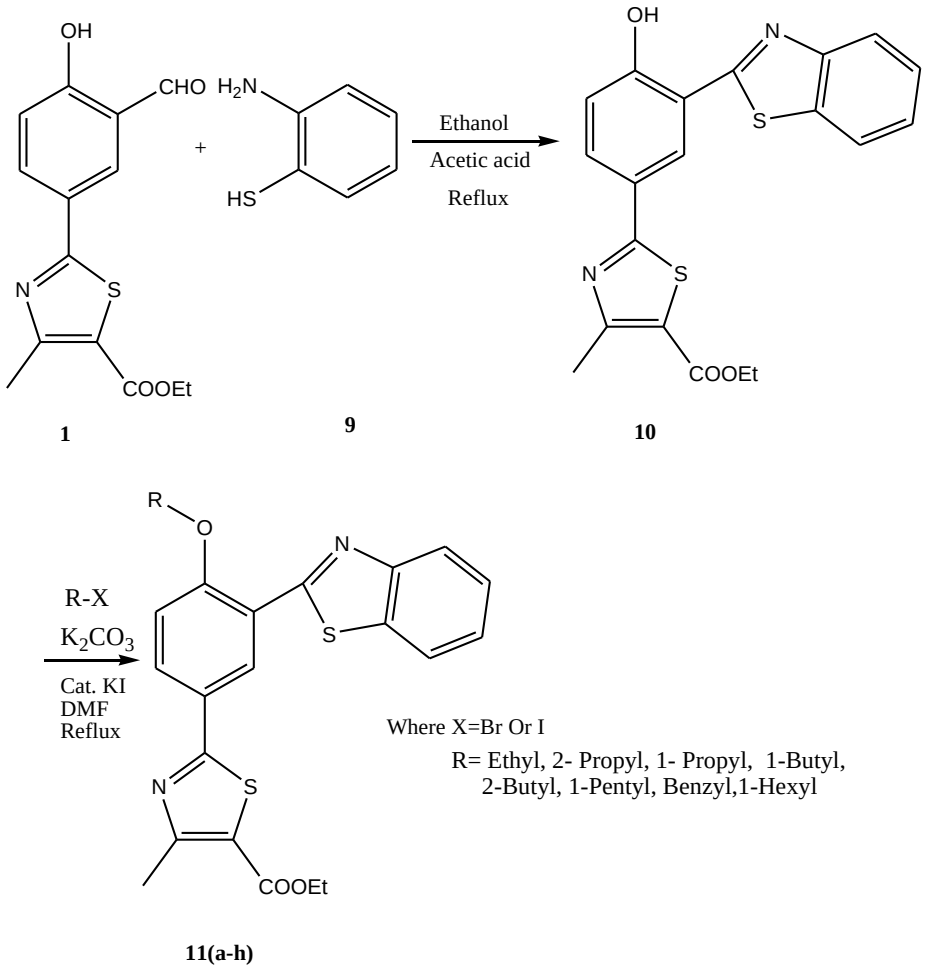
--: no inhibition

III.PRESENT WORK

In present work benzothiazoles were obtained from ethyl 2-(3-formyl4-hydroxyphenyl)-4-methylthiazole-5-carboxylate and 2-amino thiophenol using ethanol as solvent added with catalytic amount of acetic acid at reflux condition. Later compound's alkyl derivatives were obtained by treating with alkyl halides in DMF and potassium carbonate along with catalytic amount of KI at reflux conditions.

IV.EXPERIMENTAL

All the melting points were recorded by open capillary method and are uncorrected. IR spectra were recorded on Shimadzu IR Affinity 1 spectrophotometer in KBr disc. 1 H NMR were recorded on a BRUKER AVANCE II 400MHz spectrometer in $CDCl_3$/ DMSO d^6, chemical shifts are in ppm relative to TMS. Mass spectra were taken on a Macro mass spectrometer by electron spray method (Es). The structures of various synthesized compounds were assigned based on spectral studies and it has been reported in experimental protocols. The progress of the reaction was monitored on Alumina-coated TLC plates in ethyl acetate and n-hexane systems. Ethyl 2-(3-formyl-4-hydroxyphenyl)-4-methylthiazole-5-carboxylate (1) on condensation with 2-amino thiophenol (2) gave ethyl 2-(3- (benzo[d]thiazol-2-yl)-4-hydroxyphenyl)-4-methylthiazole-5-carboxylate (3) thus the compounds obtained 3 was then treated with various alkyl halide for alkylations of phenolic OH group using K_2CO_3 and DMF at reflux conditions.



Scheme 1: Synthesis of alkoxy bezothiazole derivatives

Synthesis of ethyl 2-(3-(benzo[d]thiazol-2-yl)-4-hydroxyphenyl)-4- methylthiazole-5-carboxylate (10): To a mixture of ethyl 2-(3-formyl-4-hydroxyphenyl)-4-methylthiazole5-carboxylate (2.91 gm, 0.01 mole) and 2-aminothiophenol (9) (1.25 gm, 0.01 mole) in 25 mL of ethanol 0.5 mL of acetic acid was added. The resulting mixture was stirred for 5 minutes at 60 ◦ C and then refluxed for 3 hours. The resulting reaction mixture was allowed to cooled and poured over 100 gms of crushed ice. The yellow solid obtained was filtered and recrystallized using ethanol. Yield: 3.39 gm (85 %); mp: 174-175 ◦ C; IR(KBr, cm^{-1}): 2978 (CH), 1703 (C=O ester), 1591, 1507 (C=C), 1278, 1099 (C-O); ^{1} H NMR (DMSO-d^6, δ ppm): 1.36 (t, 3H, CH_3), 2.72 (s, 3H, Ar-CH_3), 4.31 (q, 2H, CH_2), 7.17 (d, 1H, Ar-H), 7.43-7.57 (m, 2H, Ar-H), 7.94-7.97 (m, 1H, Ar-H), 8.06-8.10 (m, 2H, Ar-H), 8.74 (d, 1H, Ar-H), 12.20 (s, 1H, OH); M.W.= 396; (M+1) = 397

General Method of synthesis of ethyl 2-(3-(benzo[d]thiazol-2-yl)-4- (alkyloxy)phenyl)-4-methylthiazole-5-carboxylate 11(a-h): To the mixture of ethyl 2-(3-(benzo[d]thiazol-2-yl)-4-hydroxyphenyl)-4- methyl thiazole-5-carboxylate (0.396 gm, 0.001 mole) and alkyl halide (0.0011 mole) in 10mL of DMF, potassium carbonate (0.207 gm, 0.0015 mole), a pinch of potassium iodide was added and refluxed using water condenser for 6 hours with continuous stirring. Then the reaction mixture was allowed to cool and poured over crushed over 100 gms of crushed ice. The solid obtained was purified using column chromatography using a hexane-ethyl acetate (9: 1 v/v) system. The yield and melting points are summarized below.

TABLE III CHARACTERIZATION DATA OF ETHYL 2-(3-(BENZO[D]THIAZOL-2-YL)-4-(ALKYLOXY)PHENYL)-4-METHYLTHIAZOLE-5-CARBOXYLATE

Alkyl Halide	Comp.	R	Yield (%)	M. P. (0C)
Ethyl iodide	11a	Ethyl	82	124-125
iso Butyl bromide	11b	iso Butyl	67	49-50
1- Propyl bromide	11c	1- Propyl	62	52-53
1-Butyl bromide	11d	1-Butyl	57	47-49
2-Butyl bromide	11e	2-Butyl	63	43-44
1-Pentyl bromide	11f	1-Pentyl	60	42-43
1-Hexyl bromide	11g	1-Hexyl	54	39-40
Benzyl bromide	11h	Benzyl	64	87-88

Spectral analysis:

(11f): IR: (KBr, cm^{-1}) 2932 (CH), 1709 (C=O ester), 1607, 1518 (C=C), 1266, 1098 (C-O); 1H NMR (DMSO-d^6, δ ppm): 0.94 (t, 3H, CH_3), 1.31 (t, 3H, CH_3), 1.39-1.60 (m, 4H, , $2CH_2$), 1.96-2.01 (m, 2H, CH_2), 2.73 (s, 3H, Ar-CH_3), 4.29-4.40 (m, 4H, $2CH_2$), 7.43-7.60 (m, 3H, Ar-H), 8.12-8.19(m, 3H, Ar-H), 9.08 (d, 1H, Ar-H); M.W.= 466; (M+1) = 467

(11h): IR: (KBr, cm^{-1}) 2978 (CH), 1714 (C=O ester), 1607, 1512 (C=C), 1249, 1098 (C-O); 1H NMR (DMSO-d^6, δ ppm): 1.35 (t, 3H, CH_3), 2.73 (s, 3H, Ar-CH_3), 4.30 (q, 2H, CH_2), 5.52 (s, 2H, CH_2), 7.36-7.61 (m, 8H, Ar-H), 8.00-8.13 (m, 3H, Ar-H), 9.07 (d, 1H, Ar-H); M.W.= 486; (M+1) = 487

V. CONCLUSION

A series of alkoxy derivatives of benzothiazole were synthesized and screened for antimicrobial activity against multi-drug-resistant E. Colie bacteria and compared with Tetracycline. Compounds 11a, 11c, 11d, 11e, 11f, and 11h, showed no activity while compounds 11b and 11g showed activity. Compound 11b showed moderate activity as compared to the standard Tetracycline. The compound 11g showed comparable activity at lower concentrations while at higher concentrations showed better activity than Tetracycline.

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Surface Water Contamination of Heavy Metals Near the Industrial Area M.I.D.C. Roha, Maharashtra, India

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ABSTRACT
The surface water quality in the industrial area of Roha M.I.D.C. was examined; as this water is used for household and irrigation needs, it needs to be evaluated. The main causes of the increasing strain on the water resources in the region are rising urbanization and rapid industry. Thus, the current study was conducted to evaluate surface water contamination caused by heavy metals in light of this important issue. Water samples were taken every month from the river across the industrial area and from Nalas throughout the year. The heavy metals iron, copper, zinc, manganese, nickel, chromium, and cobalt were measured using an atomic absorption spectrophotometer (Perkin Elmer manufacture model No. Aanalyst 200). Most surface water samples have heavy metal concentrations below the maximum permissible level, according to a comparison of the samples with WHO (1993) and BIS (1991) standards.
Key words: Surface water, Heavy metal, Industrial waste

I. INTRODUCTION

Water is a vital component of life, required by all biotic organisms. Water is never totally chemically clean (Agale et al., 2013). Water contains few contaminants, but growing urbanisation, overcrowding, unregulated chemical usage, and contamination of water undermine the aquifer's equilibrium (Ramesh et al., 2014). Drinking water must be devoid of radioactive elements, living and non-living creatures, and excessive concentrations of minerals that may be hazardous to one's health. Some metals are found naturally in the body and are necessary for human health. Iron, for example, prevents anaemia, while zinc is a cofactor in over 100 enzyme reactions. They are referred to as trace metals due to their low concentration (Harte et al., 1991). In other circumstances, industrial effluents or waste percolate through the subsoil and into the water table, forming a polluted pool that impairs the natural water quality by changing its chemical composition. Irrigating with polluted water degrades soil quality and crop health.

II. MATERIAL AND METHODS

The Roha M.I.D.C. study site is located on the Arabian Sea, south of Mumbai, in the coastal Kokan region of Maharashtra. The chosen region's geographical coordinates are Latitude 18°6'12"N and Longitude 73°28'40"E, with an elevation above mean sea level (metres) of roughly 177.5 metres.

Water samples were obtained from M.I.D.C. (Maharashtra Industrial Development Corporation) facilities in Roha, Raigad District. The research area includes factories producing fertiliser, agrochemicals, acids, dyes, paints, machine tools, and resins. Fifteen water samples were taken, and metals were evaluated using the appropriate standards from APHA (1998) and Trivedy and Goel (1986) techniques. AR-grade chemicals and reagents are used. The reagents are prepared using double-distilled water.

III.RESULTS AND DISCUSSION

Over the course of the year (August 2018 to July 2019), the physicochemical properties of the water in Roha MIDC, Maharashtra, changed. The findings of the evaluation of the water quality are displayed in Table 1.

Table 1. Month-wise metals concentration of surface water around Roha MIDC, Maharashtra

Metal	Statistical	Data	August	Sept	Oct	Nov	Dec	Jan	Feb	March	April	May	June	July
Fe(ppm)	Mean	0.081	0.116	0.067	0.069	0.063	0.0742	0.077	0.089	0.102	0.07	0.057	0.11	0.074
	Min.	0.025	0.054	0.044	0.04	0.032	0.044	0.049	0.059	0.044	0.025	0.034	0.04	0.053
	Max.	0.648	0.648	0.081	0.081	0.109	0.119	0.122	0.132	0.162	0.103	0.11	0.398	0.089
Cu(ppm)	Mean	0.057	0.054	0.101	0.071	0.062	0.064	0.067	0.078	0.077	0.014	0.033	0.028	0.033
	Min.	0.025	BDL	BDL	0.032	BDL	0.032	0.032	0.032	0.028	BDL	BDL	BDL	BDL
	Max.	0.708	0.518	0.708	0.102	0.108	0.095	0.092	0.102	0.092	0.048	0.094	0.049	0.218
Zn(ppm)	Mean	0.048	0.045	0.046	0.051	0.055	0.049	0.048	0.048	0.046	0.049	0.045	0.044	0.048
	Min.	0.022	0.028	0.032	0.039	0.039	0.032	0.027	0.032	0.022	0.039	0.038	0.032	0.035
	Max.	0.089	0.073	0.058	0.061	0.083	0.077	0.089	0.072	0.083	0.06	0.077	0.061	0.069
Mn(ppm)	Mean	0.040	0.033	0.025	0.044	0.017	0.029	0.03	0.032	0.035	0.073	0.084	0.046	0.034
	Min.	0.010	0.021	0.017	0.011	0.01	0.013	0.015	0.017	0.021	0.06	0.079	0.019	0.022
	Max.	0.08	0.059	0.04	0.07	0.02	0.059	0.05	0.05	0.053	0.08	0.08	0.08	0.05

		9			9	5		6	9		2	9	7	9
Ni(ppm)	Mean	0.038	0.032	0.033	0.03	0.034	0.028	0.026	0.033	0.051	0.05	0.047	0.052	0.039
	Min.	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL
	Max.	0.348	0.073	0.059	0.059	0.054	0.049	0.049	0.049	0.348	0.08	0.082	0.086	0.07
Cr(ppm)	Mean	0.032	0.024	0.021	0.059	0.024	0.026	0.026	0.029	0.029	0.041	0.039	0.034	0.027
	Min.	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	0.019	0.02	BDL	BDL
	Max.	0.508	0.048	0.044	0.508	0.05	0.053	0.042	0.058	0.059	0.082	0.079	0.059	0.052
Co(ppm)	Mean	0.008	0.002	0.005	0.004	0.003	0.007	0.01	0.011	0.009	0.011	0.026	0.005	0.001
	Min.	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL	BDL
	Max.	0.072	0.003	0.013	0.007	0.006	0.049	0.049	0.04	0.014	0.038	0.072	0.019	0.004

Iron

The mean value of the iron concentration in surface water during the research period was 0.081 mg l^{-1}, and the concentration ranged from 0.025 to 0.648. Comparably, Al- Khuzaie et al. (2020) reported that the iron concentration ranged from 0.271 to 0.603 mg l^{-1}, while Nyandeo Gorakhe (2020) reported that the iron concentration in the Mula-Mutha river in Pune was 1.57 to 11.49 mg l^{-1}. Higher concentrations of iron in water were found during the monsoon and winter due to the leaching of industrial wastes during the rainy season and the naturally occurring occurrence of iron oxides in laterite soil (Thomas et al., 2011).

Copper

The alkalinity of the water affects the toxicity of copper to marine life; aquatic fauna is more sensitive to lower alkalinities (Train, 1979). According to the research, the copper concentration in surface water ranged from BDL to 0.708 mg L^{-1}, with a mean of 0.057 mg L^{-1}. Similarly, copper in Almuthana Province, Iraq, ranged from 0.0088ppm to 0.0716ppm (Hussain Ali Shaheed, 2019). Additionally, copper concentrations at all research stations BDL in Bijnor District, Uttar Pradesh, India, were recorded by Matta Gagan (2020).

Zinc

In the same way, the concentration of zinc in Mahi Estate in Gujarat, India, varied from 0.02 mg l^{-1} to 0.63 mg L^{-1} with a mean value of 0.170 mg l^{-1} during the summer months. The content of zinc in surface water ranged from 0.022 to 0.089 mg l^{-1}. In a similar vein, Pallavi Sharma (2020) discovered that the average concentration of zinc in the water of Brahmhaputra, Assam, ranged from 2 ppb to 270 ppb. According to Thomas et al. (2011), the concentration of zinc was higher in the summer and winter due to water depletion, which raised metal concentrations and the concentration impact, and lower during the monsoon season due to the dilution effect of rainwater.

Manganese

In surface water, manganese concentrations varied from 0.01 mg l^{-1} to 0.089 mg l^{-1}, with an average value of 0.040 mg l^{-1}. Recently, Mohana et al. (2020) conducted an analysis on Mn concentration and discovered that average values were 0.605 mg/l and 0.526 mg/l during pre-monsoon and post-monsoon seasons, respectively. According to the current investigation, manganese concentrations in water are higher in the summer and progressively decline before the winter season. In the natural world, manganese compounds are present as tiny particles in water and as a solid in soil. Usually, they are released as dust particles onto the ground. The use of fossil fuels and industrial processes raise airborne manganese concentrations. Chrome was stored as adsorbed ions due to human activities like industrial effluents, outdated plumbing, and household waste (Warmate, 2011); additionally, nearby industries like tanneries and chemical processing discharged their waste, and a significant amount of particular matter was found in the river (Mandol et al., 2011).

Nickel

The main applications for nickel are in the production of super alloys, nonferrous alloys, and stain-less steel, all of which are products of the steel industry. The mean content of nickel in surface water was 0.038 mg l^{-1}, with a range of BDL to 0.348 mg l^{-1}. The Ni concentration was found by Dnyandeo Gorakhe (2020) to be between 0.009 and 0.59 ppm. Due to the leaching effect of heavy metals and the presence of water-soluble salts, most water samples include concentrations of nickel in the water that are higher than what is safe to drink (BIS, 1991; WHO, 1984). (2013) Bharti et al. A low pH often promotes the concentration of soluble and exchangeable nickel (Parth et al., 2011).

Chromium

With a mean value of 0.032 mg l^{-1}, the variation in chromium in water varied from BDL to 0.508 mg l^{-1}. In a similar vein, Dnyandeo Gorakhe (2020) examined the metal concentration in Pune's Mula-Mutha River and found that it varied between 0.096 and 0.762 mg/l.

Cobalt

Over the course of a year, surface water cobalt concentrations varied from BDL to 0.072 mg l^{-1}, with a mean of 0.008 mg l^{-1}. Similarly, P. Mohana's research from 2020 shows that the average cobalt content was 0.011 ppm during the pre-monsoon and 0.008 ppm during the post-monsoon period.The range of cobalt in the Ganga River was reported by Akansha Patel (2021) to be 10.50 μg l^{-1} to 20.77 μg l^{-1}.

IV.CONCLUSION

The bulk of the water samples had heavy metal concentrations below the permitted level, whereas nickel concentrations were over the permissible limit in water, in accordance with BIS and WHO criteria, according to the analytical data. But this study emphasizes how crucial it is to regularly monitor water quality in order to identify pollution activity and promptly implement efficient management strategies to lower the intensity of pollution.

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A Review on Bioactivity and Catalytic Activity of Transition Metal Complexes

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ABSTRACT
Complexes exhibit a wide range and much attention in recent year due to unique biological activities including antifungal, antibacterial, antiviral, antitumor, and anticancer properties. Which have led to several reports being published on them? Numerous Schiff base complexes composed of metal ions exhibit high catalytic activity of some metals and were also utilised as catalysts in the polymerization and exhibit greater selectivity in various reactions, including oxidation, hydroxylation, aldol condensation and epoxidation. A number of Schiff base complexes have excellent heat and moisture stabilities, which made them valuable catalysts for high-temperature processes. Complexes are analysed with the help of conductivity measurements, magnetic susceptibility, UV-Vis, IR, thermal analysis, 1H- and 13C-NMR etc. In this review we are evaluate transition metals complexes of bioactivity, catalytic properties.
Keywords: Transition Metal Complexes, Bioactivity, catalytic activity etc.

I. INTRODUCTION

From the few years ago Schiff base complexes determine their use in both homogeneous and heterogeneous catalysis. The number of transition metal complexes is fascinating due to it discusses a grate luminosity of structural, Bio-physico chemical and catalytic properties[1]. Some of the transition metal complexes bioactivity has been investigate by molecular docking with DNA and various proteins, also to be involved in proliferation of viral diseases or progression of cancer[2]. A large variety of transition metal complexes and ligands possessing O, N and S atoms as a donor have been reported as structural and functional mimics of biological systems[3].We are reveals the on- going features of biological activities of metal complex such as anticancer, antifungal, antimalarial, antibacterial, antiproliferative, anti-inflammatory, and antipyretic. Apart from the biological activities of the metal complex it also shows excellent catalytic activity due to the thermal and moisture stabilities[4]. Our study focuses on the biological activities of protein binding, DNA binding, cytotoxicity, and antibacterial properties, and also examines molecular dynamics. The research field for these types of metal complexes is extensive and encompasses many interdisciplinary fields, including biology[5]. The interaction of DNA with metal complexes has been well studied and has led to development of new metal–based drugs and as

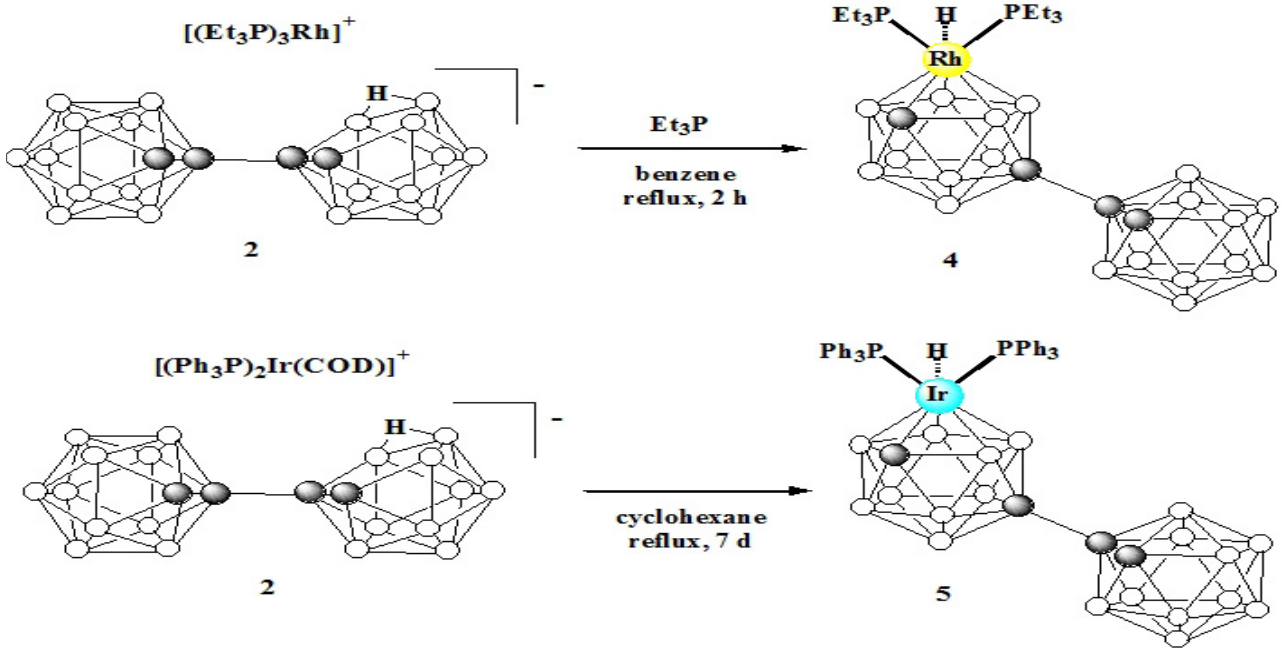
a DNA cleavage agents[6]. The heterocyclic Schiff base ligands and their metal complexes have been the subject of extensive investigation because of their wide use in biological field [7]. Schiff base complexes showed significant applications in reduction of ketones to alcohols[8]. Heterocyclic compounds possess impressive biological activity due to the strong aromaticity of the ring containing heteroatoms such as O, S, and N. Transition-metal complexes are widely used in the physical and biological sciences. They have essential roles in catalysis, synthesis, materials science, photo physics and bioinorganic chemistry. we thought it appropriate to devote one of the parts of this review to organic derivatives of 1, 10-bis (ortho-carborane) and this is various types of transition metal complexes with based ligands will be considered including those in which it acts as a deprotonated 6-ligand, or as a p-ligand formed by decapitation or reduction of the carborane cage as well as complexes based on phosphine derivatives of 1, 10-bis (ortho-carborane). There are two main types of metallacarborane based on icosahedral carboranes[9].

These structurally varied metal complexes have broad applications in the field of optoelectronics [10.] The Optoelectronic devices rely on light–matter interactions and electronic properties of matter to convert light into electrical signal or vice versa. There has always been a drive to improve light–matter interactions in semiconductor materials to make better optoelectronic devices. Solar cells[11] organic field effect transistors (OFETs) [12] and electrochromic devices.[13] an electrochromic device (ECD) controls optical properties such as optical transmission, absorption, reflectance and/or emittance in a continual but reversible manner on application of voltage (electrochromism). This property enables an ECD to be used for applications like smart glass, electrochromic mirrors, and electrochromic display devices. On the information of various researches paper the complexes of chromium (III) gives imminent antimicrobial properties.

II. RESULT AND DISCUSSION

I. B. Sivaev and Vladimir I. Bregadze[14]: The 1, 10 –bis (ortho-carborane) has capacity to undergo similar reactions to single-cage carboranes but with two important differences, specifically 1) reactivity at a single cage is significantly influenced by the presence of a bulky electron withdrawing substituent and 2) the reactions could occur at both cages and such reactivity could be either isolated or cooperative. They play important roles in the chemistry of transition metal complexes with 1, 10 –bis (ortho-carborane)-based ligands. In particular, the large size and strong electron withdrawing effect of ortho-carborane cage as substituent has strong impact on the stability of certain isomers of metalla -carboranes based on decapitated 1,10 –bis (ortho-carborane). All this makes the chemistry of 1, 10 -bis (ortho-carborane) and their transition metal complexes extremely exciting and one which attracts the growing interest of researchers. Since some of the transition metal complexes described from derivatives of 1, 10-bis (ortho-carborane), At first of all, it should be noted that organic chemistry of 1, 10-bis (ortho-carborane) is much less explored then its organometallic chemistry. Despite the fact that the CH groups of 1, 10-bis (ortho-carborane) are easily metalized, to using this way very less number of its organic derivatives were obtained. It was found that the carboranyl group in the 2,1,8-metallacarboranes 1,10-bis(ortho-carborane) 1 produces a racemic mixture of closo-nido-bis(carborane) enantiomers, and the second cage results in a mixture of racemic and meso nido-nido-bis(carborane) diasteromers 3 ([8-(10,20-closo-C2B10H11-10-)-2-(p-cymene)-2,1,8-closo-RuC2B9H10] (7), [8-(10,20-closo-C2B10H11-10-)-2-Cp-2,1,8-closo-CoC2B9H10] (9) and [8-(10,20-closo-C2B10H11-10-)-2-Cp*-2,1,8-closo-CoC2B9H10]. It should be noted that the presence two polyhedral with a different arrangement of metal and carbon atoms makes it difficult or impossible to establish the exact11B-11B structure of Metalla-carboranes

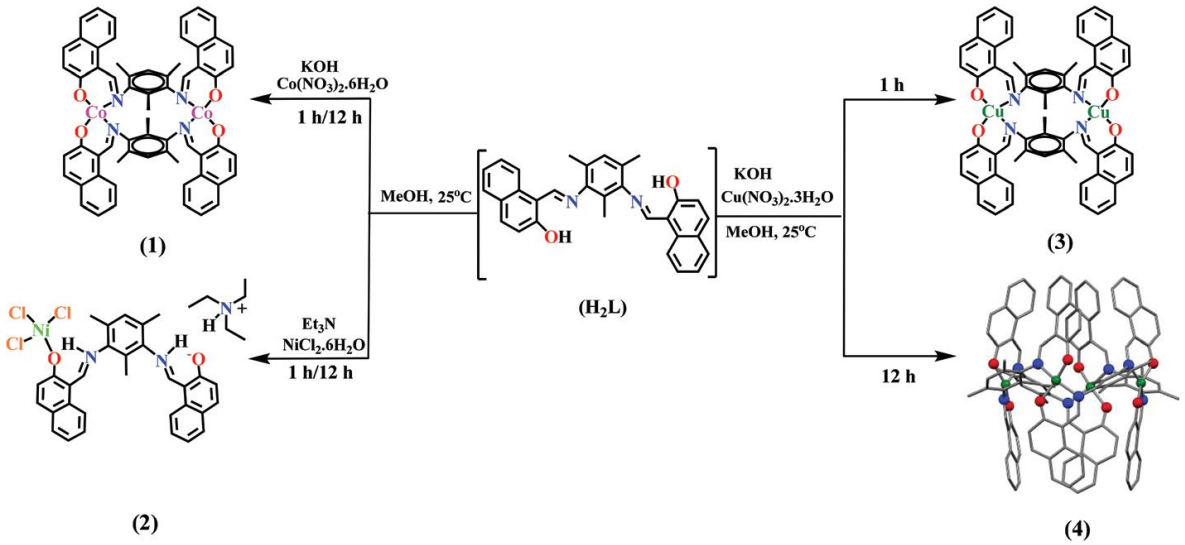
using COSY, NMR spectroscopy due to signal overlapping. Therefore, X-ray diffraction is critical for determination of molecular structures.



Enas S. Dafallah, et al[15]:

The complexes C_1, [VO_2(Sal-DAP)] and C_2, [VO_2(Sal-PA)] are characterized by conductivity measurements, magnetic susceptibility, UV-Vis, IR, thermal analysis, ^{1}H- and ^{13}C-NMR.The molecular structure of these complexes were confirmed using the DFT calculation to obtain the optimized geometries using the Gaussian09 program at the B3LYP/LANL2DZ level of theory. Synthesis, Characterization and DFT Calculations of Schiff base Vanadium (V) Complexes Derived from Salicyldehyde with 1, 2-Diaminopropane or 2-Picolylamine A Various vanadium complexes with ligands bearing oxygen and nitrogen donors have been reported as structural and functional mimics of biological systems. Vanadium complexes play an important role in biological as well as in catalytic processes[10]. In general, this leads to the presence of diasteromers generated by the additional chiral center at the vanadium site[16].

Anoop Kumar Saini et al[12]: they have designed and synthesized four new complexes with varying reaction conditions for their biological activity. The expressed various structure design that from monomeric to dimeric to tetrameric complexes by slightly neutering the reaction conditions. These complexes determine a strong interaction between complex 1 and 4 with BAS protein and DNA through Molecular docking and emission titration results are in agreement. The bioactivity of **1**–**3** have been investigated through molecular docking with DNA and various proteins, known to be involved in proliferation of viral diseases or progression of cancer. Complex **1** shows the best results, through strong binding affinity with NS2B/NS3 Protease (Dengue Virus) in terms of binding energy (11.21Kcal/mol.) and inhibition constant (6.02 nM). The experiment evidence for effective binding of **1**–**4** with Bovine Serum Albumin (BSA) protein and calf thymus DNA (CT–DNA) is in agreement with our molecular docking results. In addition, the cytotoxicity and antibacterial activity of **1**–**4** were examined and found to be compatible in biological system, with **4** showing highest antibacterial activity. The order of antibacterial activity towards Gram negative bacteria was found to be: 4 >1 > 3 > 2 determined. All four complexes were analysed by elemental analysis and UV/vis analysis, and their molecular structures were authenticated by single crystal X-ray studies.



Debdulal Maity[19]. **:** The transition metal complexes of ligands containing some hetero atoms, like oxygen, nitrogen and Sulfur donors show the carcinostatic, antitumour, antiviral, antifungal and antibacterial activities. Therefore, the research field involving these types of metal complexes is very extensive and includes a number of interdisciplinary areas such as bioinorganic chemistry, catalysis, magneto chemistry and photochemistry. Furthermore, with the developments in inorganic chemistry research people are having new ideas regarding versatile uses of metal complexes as therapeutic agents and as drugs for the treatment of several human diseases. Due to their potential applications in pharmaceuticals, antibacterial, antifungal, anticancer and anti-inflammatory actions synthesis of Schiff base metal complexes, particularly those of transition metal ions, with different molecular topologies and sets of donor atoms is becoming an emerging area of research[17].

Copper (II) complexes shows different properties like antifungal, antitumor, and antibacterial, leukaemia also the ligand containing thiosemicarbazide or semicarbizide group gives antimalarial property[18]. The ruthenium hexagonal coordination complexes shows antifungal property but it is toxic due to ligands are chelated form compare to free ligand complexes. With increases metal chelate toxicity will increase.

Fe (III) or Co (II) or Ni (II) or UO_2 (II) showed an excellent antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa and Staphylococcus pyogenes*. Fe (III), Cu (II), Zn (II) and UO_2 (II) complexes can inhibit the growth of *E. coli*. Thus, these complexes could be applied fairly to prevent some common diseases caused by *E. coli*. Again the growth of Gram-positive bacterial strains (*Staphylococcus pyogenes* and *P. aeruginosa*) could be inhibited by using Fe (III), Co (II), Cu (II), Zn (II) and UO_2 (II) Schiff base complexes. As well as the Platinum(II) complexes are more active antimicrobials than the precursor Schiff base ligands against one or more microorganisms as well as it shows antibacterial property against *E. coli*, *Bacillus subtilis*, *P. aeruginosa*, *Staphylococcus aureus* Containing with salicylaldehyde and o/p –furaldehyde Schiff base complexes. Co (III) complex of a new hybrid amine-imine-oxime ligand derived from the condensation reaction of diacetylmonoxime with benzidine was reported to have antibacterial activity against *Bacillius subtilis*. But it has no activity against *Staphylococcus aureus* or the Gram-negative bacteria *Escherichia coli* and *Enterobacter fecalis*[20].The cobalt (III) complexes of such ligands found to be important due to their antibacterial or antiviral activities. In 1998, Epstein and co-worker's reported a series of Co (III) complexes (**1d**) containing N, O donor ligands of the following type for their use in the treatment of blindness in industrial nations, known as epithelial herpetic keratitis[21].

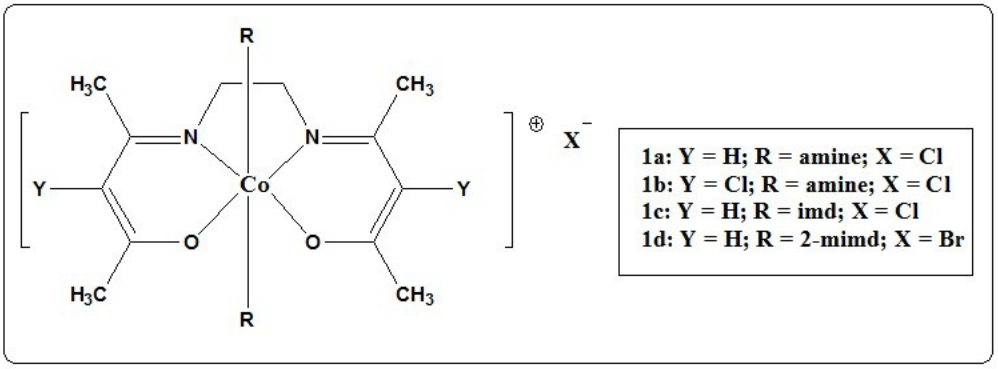
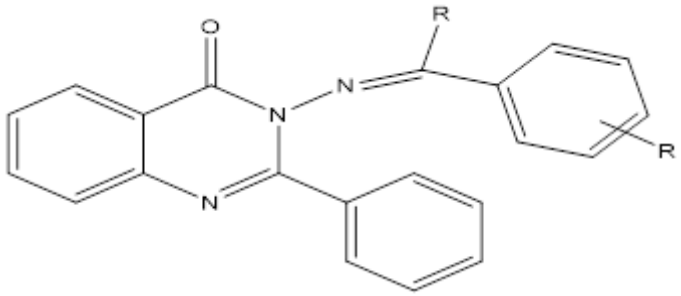


Fig. 1d.

These Co(III) Schiff base complexes have a capacity to inhibit Sp1, a DNA binding zinc finger protein and used in the treatment of human immunodeficiency virus type 1 (HIV-1)[22].

K.S. Kumar et al. synthesized a group of Schiff Base compound based on 3-(benzylideneamino)-2-phenylquinazoline-4(3H)-one and presented a detail report of anti-viral activity of these compounds against herpes simplex virus-1 (KOS), herpes simplex virus-2 (G), vaccinia virus, vesicular stomatitis virus, herpes simplex virus-1 TK- KOS ACVr, Para influenza-3 virus, reovirus-1, Sindbis virus, Coxsackie virus B4, Punta Toro virus, feline corona virus (FIPV), feline herpes virus, respiratory syncytial virus and influenza A H1N1 subtype, influenza A H3N2 subtype, influenza B[23].



Garcıa-Friaza et al.: Reported some Pd (II) and Pt (II) complexes with the following Schiff bases and studied anti-tumour activities, changing the substituents on the Pyridyl and toluene rings. In these two metals the Pd (II) complexes shows more activity than the Pt (II) complexes. All the complexes possess potential anti-cancer activities[24].

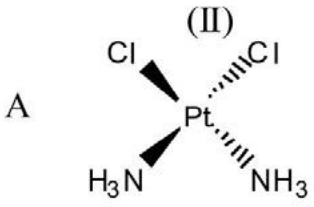
Mokhles M. Abd-Elzaher et al. The Schiff bases of Salicyldehyde with 2- amino-4- phenyl-5-methyl thiazole of some metal complexes were studied against different human tumour cell lines: breast cancer MCF-7, liver cancer HepG2, lung carcinoma A549 and colorectal cancer HCT116 in comparison with the activity of doxorubicin as a reference drug. The study showed that Zn (II) complex showed potent inhibition against human TRK in the four cell lines (HepG2, MCF7, A549 and HCT116) by the ratio 80, 70, 61 and 64% respectively as compared to the inhibition in the untreated cells[25].

Dongfang et al. 2008 Five ternary complexes of the rare earth ions with o-phenanthroline and Schiff base salicylaldehyde L-phenylalanine were used to test the anticancer effect of the complexes with K562 tumour cell. The complexes could inhibit K562 tumour cell's growth, generation, and induce apoptosis. This inhibition can be accelerated by increasing the dosage. They have reported that three metal complexes (Cu (II), Zn (II), and Cd (II)) of a ligand derived from 2-acetylpyridine and L-tryptophan have anticancer activities on MDA-MB-231 of breast cancer cells.

Zhang et al. 2012. (Where Ln (III) = La, Eu, Gd, Tb, Dy, Ho and Er) among the complexes of La and Eu are most potential in anti-tumor activity with percentage inhibition of 87.1 and 78.5%, respectively against leukaemia cells. Cu (II), Ni (II), Pd (II) and Pt (II) among the complexes Ni (II) have more efficient property against human breast cancer[26]. A series of Cu (II)-salicylidene-amino acid Schiff bases-Phen(Bipy.) ternary complexes of the following Schiff base ligand were reported by Wang et al. All the compounds showed fair anticancer activities[27]. reported some mononuclear complexes of Cu (II), Mn (II), Co (II), and Ni (II) with *bis*- Schiff base ligand derived from 2,3-butanedione and thiosemicarbazides about their synthesis and anti-cancer activities. The cytotoxicity assay was done against five different kinds of cells lines (HL-60, Spca-1, Tb, MGC, and K562). Among them, the Cu (II) complex was found to have highest anti-tumour activity[28]. Copper complexes of a tridentate ligand containing two pyridine and one imine nitrogen donor atom and the complexes possess anticancer activities[29]. Complexes of Cu and Zn showed potential activities against larynx cancer cells with IC50 values of 0.47 and 0.60 μg/mL, respectively[30-32].

K. C. Gupta and A. K. Sutar.: The catalytic activity of metal complexes of binaphthyl, binaphthol and their combinations, The Pyridyl bis(imide) and pyridine bis(imine) complexes of cobalt(II), iron(II) ions have been used as catalysts in the polymerization of ethylene and propylene. The phenoxy-imine (FI) complexes of zirconium, titanium and vanadium and Schiff base complexes of nickel(II) and palladium(II) were also used as catalysts in the polymerization of ethylene[33]. The zirconium complexes combined with $MgCl_2$/RmAl (OR ^{n} displayed strikingly high activities. The titanium complexes also showed catalytic activity, the vanadium complexes showed activity at elevated temperatures and iron(III) and cobalt(II) complexes of pyridine bis (imine) ligands 43 showed significant activity in the polymerization[34-36]. Metal complexes with unsymmetrically-substituted tetradentate SBs are one of the most important classes of coordination compounds. They have been found in a lot of biologically active drugs[37-40].

Xiang Liua,* and Jean-René Hamonb. The study of multidentate Schiff base metal complexes is crucial to accurately and thoroughly comprehend structure–property relationships in order to optimise and improve their use in a wide range of applications, given the simplicity and accessibility of multidentate Schiff bases and their metal complexes with multiple properties[41]. The complex [NiLOAc] excelled in halting proliferation of the cervical and colon cancer cells with median inhibitory concentration (IC50) values of 28.33 and 34.4 μM, respectively. The complex, [PdLOAc] demonstrated selective cytotoxicity against breast cancer line MCF-7 with IC50= 47.5 μM, also showed inhibitory effect against colon cancer cell line (HCT-116) with IC50 = 55.66 μM. The complex, [PtLdmso] showed mild activity against breast cancer (MCF-7) and cervical cancer (Hela) cells. It displayed insignificant cytotoxicity against human endothelial cells (EA.hy926)[42.] Cisplatin was approved for treating humans against cancer in 1978. Cisplatin was synthesized by Pyrone in 1844.



Cisplatin

However, its biological effects on cancer were accidentally discovered by Rosenberg and co-workers in 1965. Na[NiLOAc], Na[PdLOAc] and Na[PtLdmso]. The synthesized compounds were fully characterized and evaluated for their antiproliferative effects. The compounds were tested against three human cancer cell lines

and one normal cell line to screen for their cytotoxic potential and as anticancer agents against colon, breast and cervical cancers[43].

III.CONCLUSION

A significant part of bioinorganic chemistry, as well as a wealth of structural, physico-chemical, and catalytic features are revealed by the synthesis and structure of multidentate Schiff bases and their metal complexes. This review focused on some background and recent progress in the synthesis of Schiff bases and their mono-nuclear transition metal complexes, structural and physico physico-chemical properties (like catalysis, spin crossover etc.). Aalso applications found in polymeric materials photovoltaic materials, energy materials, nuclear medicine and as components of pharmaceutically active co-crystals. However, transformation of metal complexes into human drugs is not an easy task, as accumulation of metal ions in the body fluids can be potentially hazardous to health. Hence, biocompatibility of the metal complexes, in addition to their bio efficacy, is an Imperative factor to be considered first. The Schiff base metal complexes are crucial to accurately and thoroughly comprehend structure–property relationships in order to optimise and improve their use in a wide range of applications. These complexes demonstrated cytotoxic and antitumor activity due to which they can be used for therapeutic purposes, while DNA protection activity was observed. The various metal complexes acting as drug medicine on various diseases such as antitumor, leukaemia, breast cancer, antimalarial, antifungal etc.

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Synthesis of Nanoparticles and Its Catalytic Applications

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ABSTRACT
In recent years the nanoparticles gain enormous attention. Various technologies have main a focus on the synthesis of nanomaterials. Nanoparticles are synthesized by different methods depending on the types and nature of nanoparticles. in addition to nanomaterials possess a broad scope of applications in research area. Present article focus on the different synthetic methods of nanoparticles used by the scientists, which are being used to synthesize nanomaterials generally CVD, Sol-gel, combustion etc.the main intention of this article is to create awareness regarding the knowledge of nanoparticles and its uses in different fields. The present review basically focuses on the various synthesis processes and applications in the field of nanomterials.
Keywords: Nanoparticles, synthesis methods, applications.

I. INTRODUCTION

The Particles size nanoparticles range from 1 to100 nm as nanoparticles differ in size, shape apart from materials in nanotechnology [1] Nanoparticles are an entity that followthe importance of their unique benefits.
Nanomaterials have become important in today's technology due to their unique electrical properties and applications in the fields of catalysis, imaging,
photonics, nanoelectronics, sensors, biomaterials and biomedicine.
Nanoparticles and bulk materials exhibit different properties of the same material.There are many systems that work to reduce the production costs of nanoparticles.Nanotechnology holds the key to a clean and sustainable future. Synthesis of nanomaterials that require qualification is one of the most exciting things in nanoscience and nanotechnology today[2].

Most of nanoparticles having higher reactivity and having lots of importance in modern medicine due to their multiple oxidation states that's why nanomaterials possess a broad scope in applications. It plays an key role in imaging to carriers for drug and gene delivery into tumors. Nanomaterials also have unique environmental and social challenges particularly in regard to toxicity Nanomedicine aids in early detection and prevention enhanced diagnosis and follow up of disease. The most unusual aspect of nanomaterials is that they retain a

large surface area due to micro size of particles when compared to their bulk counterpart this property of nanomaterials helps for higher reactivity and denotes specialized properties of them, due to these properties of nanoparticles to applied in chemical, biological and industrial fields.

There are many synthesis methods such as bottom-up approach and top-down approach.applications of nanoparticle are now used in the production of scratch resistant glass, scratch resistant wall paint, clen sunscreens, self-cleaning windows and much more .

In this review, we discuss all the important aspects of synthetic methods, types and applications. Nanoparticles and nanomaterials have won prominence in technological advancements due to their adjustable physiochemical traits such as melting point, wet ability, electric and thermal conductivity, catalytic activity, mild absorption and scattering resulting. in stronger performance over their bulk counterparts.[3,4]

Numerous synthesis methods are either being developed or improved to enhance the properties and reduce the production costs. Some methods are modified to achieve process specific nanoparticles increase their optical, mechanical, physical and chemical properties [5]. Nanoparticles have been prepared from various materials such as metals, dielectrics, semiconductors, in addition to this, hybrid structures such as core-shell, nanoparticles have also been prepared. Semiconductor nanoparticles are also termed as quantum dots (QDs) when their size is small enough to demonstrate quanisation of energy levels. These nanoparticles have diverse applications in medicine as drug carriers or imaging agents.

A vast development in the instrumentation has led to an improved nanoparticle characterisation and subsequent applications.. nanoparticles are now used in every objects like from cooking vessel, electronics to renewable energyand aerospace industry. Nanotechnology is the key for a clean and sustainable future.

II. METHODS OF NANOPARTICLES

Many methods exist to synthesize of nanoparticles.These methods are divided into bottom-up and top-down approaches.currently there are two approaches available for preparing ultrafine particles.Intially it is breakdown of molecules (top-down) method by particles. The next is the build-up (bottom-up) method that produces nanoparticles starting from atoms of gas or liquids based on atomic transformations by molecular condensation.

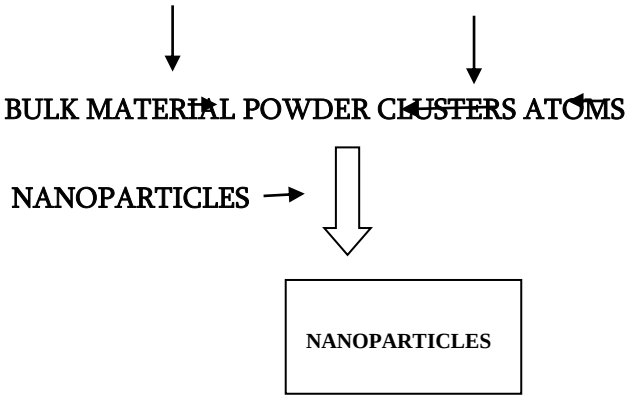
Bottom-Up Method

The Bottom-up or constructive methods involves the build-up of material from individual atoms or clusters to nanoparticles in complex manner the methods are Sol-gel, spinning, chemical vapor deposition (CVD), pyrolysis , and biosynthesis are the most commonly used bottom-up methods for nanoparticle production.

Top - Down Method

When bulk material is reduced to nanometric particles using top-down or destructive method ,the result is a nanometric size product. Mechanical milling, nanolithography, laser ablation, sputtering, and thermal decomposition are some of the most widely used nanoparticle synthesis methods.Assembling basic units into larger structures is accomplished through the use of chemical or physical forces at the nanoscale through bottom-up apporoaches to nanofabrication Many Bottom-up approaches developed for producing nanoparticles.

TOP-DOWN METHOD BOTTOM-UP METHOD



1. **Sol-gel:**

The sol – it's a colloidal suspension of solid particle in a liquid phase. The gel – colloidal solution of a liquid dispersed in solid is called gel. Recently Sol-gel is the most favor technique for bottom-up method due to its clarity and mostly the nanoparticles are prepared by this method. Sol-gel is a wet-chemical process possess chemical solution is a precursor for an integrated system of discrete particles. In sol-gel method normally Metal oxides and chlorides are used as precursors [6].

2. **Chemical Vapour Deposition (CVD):**

Chemical vapor deposition is the deposition of a thin film of gaseous reactants on a substrate. Deposition is acco mplished by oil molecular bonding at ambient temperature in the reaction chamber. Chemical reactions occur when the heated substrate comes into contact with the fuel mixture [7].

3. **Microemulsion:**

The microemulsion process is one of the best methods for the preparation of inorganic nanoparticles synthesis that forms spontaneously at room temperature are thermodynamically stable, and have a large interfacial area

4. **Pyrolysis**

Pyrolysis is the most commonly used process in industries for largescale productionof nanoparticle. It involves burning a precursor with flame. The precursor is either liquid or vapourthat is fed into the furnace at high pressure through a small hole where it burn [8]. The combustion orby-product gases is then air classified to recover the nanoparticles. Some of the furnaces use laser andplasma instead of flame to produce high temperature for easy evaporation [9]

Top –Down Method

Top-down approach is the reduction of a bulk material to nanometric scale particles. Mechanical milling, nanolithography, laser ablation, sputtering and thermal decomposition are some of the most broadly used nanoparticle synthesis techniques.

1. **Mechanical milling:**

Among the various topdown methods, grinding is the most
widely used method to produce a variety of nanoparticles. Mechanical grinding after grinding and annealing of nanoparticles during synthesis where the difference is ground in an inert atmosssphere.[10]

2. **Laser ablation**;

Laser ablation synthesis in solution (LASiS) is a method for producing nanoparticles from a variety of solvents. Irradiating a metal immersed in a liquid solution, the laser
beam intensifies a plasma cloud producing nanoparticles [11].

3. **Thermal decomposition**

Pyrolysis is an endothermic decomposition produced by heat that destroys chemical compounds [12]. The specific temperature of chemical decomposition of the resulting product is called the decomposition temperature.

Nanoparticles are made from metals that decompose at high temperatures to become chemically produced secondary products.

4. Sputtering.

Sputtering is the deposition of nanoparticles on a surface by ejecting particles from itby colliding with ions [13]. Sputtering is usually a deposition of thin layer of nanoparticles followedby annealing. The thickness of the layer, temperature and duration of annealing, substrate type, etc. determines the shape and size of the nanoparticles [14].

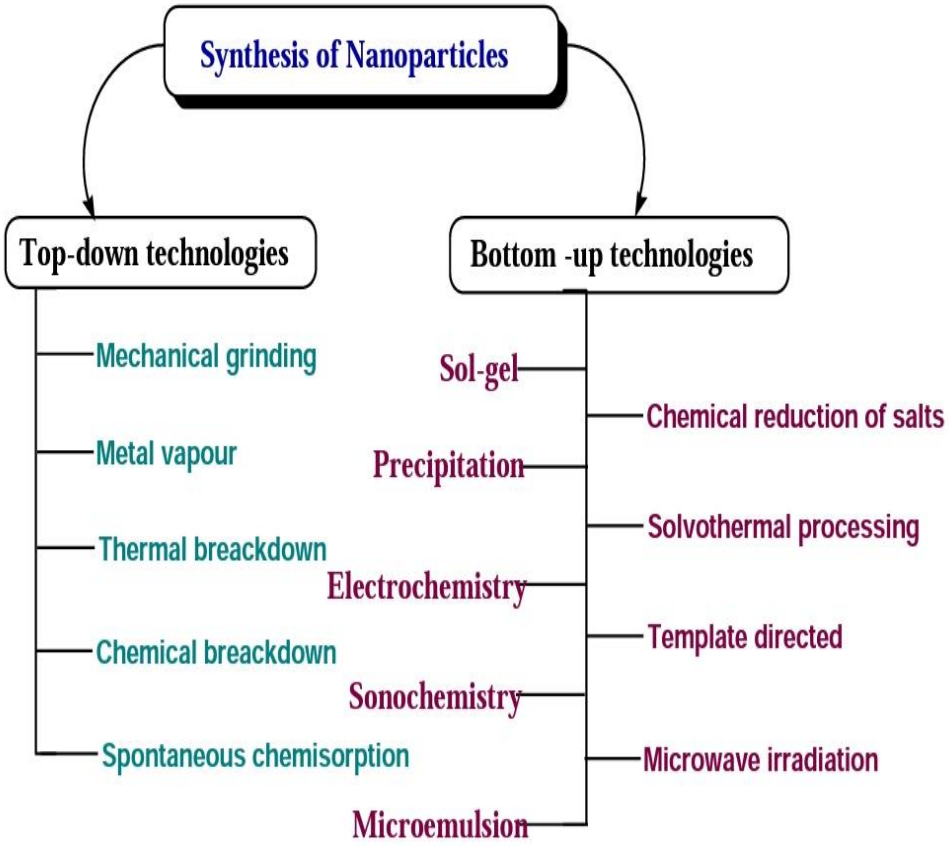


Fig ; Synthesis Methods of Nanoparticles

III.APPLICATIONS OF NANOPARTICLES

Nanoparticles are used increasingly in catalysis to boost chemical reactions.

1) Nanomedicine :

Nanomedicine refers to the use of nanotechnology in medicine. It includes the medical use of nanomaterials and biodevices, nanoscale biosensors.etc[15] Next generation applications include nanoscale biosystems, however, the potential for toxicity and environmental impact of nanomaterials is a major concern. Nanotechnology has improved medicine through the use of nanoparticles in drug delivery.

Drugs can be delivered to specific cells using nanoparticles [16]. Tissue engineering can replace traditional medi cal treatments such as organ transplants.
One such example is the development of skeletal carbon nanotube scaffolds.

2) Food:

The improvement, processing, maintenance and packaging of meals products can be executed using nanotechnology. For example, nanocomposite coatings in meals packaging have at once introduced antimicrobial sellers to the coating [17]

3) Construction;

Nanotechnology improves the construction process, making it faster, cheape
and safer. For example, when nanoscale silicon dioxide (SiO_2) is mixed with ordinary concrete, nanoparticles ca n improve the mechanical properties and durability of concrete. Nanotechnology has progressed the development strategies with the aid of making them faster, inexpensive and safer. For example when nanosilica (SiO_2) is blended with the regular concrete, the nanoparticles can enhance its mechanical houses, and additionally upgrades in durability [18]. The addition of nanoparticles in paints additionally improves its overall performance via making them lighter with more suitable houses [19].

4) Catalysis:

Nanoparticles have a high surface area, which provides greater catalytic activity Due to their large surface area/ volume ratio, nanoparticles act as effective catalysts in
drug production [20]. Catalysis is one of the pioneering application
of nanoparticles. Various materials such as aluminum, iron, titania, clay and
silica have been used as nanoscale catalysts for many years. Catalytic properties For example, the conversion an d selectivity of nanocatalysts are greatly affected by the size of metal nanoparticles [21].

5) Cosmetics and Sunscreen:

Regular use of UV protection against the sun is not sustainable in the long run. Sunscreens containing nanoparticles such as titanium dioxide have many advantages
Titanium dioxide and zinc oxide nanoparticles are used in some
sunscreens because of their UV protection properties their transparency to light
and their ability to absorband reflect UV rays. Metal oxide nanoparticles are used as pigments in some lipsticks. [22]

6) water treatment;

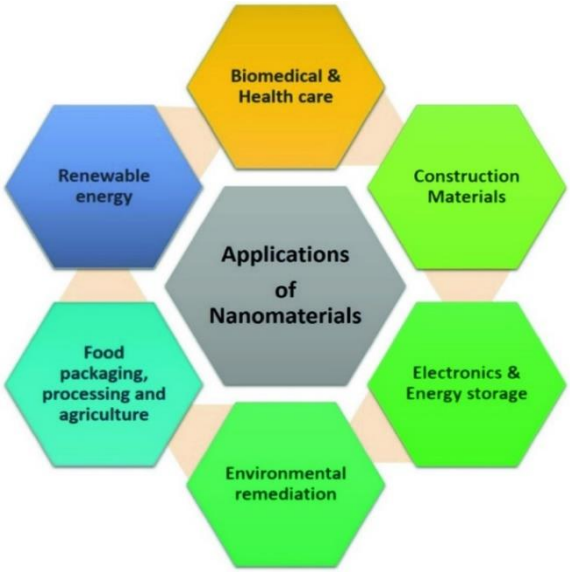
The use of nanomaterials in water and wastewater treatment has attracted a lot of attention. Nanomaterials have strong adsorption capacities and reactivity due
to their small size and large surface area. Various nanomaterials have been
reported to successfully remove heavy metal [23], organic pollutants [24] inorganic anions [25] and bacteria [26].

7) sensors;

The development of numerous nanomaterials has paved the manner for their application within the layout of excessive-overall performance electrochemical sensing gadgets for scientific, environmental and meals protection.[27] The overview is confirmed that exceptional substances may be used for the electrochemical dedication of some components and pollutants, which includes hydrazine (N_2H_4), malachite green (MG), bisphenol A (BPA), ascorbic acid (AA), espresso Caffeine. , caffeic acid (CA) is normally found and synthesized in foods and beverages.[28]

8) Energy storage;

Platinum-based nanomaterials have been attracted an lousy lot interest for there promising potentials in the fields of strength-related and environmental catalysis [29] one of the most promising areas of nanotechnology for renewable energy is the development of nanomaterials for solar cells.these materials can improve the efficiency , stability and cost-effectivness of converting sunlight into electricity.



Fig; Applications of Nanomaterials

IV.CONCLUSION

Varity of strategies have been explored to synthesize nanomaterials of desired size, shape, and orientations. Such defects can significantly affect the physical and chemical residences of nanostructures and nanomaterials. As senior agencies, organizations, and agencies boom their research. The nanometer statistics has obtained huge interest. The application of nanomaterials has grow to be an advanced studies and giant studies has been accomplished to apply the generation. Due to the fact has the first suitable of the future due to its performance and environmental friendliness, it is being examined for plenty new packages to enhance the satisfactory and overall performance of merchandise or procedures to lessen charges so everybody can use nanotechnology. This evaluate highlights the statistics approximately techniques and programs of nanomaterials further more reuse modern art work in this place. Society have more advantages from nanotechnology, therefore importance of nanotechnology and nanomaterials are enhance day to day.

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New Synthetic Methodology for The Synthesis of Nitrogen Containing Bioactive Heterocyclic Compounds

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ABSTRACT
The Biginelli reaction is a multiple-component that creates 3,4-dihydropyrimidin-2(1H)-ones4from ethyl acetoacetate 1, an aryl aldehyde(such as benzaldehyde2), and urea3.[1][2][3][4] It is named for the Italian chemist Pietro Biginelli.[5][6]. Present paper is comparative study of synthesis of 3,4-dihydropyrimidin-2(1H)-ones with respect to yield, reaction time and reaction conditions. All products (3a- j) are characterized by spectral data and elemental analysis.
Keywords: Dihydropyrimidin-2(1H)-ones, Biginelli reaction ,Comparative study.

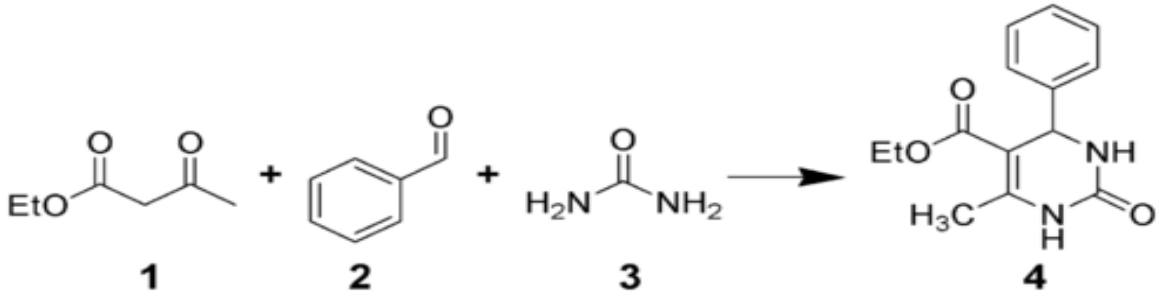
I. INTRODUCTION

Heterocyclic compounds are naturally occurring compound and found in various plants in large quantities. Heterocyclic compounds are biologically active compound used in various aspects like cosmetics, medicines and pharmaceutical industries [1]. N-Heterocyclic compounds molecules are recently used in anti- tuberculosis and anti- AIDS [2]as active drugs. So it is interesting to study the molecule and its derivatives. It is well known that the Dihydropyrimidin-2(1H)-ones derivatives represent an important class of oxygen containing heterocyclic compounds. They are widely used as additives in foods, perfumes and in the preparation of optical Brighteners [3] as well as laser dyes [4].

Dihydropyrimidines have been synthesized by several routes including Beginelli reaction [5], Perkins [6], Knovengeals [7], Reformatskys [8], and Witting [9]reaction. Among the methods applied, Beginelli reaction is the most widely applied methods for synthesizing dihydropyrimidin-2(1H)-ones. Beginelli involves the condensation of Aldehydes with β- keto esters in the presence of variety of bases. Various acid types like Lewis [10], Protic [11], Solid acids [12], acid anhydrides [13], and in different ionic liquids [14], as well as solvent free condition [15].

In continuation of our interest, the current work represents the comparative study of synthesis of dihydropyrimidin-2(1H)-ones by Beginelli reaction using different procedures and its influence with various aspects like yield, reaction time and conditions.

REACTION SCHEME:



II. MATERIALS AND METHODS

The melting points of the compounds were determined in open head capillary and are uncorrected. The IR spectra of the compounds were recorded in the region of 4000-400 cm-1 by using KBr pallet on FT-IR Perkin spectrophotometer.H1 NMR spectra were recorded on a DRX-300 Bruker FT-NMR spectrophotometer in CDCl3. The values of chemical shift are expressed in δ ppm as a unit. All the compounds were checked for purity by thin layer chromatography (TLC). The sonicator was used with 100 wattspower of 230 V AC suppliers.

Synthesis of Dihydropyrimidin-2(1H)-ones (3a) by conventional method [16] with cerric ammonium nitrate as Catalyst:

A solution of 1.1 gm of Benzaldehyde and 1.3 gm of EAA was added drop wise with stirring to 10mg of Urea. So that the temperature of reaction mixture did not raise above the 100Cthe reaction on complete addition mixture was kept at ambient temperature for 18 hr. and then poured with vigorous stirring to the mixture of ice and water. The precipitated was filter off and washed with cold water then dried under reduced pressure to afford the crude solid mass. On recrystallised from aqueous alcohol gives final compound. (3a)

Synthesis of Dihydropyrimidin-2(1H)-ones (3b) by Microwave Irradiation method [17]:

Equimolar amount of solution of Benzaldehyde and EAA was mixed well with the help of glass rod for five minutes with 1 ml of conc. Urea and placed in an open conical flask in domestic microwave oven containing 2mg magnesium sulfate and irradiated for 5 min at 350 watts (TLC monitor) and pour to ice water mixture ,obtained precipitate filter off and recrystallized by using aqueous alcohol.

Synthesis of Dihydropyrimidin-2(1H)-ones (3c) by Infra-Red lamp heating method[18]: Equimolar amount of solution of Benzaldehyde and EAA was mixed with a glass rod for few minute containing 1 ml of and heated with medicinal Infra Red lamp (250watts) for 8-10 hours, the temperature of the reaction mixture did not exceed above 750C . After completion of reaction (TLC) poured to ice- water mixture then filter it off and recrystallised from aqueous alcohol.

Synthesis of Dihydropyrimidin-2(1H)-ones (3d) by Sonicator method [19]:

Equimolar amount of solution of Benzaldehyde and EAA was mixed in 50 ml of round bottom flask followed by addition of water (5ml). The mixture was irradiated in the water bath of an ultra sound cleaner (100 watts) for 30 min, after completion of reaction, monitor by TLC, the solid product was filtered, washed by cold water and dried under vacuum. The crude product was recrystallised in ethanol (20 %) The yield of the product was listed in table 1.

Synthesis of Dihydropyrimidin-2(1H)-ones (3e) by conventiona method [20] without any catalyst: Equimolar amount of solution of Benzaldehyde and ethyl β- amino crotonate (Enamine derivatives of EAA) heated at

1800C without any catalyst, after completion of reaction, monitor by TLC, the reaction mixture was cooled and poured to cold water, obtained solid was washed with cold water and finally solid mass was recrystalised from aqueous alcohol to afford a pure product. The yield of the product was listed in table 1.

Synthesis of Dihydropyrimidin-2(1H)-ones (3f) by conventional method [13] with solid state Catalyst: To a mixture of Benzaldehyde (1 mmol) and β-keto ester (EAA) (1.2mmol) in a RBF was added silica supported Boric trisulfuric acid anhydride as a solid catalyst (40 mol%) then the flask was immersed in an oil bath adjusted at 850C, equipped with a condenser and the mixture was stirred for suitable period of time, monitored by TLC. After completion of reaction, the oil bath was removed and the flask was allowed to attained room temperature. Afterwards CHCl3 was added and the suspension was filtered to remove the catalyst. The obtained solution was then washed with water and evaporated. Finally, the residue was recrystallised from aq. Ethanol to obtain the pure compounds.

Synthesis of Dihydropyrimidin-2(1H)-ones(3g) by ionic liquid Catalyzed method [21]:

A mixture of Benzaldehyde (1 mmol), β-keto Ester (EAA) (1 mmol) and ionic liquid [(4-sulfo-butyl) tris (4-sulfophenyl) phosphonium hydrogen sulphate] (10 mol %) as a catalyst were mixed without any solvent and stirred at room temperature for an appropriate time (20 min). After completion of reaction, indicated by TLC, 2 ml of water was added and the mixture was stirred for an additional 5 min. the precipitated product was filtered, washed with cold water, dried and crystallized from ethanol. The aqueous layer containing ionic liquid was recovered under reduced pressure, washed with acetone, dried and reused for subsequent reactions. The yield of the product was listed in table 1.

Synthesis of Dihydropyrimidin-2(1H)-ones (3h) by solvent free (Neat Reaction) method [22]:

A mixture of Benzaldehyde (1 mmol), β- keto Ester (EAA) (1 mmol) and PEG-SO3H10 mol %) as a catalyst was stirred at room temperature under solvent free condition for period of 20min. Completion of reaction is compared by TLC. After completion of reaction, water (5ml) was added to reaction mixture and stirred for another 2 min, filtered and recrystallised from ethanol to afford desire product in good yield. The yield of the product was listed in table 1.

Synthesis of Dihydropyrimidin-2(1H)-ones (3i) by using Phase transfer catalyzed method [23]:

A solution of Benzaldehyde (5mmole), EAA (5mmole) in benzene (20 ml) with saturated aqueous potassium carbonate solution (20 ml) and tetra n butyl ammonium hydrogen sulphate (1.2 mmol) were stirred magnetically at room temperature for 30 min. The completion of reaction is checked by TLC. The benzene layer separated washed with water, and benzene removed by distillation under reduced pressure. The residue thus obtained was crystallized from methanol ,to give good yield of Dihydropyrimidin-2(1H)-ones(3i)

Synthesis of Dihydropyrimidin-2(1H)-ones (3j) by simple grinding technical method [15]:

To an equimolar mixture of Benzaldehyde and Ethyl aceto acetate was added TsOH in a mortar and ground it well with a pestle at room temperature. The Mixture was heated at 600C for 10 min., after cooling, water was added to the reaction mixture and obtained solid products were collected by filtration to give Dihydropyrimidin-2(1H)-ones in very good yield. The crude crystals thus obtained were recrystallized by ethanol to afford pure colorless prisms. The yield of the product was listed in table 1.

Table No.1 Table showing Reaction condition, Time, Temperature and Yeild of Compounds 3

Sr. No.	Compounds	Time With Temp.	Yield	Reaction Condition
1	3a	Overnight at RT	85%	Conc.H2SO4,addition at 00c, Overnight at RT.

2	3b	5min at 350 Watts	95%	MW Irradiaton
3	3c	8-10 hrs at 250 Watts	50%	IR lamp heating.
4	3d	30 min at 100 Watts	65%	Ultra sound Irradiation.
5	3e	20 min at 1800c	85%	Without any solvent and catalyst
6	3f	25 min at 850C	93%	BTSA-SiO2 catalyst
7	3g	20min at RT	97%	Ionic Liquid catalyzed, without any solvent.
8	3h	20min at RT	95%	PVS Acid Catalyzed, without any solvent.
9	3i	30 min at RT	80%	PTC Catalyzed.
10	3j	10 min at 600C	98%	Simple grinding Technique at RT, then 600C for 10 min

III.CONCLUSION

In conclusion, here we reported comparative study of preparation of N Containing heterocyclic compounds by various methods. Among which this study prove that green synthetic method (3j) is most efficient via by simple grinding Technique obtain product within few minutes.

IV.ACKNOWLEDGEMENT

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Potentiometric Study of Cholecalciferol Complexes with Transition Metal Ions in 92% (v/v) Acetonitrile–water Medium

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ABSTRACT

Cholecalciferol is the type of vitamin D and it is known as vitamin D3. This is important for maintaining calcium levels and promoting bone health and development.Cholecalciferol complexes with transition metal ions in 92% (v/v) acetonitrile-water medium. The dissociation constant and stability constants were determined at 298K and at0.1M ionic strength using potentiometric method. The values of dissociation constant and stability constants were evaluated and are quoted. The ionic strength was maintained by using potassium nitrate solution. The dissociation constant and stability constants were determined.

Key words: Cholecalciferol, ionic strength, transition metals, complexes, stability constant, chelate effect.

I. INTRODUCTION

Vitamins may be defined as specific chemical substances necessary for the proper functioning of the complete organism. The word vitamin has its origin from the Latin word Vita and the protein fraction amin[1]. Vitamins are essential substances, which are necessary for normal health and growth. The vitamins are organic compound that are necessary in very small amounts in the diet and are effective in small amounts. They do not furnish energy and are not utilized as building unit for the structure of organisms but are essential for the transformation of energy and for the regulation of the metabolism of structural units. If this intake is insufficient or if special dietary requirements exist, multivitamin preparation should be taken in order to prevent vitamin deficiency.

Vitamins are usually present as chemical individuals in pharmaceutical preparations, but in food products individual vitamins occur in several forms and are present in significantly smaller amounts2. Vitamins traditionally have been considered to be “accessory food factors” [2].

Classification of vitamins

Vitamins are mixed group of compounds that are not similar to each other but are grouped by functions and are differentiated from trace elements by their organic nature. On the basis of their solubility, these are classified into two classes.

1. Water soluble vitamins 2. Fat soluble vitamins

Vitamins are essential nutrients found in foods. The requirements are small but they perform specific and vital functions essential for maintaining health. Water soluble vitamins dissolve in water and are not stored; they are eliminated in urine. We need a continuous supply of them in our diets. The water soluble vitamins are B-complex group and vitamin C.

Fat soluble vitamins are essential nutrients to maintain normal body metabolism and are vital for animal growth, skeleton and vision development, reproduction and immune function5. Fat-soluble vitamins include biologically active members of vitamin A (diterpenes), vitamin D

(modified triterpenes), vitamin E (tocochromanols), vitamin K (naphthoquinones) families, and related compounds, of which some act as their precursors.

Vitamin D

The vitamin D which occurs naturally in unfortified foods is generally derived from animal products. Saltwater fish, such as herring, salmon, sardine and fish liver oils are extremely rich sources. However eggs, veal, beef, unfortified milk, and butter supply only small quantities of the vitamin. Plants are extremely poor sources of vitamin D, fruits contain no vitamin D and vegetable oils contain only negligible amounts of the provitamin. The two most prominent members of this group are ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3).Cholecalciferol is the form of vitamin D obtained when radiant energy from the sun strikes the skin and converts the precursor 7-dehydrocholesterol into vitamin D3. It is more accurate to call vitamin D a proharmone. It maintains calcium homeostasis with two peptide hormones, calcitonin and parathyroid hormone (PTH). It is also important for phosphorus homeostasis[3,4].

In the recent years science literature is receiving numerous reports on the study of metal complexes which describe their importance applicability in the field of scientific interest like,

biochemistry, medicine, pathology, agriculture industries. It will not be exaggeration to say that metalcomplexes have vital role in modern scientific age to achieve advancement in any chosen field ofsciences. Therefore in the present work, attempts have been made to report in the complex formation of cholecalciferol with transition metal complexes in 92% (v/v) acetonitrile– water mediumat 298K and at ionic strength 0.1M KNO_3.

II. METHODS AND MATERIALS

Cholecalciferol was obtained from Himedia in pure form. The solvent acetonitrile was used Anala R grade. The metal ion solutions, acid solution, KNO_3 solution and NaOH solution were prepared in doubledistilled water. The conductivity and pH of this distilled water was found to be 1.60 x 10-6 mhos and 6.8 respectively. NaOH was standardized with oxalic acid solution and it was used for further potentiometric titrations. The concentration of metal ions in solutions was estimated by standard procedures[5-7]. Borosil quality glasswares were used in the experiments. The micro burette with graduation of 0.02 ml was calibrated by the method of Vogel[8]. An Elico model LI-120 digital pH meter in conjuction with an Elico combined glass electrode consisting of glass and reference electrodes entity of the type CK-61/CN-91/CM-51 were used for the pH measurement. The precautions suggested by Bates[9], Albert andSergeant[10] were adopted for smooth handling of the electrode.

The experimental procedure for binary metal complexes involves following titrations

(1) Free HNO_3
(2) Free HNO_3 + Cholecalciferol
(3) Free HNO_3 + Cholecalciferol + metal ion solution

The method for the determination of the formation functions was described by Irving and Rossotti[11] and Hearon and Gilbert[12]. The potentiometric titration techniques used by Irving and Rossotti, which was used earlier by Calvin and Melchior[13] and now known as Calvin-Bjerrum titration technique.

III.RESULTS AND DISCUSSION

The complex formation of transition metal ions with cholecalciferol in 92% acetonitrile-water medium was performed at 298K by maintaining ionic strength at 0.1M KNO_3.The stability constants of cholecalciferol were evaluated with transition metal ions. The proton ligand stability constant and metal ligand stability constants of cholecalciferol in 92% (v/v) acetonitrile– water medium at 298K and at μ= 0.1M KNO_3 are quoted in Table 1. The metal ions and hydrogen ions act as Lewis acids. pH decreases, if a neutral metal ion is added to the ligand solution The metal- ligand titration curve lie below the pure ligand titration curve.The determination of proton – ligand stability constant of the ligand is a prerequisite for the evaluation of metal – ligand stability constant.

Formation constants, Free energy, Enthalpy, Entropy changes in the complexation of transition metal ions with cholecalciferol in 92% (v/v) acetonitrile– water medium.

Metal	V(II)	Mn(II)	Fe(III)	Co(II)	Cu(II)	Zn (II)	Cd(II)	Pb(II)
$\log K_1$	3.0898	2.9583	2.9856	2.9215	2.9258	2.7524	3.0012	3.1415
ΔG	-17.6307	-16.8804	-17.0362	-16.6704	-16.6949	-15.7055	-17.1252	-17.9257
ΔH	2.7044	3.8587	2.8314	3.7166	2.8354	2.8212	4.1927	2.1756
ΔS	0.0682	0.0695	0.0599	0.0684	0.0655	0.0621	0.0715	0.0674

Table 1

The values of ΔG are negative and values obtained for ΔH and ΔS are positive as well as values of logK indicates that there must be strong interaction between metal ion and the chelating reagents. The positive values of entropy were accounted towards the interaction of positive and negative ions[14-17].

The Chelate effect

The ligand effect is classified in to two types i) the electrostatic effect ii) the rest effect. The electrostatic effect represents the effect of any ionic charge on the ligand. This shows the effect of co-ordination of a charged ion on the already charged species of the complex. Magnitude of the electrostatic effect is related to the work done to bring an electrically charged ligand L to a complex MLn to give MLn + 1.

The rest effect shows that the ligand molecule affects the ability of further ligand molecules to attach themselves to the lower complex already formed. Since in the present investigation the ligand do not contain nitrogen therefore the involvement of OH group takes place.

IV.CONCLUSIONS

In the present work, pH metric study was performed to determine stability constants and to assess binary species for Cholecalciferol with transition metals ions in 92% (v/v) Acetonitrile-water medium in pH range of 2.0-7.5. The higher negative value of free energy indicates stable metal complex is formed. The positive values of entropy were accounted towards the interaction of positive and negative ions. Thus the dielectric constant of the medium strongly affects the stability constants of metal complexes.

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A Review On Phytochemistry and Pharmacology of Medicinal Plant Rhynchosia

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I. INTRODUCTION

Rynchosia is commonly known as Teen Pani is a pharmacologically diverse medicinal plant.(H.M. Burkul et al 1985 [1] Various parts of this plant, specifically Leaf , have an immense range of medicinal uses in folk medicine directed for a number of ailments (L.M. Bakshiet al 2002 [2]. A plethora of active phytochemical constituents of this plant have been revealed so far, namely, Steroids, Flavonoids, terpenoids several studies demonstrated the exploration of pharmacological potential of various parts such as leaves (Jeevan Ram et al 2004 [3]. It is used to treat skin diseases, particularly india. Rynchosia is used to treat upper respiratory ailments, swelling and joint pains. According to ethno medicinal reports provided by a South African traditional healer, the leaves are used to treat and prevent heart or chest pain and diseases. The seeds extract was found to have agglutinating effects against human red blood cells.(C.C.Blyth et al 2007[4] Rynchosia used to treat some of the symptoms observed in IFI patients; hence this research sought to isolate and screen the identified compounds from the leaves against *C. albicans* and *C. neoformans*. (R. Di et al 2010[5] In our search for essential oils for the medical, cosmetics, perfumery, fragrance or flavors industries, The pulmonary form often presents in patients with symptoms such as coughing, chest pains, fatigue, skin rash and even bruises.

Taxonomic Classification and Common name:

Familia: Fabaceae
Subfamilia: Faboideae
Tribus: Phaseoleae
Subtribus: Cajaninae
Genus: Rhynchosia
Species: Rhynchosia aurea

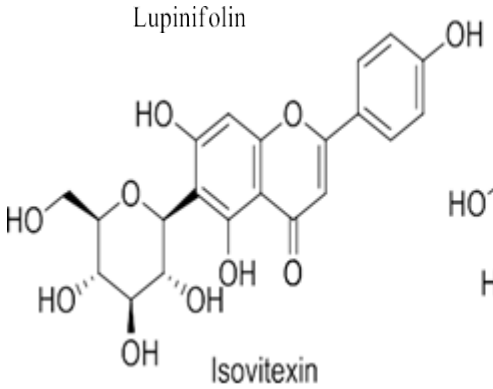
Method:

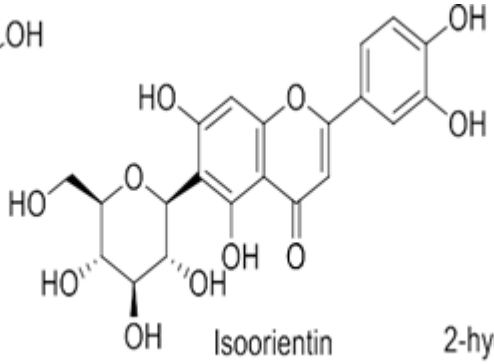
The present review covered the literature published prior to the year 2023. The information about Phytochemicals from *Rynchosia* and its pharmacological properties was gathered from search engines like

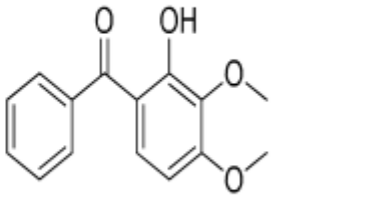
Google Scholar, NCBI, Scientific Research and Science Direct. Literature abstracts and full-text articles available from scientific revues were analyzed and bioactive compounds extracted from *Rynchosia* were included in this review.(Y.S. Lee et al 2011[6])

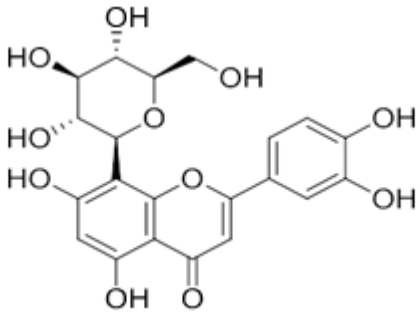
Phytochemical studies:

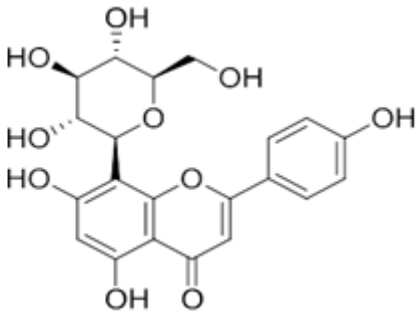
The phytochemical studies revealed that extracts of Rynchosia species s have been reported several Chemicals as isovitexin , Isoorientin , 2 hydoxy 3,4 dimethoxybenzophenone , orientin , vitexin, (M.A. pfailer 2012[7]

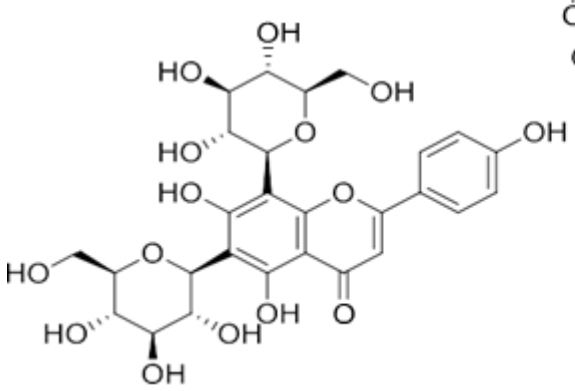


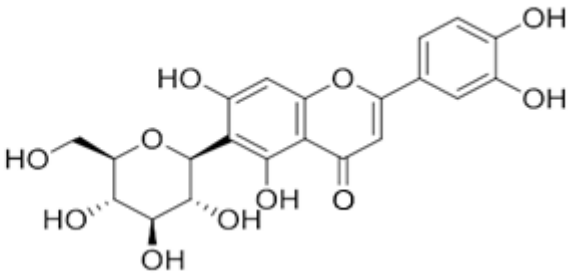


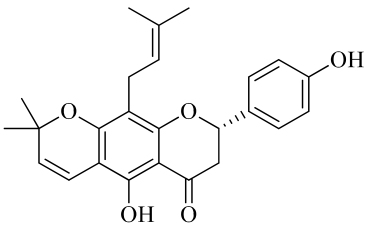


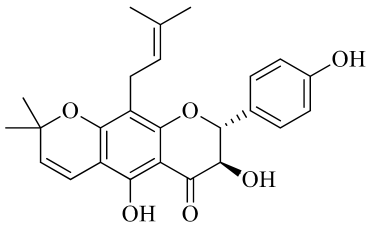


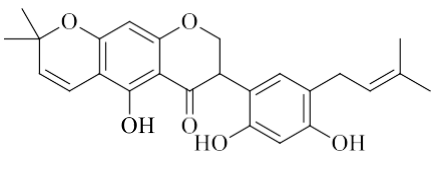


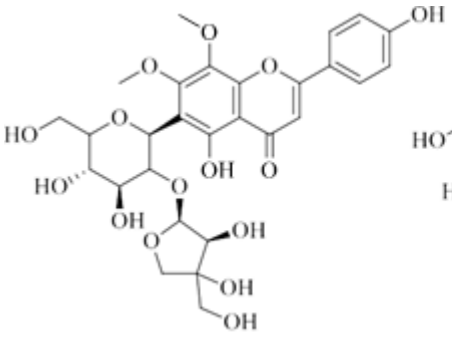




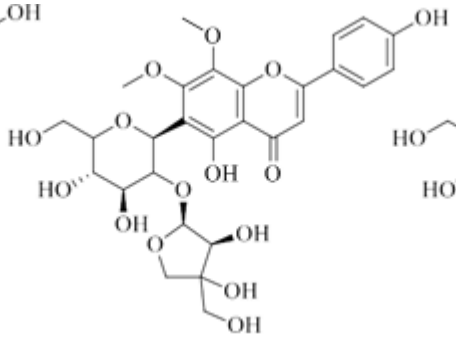




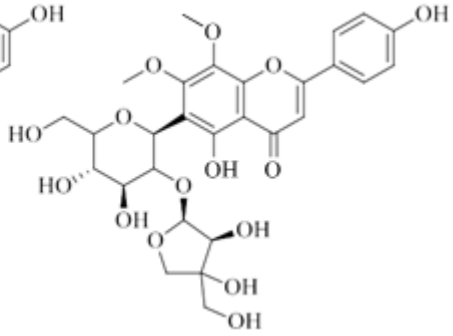




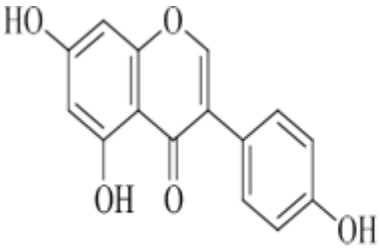
Precatorin C



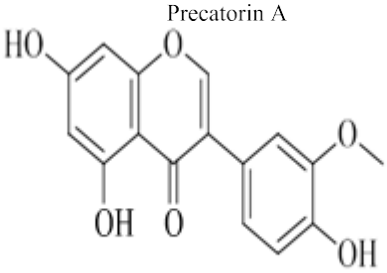
Precatorin A



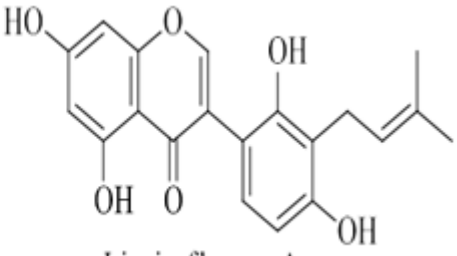
Precatorin B



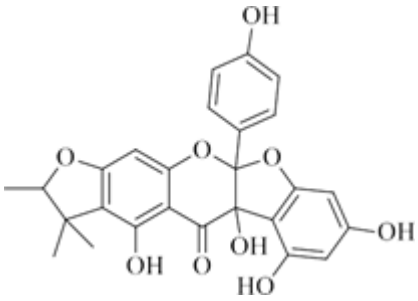
Genistein



3'-O-methylorobol



Licoisoflavone A



Sophoraisoflavone A

Pharmacology:

Most of the reports are either isolation of chemical constituents or preliminary pharmacological screening of plant extracts of Rhynchosia species. There are very few reports are on the bioassay guided isolation of natural compounds and their biological activity studies.(Coronado 2017) In the above section, under traditional uses, we have summarized the activity studies of plant extracts of Rhynchosia members and in the current section, the study focusing mostly on stated biological activities of isolated compounds of Rhynchosia members. Most of the reported activities are antibacterial, allelopathic activity, anti-angiogenic activity (D. Gozalbo et al 2014[8]

Antioxidant studies:

Flavonoids make up the largest category of secondary metabolites that can be found in plants. They exhibit a diverse array of medicinal uses, including antioxidant properties, and are the most abundant of these metabolites. The Isovitexin, isoorientin, mangiferin, and 2-hydroxy-3,4-dimethoxybenzophenone were the four flavonoids that were isolated from the flowers of *Rhynchosia* using a bioassay as a guide. These flavonoids were then put through tests to determine whether or not they had 1,1-diphenyl-2- picrylhydrazyl (DPPH) radical scavenging activity. Mangiferin and isoorientin had significant antioxidant activity. (Z. Jiang et al 2015[9]

Antimycobacterial activity:

The bacterial organisms used in the present study included: Acenotobacter calcoacetilus (NCIB 8250), Bacillus subtilis (NCIB 3610), Citrobacter freundii (NCIB 11490), Clostridium perfringens, Clostridium sporogenes (NCIB 10696), Escherichia coli (NCIB 8879), Klebsielia pneumoniae (NCIB 4184), Proteus vulgaris (NCIB 4175), Pseudomonas aeruginosa (NCIB 950), Salmonella typhii, Staphylococcus aureus (NCIB 6751) and Yersinia enterocolitica (NCIB 10460). The Antimycobacterial Activity.Isovitexin, isoorientin, quercetin-7-O-methylether, and biochanin A are the names of the four flavonoids that were recently identified from the flowers of *Rhynchosia* . Using the disc diffusion technique, each chemical was examined to see whether or not it has any antibacterial activity against gram-positive and gram-negative bacteria as well as fungi. (A.N. Moteetee et al 2016[10]

Anti-inflammatory and anti-angiogenic activities:

The compounds include genistein, 3′-O- methylorobol, licoisoflavone A, sophoraisoflavone A, and Rhynchoviscin, a completely new chemical. In addition, the isolated compounds were put through an LPS-enhanced leukocyte migration experiment to determine whether or not they have anti- inflammatory properties. Licoisofavone A, one of the other two 3′-O-methylorobols, did not demonstrate any substantial inhibition. Additionally, a Zebrafish-based vascular outgrowth assay was used to test the angiogenic activity of the extracts and compounds. (R. Rajashingham et al 2017[11]

Antibacterial activity:

A pour plate method was adopted for anti-petriplates and allowed to solidify. Wells (6mm) were made with sterile gel puncture and 10 mL of plant extract was aseptically added to each well. A control drug, ampicillin (10 mg/mL), was used as standard positive antibacterial agent along with plant extract samples.

These nutrient agar plates were incubated at 37° C for 24 h. The diameter of zone inhibition was measured in mm using a Himedia zone reader. The minimum inhibitor concentration (MIC) was determined by an agar diffusion method. The extracts were incorporated into nutrient agar at concentrations from 1 mL to 10 mL. A control plate without the extract was also set up. The lowest concentration of extract that inhibited the grow The antimicrobial activity of the four solvent extracts of Rynchosia was evaluated using the Zone Inhibition Test on MHA for bacteria and SDA for fungi [18]. In brief, Sterile filter paper discs (6 mm diameter) were impregnated with different concentrations loaded (125, 250, 500, and 1000 µg/disk for bacteria and 125 to 5000 µg/disk for fungi) and were placed on the agar plates previously inoculated with test microorganisms (Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Candida albicans, and Aspergillus niger). Ciprofloxacin (10 µg/disk) and fluconazole (25 µg/disk) were used as positive controls for bacteria and fungi, respectively. The plates were kept in an incubator at 37 degrees Celsius for 24 hours to grow bacteria and at 30 degrees Celsius for 48 hours to grow yeast. The diameter of the inhibition zone around each disc was measured in millimeters (mm) and recorded as the mean of three replicates (D. G. Pappas et al 2018[12]

Anticancer activity:

Fresh tissue specimens were taken from cancer patients undergoing therapeutic debulking procedures. All tissue specimens were washed several times with Leibovitz (L15) medium, minced, and subjected to enzymatic proteolysis for 2 h at 37°C with gentle shaking in Leibovitz medium containing collagenase type I (200 units/mL), hyaluronidase (100 units/mL) (Sigma-Aldrich), penicillin (1000 units/mL), streptomycin (1 mg/mL), and amphotericin B (2.5 μg/mL). Tissue preparations were centrifuged for 10 min at 200 g, and the pellets were suspended in RPMI 1640 medium containing all supplements and plated in 100 mm petri dishes. After 1–3

weeks, when the cultures had reached a density of cells/plate, histopathological diagnoses and cell viability assays (see below) were performed. The chemicals include lupinifolin, lupinifolinol, cajanone, precatorin C, precatorin A, and precatorin B. In addition, the roots of Rhynchosia as well as its separated chemicals (with the exception of lupinifolinol) were tested for their potential cytotoxic action against murine macrophage cells.(C.firacative et al 2020[13]

II. RESULT AND DISCUSSION:

This survey of writing features one of the significance of certain plants of variety Rhynchosia having a place with the family Fabaceae. The presence of compounds such as isovitexin , Isoorientin , 2 hydoxy 3,4 dimethoxybenzophenone , orientin , vitexin, Lupinofoline etc. its most use in medicine and traditional medicines. It gives a scope for further studies of in vitro and in vivo activities like antiulcer activity, hypertension, rheumatic pains, anticonvulsant, anti-nociceptive activity.This study may thus provide a bird's eye perspective for the future experimental research that will be conducted in the search for novel medication

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An Efficient and Green Method for The Preparation of 2,3 – Dihydro-2-Phenyl-1 H-Naphtho-[1,2-E] [1,3] Oxazine by Using Tannic Acid

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ABSTRACT

A Novel route one-pot three-component reaction was developed for the synthesis of 2,3-Dihydro-2-phenyl-1-H-Naphtho-[1,2-e] [1,3] Oxazine by using Substituted Aniline, Formalin & β-Naphthol in the presence of Tannic acid (10 Mol %) as catalyst. The reaction is observed by using TLC, after completion of reaction product is characterized by 1H, NMR, 13C NMR, IR and Mass Spectra.

Keywords: Substituted Aniline, β-Naphthol, Formalin and Tannic acid.

I. INTRODUCTION

Derivative of oxazine are among the most important heterocyclic chemicals that have attracted substantial attention in synthetic chemistry because of wide array of pharmaceutical effects [1].

Oxazine is a compound that may be synthesized by the substitution of carbon (C) atoms with nitrogen (N_2) & oxygen (O_2) in benzene and its reduction products [2]. Oxazines are a class of heterocyclic compounds characterized by the presence of single nitrogen and a single oxygen atom [3]. Three isomers exist based on the respective positioning of heteroatom & relative positioning of double bonds [4]. The synthesis of oxazines (aromatic) was firstly accomplished in 1944 by Holly & Cope using Mannich processes. There has been a limited amount of research conducted on basic derivatives of these ring systems, with the majority of studies focusing on the reduced 1, 3 and 1, 4 molecules. One of the most significant examples of a simple 1,4-oxazine compound morpholine, also known as tetrahydro-1,4-oxazine. Morpholine the white liquid that exhibits miscibility with water [5].

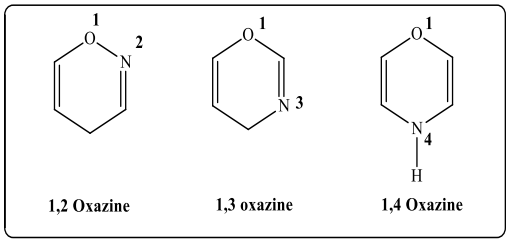
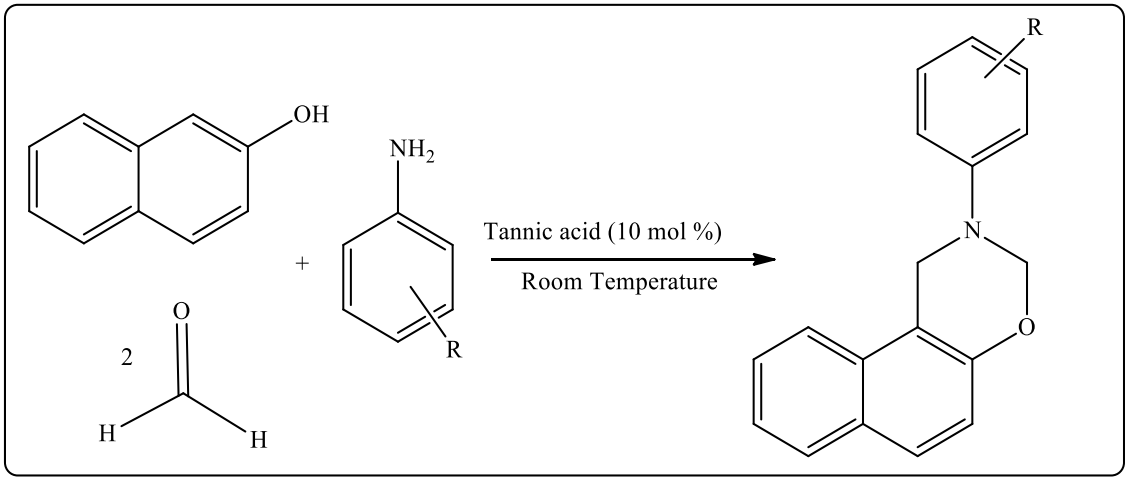


Fig 1. Isomers of Oxazine

The field of Oxazine chemistry has been the subject of much scientific research worldwide. Oxazines are a class of heterocyclic compounds characterized by a six-membered ring structure consisting of one nitrogen atom, one oxygen atom (O_2), that possess significant biological activity [6].The significance of oxazine derivatives has seen a recent surge of attention due to the diverse range of pharmacological effects demonstrated by molecules containing the dihydro [1,3]Oxazine ring system, as well as their use as synthetic intermediates [7].Furthermore, it has been shown that naphthoxazine derivatives have promising therapeutic properties that might be used in management of Parkinson's bug [8]. "Trifluoromethyl-1,3-oxazine-2-one", a chemical molecule, has been recognized as a very effective non-nucleoside reverse transcriptase inhibitor. It has notable efficiency against several mutant strains of the HIV-1 virus. Consequently, extensive research has been carried out to examine the features and characteristics of 1,3-oxazine derivatives by means of synthesizing these compounds by a three-component cyclo condensation technique. The documented biological actions of the subject include anti-inflammatory, anti-tubercular, anti-diabetic, anticancer, antioxidant, diuretic, and antiviral activities, among others. In addition to their biological activities, benzo-1,3-oxazines possess pharmacological properties and are considered a significant class of chemical pigments. Several techniques are available for production of several oxazines, although necessitating the use of costly and hazardous materials, as well as specific reaction conditions [9]. Boeini and Co-worker did a work whereby they synthesized novel "naphtho [1, 2-e] [1,3] Oxazines" including an aryl sulfonamide moiety. The synthesis was achieved using a one-pot technique, employing an ecologically benign reaction medium. The characterization of the "naphtho [1,2- e] [1,3] Oxazine" derivative was performed by utilization of ^{1}H NMR, ^{13}C NMR, and LC-MS techniques. The in vitro effectiveness of the newly synthesized compounds in inhibiting cancer growth was assessed using breast, colon, & BCLL cancer cell lines [10]. Botla et al. investigated on a wide range of "2,3-dihydro-1H-benzo [2,3] benzofuran [4,5-e] [1,3] Oxazine" derivatives. These compounds were synthesized by a Mannich type condensation chemical reaction of dibenzofuran-2-ol with different amines, utilizing water as the solvent. The ortho-amino methylation process of dibenzo furanols was seen to proceed smoothly in presence of various "aromatic/aliphatic amines & para formaldehyde", resulting in subsequent cyclization [11]. In current times, there has been a rising interest in the investigation to the 1,3-oxazine heterocycles due to their diverse biological features. These qualities include analgesic, anti-convulsant, anti-tubercular, anti-bacterial, & anti-cancer activities [12]. Significance of "1,3-oxazine" derivatives has been recognized in their role as intermediates and their utility in the synthesis of diverse pharmaceutical compounds .Several established methodologies have been documented for their preparation, including the utilization of dehydrated alc. ammonia, ammonium acetate, copper acetate/ zinc chloride, Au(I) complexes, 2-azadienes in combination with alkynes, Bu_4NF/ethyl iodide, & p-TsCl, DMAP/DCM, operating under basic conditions. This study focuses on the production of "2, 3-dihydro-2-phenyl-1H-naphtho-[1,2-e] [1,3] Oxazine" derivatives by the utilization of tannic acid [13].



Scheme 1: Preparation of 2, 3-Dihydro-2-Phenyl-1*H*-Naphtho [1,2-e] [1,3] Oxazine

II. RESULT & DISCUSSION

Here, we hope to introduce the use of tannic acid as a catalyst to promote the synthesis of 3,4-dihydro-3-substituted-2H-naphtho[2,1-e][1,3] oxazine derivatives (Scheme 5.3.3). We use the reaction of 2-naphthol (1 mmol), formalin (2 mmol), and 4-methoxy aniline (1 mmol) stirred at room temperature as the reaction model. To determine the suitable concentration of the catalyst Tannic acid, it has been investigate the model reaction first with no catalyst and a smaller amount product is obtained at various concentrations of catalyst like 2.5 , 5 , 7.5, 10 & 12.5 mol % the product produced in 58 , 71 , 82 , 92 and 92 % yields, correspondingly (Table 1). This shows that 10 mol % tannic acid is sufficient to obtain good results in terms of reaction time and product yield. To study the catalyst loading concentration of the reaction model, the procedure was optimized using various molar concentrations of Tannic acid under RT stirring condition. Excellent yield of product was observed by using 10 mol% of catalyst. From that result, it can be seen that the catalyst concentration plays an important role in improving the results to a greater extent. It was also observed that, there is no larger change in yields of product more than 10 mol % of catalysts.

Table 1: Effects of Catalyst Concentrations [a]

Sr. No.	Conc. (mol %)	Yield (%) [b]
1	2.5	58
2	5	71
3	7.5	82
4	10	92
5	12.5	92
[a]Reaction conditions: **1** (1 mmol), **2** (2 mmol), **3a** (1 mmol), Tannic acid (10 mol %) at room temp. [b]Isolated yield		

To evaluate the solvent effect, various solvents such as tetrahydrofuran, acetonitrile, dichloromethane, water, water: ethanol (1:1), methyl alcohol, ethyl alcohol and H_2O: ethyl alcohol (1:9) was used for the model reactions. The preferred product was obtained in 33, 62 54, 50, 60, 84, 86 , and 90 % yields correspondingly after respective time at room temperature conditions. Ethyl alcohol: Water: (1:9) stand out as the solvent of

selection amongst the solvents tested. Because of the speedy conversion & desired product obtained higher yield (Table 2, Sr.No. 8), whereas the product formed in lesser yield (30-85%) in longer time by using varies ratio of water & ethyl alcohol solvents.

Table 2: Screening of solvents

Sr.No.	Solvent	Yield (%)
1	Tetrahydrofuran	33
2	Acetonitrile	62
3	Dichloromethane	54
4	Water	50
5	Water: ethanol (1:1)	60
6	Methyl alcohol	84
7	Ethyl alcohol	86
8	Water: Ethyl alcohol (1:9)	90

To extend this method, we also treated various other amines of the reaction with electron donating group and electron withdrawing group to obtain the corresponding [1, 3] Oxazine derivative. As shown in (Table 3) in most cases the yields were good to excellent.

Table 3: Preparation of 2, 3-Dihydro-2-Phenyl-1*H*-Naphtho-[1, 2-E] [1, 3] Oxazine by use of Tannic Acid.

Sr. No.	Ar-NH_2	Product	Time (min)	Yield (%)	M. P °C
1	4-OCH_3-C_6H_4-NH_2	4a	07	92	88-90
2	3-NO2-C_6H_4-NH_2	4b	10	89	132-134
3	4-NO2-C_6H_4-NH_2	4c	12	83	168-170
4	4-Br-C_6H_4-NH_2	4d	10	89	114-116
5	2-NO2-C_6H_4-NH_2	4e	15	84	109-110
6	3-OCH3-C_6H_4-NH_2	4f	09	90	46-48
7	C_6H_5-NH_2	4g	10	89	48-50
8	3-CH3-C_6H_4-NH_2	4h	10	90	70-72
9	2-CH_3-C_6H_4-NH_2	4i	12	87	58-60
10	4-F-C_6H_4-NH_2	4j	11	86	136-138
11	4-OC_2H_5-C_6H_4-NH_2	4k	07	91	69-71
12	4-OCH_3-C_6H_4-NH_2	4l	05	94	78-80
13	3-OCH_3-C_6H_4-NH_2	4m	07	91	76-78

[a]Reaction conditions: **1** (1 mmol), **2** (2 mmol), **3a** (1 mmol), tannic acid (10 mol%) at room temperature. [b]Isolated yield.

III.EXPERIMENTAL

Method & Material:

All amines were obtained from freshly opened containers and used without further filtration. The melting point is determined in an open capillary tube in a paraffin bath. The progress of the reaction was observed by TLC (thin layer chromatography). IR spectra were recorded on a Bruker spectrometer on KBr disks. ^{1}H NMR

spectra were recorded on Bruker spectrometer (400 MHz). NMR spectrometer with chemical shift values in units of δ (ppm) with respect to DMSO as solvent and TMS as internal standard.^{13}C NMR also recorded on Bruker spectrometer & Mass spectra recorded on LCMS Water's Synapt-XS Maldi TOF HDMS spectrometer.

General Procedure

A mixture of β-naphthol (1 mmol), formalin (2 mmol), aryl amine (1 mmol) and Tannic acid (10 mol %) as catalyst was stirred at reflux temperature for 90-180 minutes. The development of the reaction was observed by TLC. After completion of reaction transformation, the reaction mixture was pour on crushed ice. The obtained crude product was filtered, dried and recrystallized in ethyl alcohol.

IV.CONCLUSION

In this Work we have developed the new methodology for the simple and efficient preparation of [1, 3] Oxazine derivatives by use of Tannic acid Catalyst. The protocol followed was simple and easy associated with good yield of the product generated 83 to 94% of the product. The major benefit of this method was easy setup, easy workup and less time required to complete the reaction.

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Spectrophotometric Quantification of Lamivudine in Pure and Pharmaceutical Formulations Via Extractive Methodology

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ABSTRACT
A novel spectrophotometric technique has been devised to quantify lamivudine (LVD) in both its pure form and pharmaceutical formulations. The method hinges on the interaction between the target drug LVD and bromocresol purple (BCP), resulting in the formation of ion-pair complexes in acidic buffers. These complexes are amenable to extraction in chloroform, and their maximum absorbance is measured at 429 nm. Rigorous exploration of all variables was undertaken to refine the reaction conditions. The linearity of the method spans concentrations from 50 to 250 ppm for LVD. Successful application of this method in determining LVD in pharmaceutical preparations underscores its efficacy. Importantly, the presence of excipients in pharmaceutical formulations does not impede the accuracy of the analysis. The obtained results support the recommendation of the proposed method for applications in quality control and routine analysis within the pharmaceutical domain.
Keywords: spectrophotometric method, lamivudine, bromocresol purple, ion pair complex, acidic buffer

I. INTRODUCTION

Lamivudine (LVD) belongs to the class of synthetic nucleoside analog reverse transcriptase inhibitors (NRTIs), exhibiting potent activity against the human immunodeficiency virus (HIV). Its use has been well-established over an extended period in the treatment of HIV-infected patients[1,2]. The available literature presents diverse methodologies for quantifying the mentioned drug substances in biological fluids and pharmaceutical preparations, including the utilization of UV-visible spectrophotometry[3-5].for LVD. The need for straightforward, discriminating, and highly sensitive spectrophotometric techniques is evident in the determination of these substances. The absence of a chromophore group in their structure renders direct UV detection impractical. In such instances, the formation of ion-pair complexes facilitates UV-visible detection. Existing literature reflects various studies on drug analysis that rely on this complex composition, employing different dyes like bromocresol purple, bromocresol green, methyl orange, and methylene blue[7, 8-11]. The objective of the suggested research is to establish a cost-effective spectrophotometric method utilizing bromocresol purple (BCP) for the determination of lamivudine (LVD), suitable for routine laboratory use without the need for expensive equipment. Additionally, the developed method aims to be characterized by its

simplicity, rapidity, accuracy, precision, and sensitivity in quantifying LVD in both its pure and pharmaceutical forms.

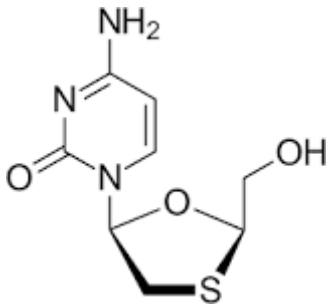

Fig. 1 Structure of LVD

The literature reveals various methods for the determination of the mentioned drug substances in biological fluids and pharmaceutical preparations such as UV-visible spectrophotometry[3-5], HPLC[12-18], capillary zone electrophoresis[19] for LVD,

Simple, selective, and sensitive spectrophotometric methods are required for the determination of LVD. But lack of chromophore group in their structure makes direct UV detection inapplicable. In this case, formation of ion-pair complexes enables UV-visible detection. There are some studies in the literature for drug analysis depending on this complex composition by using different dyes such as bromophenol blue, bromocresol green, methyl orange, and methylene blue[7,8-11].

The aim of the proposed study is to develop a spectrophotometric method by using bromocresol purple (BCP) for LVD that can be used in routine laboratories without requiring high cost equipment and sophisticated operator such as HPLC. Moreover, the developed method is simple, rapid, accurate, precise, and sensitive for the determination of LVD in bulk and pharmaceutical forms.

II. EXPERIMENTAL

Apparatus

The data acquisition was performed using a Systronic UV instrument fitted with a Xenon lamp and utilizing 1 cm quartz cells for measurements. pH assessments were conducted using a digital pH meter, calibrated with a buffer solution of pH 7.0.

Reagents and Solutions

All chemicals and reagents utilized in the study were of analytical-reagent grade. Lamivudine (LVD) and its pharmaceutical preparations, specifically Lamivir (containing 150 mg of LVD per tablet), were generously provided by Cipla Pharmaceuticals. Bromocresol purple (BCP) was sourced from Merck India, and distilled water served as the primary solvent throughout the experimental work. A solution of BCP (0.05%) was prepared in a mixture of 10% ethanol and water. Furthermore, stock solutions of LVD (1 mg mL–1) were meticulously prepared using water as the solvent.

Procedure

The experimental procedure involved transferring various volumes from LVD stock solutions into stoppered glass tubes, and then adjusting the LVD solution volume to 1 mL by adding water. Subsequently, 2 mL of phthalate buffer (pH 2.0) were added to each tube, followed by the addition of 2 mL of a 0.05% BCP solution. Each resulting reaction mixture, totaling 5 mL in volume, underwent extraction with 5 mL chloroform through vigorous mixing for 2 minutes using a vortex mixer. The two phases were allowed to separate, and the chloroform layers were then passed through anhydrous sodium sulfate. The organic layers were adjusted to a final volume of 5 mL with chloroform in volumetric flasks. The absorbances of the resulting yellow-colored chloroformic extracts were measured at 429 nm at room temperature, referencing against a blank solution prepared in a similar manner, with the exception of the addition of the drug substances.

Sample Preparation

Twenty tablets were weighed, and an amount equivalent to one tablet (each containing 150 mg LVD) was precisely weighed and transferred into 100 mL calibrated flasks. To each flask, 50 mL of water was added, and the mixtures were subjected to mechanical shaking and sonication in an ultrasonic bath for a total of 30 minutes. Afterward, the mixtures were diluted with water, thoroughly mixed, and then filtered. A 10 mL portion of each filtrate was further diluted to 50 mL, and appropriate aliquots were utilized for analysis following the aforementioned procedure.

RESULTS AND DISCUSSION

Optimization of the Analytical Procedure

Optimum conditions necessary for rapid and quantitative formation of colored ion-pair complexes with maximum stability and sensitivity were established by a number of preliminary experiments.

Absorption Spectra

LVD react with BCP in acidic buffer to give chloroform soluble yellow-colored ion-association complexes which exhibit absorption maximum at 429 nm. Under the experimental conditions, the reagent blank showed negligible absorbance as shown in Figure 2.

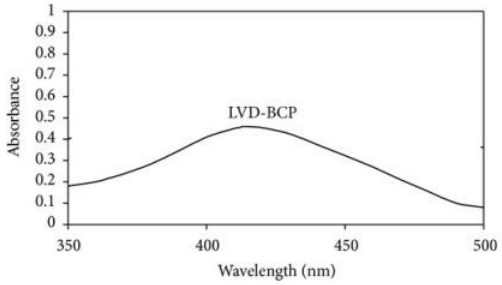

Fig. 2 Absorption maximum of LVD

Effect of pH

The effect of pH was studied by extracting the colored complex in the presence of various buffers such as phosphate buffer (pH = 2.5–8.0), phthalate buffer (pH = 2.0–8.0), and acetate buffer (pH = 3.5–6.0). It was found that the maximum color intensity and constant absorbance were observed in phthalate buffer of pH 2.0 for LVD-BCP (Figure 3)

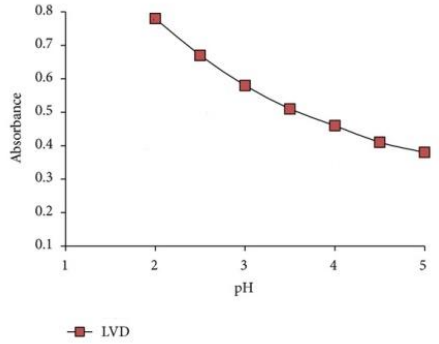

Fig. 3 Effect of pH on the ion-pair complexes

Effect of Solvent

The effect of extraction solvent on the ion-pair complexes was examined. Chloroform, ethyl acetate, ether, dichloromethane, benzene, and methyl isobutyl ketone were tested as extraction solvents for effective extraction of colored species from aqueous phase. Chloroform was selected because of its slightly higher efficiency on color intensity and selective extraction of the drug-dye complex from the aqueous phase. It was observed that only one extraction with chloroform was adequate to achieve a quantitative recovery of the complex.

Effect of Reagent Concentration

The effect of dye concentration on the intensity of the color developed was tested using different volumes of the reagent. The results show that 2 mL of BCP were found to be optimum and excess of dyes does not affect the color of the complex or the absorbance.

Effect of Temperature on the Colored Complexes

The effect of temperature on the colored complexes was studied at different temperatures. It was found that the colored complexes were stable up to 35°C. At higher temperature the drug concentration was found to increase due to volatile nature of chloroform. As a result, the absorbance of colored complexes increases. Besides, the resultant complexes were stable 48 h at 25 ± 1°C in the dark.

Effect of Shaking Form and Time

Ion-pair complexes were formed by using vortex mixer and shaking times ranging from 0.5 to 5 min were studied. Optimum shaking time as 2 min was selected for this method.

Stoichiometric Relationship

To ascertain the molar ratio between the investigated drug substances and BCP, Job's method of continuous variation was employed. In this method, solutions of drugs and dyestuff with identical molar concentrations were blended in varying volume ratios, ensuring that the total volume of each mixture remained constant. The results of these measurements revealed that the stoichiometry of the reactions was determined to be 1 : 1.

III.QUANTIFICATION

Linearity and Range

In Table No. 1, the Beer's law range, molar absorptivity, Sandell's sensitivity, regression equation, and correlation coefficient are detailed for each method. Notably, a linear relationship was established between the absorbance and the concentration of the drug within the range of 25–250 μg mL–1 for LVD. Regression analysis of Beer's law plots at this range revealed a strong correlation. The regression equations were derived using the

least-squares method. The high molar absorptivities observed for the resultant colored complexes underscore the method's elevated sensitivity.

Table 1 Optical characteristics and statistical data of the regression equations for LVD with BCP.

Parameter	LVD
Wavelength (nm)	429
Beer's law limit (μg mL^{-1})^{b}	25–250
Molar absorptivity (l mol^{-1} cm^{-1})	3.59×10^{3}
Sandell's sensitivity	1.597×10^{-5}
Regression equation	
Slope ± SD	0.0034 ± 0.00017
Intercept ± SD	–0.0148 ± 0.000047
Correlation coefficient,	0.999
LOD (μg mL^{-1})	0.105
LOQ (μg mL^{-1})	0.321
Intra-day	0.67
Inter-day	0.86

Validation of the Method

The method's applicability for the analysis of LVD in its pure state and formulations was evaluated by subjecting samples to the proposed procedure. The outcomes for the pure drug are outlined in Table No. 1. To assess precision and accuracy, six replicates of the drug were analyzed within the limits of Beer's law. The method exhibited good precision and reproducibility, as evidenced by the low values of relative standard deviation (RSD). The analysis of dosage forms, as presented in Table No. 1, also yielded reproducible results with low RSD values.

Table No. 2 Determination of LVD in dosage forms by standard addition method.

	Amount of taken drug (μg)	Amount of pure drug added (μg)	Total amount found (μg) (Mean ± S.D.)	RSD (%)	Recovery of pure drug added (%)
LVD	100	25	125.11 ± 1.10	0.98	100.17
	100	100	200.55 ± 1.04	0.46	100.67
	100	150	251.68 ± 1.96	0.87	101.10

To evaluate the accuracy of the method, recovery experiments were conducted using the standard addition technique. Various amounts of pure sample solutions of LVD were added to two different concentrations of the standard drug solution and then assayed. The obtained results are presented in Table No. 2, revealing average percent recoveries in the range of 100.17–101.10% for LVD.

Analysis Pharmaceutical Preparations

The developed and validated method was applied to analyses of the drug substances in their pharmaceutical preparations. The results were compared statistically by Student's -test and -test with the results obtained by the HPLC methods described in the literature [6, 7]. The calculated - and -values did not exceed the tabulated values, indicating that there is no significant difference between the developed method and valid HPLC methods in the respect of mean values and standard deviations at 94% confidence level. Statistical results are given in Table No.3

Table 3 Determination of LVD in dosage forms by the proposed and reference methods.

Statistical value	LVD	
	Proposed method	Reference method[26]
Mean	100.12	100.13
Recovery (%)	100.12	100.13
RSD (%)	0.15	0.198
t-test of significance	0.003	-
f-test of significance	1.72	-

IV.CONCLUSION

An advantageous aspect of the extractive spectrophotometric method lies in its ability to determine compounds within a multicomponent mixture. Unlike gas chromatography and HPLC procedures, the instrumentation required is straightforward and does not entail high costs. The method exhibits favorable sensitivity, measured by molar absorptivity, and impressive precision, indicated by a low relative standard deviation (RSD), making it well-suited for quantifying lamivudine (LVD) in both its pure and dosage forms.

The proposed method employs a cost-effective and readily available reagent, and the procedures do not involve intricate reaction conditions or cumbersome sample preparation steps. Notably, commonly used additives like magnesium trisilicate, magnesium stearate, lactose, starch, and carboxy methyl cellulose do not pose interference in the analysis.

Characterized by simplicity and speed, the proposed method demonstrates high precision and accuracy in comparison to various reported methods. Its utility extends to the analysis of these drug substances in quality control, research, and routine laboratory settings.

V. CONFLICT OF INTERESTS

The author certifies that there is no conflict of interests with any financial organization regarding the investigated drug substances and used chemicals in the study.

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Redefine The Approach: Spectrophotometric Analysis for Quantifying Lamivudine in Both Its Pure Form and Pharmaceutical Formulations

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ABSTRACT
A novel spectrophotometric technique has been developed to quantify lamivudine (LVD) in both its pure form and pharmaceutical formulations. The active pharmaceutical ingredient (API) is dissolved in distilled water, and the maximum absorbance of the resulting solution is measured at 271 nm. Systematic exploration of various parameters was conducted to optimize the reaction conditions. The established method exhibits a linear range of 10-50 ppm for LVD. Successfully applied to analyze pharmaceutical preparations, the method demonstrates that excipients present in these formulations do not interfere with the analysis. Based on the findings, the proposed method is deemed suitable for quality control and routine analysis applications.
KEYWORDS: Lamivudine, Spectrophotometry, Validation

I. INTRODUCTION

Lamivudine (LVD, 2'-Deoxy-3'-Thiacytidine) (Figure 1) is a synthetic nucleoside analog reverse transcriptase inhibitor (NRTI) known for its efficacy against the human immunodeficiency virus (HIV) and has been extensively utilized in HIV-infected patients [1, 2]. Various methods have been reported in the literature for determining these drug substances in biological fluids and pharmaceutical preparations, including UV-visible spectrophotometry [3–5], specifically for LVD.

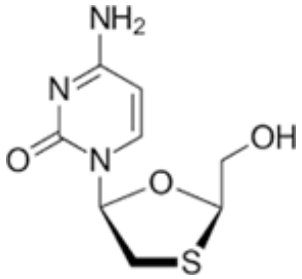

Fig 1: Chemical Structure of Lamivudine

The determination of these substances calls for spectrophotometric methods that are simple, selective, and sensitive. In light of this, our study aims to establish a spectrophotometric method for LVD, emphasizing its applicability in routine laboratories without the need for high-cost equipment. The proposed method is not only simple and rapid but also proves to be accurate, precise, and sensitive in the determination of LVD in both its pure form and pharmaceutical formulations.

II. EXPERIMENTAL

Apparatus

The determination of the drug's wavelength was conducted using the Systronic Double Beam Touch Screen UV-Vis Spectrophotometer (Type AU 2702). Spectra were recorded within the range of 200-400 nm against a solvent in 1 cm quartz cells. For precise measurements, an electronic analytical balance, specifically the Contech Electronic Balance, was employed in the experimental setup.

Reagents and Solutions

All chemicals and reagents employed in this study were of analytical-reagent grade. Lamivudine (LVD) and its pharmaceutical preparations, notably Lamivir (containing 150 mg of LVD per tablet), were generously supplied by Cipla Pharmaceuticals.

Reference Standard: Lamivudine (% Purity - 99.57%)

The reference standard, with a certified purity of 99.57%, was acquired as a gift sample. The authenticity and purity of the sample were certified by the same source.

EXPERIMENTAL PROCEDURE

The experimental procedure for the determination of lamivudine is as follows:

Weighing and Transfer:

- Accurately weigh 50 mg of lamivudine.
- Transfer the weighed lamivudine to a 100 ml volumetric flask.

Dissolving the Drug:

- Add 50 ml of water to the volumetric flask containing lamivudine.
- Dissolve the drug completely by vigorously shaking the solution.

Preparing Standard Stock Solution:

- Adjust the volume with the same solvent up to the mark on the volumetric flask.
- Create a standard stock solution with a concentration of 1000 ppm.

Scanning Across UV Range:

- Scan working standard solutions of 1000 ppm across the entire UV range of 400-200 nm.
- Determine the λmax, which was found to be 271 nm.

Preparing Solutions for Calibration Curve:

- From the standard stock solution (1000 ppm), pipette aliquots of 1 ml, 2 ml, 3 ml, 4 ml, and 5 ml into volumetric flasks.
- Make up the volume with distilled water to obtain solutions with concentrations ranging from 10 to 50 ppm of lamivudine.

Area Measurement:

- Measure the area under the curve of these solutions between 265 nm to 275 nm.

- Utilize a reagent blank in spectrum mode as a reference.

Calibration Curve:

- Plot a calibration curve of the area against concentration.
- Establish linearity and determine the regression equation.

Sample Preparation:

- Accurately weigh and powder twenty tablets of the marketed formulation.
- Transfer a quantity of powder equivalent to 50 mg of lamivudine to a 100 ml volumetric flask.
- Dissolve the powdered lamivudine in water, and adjust the final volume to the mark, resulting in a concentration of 1000 ppm.

Preparation of Standard Solutions:

- From the above stock solution (1000 ppm), transfer 1 ml, 2 ml, 3 ml, 4 ml, and 5 ml to 10 ml volumetric flasks.
- Dilute each of the solutions with water up to 10 ml, producing concentrations ranging from 10 to 50 ppm of lamivudine.

VALIDATION[6-8]

The ultraviolet spectrophotometric method was validated for accuracy, precision, linearity, detection limit, quantitation limit and robustness.

Linearity & Range[9]

Linearity refers to the method's ability to provide test results that are directly proportional to the analyte concentration within a specified range.

Precision[10]

Precision measures the degree of agreement among individual test results when the method is repeatedly applied to multiple samples from a homogeneous batch.

System Precision: Evaluated by measuring the peak response of the drug for replicate injections of a standard solution prepared according to the proposed method.

Method Precision: Determined by preparing samples from a single batch of tablet formulation six times and analyzing them using the proposed method.

Accuracy[11]

Accuracy denotes the exactness of an analytical method in determining true and observed values.

Ruggedness[12]

Ruggedness is evaluated by analyzing samples from homogenous lots in different laboratories, using different analysts, and employing varied operational and environmental conditions while staying within specified limits.

Robustness[13]

Robustness measures an assay's capacity to remain unaffected by small, deliberate variations in method parameters, providing an indication of reliability in the face of normal range degradation and variations in chromatography column, mobile phase, and method development.

Limit of Detection (LOD)[14]

The limit of detection is the lowest concentration of the analyte in a sample that can be reliably detected under specified experimental conditions, usually expressed in units such as micrograms per milliliter (ug/ml).

Limit of Quantification (LOQ)[15]

The Limit of quantification is the lowest concentration of the analyte in the sample that can be determined quantitatively with an acceptable level of accuracy and precision under the stated operational conditions of the method.

III.RESULTS AND DISCUSSION

Optimization of the Analytical Procedure:

The optimization process aimed to establish conditions that ensure sensitivity and yield precise and accurate results. Identifying the optimum conditions is crucial for the success of the analytical method.

Effect of Solvent:

Lamivudine exhibits solubility in various organic solvents such as ethanol, Dimethyl Formamide (DMF), Dimethyl Sulfoxide (DMSO), and distilled water. In this method, distilled water was chosen as the solvent. This decision was based on several factors, including the slightly higher solubility of lamivudine in distilled water compared to ethanol and other organic solvents. Additionally, the ready availability of distilled water further supported its selection as the solvent for this analytical procedure. The solvent choice plays a pivotal role in the effectiveness of the method, and in this case, the decision was made to prioritize the advantages offered by distilled water in terms of solubility and accessibility.

Table No.1 Method Optimization

Parameters	Lamivudine (LVD)
Max. wavelength	271 nm
Beer's law limit	10 – 50 ppm
Solvent	Distilled Water
Slope ±SD	0.03252
Intercept ±SD	0.016
Correlation coefficient, r	0.999834

Linearity

Table No.2 Linearity

Sr.no	Concentration(ppm)	Wavelength (nm)	Absorbance	calculation
1	10	271	0.302	Mean =0.9598
2	20	271	0.652	SD=0.514
3	30	271	0.964	CC=0.999
4	40	271	1.253	Slope=0.032
5	50	271	1.628	%RSD=53

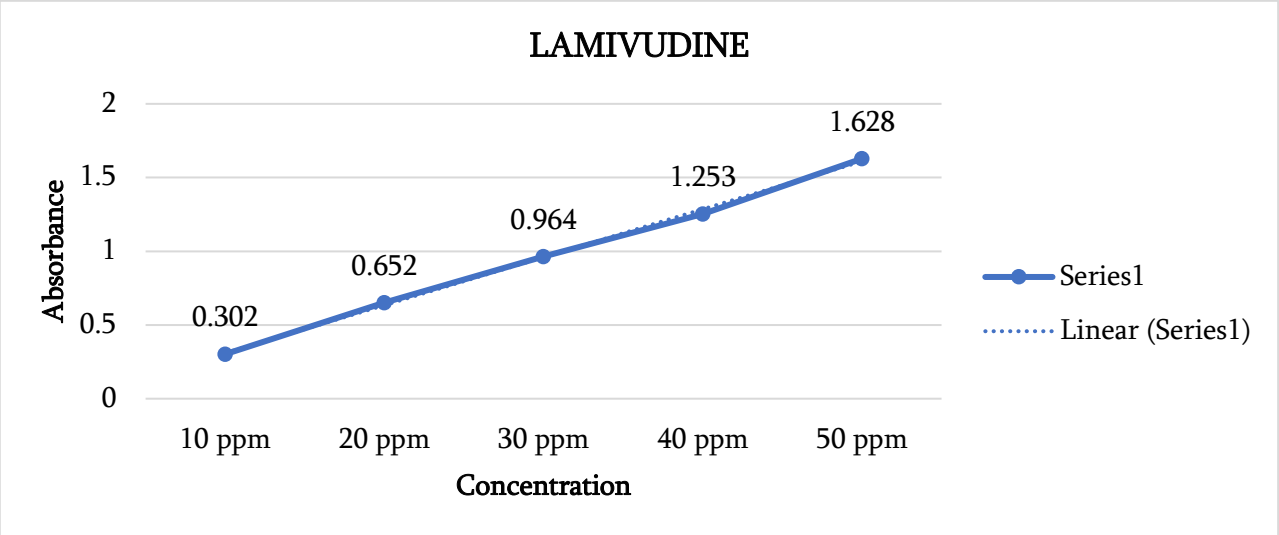

Fig. No.2 Calibration Curve of Lamivudine

Precision

The procedure is applied repeatedly to separate, identical samples drawn from a homogeneous batch, and precision is expressed as the coefficient of variation, reflecting the scatter of individual results from the mean.

Intraday Precision

Table No.3 Intraday Precision

Sr. No	Concentration (ppm)	Time (hrs.)	Absorbance	calculation
1	20	0	0.652	Mean=0.646
2	20	2	0.630	SD=0.0088
3	20	4	0.645	%RSD=1.36
4	20	8	0.648	
5	20	12	0.655	
6	20	24	0.650	

Interday Precision

Table No.4 Interday Precision

Sr. No	Time (hrs.)	Concentration (ppm)	Absorbance (Day 1)	Absorbance (Day 2)	Absorbance (Day 3)
1	0	20	0.652	0.638	0.640
2	2	20	0.630	0.640	0.635
3	4	20	0.645	0.635	0.634
4	8	20	0.648	0.633	0.636
5	12	20	0.655	0.640	0.632
6	24	20	0.650	0.642	0.630
	Mean		0.6466	0.638	0.6345
	SD		0.00884	0.003405	0.00344
	% RSD		1.36	0.5	0.54

Accuracy:

Accuracy is assessed by applying the analytical method to samples that include all components of the material, comparing the results with known added amounts of the analyte. Accuracy is calculated as the percentage of recovery by assaying the known added amount of the analyte in the sample or the difference between the mean and accepted values.

Table No.5 Accuracy

Sr. No	Concentration (ppm)	Absorbance	Calculation
1	16	0.539	Mean=0.534
		0.530	SD=0.004
		0.535	%RSD=0.8
2	20	0.648	Mean=0.65
		0.652	SD=0.002
		0.650	%RSD=0.3
3	24	0.756	Mean=0.753
		0.753	SD=0.002
		0.752	%RSD=0.2

Ruggedness:

Table no.6 Ruggedness

Sr.no	Parameters	Set A	Set B
1	Analyst	04/19	18/19
2	Day	Wednesday	Thursday
3	Time	Morning	Evening
4	Place	Machine room	Analysis lab.
5	Instrument	Systronics	Schimadzu
6	Concentration	20 ppm	40 ppm
7	Absorbance	0.652	1.253
		0.650	1.251
		0.651	1.252
Mean=		0.651	1.252
SD=		0.001	0.001
%RSD=		0.1	0.07

Robustness:

Table No7 Robustness

Sr. No	Concentration (ppm)	Wavelength	Absorbance	Calculation
1	20	(+5nm)	0.691	Mean= 0.696
	20	271	0.702	SD=0.0055
	20		0.696	%RSD=0.7
2	20	(-5nm)	0.681	Mean=0.681
	20	271	0.679	SD=0.0030
	20		0.685	%RSD=0.4

LOD and LOQ:

Table No.8 LOD and LOQ

Sr. No	Parameters	Concentration (ppm)	Absorbance	Calculation
1	LOD	20	0.652	Mean=0.653
		20	0.653	SD=0.0015
		20	0.655	%RSD= 0.2
				LOD=0.154
2	LOQ	20	0.651	Mean=0.653
		20	0.655	SD=0.0020
		20	0.654	%RSD=0.3
				LOQ=0.63

Marketed Pharma Assay of Tablet

Twenty tablets obtained from the commercial sample were collectively weighed and uniformly crushed using a mortar and pestle. An accurately measured powder sample, equivalent to 100 mg of lamivudine, was carefully transferred into a volumetric flask containing 25 mL of methanol solvent. Subsequently, the contents underwent sonication for approximately 5 minutes to facilitate dissolution, ensuring completion within 15 minutes. Following this, 10 milliliters of the resulting supernatant solution were extracted and further diluted to a final volume of 100 mL with methanol solvent.

Table No.9 Analysis data of tablet formulation

Sample	Label claim (mg/tablet)	Amount obtained (mg/tablet)	Percentage	Relative standard deviation (n=6)
Lamivir 150 mg	150	98.9	98.9	0.38%

IV.CONCLUSION

The spectrophotometric method presented in this study offers a substantial advantage for determining compounds in a multicomponent mixture. In contrast to gas chromatography and high-performance liquid chromatography (HPLC) procedures, the instrumentation required is simple and not prohibitively expensive.

The method demonstrates favorable sensitivity, as indicated by the molar absorptivity, and precision, as reflected in the relative standard deviation (RSD). These attributes make the method highly suitable for the determination of lamivudine (LVD) in both its pure form and dosage forms.

An additional strength of the proposed method lies in the cost-effectiveness and easy accessibility of the reagent employed. Furthermore, the procedures do not entail critical reaction conditions or laborious sample preparation steps.

The simplicity and rapidity of the proposed method, coupled with its high precision and accuracy relative to other reported methods, highlight its efficacy. This method proves valuable for the analysis of the specified drug substances in quality control, research, and routine laboratories.

In summary, the proposed spectrophotometric method stands out as a practical and efficient approach, offering advantages in terms of simplicity, cost-effectiveness, and suitability for a range of applications in pharmaceutical analysis.

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Exploring The Antifungal and Antibacterial Activities of Cu(II), Ni(II) Complexes Incorporating Amino Acids Schiff Base Ligands: Synthesis and Spectroscopic Investigations

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ABSTRACT
In this study, Schiff base ligand (E)-2-(5-fluoro-2-hydroxybenzylideneamino) acetic acid (HL1) and (E)-2-(5-chloro-2-hydroxybenzylideneamino)-3-phenylpropanoic acid (HL2) based Cu(II), Ni(II) complexes (C1-C4) were synthesized for acquiring a potential antibacterial and antifungal activities against. The synthesized compounds were characterized by 1H-NMR, 13C-NMR, ultraviolet–visible (UV–Vis), FT-IR, mass spectrometry. The study reveals that the tridentate Schiff base ligands coordinated via oxygen and nitrogen atom with Cu(II) and Ni(II) resulting in hexa-coordinated complexes. The thermal features of the ligand and complexes were studied using thermal (TGA and DTG) techniques. The pharmacological behaviour of the Schiff base and its complexes was assessed by examining their reactivity against E. Coli and A. Niger strains with streptomycin as a standard. The complex C1 and C3 exhibited the highest inhibition activity against bacterial and fungal strains. The results advocate that complexes can be utilized as antimicrobial drugs.
Keywords: Schiff base, antibacterial, antifungal, metal complexes.

I. INTRODUCTION

In recent years, the surge in multidrug-resistant microbial strains has underscored the urgent need for innovative antimicrobial agents [1]. Metal complexes, particularly those involving transition metals like copper (Cu) and nickel (Ni), have gained considerable attention for their potential as antimicrobial agents due to their unique chemical properties. Schiff base ligands derived from amino acids add an additional layer of complexity and versatility, offering tailored coordination environments for these metal ions[2].

The present research article delves into the synthesis and characterization of Cu(II) and Ni(II) complexes incorporating Schiff base ligands derived from amino acids, aiming to explore their antifungal and antibacterial activities. Schiff bases, formed by condensation reactions between amino acids and aldehydes possess inherent biological relevance owing to the presence of nitrogen and oxygen donor atoms in their structure. When coordinated with metal ions, these ligands may impart enhanced biological activities to the resulting complexes [2].

The inclusion of Cu(II) and Ni(II) ions in these complexes is of particular interest, given their well-documented biological activities and potential for redox chemistry. Copper, in its divalent state, has been recognized for its ability to generate reactive oxygen species, while nickel complexes have displayed diverse coordination geometries that may influence their biological behavior. By combining these metal ions with amino acid Schiff base ligands, we aim to design compounds with improved selectivity and potency against pathogenic fungi and bacteria [3].

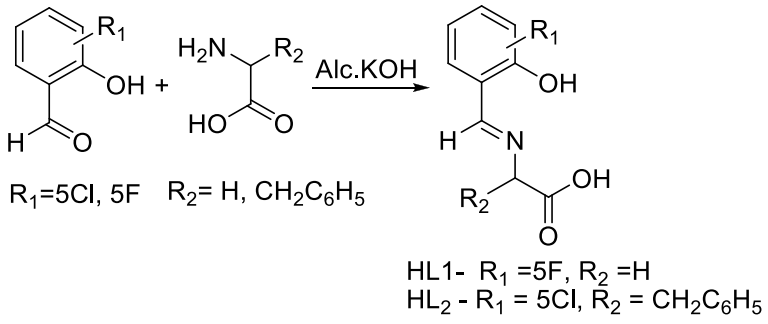
This article reviews the recent advancements in the synthesis methodologies of Cu(II) and Ni(II) complexes with amino acid Schiff base ligands and systematically examines their structural, spectroscopic, and physicochemical properties. Furthermore, a comprehensive analysis of their antifungal and antibacterial activities will be presented, drawing insights from the latest experimental findings and comparative studies. The referenced literature serves as a foundation for understanding the mechanisms underlying the bioactivity of these metal complexes, thereby contributing to the ongoing efforts in developing effective microbial agents [4].

II. METHODS AND MATERIAL

All chemicals and solvents were commercial grade materials and used without further purification. Ethanol and ether were distilled by standard methods before use. Purification of products was carried out by column chromatography using commercial column chromatography grade silica gel (60-120 mesh) purchased from s. d. fine-chemicals ltd. using mixture of ethyl acetate and n-hexane as eluting agent. The melting point of ligands and its metal complexes were determined by open capillary method on digital melting point apparatus (optics technology) and melting points are not corrected. The IR spectra were recorded on a Perkin Elmer FT-IR spectrum 65 at the range of 450-4000 cm^{-1} using ATR. Samples were kept directly without KBr pallets. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker AVANCE-II 400 MHz spectrometer. All known compounds were characterized and compared with the literature reports.

General procedure for synthesis of Schiff Base (HL1 & HL2):-

The Schiff base ligands were synthesized as per the following literature procedure. To a Solution of amino acid (10 mM) in 5 ml ethanol containing (10 mM) KOH, added drop wise substituted salicylaldehyde (10 mM) in 5ml methanol as with constant stirring and reflux for 2-5 hours on oil bath at 60^0C-70^0C. Then reaction mixture was cooled to room temperature. The yellow-colored precipitate of Schiff base ligand was formed and then checked for completion by TLC. Scheme 1



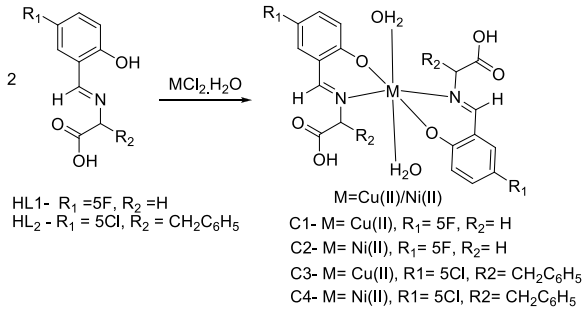
Scheme 1 synthetic route for the formation of Schiff bases

(E)-2-(5-fluoro-2-hydroxybenzylideneamino)acetic acid(HL1): yield 85% U.V. $\lambda_{max}CHCl_3$ (276)^{1}H NMR (400 MHz, $CDCl_3$) δ 12.37 (s, 1H),7.33 (s, 1H), 7.07 (d, 1H), 6.88 (d, 1H), 6.81 (s, 1H), 4.77 (s, 1H), 4.36 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.34 (s), 163.85 (s), 156.65 (d, *J* = 176.6 Hz), 122.41 (s), 119.44 (s), 117.42 (d, *J* = 97.6 Hz), 65.48 (s). FT.IR (ATR, ν cm^{-1}) 3282, 2964, 1593, 1616, 1116 mass 197.16.

E)-2-(5-chloro-2-hydroxybenzylideneamino)-3-phenylpropanoic acid (HL2): Yield 72% U.V. $\lambda_{max}CHCl_3$ (273). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.55 (s, 1H), 8.63 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.22 (m, 5H), 7.16 (d, *J* = 2.3 Hz, 2H), 6.73 (s, 1H), 4.39 (s, 1H), 3.25 (s, 1H), 2.98 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.57 (s), 159.05 (s), 158.67 (s), 137.41 (s), 134.08 (s), 129.87 (s), 129.78 – 129.38 (m), 129.29 – 128.89 (m), 127.34 (s), 125.35 (s), 121.95 (s), 118.22 (s), 80.77 (s), 35.58 (s). FT.IR (ATR, ν cm^{-1}) 3310, 2971, 1590, 1615, 1121. mass 303.74

General procedure for Synthesis of metal (II) chloride complexes (C1,C2,C3,C4):

Binary metal complexes were prepared using metal salts and ligands in 1:2 stochiometric ratio. The mixture of hot ethanolic solution of 10 mM of metal (II) chloride and ethanolic solution of Schiff base ligand [HL1/HL2] (20 mM) was refluxed for 2-4 hours at 60-70°C. The precipitate was kept aside for slow evaporation at room temperature. The solid was collected by suction filtration, washed thoroughly with ethanol and then dried in desiccator over anhydrous $CaCl_2$. An outline of synthetic procedure of ligands and respective metal complexes are as presented in Scheme 2



Scheme 2 outline of synthetic procedure of ligands and respective metal complexes

TABLE 1 Infrared spectra of Metal Complexes of Schiff base ligands

Codes	I.R. Values (υ in cm^{-1})					
	(OH)	(N=CH)	(C=N)	(C=O)	(M-O)	(M-N)
C1	3342	2692	1634	1728	452	418
C2	3303	2740	1591	1705	472	414
C3	3355	2710	1610	1724	468	412
C4	3342	2692	1634	1728	452	418

III.RESULTS AND DISCUSSION

In this investigation IR spectra of Schiff bases, new broad band at 3300-3600 cm^{-1} has been observe for all complexes which due to the presence of amino acids OH group and water molecule coordinated with metal ion [5]. In the metal complexes, azomethine (>C=N) stretching frequency has been observed at lower region than

that of corresponding free ligands [6]. This lower shift indicates coordination of imino nitrogen atom to the metal ion. The stretching frequency of Phenolic–OH group of ligands (**HL1- HL2**) is absent in complexes (**C1-C4**), which clearly indicates that phenolic–OH group of salicylic acid coordinates to the metal ion. Appearance of new bands in the spectra of all complexes in the regions 500-450 and 420-400 cm^{-1} has been attributed to M-O and M-N stretching respectively [7]. The thermogravimetric analysis (TG) of the solid complexes has been carried out from room 20°C to 850°C in a dynamic atmosphere of nitrogen (50 ml/min) using a Toshvin DTG 60H thermal analyser.

The electronic spectral data of HL1 and HL2 and their C1-C4 complexes is obtained by preparing methanolic solutions (1×10^{-5} M) of the sample at room temperature. The ligands exhibited absorption bands between 200 to 270 nm assigned to $\pi \rightarrow \pi^*$ and 408 to 426 nm $n \rightarrow \pi^*$ transitions. But these bands found to be blue-shifted at different absorbance values in the case of the metal complexes. The hypsochromic effect shows formation of the metal complexes. The ligand-to-metal charge transfer (LMCT) observed at 351 nm for Cu(II) is due to the presence of electron transitions from the highest occupied molecular orbital (HOMO) of the ligand to the lowest unoccupied molecular orbital (LUMO) of the metal.

Biological Activity of the Compounds:

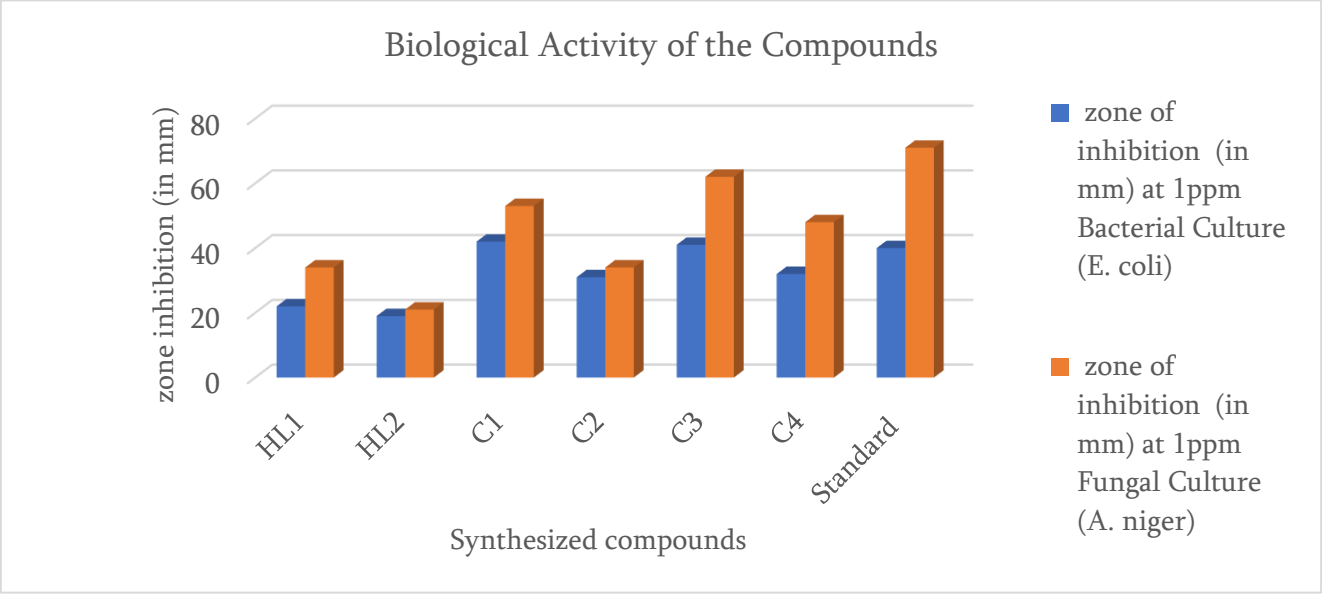


Figure 1: Antifungal and antibacterial activity of synthesized compounds

agar well plate diffusion method is use to screen antimicrobial activity of all synthesized compounds. where C1 and C3 have very promising activity against E. *Coli* and *A. Niger* strains with streptomycin as a standard [8].

IV.CONCLUSION

On the basis of different analysis, it is found that, the metal complexes have octahedral geometries with 1:2 metal as to ligand stochiometric ratio. The synthesized complexes C1 and C3 have been found to be equally potent against *E. Coli* and *A. Niger* strains when results compared with streptomycin as standard. the findings of the current work can serve as a recommendation for the synthesis and screening of new complexes which will be upstretched towards the development of new drugs in current MDR crisis.

V. ACKNOWLEDGEMENTS

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VI.CONFLICT OF INTEREST

The author(s) declare that there is no conflict of interests regarding the publication of this article.

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A Green, Efficient Protocol for Synthesis of a 3-Pyranyl Indole Derivatives by Using [Bmim]PF6 under Reflux Condition

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ABSTRACT
A green and efficient method was described for one pot synthesis of 3-pyranyl indole derivatives by reaction of 3-cyano acetyl indole, aromatic aldehydes and malononitrile in an aqueous media under reflux by using [Bmim]PF6 as a green catalyst. Simple and easy work process, use of green catalyst, green solvent, short reaction time and excellent yields of the products are the advantages of this method.
Keywords: 3-cyano acetyl indole, aromatic aldehydes, malononitrile, [Bmim]PF6.

I. INTRODUCTION

Recently 3-substituted indole and pyranyl ring containing heterocycles having structural and biological importance made them attractive moieties in organic synthesis, drug discovery and medicinal chemistry. In synthesis of such heterocyclic compounds, multicomponent reactions (MCR's) play an important role. The major benefits of multicomponent reactions are high atom- economy, operational simplicity, and high selectivity, due to substantial minimization of waste, time, labor cost [1-4].

Heterocycles containing 4H-pyrane moiety have important biological, pharmacological activities and used in wide range of therapeutic areas [5-7]. 3-Substituted indole moieties also play an important role in the synthesis of biologically active compounds. 3-Substituted indole moieties shows various pharmacological activities such as anticancer, antitumor, hypoglycemic, antiinflammatory, analgesic and antipyretic activities [8-12]. Because of pharmaceutical importance of 4H-pyrane and 3-substituted indole compounds, herein, we have developed an green an efficient protocol for the synthesis of 3-pyrane indole derivatives by using [Bmim]PF6 catalyst in an aqueous media at reflux condition(Fig. 1).

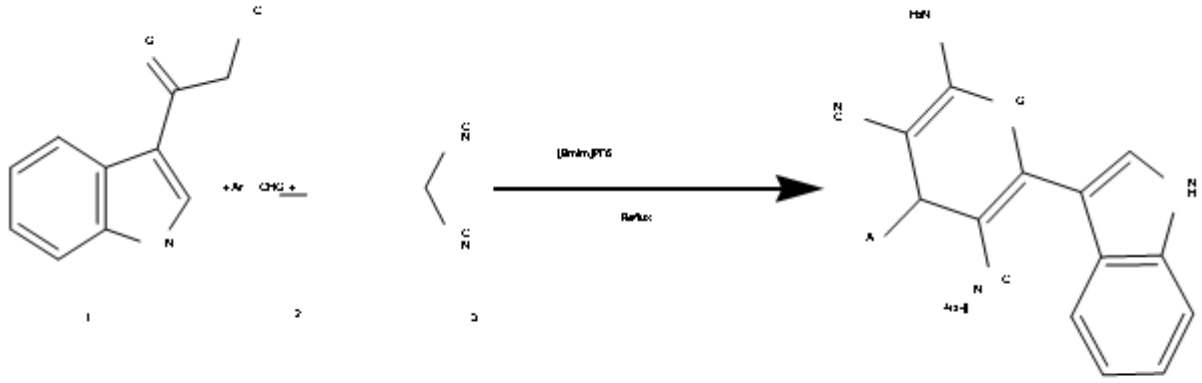


Fig.1.Synthesis of 3-pyranyl indole derivatives by using (Bmim)PF6 at reflux condition.

II. EXPERIMENTAL

2.1. General

Melting points were measured in open glass capillaries on a Veego melting-point apparatus and were uncorrected. 1H NMR was recorded at room temperature on a Bruker Avance II 400MHz Spectrometer (National Chemical Laboratory Pune) in deuterated chloroform using TMS as internal standard. IR spectra (using KBr pellets) were obtained with a Perkin Elmer Spectrum RX FTIR (Yashwant College Nanded) instrument. The reactions were monitored on thin layer Chromatography using pre-coated plates (silica gel on aluminum, Merck). All reagents were obtained from commercial sources and used without further purification. Solvents for chromatography were distilled before use. Compounds were characterized by IR and 1H NMR spectroscopy.

2.2. General procedure for synthesis of 3-pyranyl indole derivatives.

A mixture of an benzaldehyde (1 mmol), malononitrile (1.2 mmol) and 3-cyanoacetyl indole (1 mmol) was refluxed with [Bmim]PF6 (20 mol %) in 5 ml water for 25 minutes. The progress of the reaction was monitored on TLC. After completion of reaction, the reaction mixture was cooled to room temperature and the solid product was collected by filtration, washed with distilled water (5 ml x 5). The crude reaction product was collected and further purified by column chromatography (8:2 system of Pet ether:Ethyl acetate as eluent). The filtrate so obtained was concentrated under reduced pressure to recover ionic liquid which could be reused in subsequent experiments.

2.3. Spectral data for selected compound

1]2-Amino-6-(1H-indol-3-yl)-4-(naphthalen-1-yl)4H-pyran-3,5-dicarbonitrile (Table 3, entry 10):IR (KBr): 3433, 3243, 2112, 1608, 1512, 771, 733 cm;

1H NMR (400 MHz, DMSO-d6): d 5.18 (s, 1H, -CH),7.11 (t, 1H, J = 6.75 Hz, Ar-H), 7.27 (t, 1H, J = 7.45 Hz, Ar-H), 7.19 (s, 2H, –NH2), 7.38–7.46 (m, 5H, Ar-H), 7.79–7.88 (m, 3H, Ar-H), 8.17 (d, 1H, J = 7.15 Hz, Ar-H), 8.28 (d, 1H, J = 7.45 Hz, Ar-H), 12.07 (br s, 1H, –NH), MS (EI): m/z 388.42 [M+].

III.RESULTS AND DISCUSSION

In recent years, the use of ionic liquids as a green catalyst, solvent found applications in number of organic reactions. Herein we developed the use of ionic liquids as a green catalyst in an aqueous medium under reflux conditions for one pot multicomponent synthesis of 3-pyranyl indole derivatives.

In order to check the generality of the reaction, the effect of solvent on the reaction was studied at reflux condition with model reaction of benzaldehyde, malononitrile and 3-cyanoacetyl indole by using [Bmim]PF6(for 20 mol%) . The best results were obtained for aqueous media as shown in Table 1.

Table 1. Synthesis of 3-pyranyl indole derivative using different solvents.

Entry	Solvent used	Time in Minutes	Yield(%)
1	Chloroform	30	76
2	Ethanol	30	84
3	Acetonitrile	25	82
4	Water	25	94
5	Solvent free	25	81

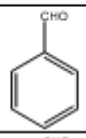
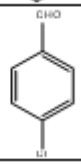
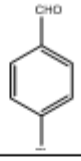
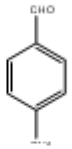
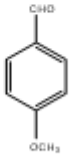
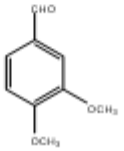
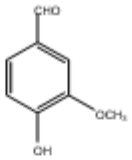
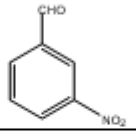
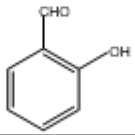
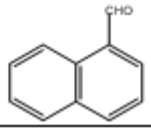
However the scope of the reactions was studied with different substituted aldehyde derivatives. The reaction undergo very smoothly with both electron withdrawing and electron donating groups substituted at different position of aromatic aldehyde. The results are summarized in Table 3.

The reuse of the catalyst is a major factor in a new synthetic green procedure. The ionic liquid can be reused after simple distillation to remove water and remaining ionic liquids was dried under vacuum and reuse for further reactions. To test this, a series of three consecutive runs for the reaction with catalyst were carried out. The results, however, demonstrated no significant change in the activity of the catalyst. The catalyst could be reused for fourth times without significant decrease in catalytic activity (Table 2).

Table 2. Reuse IL for the synthesis 3-pyranyl indole derivatives.

Cycle	Fresh	First	Second	Third
Yield (%)	94	91	88	81

Table 3: Synthesis of 3-pyranyl indole derivatives by using [Bmim]PF6 at reflux condition in an aqueous media.

Entry	Aldehydes	Products	Time (Min)	[a]Yield (%)
1		**4a**	25	94
2		**4b**	28	88
3		**4c**	28	90
4		**4d**	25	90
5		**4e**	37	87
6		**4f**	40	85
7		**4g**	35	85
8		**4h**	40	86
9		**4i**	30	87
10		**4j**	30	88

IV.CONCLUSIONS

In conclusion here we describe a highly efficient and green process for the synthesis of 3-pyran indole derivatives under reflux condition by using ionic liquid in an aqueous media. This method offers several advantages such as catalyst reusability, high yield of product, short reaction time, simple work-up procedure and easy isolation.

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Formation of Alkaline Earth and Transition Metal Complexes with Labetalol Drug in Ethanol Water Media

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ABSTRACT

The stability constant of Labetalol drug with alkaline earth metal ions Mg2+, Ca2+ and transition metal ions Fe3+, Cu2+, Zn2+were investigate using pH metric titration technique in 20%(v/v) ethanol-water mixture at 300 K temperature and at an ionic strength of 0.1M NaClO4. {Metal to ligand ratio = 1:5 and 1:1} The method of Calvin and Bjerrum as adopted by Irving and Rossotti has been employed to determine proton- ligand pKa and metal-ligand stability constant logK values. It is observed that transition metal and alkaline earth metal ion forms 1:1 and 1:2 complexes. The order of stability constants for these metal complexes was as: Fe3+ > Cu2+ > Zn2+> Mg2+ > Ca2+

Keywords: Stability Constant, alkaline earth metal, transition metal, Labetalol, pH metry

I. INTRODUCTION

The stability of metal complexes with medicinal drugs plays a major role in the biological and chemical activity. Most of the s-block and d-block elements form complexes. Mg (II) ions form complexes with several enzymes which are essential for energy release. Ca (II) is important in bone, teeth and blood clotting. It maintains the regular breathing of hearts, contraction of muscles. For the present investigation, we selected medicinal drug Labetalol (LBT), chemically described as 5-[1-Hydroxy-2-(1-methyl-3-henyl propyl amino) ethyl] salicylamide hydrochloride. LBT is considered as one of the major therapeutic drugs for the treatment of hypertension and also used to induce hypotension during surgery as it reduces blood pressure more rapidly than other beta blockers. The drug is quite sensitive, even a small dose of the drug gives sufficient blockage, thus indicating that the drug is very much confined to the cardio protective effects. It is used in the treatment of patients with angina pectoris with and without co-existing hypertension.

In continuation of our earlier work with complexation of medicinal drugs[01-15] and after literature survey we have carried out a solution study on the complexation of Labetalol with transition metal ions Fe^{3+}, Cu^{2+}, $Zn^{2+}$and alkaline earth metal ions Mg^{2+}, Ca^{2+} pH metrically in 20% (v/v) ethanol-water mixture at constant ionic strength of 0.1M $NaClO_4$.

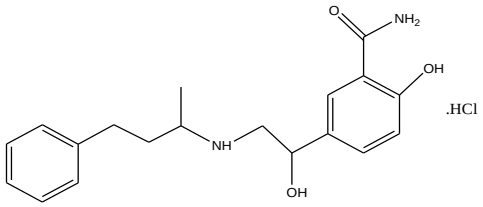

Figure 1: Labetalol hydrochloride (molecular formula $C_{19}H_{25}N_2O_3Cl$)

II. METHODS AND MATERIAL

NaOH, $NaClO_4$, $HClO_4$, metal salts were of AR grade. Labetalol is soluble in 20% (v/v) ethanol-water mixture.The solutions used in the pH metric titration were prepared in double distilled water. NaOH solution was standardized against oxalic acid solution and standard alkali solution was again used for standardization of $HClO_4$. Metal salt solutions were standardized using EDTA titration. The measurements were made at temperature 300K in 20% (v/v) ethanol-water mixture at ionic strength 0.1M $NaClO_4$. Water thermostat is used to maintain the temperature constant. pH measurement was made using Elico L_1-120 pH meter in conjunction with glass and reference calomel electrode. The instrument was calibrated at pH 7.00 and 4.00 using standard buffer solutions.

For evaluating the protonation constant of the ligand and the formation constant of the complexes in 20 %(v/v) ethanol-water mixture with metal ions we prepare the following sets of solutions.

(A) $HClO_4$ (A)

(B) $HClO_4$+Labetalol (A+ L)

(C) $HClO_4$+ Labetalol + Metal (A+ L+ M)

Above mentioned sets prepared by keeping M : L ratio, concentration of perchloric acid and sodium perchlorate were kept constant for all sets. The volume of every mixture was made up to 50ml with double distilled water and the reaction solution were pH meterically titrated against the standard alkali at temperature 300K.

TABLE 1 Proton-ligand and metal-ligand stability constant of Labetalol drug in 20% (v/v) ethanol-water medium{Metal to ligand ratio =1:5}

pKa	logK	Fe^{3+}	Cu^{2+}	Zn^{2+}	Mg^{2+}	Ca^{2+}
7.7424	$logK_1$	4.2816	4.1402	3.2344	3.2141	2.9221
	$logK_2$	4.1452	4.0566	2.9832	2.9531	2.6021
	log β	8.4268	8.1968	6.2176	6.1672	5.5242

TABLE 2. Proton-ligand and metal-ligand stability constant of Labetalol drug in 20% (v/v) ethanol-water medium {Metal to ligand ratio =1:1}

pKa	logK	Fe^{3+}	Cu^{2+}	Zn^{2+}	Mg^{2+}	Ca^{2+}
7.7424	$logK_1$	4.8920	4.7510	3.7286	3.7080	3.2571
	$logK_2$	- - - -	- - - -	- - - -	- - - -	- - - -
	log β	4.8920	4.7510	3.7286	3.7080	3.2571

III.RESULT AND DISCUSSION

Labetalol Hydrochloride is antihypertensive drug, it contains primary amine group, secondary amine group and two hydroxyl groups one is phenolic -OH and other is cyclic -OH group. It also contains one carbonyl group. The labetalol under experimental conditions shows only one protonation constant in the basic range. Instead of hydroxyl groups, carbonyl group and secondary amino group, nitrogen of primary amino group might be involved in the process of protonation. The lower value of pKa (7.7429) is attributed to strong electron withdrawing effect of carbonyl group present nearer to $-NH_2$ group.

The proton-ligand stability constant pKa of Labetalol is determined by point wise calculation method as suggested by Irving and Rossoti. Metal-ligand stability constant logK of metal ions with Labetalol drug were calculated by point wise and half integral method of Calvin-Bjerrum as adopted by Irving -Rossotti.

The order of stability constants for these metal complexes was as follows:

Fe^{3+} > Cu^{2+} > Zn^{2+} > Mg^{2+} > Ca^{2+} {Metal to ligand ratio 1:5 and 1:1}

The above stabilities of metal complexes with ligand are similar to the observations made by several research workers and are in accordance with Irving and Williams order. In the present metal ions, trivalent Iron has highest stability while divalent calcium shows minimum stability. This natural order is particularly valid for nitrogen and oxygen donor ligands, irrespective of nature of ligands. Extra stability of divalent copper complex is attributed to unique electronic configuration of Cu (II) and John-Teller effect.

IV.CONCLUSION

In the present investigation, stability constants of transition metal and alkaline earth metal complexes with Labetalol drug at 1:5 and 1:1 metal-ligand ratio were studied at 300K. It is found that stability constant of transition metal complexes when metal-ligand ratio 1:5 is greater than those of transition metal complexes when metal-ligand ratio is 1:1. **This indicates that at higher concentration of ligand more stable complexes are formed.** The stability constants of trivalent Fe show maximum stability whereas divalent Ca shows minimum stability. The metal ions forms 1:1 and 1:2 complexes with Labetalol drug.

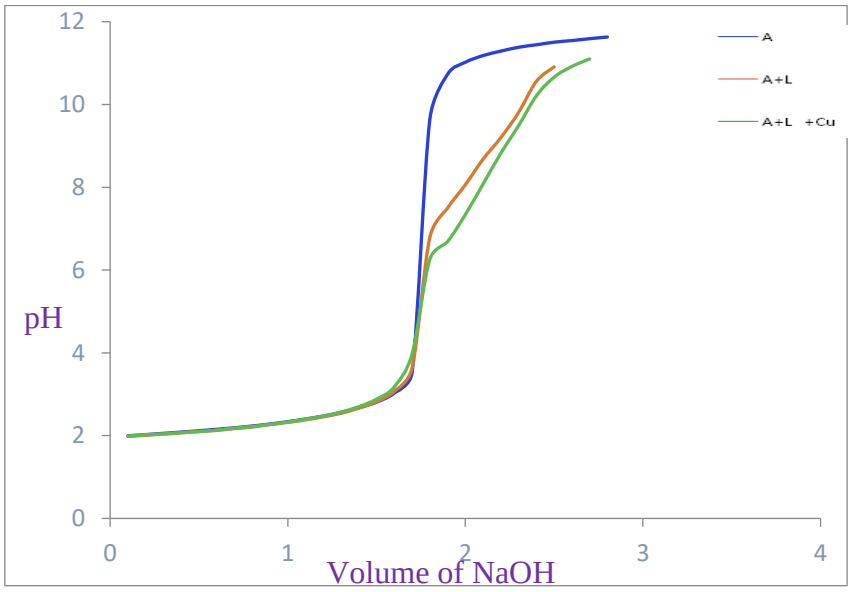

Figure 2: The pH metric titration curve for Cu (II)- Labetalol

V. ACKNOWLEDGMENTS

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Sodium Hydroxide Treated Alstonia Scholaris Leaves Powder as an Adsorbent for Divalent Nickel Ion Removal from Aqueous Media: Kinetic and Isotherm Studies

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ABSTRACT
In the current studies, the effectiveness of Alstonia Scholaris leaves powder was investigated for the adsorption of Ni2+ ion from aqueous solution by batch adsorption. The experimental data was analyzed by applying Pseudo first order kinetic model, pseudo second order kinetic model, Langmuir isotherm and Freundlich isotherm.

Key Words: Bio adsorbent, removal, economic adsorbent, adsorption

I. INTRODUCTION

Due to the environmental concern, the need of industrial effluent becomes very important factor [1]. Nickel is uses to make alloys and for other important function in different industries [2]. The human exposure to high concentration of nickel can associated with serious health issues like cancer, asthma and allergic reaction [3]. The adsorption method is mostly used to remove hazardous material from the water [4]. So in the present study the adsorption efficiency of leaves powder for divalent nickel ion was investigated.

II. MATERIALS AND METHODS

The adsorbent (leaves powder) was prepared as per the literature procedure [5]. All the chemicals used were purchased from Loba Chemie. Distilled water was used to prepare desired solution. A batch absorption experiment was carried out by taking 50 mL Ni^{2+} solution of known concentration in 250 mL conical flask, 0.1 g of adsorbent was added and the resultant solution was shaken. After scheduled time interval solution was filtered using Whattman Filter paper 41 and concentration of Ni^{2+} in solution was found. The following equation is used to determine the amount absorbed

$$q_t = \frac{(C_0 - C_t)V}{W} \quad (1)$$

Where q_t and q_e is adsorption amount at time t and equilibrium, C_o, C_t are Ni^{2+} concentration initial, at time t and equilibrium in mg L^{-1} respectively, V is volume of solution in L and W is weight of adsorbent in g.

III.RESULT AND DISCUSSION

Effect of Adsorbent dose

50 mL 20 mg/L solution and adsorbent was stirred for 30 min. The result was represented in Fig.1 and Fig 2.

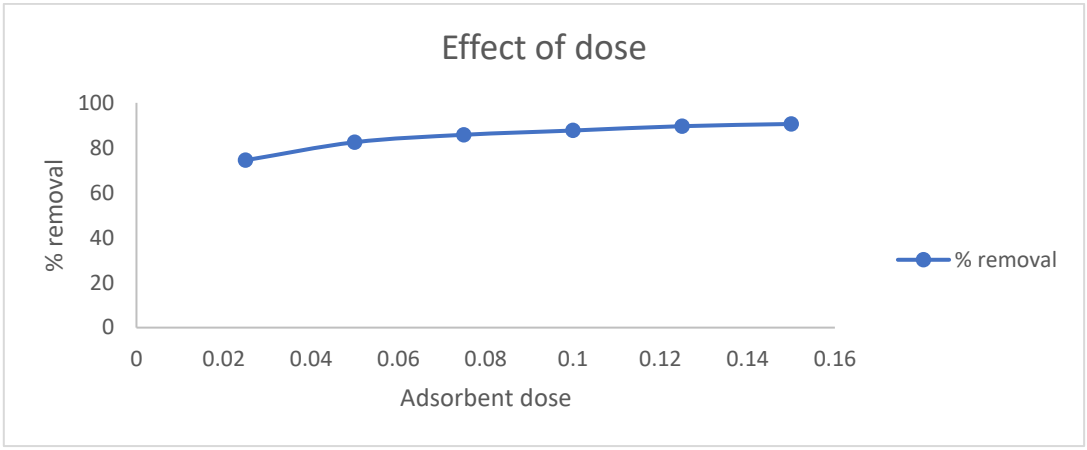

Fig. 1 Effect of Adsorbent dose (% removal)

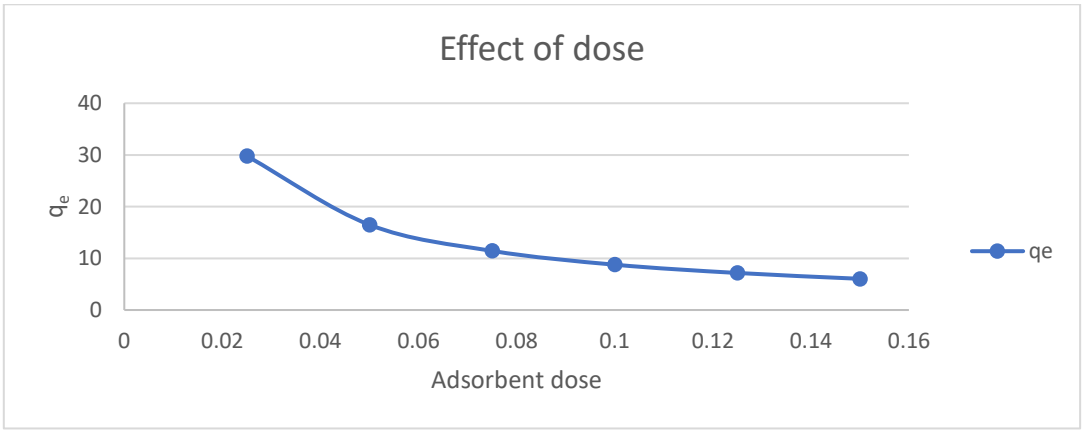

Fig 2 Effect of Adsorbent dose (q_e)

Effect of Contact time and initial metal ion concentration

Effect of contact time and initial metal ion concentration was studied by stirring 50 mL Ni^{2+} solution (10 mg/L to 40 mg/L) with 0.1 g adsorbent.

Adsorption Kinetics

Pseudo first order kinetic model and pseudo second order kinetic model were applied for present studies.

Following equation for pseudo first order kinetic model was applied [6]

$$\log(q_e - q_t) = \log q_e - \frac{k_1 t}{2.303} \qquad (2)$$

Where k_1 is rate constant, q_e and q_t are amount of dye adsorbed at equilibrium and at time t respectively.

Pseudo second order equation is represented by following equation [7]

$$\frac{t}{q_t} = \frac{1}{q_e^2 k_2} + \frac{t}{q_t} \qquad (3)$$

Where k_2 is rate constant

Table 1 Rate constants for pseudo first-order , pseudo second-order adsorption model

Dye Conc.	First order			Second order		
(mg L^{-1})	K_1	q_e	R^2	K_2	q_e	R^2
	(min^{-1})	(mg g^{-1})		(min^{-1})	(mg g^{-1})	
10	0.0329	0.362	0.982	0.329	4.385	1.0000
20	0.0454	0.658	0.924	0.186	9.001	0.9989
30	0.0739	1.12	0.931	0.135	14.064	0.9993
40	0.0439	0.923	0.9676	0.125	18.726	0.9978

Adsorption isotherms

Langmuir isotherm, Freundlich isotherm, were applied for present study

Langmuir isotherm represented by following equation was used [8]

$$\frac{C_e}{q_e} = \frac{C_e}{q_m} + \frac{1}{bq_m} \qquad (4)$$

Freundlich isotherm is represented by following equation [9]

$$\log q_e = (1/n) log C_e + \log k_f \qquad (5)$$

Table 2 Langmuir , Freundlich parameter

Langmuir Isotherm			Freundlich Isotherm		
b (L mg-1)	q_m (mg g-1)	R^2	n	Kf(mg g^{-1})	R^2
-17.04	2.679	0.892	11.33	14.71	0.996

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Synthesis, Characterization and Antimicrobial Studies of 1-(5-Bromo-2-Hydroxyphenyl)-3-(2-Bromo-5-Methoxyphenyl) Propane-1, 3-Dione and Its Metal Transition Complexes

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ABSTRACT

The ligand 1-(5-bromo-2-hydroxyphenyl)-3-(2-bromo-5-methoxyphenyl) propane-1,3-dione (L) and its transition metal complexes have been synthesized. Each metal complexes synthesized by metal nitrate with 1, 3 dione (L) in the ratio 1:2 stiochimetry. The characteration were carried out by elemental analysis, UV-Visible spectroscopy, infrared spectroscopy,1H-NMR,13C-NMR, magnetic susceptibility, molar conductance, powder XRD and TGA for structural formulae study. The synthesized 1, 3-dione and their transition metal complexes have been screened for in vitro antibacterial, and antifungal activity using Resazurin 96 well plate method. This method is simple, sensitive, rapid, and reliable. It achieves more accurate minimum inhibitory concentration (MIC). The transition metal complexes and ligand showed moderate to excellent antimicrobial activity against all tested bacteria and fungi.

Keywords: 1, 3-dione, Metal-complexes, Magnetic susceptibility, XRD, TGA, Antimicrobial activity

I. INTRODUCTION

In pharmaceutical sector metal plays important role in synthesis of drugs. In particular 3d series are more important in human body. The transitions metal ions have great ability to form bond with organic and biological fluids. The Fe ions important role in Hemoglobin which give binding side for O_2. Pt ions forms complexes with ammonia and chlorine to form cis-platin (cis-Pt $(NH_3)_2Cl_2$) which is first introduced in anti-cancer drug. Zn ions regulate the function of genes in the nuclei of cells, synthesis, storage and secretion of insulin and also supporting a healthy immune system. The 1, 3-diones uses as an antibacterial , antiviral, insecticidal , antioxidant , antitumor,HIV-1 Integrase (IN) inhibitors. [1-6] The synthesis of different hetero-cyclic compounds. [7-11] from 1, 3-diones were known's.

Here we synthesized of new 1, 3-dione and their metal complexes characterized by various spectral analyses and also look the in vitro antibacterial screening was carried out by using micro titre plate based resazurin assay against Gram positive and Gram negative bacterial cultures. The antifungal susceptibility of 1, 3-dione and its metal complexes was tested against Candida albicans and Saccharomyces cerevisiae .In micro titre plate based resazurin assay technique was used for antimicrobial analysis and colorimetric indicator is resazurin.

II. EXPERIMENTAL

All chemicals were of reagents grade, purchased from commercial source and used directly. All metal salts were used as nitrate. Melting points were recorded by the open tube capillary method and are uncorrected. The progress of the reaction and the purity of compounds were verified by thin-layer chromatography (TLC). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Jeol-400 MHz instrument in $CDCl_3$ solution. Mass spectra were taken on a macro mass spectrometer by the electrospray ionization (ESI) method. The C, H and N analyses were carried out using a Euro-E 3000. Infrared spectra were recorded on SHIMADZU FT-IR spectrometer. The conductivity of metal-complexes measured by ELICO CM 180. The TGA analysis were carried out by Ramp method using SDT Q600 V20.9 Build 20 instrument.

Synthesis of 1-(5-bromo-2-hydroxyphenyl)-3-(2-bromo-5-methoxy phenyl) propane 1,3-dione (L):

The compound 2-bromo-5-methoxy benzoic acid (0.01mol) and 5-bromo-2-hydroxy acetophenone (0.01mol) was dissolved in 20 ml dry pyridine cool the mixture below 5^{o}C add phosphorous oxychloride (1-2 ml) drop wise and continuously stirrer for 5-6 hrs form ester. The ester dissolve in pyridine and add powdered KOH and stirrer for about 2-3 hrs. Then it was poured over crushed ice and acidified with dil. HCl. The resulting solid was crystallized from ethanol. **Yield:** 66%; **M.P.**129 ^{0}C. **Elemental analysis:** calculated C= 44.89, H= 2.83 Found C= 43.92 H=3.02; **^{1}H-NMR:** 15.09 δ (s, 1H, enolic -OH), 11.94 δ (s, 1H, phenolic –OH) 7.39 δ (s, 1H, =C-H ethylene), 6.87-7.78 δ (m, 6H, Ar-H), 3.85(s, 3H, O-CH_3).

^{13}C-NMR: (400 MHz, $CDCl_3$) δ/ppm = 194.86 (C=O), 178.47 (C-O enolic), 98.10 (=C-H ethylene). 55.91 (O-CH_3)

IR: (KBr) ν_{max}/cm^{-1}; 1612 cm^{-1} (ν (C=O) ketonic), 1593 ν (C=C), 1213 cm^{-1}(C-O) enolic), 3072 cm^{-1} (ν (-OH) intramolecular H-bonding in phenolic).

UV/Vis.: (DMSO): 361.50, 257 nm. **MS:** *m/e*; 428.91

Synthesis of metal complexes of ligand (L)

A Mixture of ligand (L) (5 mmol) and 2.5 mmol of appropriate metal nitrate added in anhydrous 30 ml ethanol and the resulting mixture was refluxed at 60-65^{0}C for 2-3 hour whereupon the complex precipitation occurs after the addition of alcoholic ammonia. The precipitated colored solid complex washed with ethanol and crystallized by using dichloromethane.

Yield- 62- 72%.

IR (KBr) ν_{max}/cm^{-1}; 1605-1612 (ν(C=O) ketonic), 1550-1585 (ν(C=C) alkene), 1213-1242 (ν(C-O) enolic), 3005-3095 (ν (-OH) in phenolic), 3600-3745 (ν (-OH) in H_2O molecules), 518-534 (ν (M-O bond in metal complex).

UV/Vis. (DMSO) nm: 256.5-258 ($\pi \rightarrow \pi^{*}$), 363.5- 372 (LMCT).

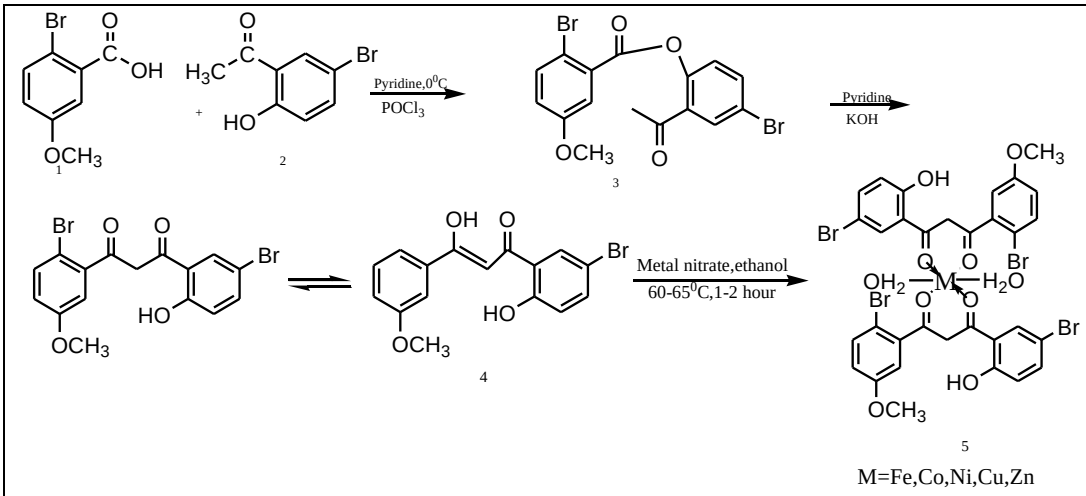

Fig. Synthetic Route of 1,3-Diones and its metal complexes

III.RESULTS AND DISCUSSION

All the metal complexes were found to be thermally very stable. All the synthesized transition metal complexes were highly soluble in dimethyl formamide and dimethyl sulfoxide and less soluble in other common organic solvents. The results of elemental analysis confirmed stoichiometry of ligand to metal 2:1 for all metal complexes. The study of TGA confirms two water molecules coordinated in the metal complexes reveals octahedral geometry. Spectral analysis data confirm the synthesis of β-diketone and its metal complexes. Physical and analytical data of the transition metal complexes are given in experimental section.

A) IR SPECTRA

The characteristic infrared spectral data of ligand (L) and their metal complexes are reported in Table 1. The carbonyl group (>C=O) stretching frequency of ligand (L) appearance at 1612 cm^{-1}. The appearance of frequency at 1593 cm^{-1} due to (-C=C-) double bond and the bond (C-O) appear at 1213 cm^{-1}. The metal complexes of ligand (L) shows IR frequency of carbonyl group (>C=O) at 1591-1612 cm^{-1} which were lower than IR frequency of ligand (L).[12] This lowering stretching frequency indicates that ligands coordinated with the transition metal ions. In addition, new band at 509-534 cm^{-1} observed due to metal–oxygen (M-O) bond vibrations in metal complexes which were absent in ligands 4.[13] This confirms of metal ions coordinate with ligand via oxygen.

Table I: FTIR (υ/cm^{-1}) data of ligand and metal complexes.

Compounds	C=O	C-O	C=C	M-O
L	1612	1213	1593	----
$(L)_2$-Fe	1605	1220	1591	518
$(L)_2$-Co	1610	1242	1581	534
$(L)_2$ –Ni	1608	1213	1585	532
$(L)_2$-Cu	1612	1242	1577	520
$(L)_2$-Cu	1610	1213	1581	532

B) ^{1}H NMR and ^{13}C NMR SPECTRA

The ^{1}H NMR spectral data of the 1-(5-bromo-2-hydroxlphenyl)-3-(2-bromo-5-methoxyphenyl)propane-1,3-dione (L) shows singlet at δ 15.09 ppm due to enolic proton, a singlet at δ 11.94 ppm due to phenolic proton adjacent to the carbonyl group which confirms the formation of β-diketone.

In the ^{13}C NMR of Ligand (L) peak appeared at δ 194.86 ppm corresponds to carbonyl carbon (C=O) and enolic carbon (C-O) at δ 178.47 ppm. The signal at δ 98.10 ppm appeared shows methine linkage.

C) MAGNETIC SUSCEPTIBILITY AND MOLAR CONDUCTANCE

The molar conductance values were obtained in $\Omega^{-1}cm^{2}mol^{-1}$ at room temperature using DMSO as a solvent and results are recorded in Table II. The molar conductance values were obtained in the range 13-20 $\Omega^{-1}cm^{2}mol^{-1}$. The conductance values show metal complexes non-electrolytic in nature.[14] All metal complexes were paramagnetic in nature except Zinc complexes were diamagnetic due to non-availability of unpaired electrons.

Table II:

Metal Complexes	Magnetic moment μeff (B.M)	Molar conductance	M. W.	Melting point	Elemental analysis (%) Found/ (Calcd.)	
					C	H
$(L)_2$-Fe	5.49	13	948.02	>300	39.94(40.54)	39.94(40.54)
$(L)_2$-Co	3.31	17	951.11	210	40.22(40.41)	2.85(2.97)
$(L)_2$ –Ni	2.48	18	950.87	230	40.03(40.42)	2.61(2.97)
$(L)_2$-Cu	1.19	20	955.72	>300	39.77(40.21)	2.72(2.95)
$(L)_2$-Cu	Dia	14	957.56	>300	39.91(40.14)	2.77(2.95)

D) UV–VISIBLE SPECTROSCOPY

The electronic spectra of the ligands (L) exhibited bands in the regions of 259.5 and 361.5 nm, which can be assigned to intramolecular $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ electronic transitions due to the aromatic and carbonyl groups. In all metal complexes intramolecular $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ electronic transitions occur but weak d-d transition not found. All metal complexes have center of symmetry the 3d orbital cannot mix with the 3p orbital in such mixing being symmetry forbidden. Octahedral complexes can be centrosymmetric. The octahedral complexes with center of symmetry so T_2g-Eg transitions were very weak not observed.

E) POWDER XRD STUDIES

X-ray powder diffraction study primarily used for phase identification of a materials and can provide information on unit cell dimensions. Single crystals of the complexes could not be prepared therefore powder diffraction data used. The average crystallite size of complexes calculated using Debye Scherrer's formula.[15] Powder xrd data recorded in the range 10^0-80^0. 2θ values. All metal complexes show monoclinic crystal system.

Table III: Summary of XRD data of Metal Complexes

Parameter	$(L)_2$- Fe complex	$(L)_2$- Cu complex
Temperature(k)	298	298
Wavalength	1.540598	1.540598
Radiation	Cu K α	Cu K α
Crystal System	Monoclinic	Monoclinic
Unit Cell Dimension		

a (A°)	6.014	11.10
b (A°)	27.38	12.5
c (A°)	9.520	10.10
α (⁰)	90	90
β (⁰)	97	104.5
γ (⁰)	91	90
Average Particle Size (nm)	10.45	9.673

F) THERMO GRAVIMETRIC STUDY OF SOME METAL COMPLEXES

The TG/DT analysis of L–Fe Complex, the temperature range usually selected 25⁰C to 600⁰C at the rate 10⁰C/Min in Nitrogen atmosphere using *a*-Al_2O_3 as reference. The thermogram curve of L–Fe Complex shows weight loss 6.018% upto 225⁰C clearly indicate removal of surface two coordinated water molecules. A sudden weight loss (48.05%) from 225⁰C to 475°C was due to loss of one phenyl ring with two hydroxy and one carbonyl group. Further, the weight loss (29 %) from 475°C to 566°C corresponds to the decomposition of two phenyl ring and a propane-1, 3-dione moiety. On further heating above 566°C the weight remained constant corresponding the formation of Ferrous oxide. In DTA graph small endothermic peak observed at 123°C which indicates dehydration process and strong exothermic at 501°C indicates thermal decomposition of L–Fe Complex.

G) ANTIMICROBIAL ACTIVITIES

Antimicroial activities of the ligand and its transition metal complexes were performed by the resazurin method.[16] The resazurin method which is simple, sensitive, rapid, robust and reliable, and could be used successfully to assess antibacterial especially the dilution protocols, and utilized a standard concentration of bacterial suspension so that a 'true' MIC value can be obtained. The MIC values of ligand and its metal complexes shows moderate activities compare to standard.

Table IV: Antibacterial activity Ligand and its complexes MIC (µg/ml).

Compound	Antibacterial Activity			
	Gram positive		Gram negative	
	B.subtilus	S.aureus	E.coli	P.aerugenosa
Fe-L	50	<50	100	100
Co–L	50	<50	100	100
Ni–L	50	<50	100	50
Cu–L	50	50	100	50
Zn-L	50	<50	100	100
L	50	50	100	100
Tetracycline	2	1	4	1

Table V: Antifungal activity of ligand and its metal complexes MIC (µg/ml).

Compound	Antifungal Activity

	C.albicans	S.cerevisiae
Fe-L	150	150
Co–L	150	150
Ni–L	150	100
Cu–L	150	100
Zn-L	100	150
L	150	150
Amphotericin B(mg/ml)	1.25	1.25

IV.CONCLUSIONS

The present research work, we synthesized new ligand and its transition metal complexes. In the metal complexes reveals that 1, 3-dione and metal 2:1 stoichiometry ratio for all the prepared metal complexes. These complexes were characterized by various physicochemical and spectral analyses. It shows non-electrolytic nature and octahedral geometry with center of symmetry. powder XRD study of complexes show monoclinic crystal system. The thermal stability were evaluated by TG method whose results revealed good thermal stability for the synthesized metal complexes. As per results, it can be seen that the newly synthesized ligand and its metal complexes shows considerable antimicrobial activity against all tested bacteria and fungi compared with antibiotics Tetracycline and Amphotericin B.

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Some Newly Developed Naphthofuran Derivatives Containing 3-Phenylquinoxaline moiety as Biological Active Compounds

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ABSTRACT

A series of substituted Chalcones (1a-e) prepared by Claisen-Schmidt condensation with substituted aromatic aldehydes. These Chalcones on reacts with bromine in acetic acid gives chalcone dibromide (2 a-e). This chalcone dibromide (2 a-e) condenses with benzene 1,2-diamine (BDA) in presence of few drops of concentrated H2SO4 in methanol medium affords substituted 3-phenylquinoxaline (3 a-e). The structures of these compounds were confirmed by analytical and spectral data. The newly synthesized compounds were screened for biological activity

Keywords: Naphthofuran, Chalcone , Antimicrobial activity

I. INTRODUCTION

Heterocyclic compounds represent an important class of biological active molecules especially those containing quinoxaline derivatives have evoked considerable attention in recent years as these are endowed.

Quinoxaline derivatives are an important class of nitrogen containing benzo heterocyclic compounds containing a ring complex made up of a benzene ring and a pyrazine ring [1,2] for medicinal chemist, since it has wide range of therapeutic uses and potential activities; acting as antimicrobial agent [3,4], cytotoxic agents[5] anxiolytic, anti HIV, antioxidant [6],anti-inflammatory[7-9],antimalarial anticancer[10],antibacterial[11],anticonvulsant[12],antiviral[13],antifungal[14]antitubercular[15],antiviral[16], analgesic[17], antiarrhythmic[18], antibiotic such as echinomycin, levomycin etc.

They are also used in the agricultural field as fungicides, insecticides [19], pesticides [20,21] consequently, many methods have been developed for the synthesis of quinoxaline.

In view of this observations and in continuation of our previous work in heterocyclic chemistry, we synthesized some new substituted 3-phenylaquinoxaline derivatives using 1-(naphtho [2,1-b]furan-2-yl)-3-phenylprop-2-en-1-one (chalcone). On starting material and tested their antimicrobial activity.

II. METHODS AND MATERIAL

All chemicals used were of analytical grade and were used without purification. Melting points were determined in open capillary method and are uncorrected. IR spectra were recorded in KBr on Bruker FT-IR(Alpha-p).^{1}H NMR spectra on Bruker "AVANCE 400" MHz spectrometer using TMS as an standard, (chemical shift in δ ppm) and mass spectrum on Shimadzu GCMS QP 5050 A. Japan model DI mass spectrometer operating at 70 eV. Progress of the reaction was monitored by TLC. The entire compounds have been recrystallized from ethanol.

A. Experimental:

Typical experimental procedure for synthesis of 3-(4-hydroxyphenyl)-1-(naphtho [2,1-b] furan-2yl) prop-2-en-one.(1a-e)

Flask was charged with mixture 2-acetylnaphto [2,1-b] furan (2.10 gm,0.011 mole) and p-hydroxy benzaldehyde (1.34 gm, 0.011 mole). It was stirred in ethanol (25 mL) and then potassium hydroxide (50%) (5 ml) was added portion wise, keeping the temperature below the 10^{0}C throughout the Addition. The mixture was kept for 36 hrs at room temp., after completion of reaction, reaction mixture was poured into crushed ice and the solid obtained was filtered under vacuum. It was washed firstly with sodium carbonate solution and then with water, dried and the product was recrystallized from ethanol to afford the pure product in 60-70% yield (1a-e). Same procedure is extended for other compounds of this series by using appropriate aldehyde. Yield 78% M.P. 156^{0}C

Spectral discussion of synthesised 1-(naphtho[2,1-b]furan-2-yl)-3-(4-hydroxy) phenylprop-2-en-1-one) (1e)

IR (KBr, vcm^{-1}): 3310 cm^{-1} (Ar-o-H str.), 3058 cm^{-1}(-CH str. of. Ar), 1644 cm^{-1}(C=0 str. in ketone),1586 cm^{-1}(C=C str.) 1515 cm^{-1} (C=C str. in Ar), 1443 and 1359 cm^{-1}(CH_3 def.), 1153 and 1167 cm^{-1} (C-O-C str) 830 cm^{-1}(-CH str.) 747 cm^{-1}(Ar-H-opb)

^{1}H NMR ($CDCl_3$ in δ pmm): 6.35(d, 1H-CO-CH), 6.95(d,^{1}H, C=CH),7.21-8.24 (complex m, 11 H, Ar-protons), 10.32 (s,^{1}H, phenolic-OH) proton

Mass (m/z): 314[M]$^+$,221,195,147,119,118,91,69,65,43

Synthesis of 2,3-dibromo-3-(4-Substituted phenyl)-1-(naphtho[2,1-b]furan-2-yl)propan-1-one (2a-e)

A mixture of 1-(naphtho[2,1-b]furan-2-yl)-3-chloro phenyl prope-2-en-1-one (chalcone) (1b) (0.005 mole) was dissolved in glacial acetic acid by warming and solution was cooled. A solution of bromine in acetic acid (3.2ml, 25% w/v) was added to this solution with stirring. After 15 minutes the dibromide prepared was filtered and washed with little alcohol followed by petroleum ether to get (2b) solid. M.P.189^{0}C yield 67 %.

Spectral discussion of 2,3-dibromo-3-(4-chlorophenyl)-1-(naphtho[2,1-b]furan-2 yl) propan-1-one.(2b)

IR (KBr, vcm^{-1}): 3315cm^{-1} (Ar-o-H str.), 3067 cm^{-1} (-CH str. of. Ar), 1635 cm^{-1}(C=0 str.in ketone),1578 cm^{-1}(C=C str.) 1509 cm^{-1} (C=C str. in Ar), 1148 and 1178 cm^{-1} (C-O-C str) 832 cm^{-1}(-CH str.) 757 cm^{-1}(Ar-H-opb), 556 cm^{-1} (C-Br str.)

^{1}H NMR ($CDCl_3$ in δ pmm): 5.09 (d,1H, -CO-CH-Br),5.35(d, 1H, Ar-CH-Br),7.19-7.67 (complex m, 6H, Ar-protons), 7.49 (singlet, 1H, Aromatic proton of Furan)7.06-7.22 (Complex multiplet , 3H, chlorophenyl protons

Mass (m/z):489[M]$^+$

Synthesis of 2-((naphtho[2,1-b]furan-2yl)methyl)-3-p-substitutedquinoxaline.(3a-e)

A mixture of 2-((naphtho[2,1-b]furan-2-yl)methyl)-3-p-tolylquinoxaline (2c) (0.01 mole) and benzene 1,2 diamine (BDA) (0.01 mole) was taken in 25ml methanol and 2,3 drops of concentrated H_2SO_4 was added. The

reaction mixture was heated on water bath for about 30 minutes. It was then diluted with water, crude mass extracted with solvent petroleum ether. (to remove insoluble BDA).Ether was evaporated and solid mass was recrystallized from ethanol. (3c) M.P.203^{0}C ,yield 64 %.

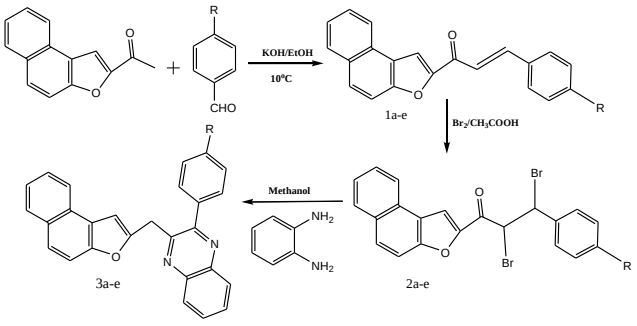
Spectral discussion of 2-((naphtho[2,1-b]furan-2-yl)methyl)-3-p-tolylquinoxaline (3c)

IR (KBr, vcm^{-1}): 3320 cm^{-1} (Ar-o-H str.), 3048 cm^{-1}(-CH str. of. Ar), 1581 cm^{-1}(C=C str.) 1518 cm^{-1} (C=C str. in Ar), 1448 and 1364 cm^{-1}(CH_3 def.), 830 cm^{-1}(-CH str.), 1665and 1585 cm^{-1} (C-C str.)747 cm^{-1}(Ar-H-opb),1446 cm^{-1}(-C=N str.)

^{1}H NMR ($CDCl_3$ in δ pmm): 2.45(s, Het-Ar-CH_2-Ar), 7.19-7.78 (complex m, 6H, Napthyl protons), 6.49 (singlet, 1H, Aromatic proton of Furan)7.16-7.32 (Complex multiplet , 4H,Aromatic protons), 2.35 (s,Ar-CH_3 protons),7.71-8.32(Aromatic ring fused with quinoxaline ring)

Mass (m/z): 400

Reaction Scheme:



Where R= H,Cl,CH_3,OCH_3 &OH

Table-1 Physical and analytical data of synthesised compounds

Mol.for.	Mol.wt.	Yield	M.P. oC	Elemental % calc.(Found)			
				C	H	N	X
Code 3a ($C_{27}H_{18}N_2O$)	386	64	186	83.9 **83.1**	4.6 **4.3**	7.2 **7.4**	-
Code 3b ($C_{27}H_{17}ClN_2O$)	420	74	196	77.0 **77.2**	4.0 **3.9**	6.6 **6.4**	8.4 **8.1**
Code 3c ($C_{28}H_{20}N_2O$)	400	67	203	83.9 **83.4**	5.0 **4.9**	7.0 **6.9**	-
Code 3d ($C_{28}H_{20}N_2O_2$)	416	69	145	80.7 **80.4**	4.8 **4.6**	6.7 **6.3**	-
Code 3e ($C_{27}H_{18}N_2O_2$)	402	74	133	80.5 **80.1**	4.5 **4.2**	6.9 **6.4**	-

III.RESULTS AND DISCUSSION

Antimicrobial activity: Newly synthesized compound 3a-e were evaluated for antimicrobial activity against two Gram-negative bacteria viz. *Eschricha coli, Salmonella typhi* and two Gram-positive bacteria viz. *Staphylococcus aureus, Bacillus subtitles* and four fungal strain viz. *Aspergillus niger, Penicillum chrysogenum, Fusirium moneliforme and Candida albicans* were determined by cup-plate method. The samples (20mg) were

dissolved in dimethyl sulfoxide(5ml) against all organisms. Penicillin and Griseofulvin were used as standards for antibacterial and antifungal activities respectively. Control (DMSO) (-ve)- means no activity.

The solvent DMSO were used as negative controls and penicillin and Griseofulvin were used as standard calculated average diameter of the zones of inhibition (in mm) for test samples were compared with that procedure by the standard drug. Almost all tested compounds were found to exhibit antimicrobial activities. Analysis of antimicrobial data suggested that compounds 3a, 3d, 3e were found to be the most active against bacterial and fungi and remaining compounds showed moderate activity against all the organisms.

Table-2 Antimicrobial activity of synthesised compounds

Comp.	Antibacterial activity				Antifungal activity			
	E.coli	*S.typhi*	*S.aureus*	*B.substilis*	*A.niger*	*P.chryso.*	*F.monelif.*	*C.albicans.*
3a	14	10	18	11	- ve	+ve	+ve	-ve
3b	09	07	20	22	+ve	+ve	+ve	+ve
3c	12	16	13	10	+ve	+ve	+ve	-ve
3d	08	**20**	**25**	23	+ve	+ve	+ve	+ve
3e	**16**	17	18	**25**	+ve	+ve	-ve	+ve
Penicillin	20	22	32	29	--	--	--	--
Griseo fulvin	--	--	--	--	+ve	+ve	+ve	+ve

IV.CONCLUSION

In conclusion a series of 2-((naphtho[2,1-b]furan-2yl)methyl)-3-p-substitutedquinoxaline were prepared. The antimicrobial activity of these compounds was evaluated against various Gram + ve and Gram –ve bacteria and fungi. Most of the compounds showed a moderate degree of antimicrobial activity. Among them compounds 3e shows higher degree of antibacterial activity for *E.coli and B.substillis* where 3d shows higher degree of antibacterial activity for *S.typhi and S.aureus.*

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Development of Proficient Route for The Synthesis of 5-Amino-1,3-Diphenyl-1H-Pyrazole-4 Carbonitrile Derivative Mediated by Si-PTA as A Catalyst

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ABSTRACT

In the present study, novel Si-PTA catalyst as an eco-friendly catalyst was synthesized and explored in the one pot multicomponent synthesis of pyrazole derivatives from Aromatic aldehyde, malononitrile and phenyl hydrazine under optimized reaction conditions in excellent yield. This eco-friendly approach of catalyst offers several advantages such as the use of a green solvent system, mild reaction conditions, shorter reaction times and excellent yield. In addition, the synthesized catalyst was characterized by using different spectroscopic techniques. Therefore, the work and results obtained present clear significant advancements over the previously reported synthesis methods.

Key words: Si-PTA, pyrazole derivatives, one pot multicomponent reaction.

I. INTRODUCTION

Nitrogen-linked heterocyclic compounds have received considerable attention in recent times due to their wide applications. Pyrazole containing structural moieties are of biological interest because they are the key structures in various therapeutic compounds. Pyrazole moiety is an important template for many biologically active compounds. The 1-pyrazolyl alanine was the first natural pyrazole which was isolated from the seeds of watermelon in 1959 [1]. Pyrazole is a magnificent ring among heterocyclic compounds as pyrazole compounds are involved in approximately all applications, including; industries, medications, pharmaceutics, agriculture, polymers, dyes, etc. [2-3]. Synthesis of such heterocyclic compound several methods are presented including multi-component reactions (MCRs) [4-6]. Synthesis by MCRs is more accepted aspect because it is effective, required less energy, decrease cost, time & generation of by-products, mild conditions, simplicity, environmental friendliness, elimination of waste production, atom economy, energy efficiency, fewer side reactions, costly purification processes [7-9] . Therefore, the formation of new MCRs with green procedure has attracted more attention. Pyrazole compounds prepared by chemists and biologists have gained widespread

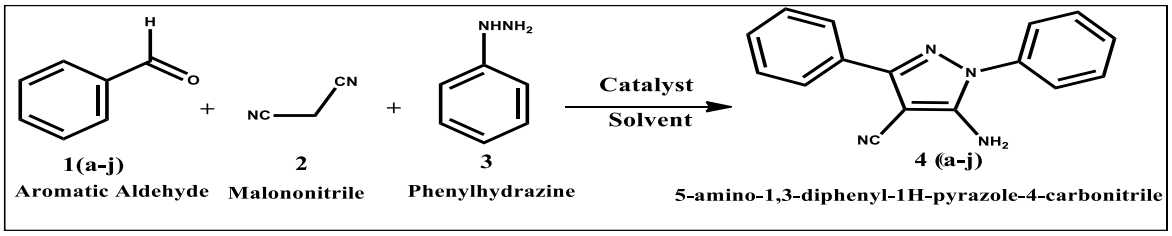
attention as they have become fairly accessible and show diverse properties [10]. These compounds are known to display anti-bacterial [11–12], anti-fungal [13], analgesic [14], anti-depressant [15], anti-convulsant [16], antimalarial [17], and anti-viral activities [18-19], antimicrobial [20], anti-inflammatory [21], antioxidant [22] , anticancer [23], cardiovascular [24], antihypertensive [25], antibiotic [26], antihyperglycemic activity [27]. Although several efforts have been taken to synthesize pyrazole derivatives from different starting material, it is still highly desirable to further explore them under this topic in pursuit of transformation efficiency and molecular diversity. Therefore, the construction of pyrazole derivative has also attracted the long-standing interest for researcher [28]. In the strategies developed, substituted hydrazones, versatile synthetic intermediates, have been commonly used as the starting materials for the preparation of pyrazole.

The methods developed for the synthesis of polysubstituted pyrazoles used different catalysts. Some of these comprises trisodium citrate dehydrate [29-30], ZrO_2 nanoparticles [31], cesium fluoride [32], I_2 [33], $Sc(OTf)_3$[34], LiOH [35], [BMIM]OH [36], $Cu(OAc)_2$ [37], oxone [38], silica chloride [39], alum [40], AgOTf [41], sodium ascorbate [42], graphene oxide–TiO_2 [43], piperidinium acetate [44], palladium and copper [45], lipase [46], cetyltrimethylammonium chloride (CTACl) [47], nickel nanoparticles [48], and juice of Citrus lemon [49]. Use of this catalyst complies with the timely topics mentioned above. In addition, one of the novel aspects of the present work is that the catalyst can act in a highly efficient and general way for reactions.

In continuation, a simple and an efficient one-pot synthetic approach were used for the preparation of pharmaceutically important pyrazoles derivatives with high functionality by means of three-component reactions of accessible starting materials such as arylaldehydes, malononitrile and phenyl hydrazine.

Phosphotungstic acid has been found to be the strongest acid among heteropoly acid [50], According to data observed in the literature, the direct connectivity of heteropoly acid with the surface of silica caused strong bonding [51] also the acidity of the catalyst could be enhanced [52].

In continuation of our research endeavor focused on the development of novel and efficient heterogeneous catalysts for heterocycles synthesis, we synthesized Si-PTA (silica-supported phosphotungstic acid) and successfully employed it as an effective catalyst for the synthesis of pyrazole derivatives (Scheme 1).



Scheme-1

II. RESULTS AND DISCUSSION

2.1. Characterization of Si-PTA:

The desired catalyst Si-PTA was prepared by treating Silica with 1 M hydrochloric acid. A mixture of 12 g of silica and 50 ml of 1 M hydrochloric acid was combined with 120 ml round-bottomed flask with continuous stirring for 5 hr at room temperature, the processed silica was collected by filtration, washed by means of distilled water up to three times, then dry in an microwave oven at 90 ◦C for 6 h. Catalyst was prepared with facilitate of the impregnation method. Phosphotungustic acid 1.5 g, pretreated silica 2.5 g , and 30 ml of distilled water were placed into a 100 ml flask, the resultant reaction mixture was refluxed with stirring in an

oil bath for 6 h at 110°C, then evaporated completely to dryness at 100°C, and further dry in an microwave oven till complete dryness.

The FT-IR spectrum of Si-PTA are observed at 800, 875 and 900 cm^{-1} are more intense in Si-PTA compared to pure silica which shows the peak at 720 cm^{-1} shown in (figure 1), so it displayed the modification of catalyst. In comparison to pure silica with Si-PTA shows broad range bands due to change in structure.

The XRD pattern of pure Silica and Si-PTA are depicted in Figure 2. The broad band centered peak of pure silica is obseved at 2θ = ~27°. When Silica is doped with phosphotungustic acid the change in peaks assigned to PTA are analogous to those obseved for the Si-PTA, which confirms retention of their crystalline structure. As seen in Figure 2, the peak of Si-PTA showed decrease at 27° in comparision to silica which refers surface of silica was occupied by particles of phosphotungustic acid with highly intensive peak which proves no change in structure of phospotungstic acid, confirmed by Fourier Transform IR spectra.

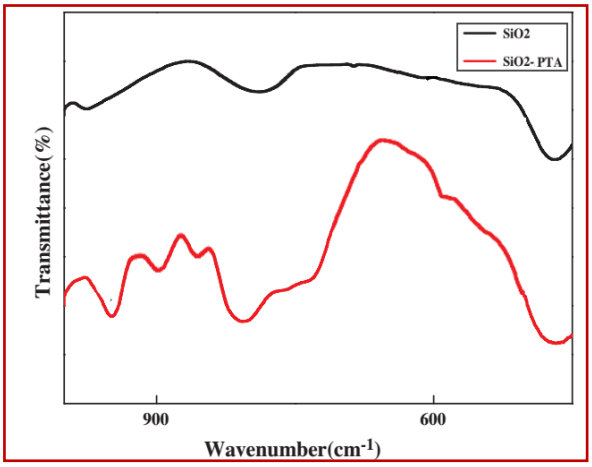


Fig 1- FT-IR Spectra of SiO_2 and Si-PTA

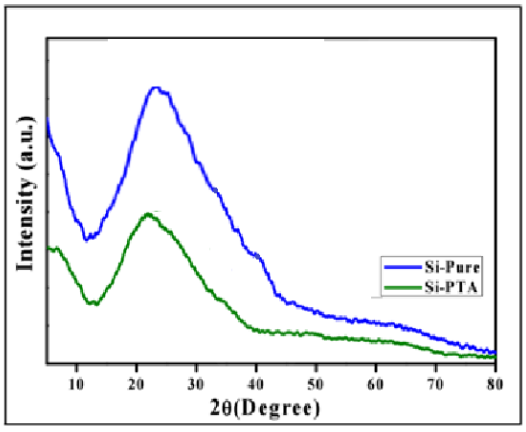


Fig 2-XRD Analysis of SiO_2 and Si-PTA

The particle size and morphology of the Si-PTA were studied by SEM analysis. Morphology study of pure Si no association of particles occurred, while Si-PTA showed the association of particles, it reveals that consistent distribution of phosphotungustic acid on pure silica in synthesized catalyst. The SEM images (figure 3. d-f) of the catalyst showed the surface morphology of functionalized silica. The image shows the change in the surface morphology of silica gel (fig 3. a-c)

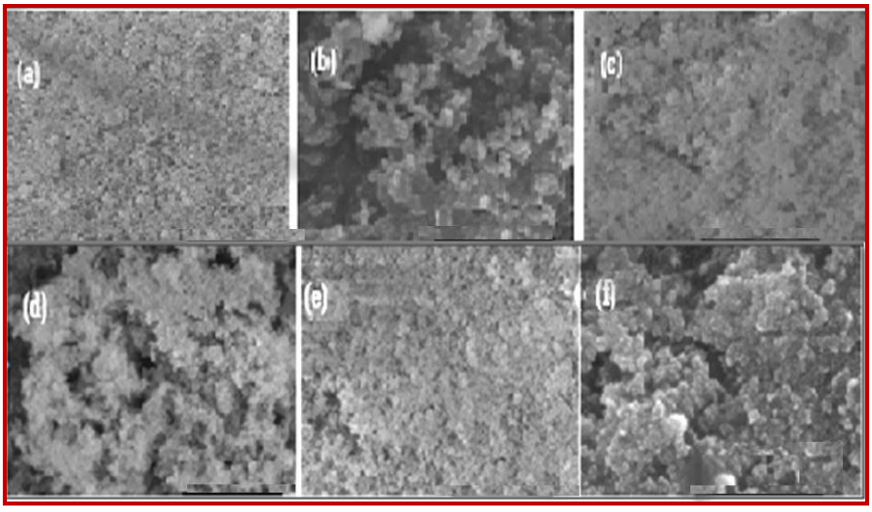
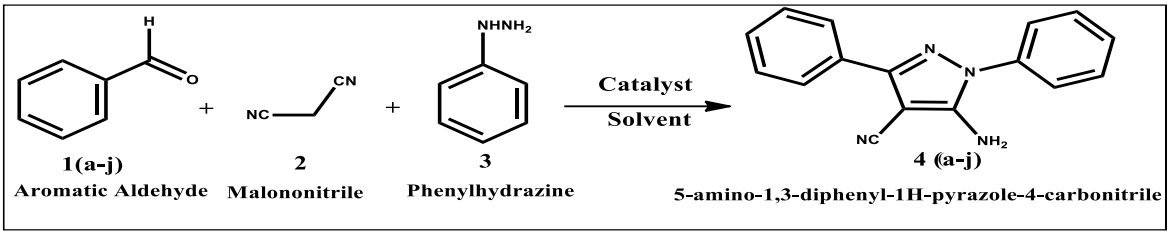


Fig 3: SEM images (a-c) for pure silica and images (d-f) for Si-PTA.

2.2. Catalytic application of Si-PTA in the synthesis of Pyrazole derivatives:

With the Si-PTA heterogeneous, one-pot reaction multicomponent of Synthesis of pyrazole derivative was completed by using and Aromatic aldehyde, malononitrile and phenyl hydrazine under optimized the reaction condition. The results of these studies are tabulated in Table 1(entries 1-11). So from all this study it was concluded that 10 wt% catalyst in acetonitrile as a solvent for the synthesis of pyrazole derivative was considered as an ideal condition.

Table 1: Screening of reaction condition for the synthesis of pyrazole derivative.

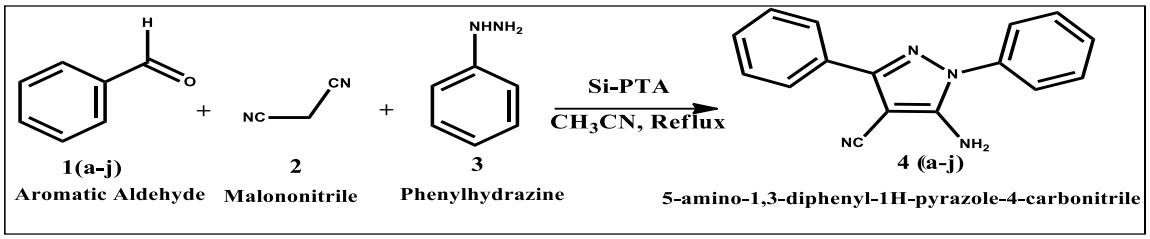


Entry	Solvent	Wt% of Si-PTA	Temp. (ºC)	Time (hr)	Yield[x] (%)
1	-	-	RT	24	0
2	-	-	Reflux	24	20
3	EtOH	10	Reflux	04	74
4	C_6H_6	10	Reflux	06	66
5	THF	10	Reflux	3.5	58
6	DCM	10	Reflux	4	64
7	CH_3CN	10	Reflux	4	86
8	CH_3CN	5	Reflux	4.5	80
9	CH_3CN	15	Reflux	4	86
10	CH_3CN	20	Reflux	4	88
11	CH_3CN	25	Reflux	4	89

Reaction proceeded at equimolar quantities of reactant refluxed in Acetonitrile as a solvent, [x] indicates isolated yield of the product.

The facile synthesis of pyrazole derivative from aromatic aldehyde, malononitrile and phenyl hydrazine was practiced with different available catalyst and their comparative study was summarized in Table 2(entries 1-8). So at last the reaction for the formation of pyrazole was preceded with synthesized Si-PTA catalyst made conversion 100% of starting material in to 86% of corresponding yield of pyrazole derivative within 4 hr (Table 2, entry 9). This particular reaction condition work dominantly over all other practices which generate the excellent yield within short of time and reaction also proceed smoothly.

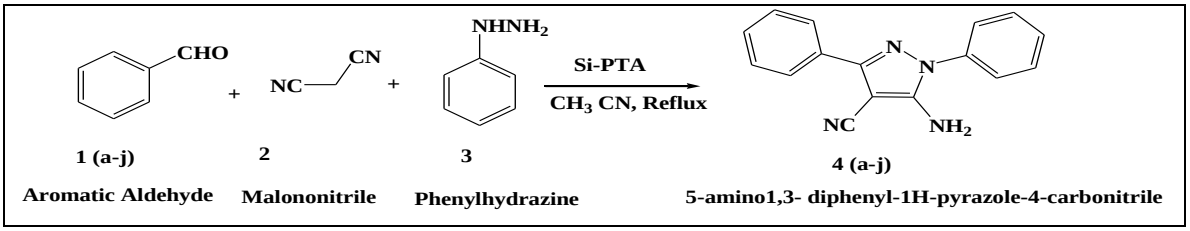
Table 2: Comparison of catalytic activity of Si-PTA and reported catalyst.



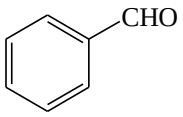
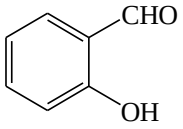
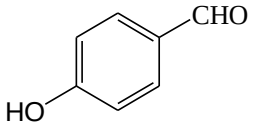
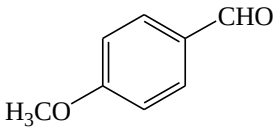
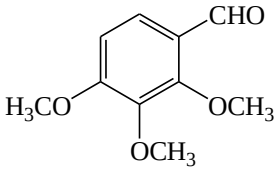
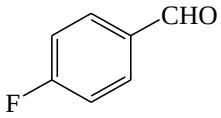
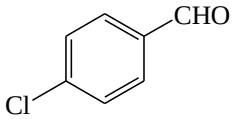
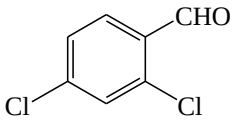
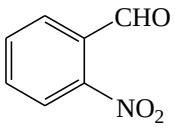
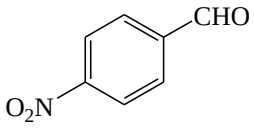
Entry	Catalyst	Time (hr)	Conv. (%)	Yield (%)
1	$FeCl_3$	8	78	52
2	$NiCl_2$	9	74	48
3	$ZnCl_2$	8	65	42
4	BF_3	6	80	55
5	$GdCl_3$	6	76	52
6	$ZrCl_4$	9	72	45
7	Me_3SiCl	7	58	38
8	$SnCl_4$	8	68	42
9	Si-PTA	4	85	86
Reaction proceeded at equimolar quantities of reactant refluxed in Acetonitrile as a solvent, [x] indicates isolated yield of the product.				

After optimization of the model reaction, we focused our consideration on substrate diversity to authenticate the generality of the protocol, using substituted aryl aldehydes, malononitrile and phenyl hydrazine (Table 3, entries 1-10). Starting with bezaldehyde which reacts with malononitrile and phenyl hydrazine refluxed under acetonitrile as a solvent using Si-PTA as a catalyst offers 86% of yield within 4 hr (Table 3, entry 1). The electron donating group containing benzaldehyde such 2-hydroxy benzaldeyde, 4-hydroxy benzaldeyde, 4-methoxy benzaldeyde and 2,3,4 methoxy benzaldehyde were allowed to react under similar reaction circumstances gave 78, 80, 85 and 82% of product yield respectively (Table 3, entries 2-5). Which indicate reduced product yield as compared with the unsubstituted benzaldehyde. In further part of study electron withdrawing group substituted aromatic aldehyde like 4-fluro benzaldehyde, 4-chloro benzaldehyde, 2,4-dichloro benzaldehyde, 2-nitro benzaldehyde, 4-nitro benzaldehyde were proceed for the reaction under same condition as described above in a separate attempt affords 90, 88, 90, 91 and 95% of corresponding yield of product respectively (Table 3, entries 6-10). So far from the study it was concluded that electron withdrawing group having major impact on the reaction so it generate greater amount of yield compared to aromatic aldehyde containing electron releasing group.

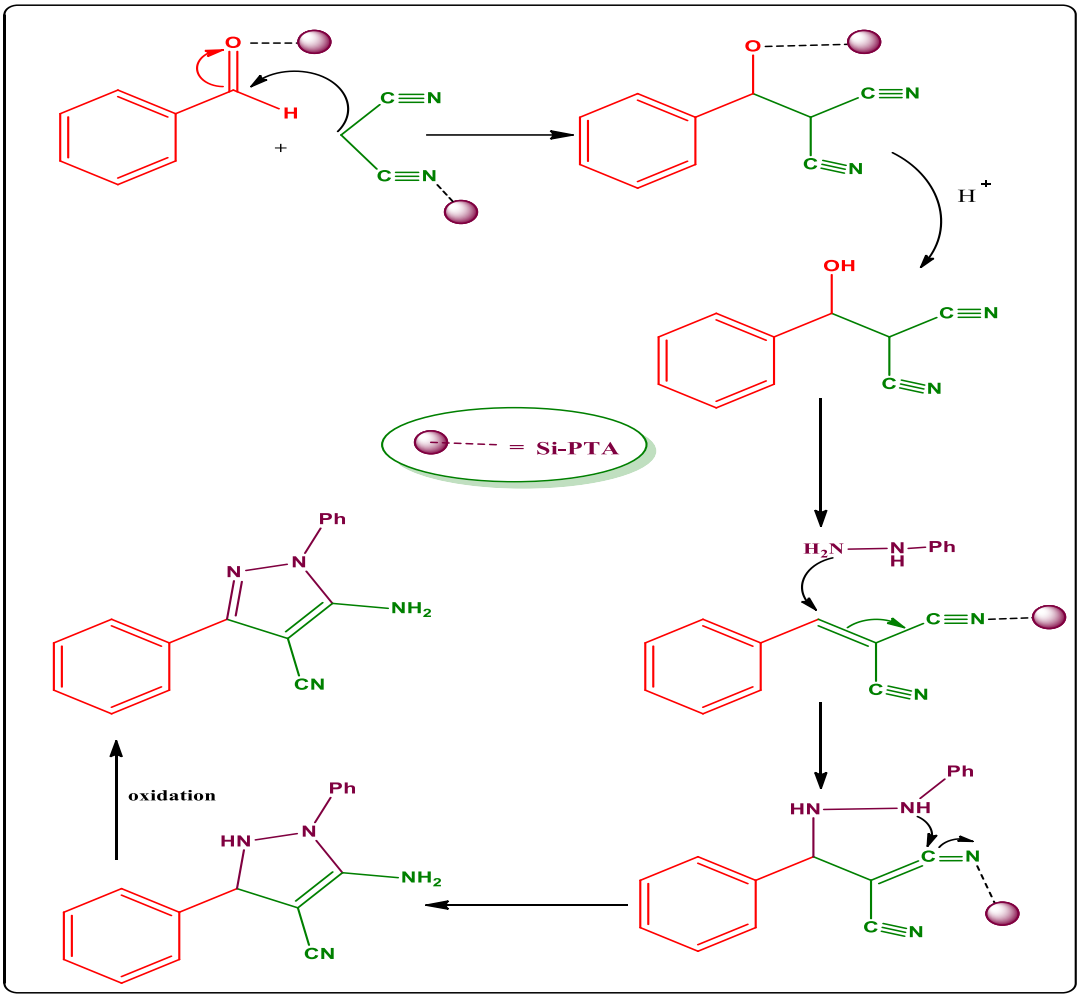
Table 3: Optimization of yield of pyrazole derivatives.



Entry	Aldehyde	Product	Time (hrs.)	Yield (%)

1		**4a**	4	86
2		**4b**	5	78
3		**4c**	5	80
4		**4d**	4	85
5		**4e**	4.5	82
6		**4f**	3	90
7		**4g**	3.5	88
8		**4h**	3	90
9		**4i**	2.5	91
10		**4j**	3	95
Reaction proceeded at equimolar quantities of reactant refluxed in Acetonitrile as a solvent, [x] indicates isolated yield of the product.				

2.3. Proposed Mechanism:



2.4. Recyclability of Catalyst:

To revise the recyclability of the catalyst, the Si-PTA catalyst was isolated from the reaction mixture by means of simple filtration procedure and washed several times with water and made ready for succeeding attempt. Recyclability of Si-PTA catalyst was studied over fifth cycles for the synthesis of pyrazole in acetonitrile as a solvent under refluxed condition, the catalyst does not lose much significant activity which is shown in fig. 4. Hence, the catalyst can be proficiently recycled for five times without significant loss in its catalytic activity and used effectively for the synthesis of pyrazole-4-carbonitrile under optimized reaction condition. These outcome shows that, the present protocol is highly significant and effective for the preparation of pyrazole derivatives.

III.EXPERIMENTAL

3.1. Materials and methods:

The Chemicals were procured from SD Fine, Sigma-Aldrich, Spectrochem and Avra. FT-IR spectroscopy were recorded using a Perkin Elmer spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 400 MHz using CDCl3 as solvent and TMS as internal standard. The purity of products checked by TLC.

3.2. General Procedure for the synthesis of Pyrazole derivative:

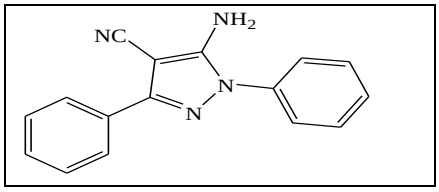
A mixture of aromatic aldehyde (1mmol), malononitrile (1mmol), phenyl hydrazine (1mmol), were added in a 25 mL Acetonitrile in round-bottomed flask connected to a condenser refluxed for appropriate times in acetonitrile as a solvent, after some time added Si-PTA (10mol%) of catalyst and confirmed the completion of reaction at different interval of time. After completion of the reaction the reaction mixture was poured in to ice cold water, the solid products were filtered off, washed with ice cold water several times and dried at room temperature. The crude products were further purified by simple recrystallization from Acetonitrile. The filtrate containing the catalyst was separated by simple filtration technique.

IV.CONCLUSION

We have developed an active and efficient protocol for the synthesis of different pyrazole-4 carbonitrile derivative mediated by Si-PTA heterogeneous catalyst in one-pot synthesis. Protocol is efficient in the synthesis and produced good to excellent yield. The few major key of this methodology was shorter reaction time, easy work process, easy separation of catalyst and reuse of the catalyst up to fifth cycle. The results disclose that the Si-PTA works as an excellent acid modified and environmentally kindly solid catalyst for the synthesis of pyrazole derivative at optimized reaction condition.

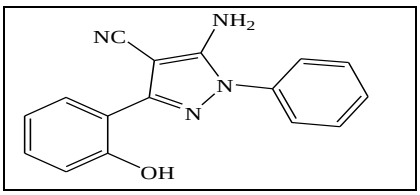
Spectra of some synthesized compound:

5-amino-1,3-diphenyl-1H-pyrazole-4-carbonitrile (Table III-4a)



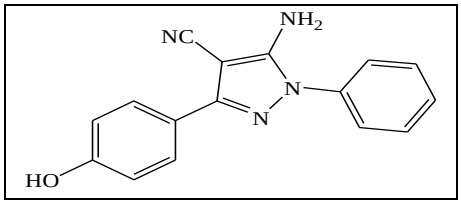
White powder, M.P. = 161 ^{0}C, **IR** (KBr, cm^{-1}) 3488, 3338, 3085, 2359, 1605, 1418, 1261, 1129, 1098, 1076. **^{1}H NMR** ($CDCl_3$, δppm): 6.88 (t, 1H), 7.22 (d, 2H), 7.31-7.38 (m, 3H), 7.45 (t, 2H), 7.68 (s, 1H), 7.70 (d, 1H), 7.86 (s, 2H). **^{13}C NMR** ($CDCl_3$, δ ppm): 111.78, 114.36, 122.58, 126.75, 138.9, 124.05, 129.79, 135.94, 139.85, 144.16, 151.48, 158.57. **MS (m/z):** 260 (M+).

5-amino-3-(2-hydroxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4b)



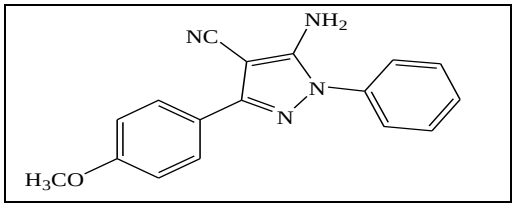
Yellow powder, M.P. = 162 ^{0}C, **IR** (KBr, cm^{-1}) 3588, 3492, 3351, 3108, 2364, 2201, 1606, 1416, 1227, 1195, 1102, 1046. **^{1}H NMR** (DMSO, δ ppm) 6.85 (t, 1H), 6.86-6.92 (m, 2H), 6.97 (d, 2H), 7.12-7.18 (m, 1H), 7.26 (dd, 2H), 7.44 (dd, 1H), 7.61 (s, 1H), 7.92 (s, 1H), 10.61 (s, 1H). **^{13}C NMR** ($CDCl_3$, δ (ppm)): 112.42, 116.64, 119.88, 120.35, 121.55, 125.35, 127.68, 130.24, 131.05, 138.18, 145.14, 149.52, 153.31, 156.57; **MS (m/z):** (M^+) 276.

5-amino-3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4c)



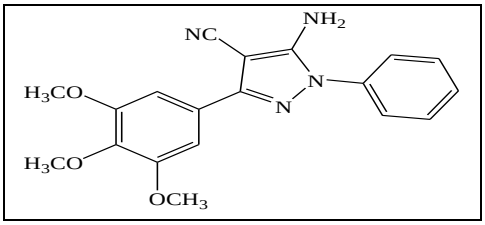
Pale yellow amorphous solid, M.P: 190 ^{0}C. **^{1}H-NMR** ($CDCl_3$, δ ppm.): 7.61 (d, 2H), 7.52 (t, 2H), 7.31 (t, 1H), 7.35 (d, 2H), 6.85 (d, 2H), 5.63 (s, 2H), 5.32 (s, 1H). **^{13}CNMR** ($CDCl_3$, δ ppm): 97.52, 116.54, 118.14, 118.72, 128.01, 128.24128.38, 129.22, 129.44, 129.51, 129.56, 135.67, 139.16, 138.41, 149.92, 156.77, 165.88. **MS (m/z):** (M^+) 276.

5-amino-3-(4-methoxyphenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4d)



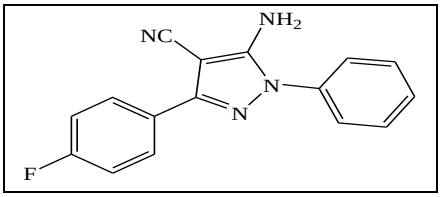
Light brown solid, melting point: 108^{0}C. **IR (KBr, cm^{-1}):** 3483, 3235, 3100, 2925, 2910, 1643, 1596, 1492, 1392, 1257, 1172, 1029, 871,802. **^{1}H NMR** (CDCl3, δppm) 3.72 (S, 3H), 6.90-7.08(m, 5H), 7.10(d, 2H), 7.25(d, 2H), 7.27(d, 2H), 7.68(s, 2H). **^{13}C NMR** ($CDCl_3$, δ ppm): 56.13, 107.20, 108.94, 113.27, 114.33, 115.21, 119.51, 121.06, 127.61, 128.02, 146.08, 153.2, 156. **MS (m/z):** 291 (M+1)·

5-amino-1-phenyl-3-(3,4, 5- trimethoxyphenyl)-1H-pyrazole-4-carbonitrile(Table III-4e)



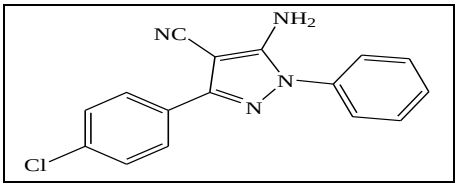
Cream colour solid, M. P.: 126 ^{0}C. **IR** (KBr, cm^{-1}): 3418, 3366, 2933, 2225, 1614, 1255, 1164. **^{1}H NMR** ($CDCl_3$, δppm): 3.95 (s, 3H), 3.42 (s, 6H), 6.78 (d, 2H), 7.22-7.29 (m, 5H), 7.61(s, 2H). **^{13}C NMR** ($CDCl_3$, δppm): 65.14, 112.34, 116.88, 119.63, 121.17, 127.42, 129.84, 130.73, 138.03, 143.12, 147.12, 151.02, 155.27. **MS (m/z):** 350 $(M)^+$.

5-amino-3-(4-fluorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4f)



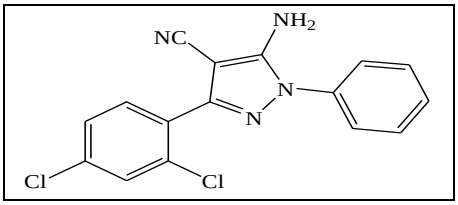
Yellow oil, **IR** (KBr, cm^{-1}): 3468, 3395, 3133, 2565, 2228, 1651, 1648, 1326, 850 cm^{-1}; **^{1}H NMR** ($CDCl_3$, δppm): 6.91–6.95 (m, 3H), 7.13 (d, 1H), 7.25-7.30 (m, 2H), 7.60-7.65 (m, 2H), 7.66 (s, 1H), 7.72 (s, 1H), 7.98 (m, 2H); **^{13}C NMR** ($CDCl_3$, δppm) 113.56, 115.17, 116.46, 118.32, 127.31, 127.88, 128.01, 130.32, 138.49, 136.34, 144.55, 144.95, 157.62; **MS (m/z):** 278 $(M)^+$.

5-amino-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4g)



White powder , M.P. = 130 ^{0}C, **IR** (KBr, cm^{-1}) 3409, 3306, 3174, 2167, 1647, 1600, 1408, 1400, 1184, 1049, 875. **^{1}H NMR** ($CDCl_3$, δppm): 6.84 (t, 1H), 6.88 (d, 2H), 7.24-7.26 (m, 2H), 7.27(d2H), 7.34 (d, 2H), 7.60(s, 2H). **^{13}C NMR** ($CDCl_3$, δppm) 112.54, 113.29, 119.55, 126.71, 127.88, 128.71, 131.94, 133.46, 137.65, 144.72, 149.21; **MS (m/z):** 296 (M+1).

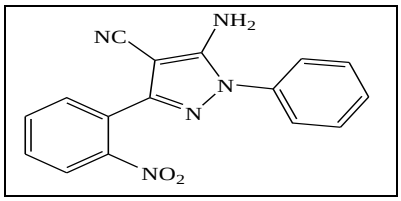
5-amino-3-(2, 4-dichlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4h)



Yellow solid; m.p: 247 ^{0}C; **IR** (KBr, cm^{-1}) 3465, 3403, 3231, 2986, 2206, 1675, 1577, 1364 ; **^{1}H NMR** ($CDCl_3$, δppm): 7.08 (s, 1H), 7.45 (t, 3H), 7.38 (d, 1H), 7.44 (d, 2H), 7.54 (d, 1H), 7.83 (s, 2H); **^{13}C NMR** ($CDCl_3$, δppm) 112.81, 113.86, 124.83, 125.76, 126.54, 127.62, 127.86, 127.82, 128.13, 132.04, 133.55, 145.52, 151.43, 152.57, 165.67.

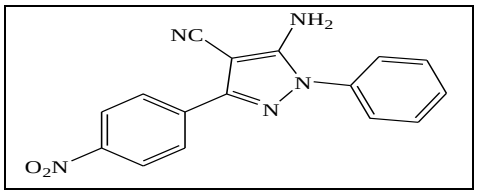
MS (m/z): 329 (M+).

5-amino-3-(2-nitrophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4h)



Red powder, **M.P.** = 160–161 ◦C, **IR** (KBr, cm^{-1}) 3442, 3312, 3054, 2352, 1605, 1523, 1459, 1356, 1323, 1321, 1256, 1143, 1133. **^{1}H NMR** ($CDCl_3$, δppm): 6.84 (t, 1H), 7.15 (d, 2H), 7.30 (t, 2H), 7.34 (t, 1H), 7.42 (t, 1H), 7.46 (d, 1H), 7.54 (d, 1H), 7.58 (s, 1H), 7.83 (s, 2H). **MS (m/z):** 305(M+).

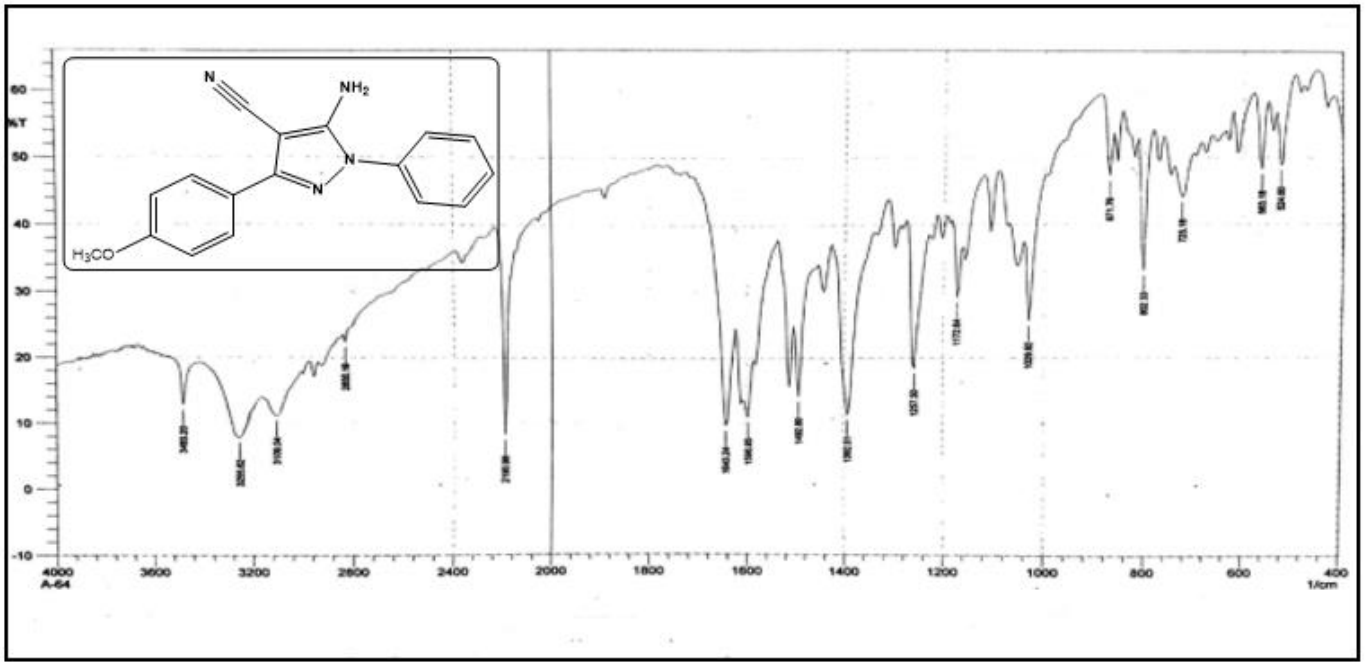
5-amino-3-(4-nitrophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (Table III-4j)



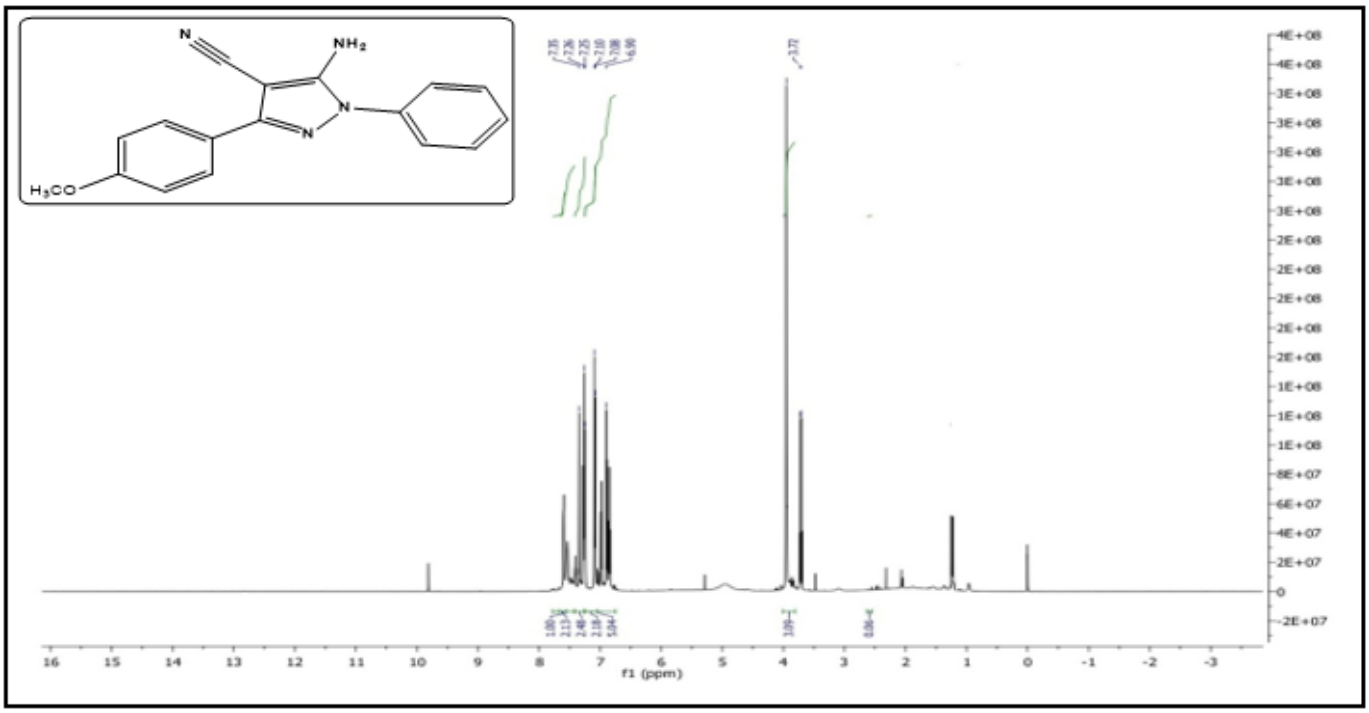
Red powder, M.P. = 164–165 ◦C, **IR** (KBr, cm^{-1}) 3464, 3356, 3105, 2363, 1604, 1418, 1463, 1342, 1254, 1121, 1110, 1092. **^{1}H NMR** ($CDCl_3$, δppm): 6.95(s, 1H) 7.23 (d, 2H), 7.27-7.34 (m, 2H), 7.75-7.82 (m, 3H), 8.06 (s, 1H), 8.34 (d, 2H). **MS** (m/z): 305 (M$^+$).

; **^{13}C NMR ($CDCl_3$, δppm)** 112.36, 113.43, 123.47, 123.88, 124.78, 128.90, 131.93, 132.24, 138.32, 137.83, 145.26, 149.56, 158.53 ; **MS (m/z):** 305 (M)+

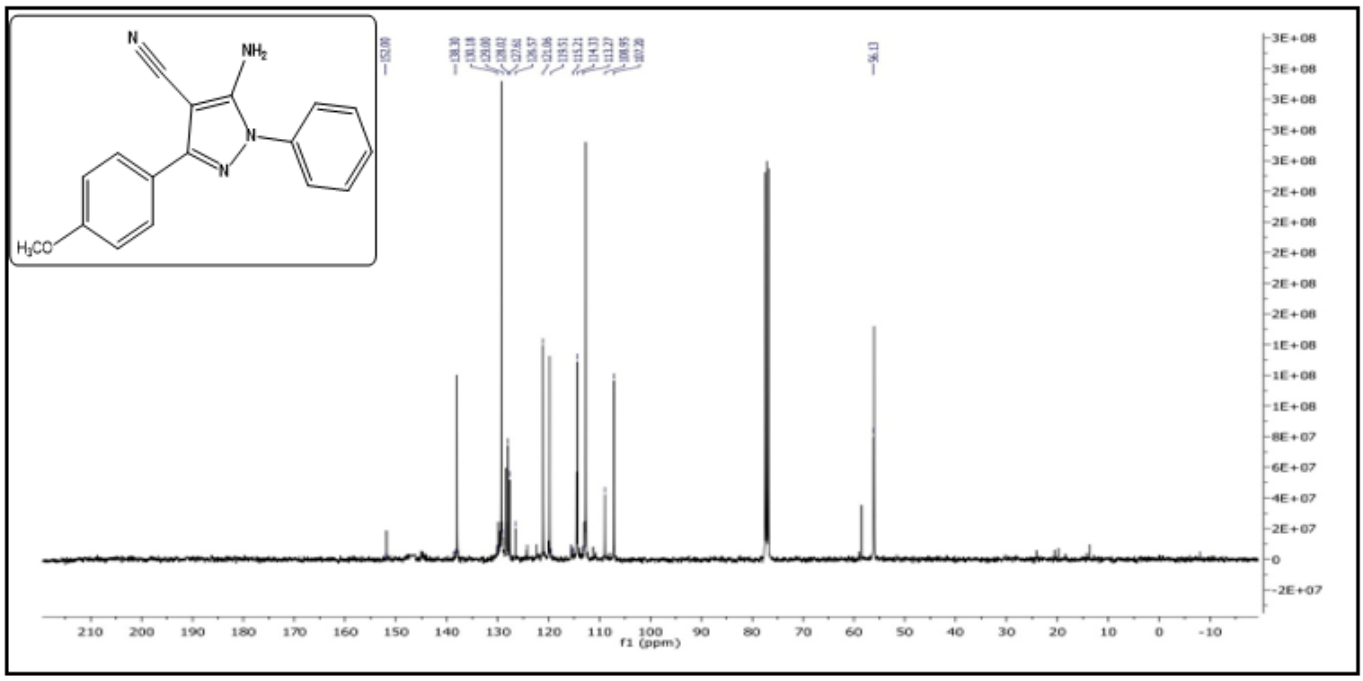
Spectrum I: IR Spectra 5-amino-3-(4-Methoxy phenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4d).



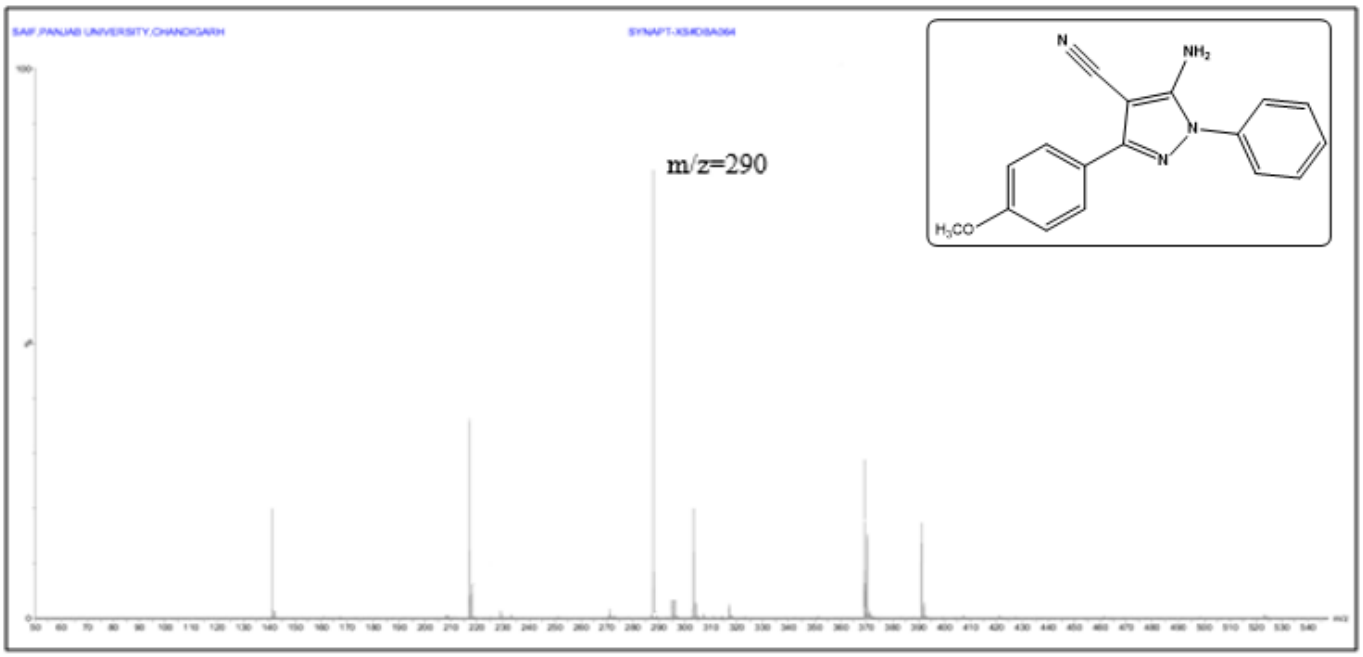
Spectrum II: ^{1}H NMR Spectra 5-amino-3-(4-Methoxy phenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4d).



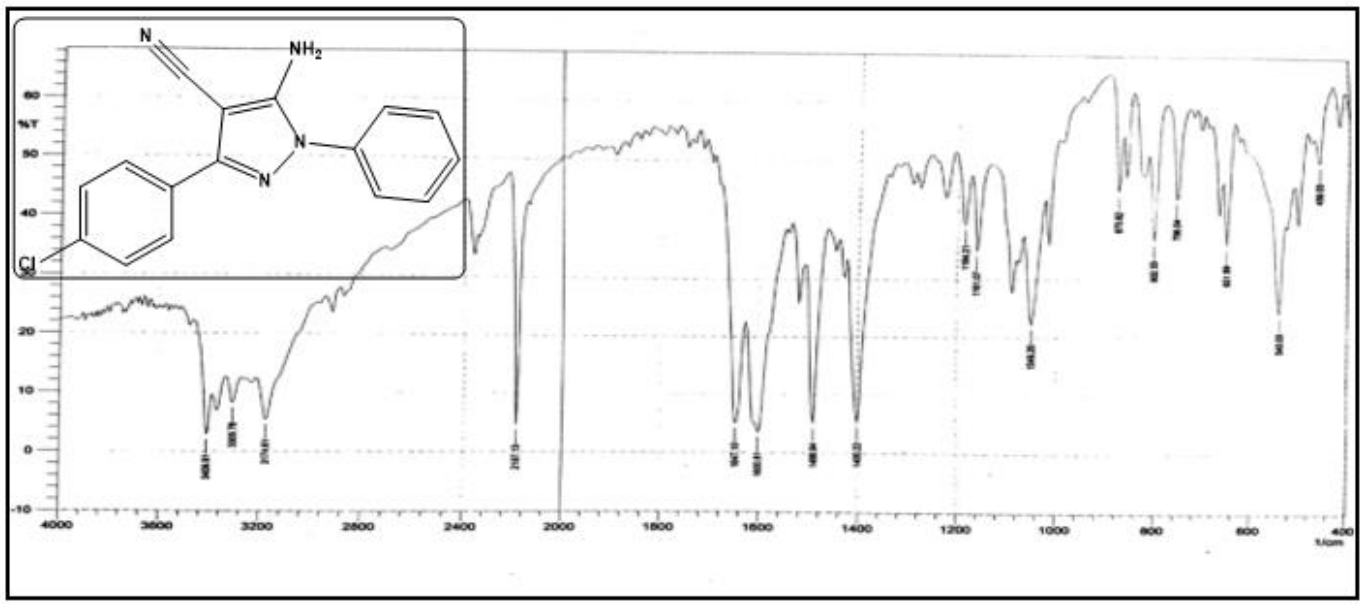
Spectrum III: ^{13}C NMR Spectra 5-amino-3-(4-Methoxy phenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4d).



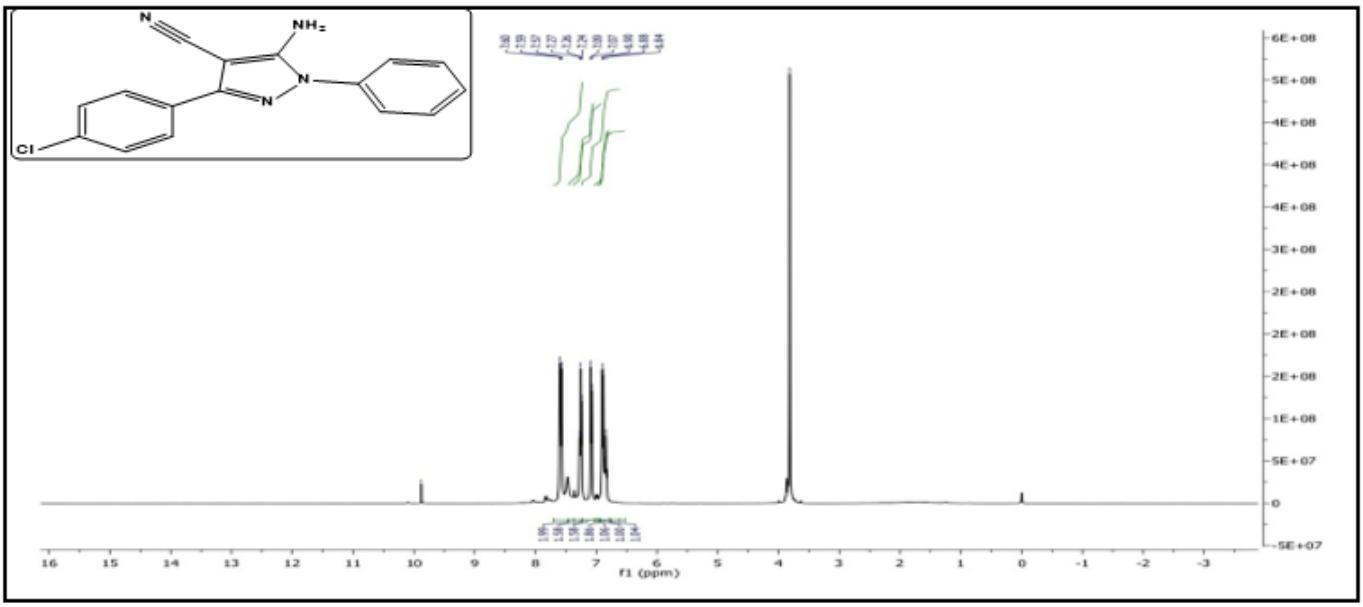
Spectrum IV: Mass Spectra 5-amino-3-(4-Methoxy phenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4d).



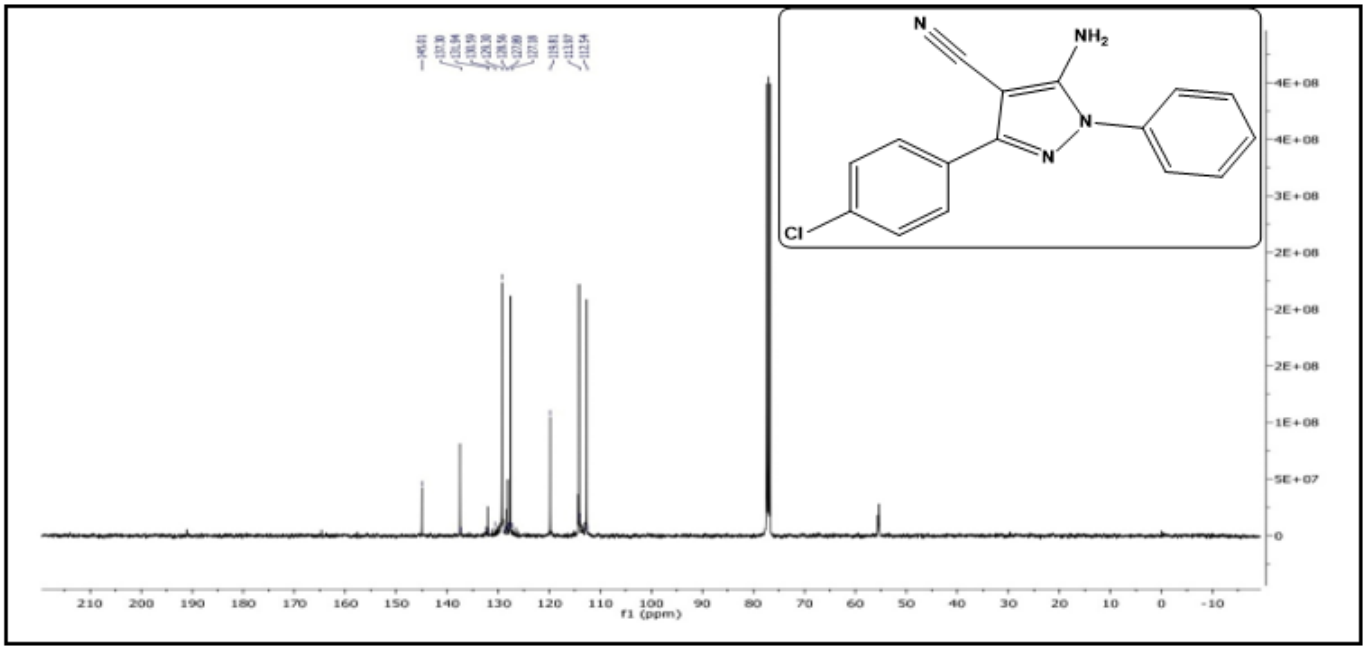
Spectrum V: IR Spectra5-amino-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4g).



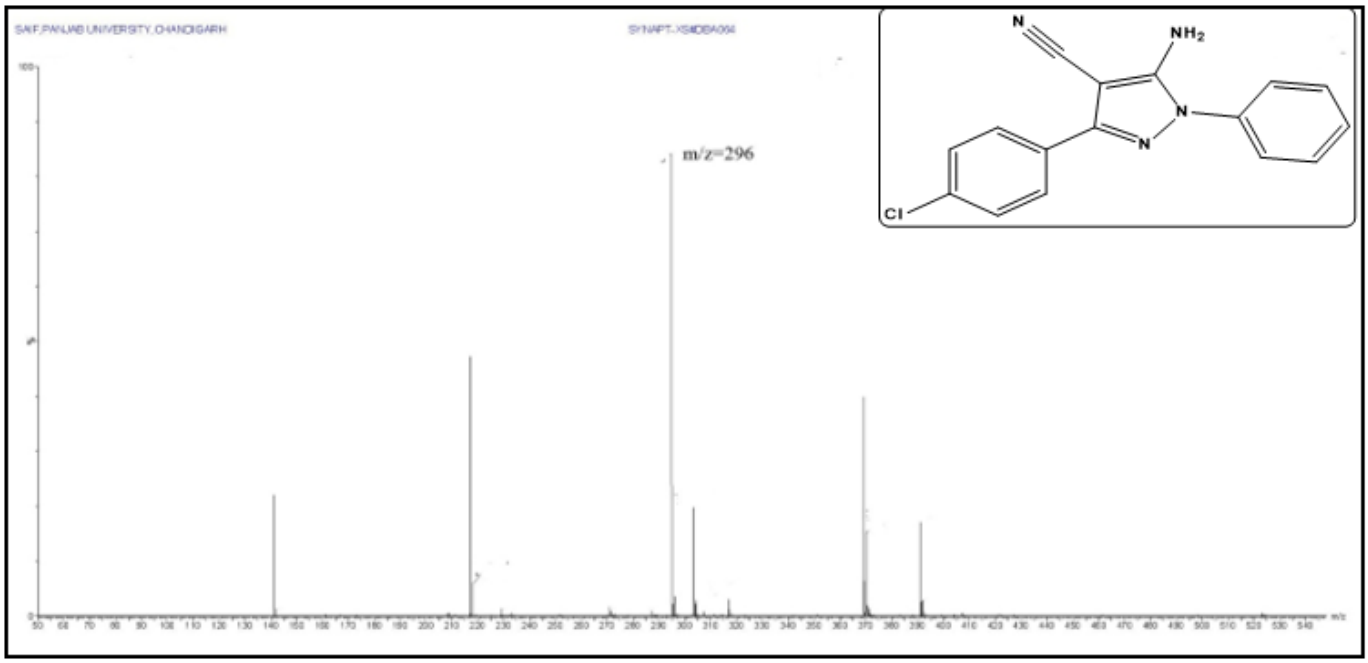
Spectrum VI: ^{1}H NMR Spectra5-amino-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4g).



Spectrum VII: ^{13}C NMR Spectra5-amino-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4g).



Spectrum VIII: Mass NMR Spectra5-amino-3-(4-chlorophenyl)-1-phenyl-1H-pyrazole-4-carbonitrile (4g).



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The Comparative Study: Chemistry of Renewable Energy Resources and their Environmental Effect for Sustainable Energy Production

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ABSTRACT

Renewable energy sources, such as solar, wind, and hydroelectric power, have gained increasing attention as a means to mitigate climate change and reduce dependence on fossil fuels. In this review article, we provide a comprehensive overview of the chemistry underlying renewable energy production and storage. We discuss the principles and mechanisms of energy conversion in various renewable energy technologies, including photovoltaic cells, wind turbines, and fuel cells. Additionally, we examine the chemical processes involved in energy storage and transmission, such as battery and hydrogen fuel production. Overall, this review provides a valuable resource for researchers and practitioners in the field of renewable energy, and highlights the potential of chemistry to drive innovation and progress towards a more sustainable future.

Keywords: Energy resources, renewable energy, solar energy, hydro energy, nuclear energy, biomass energy, solar cells

I. INTRODUCTION

The increasing demand for energy, coupled with concerns over climate change and the depletion of fossil fuels, has led to a growing interest in renewable energy sources. Renewable energy technologies, such as solar, wind, and hydroelectric power, offer promising solutions to these challenges, providing a sustainable and environmentally friendly means of meeting our energy needs. The principles of chemistry govern the mechanisms by which energy is harvested from the sun, wind, and water, and transformed into usable forms of electricity or fuel. In addition, chemistry plays a crucial role in the development of materials and processes for energy storage and transmission, from batteries to hydrogen fuel production.

II. SIGNIFICANCE

The chemistry of renewable energy sources is critical for addressing the challenges of climate change and sustainable energy production. As the world's population continues to grow, and energy demand increases, the need for sustainable and environmentally friendly energy sources becomes more urgent. Renewable energy technologies, such as solar, wind, and hydroelectric power, offer a promising solution to these challenges. By understanding the chemistry underlying these technologies, we can develop more efficient and effective systems

2.1. Meeting Energy Demands: As the global population continues to grow and economies expand, the demand for energy is increasing at an unprecedented rate. The use of renewable energy sources has the potential to meet this growing demand while reducing our dependence on finite fossil fuels.

2.2. Climate Change Mitigation: The burning of fossil fuels is a major contributor to climate change. Renewable energy technologies, such as solar, wind for energy conversion and storage.

2.3. Energy Security*:* Dependence on fossil fuels from foreign sources can create geopolitical challenges and risks. By developing domestic renewable energy sources, countries can improve their energy security and reduce their reliance on foreign energy sources.

2.4. Economic Development: The development of renewable energy technologies has the potential to drive economic growth and create new jobs in the clean energy sector.

2.5. Environmental Protection**:** The use of renewable energy sources can help to protect natural resources and ecosystems by reducing pollution and minimizing habitat destruction.

2.6. Access to Energy**:** Renewable energy technologies can also provide energy access to rural and remote communities that are not connected to traditional energy grids.

Overall, the chemistry of renewable energy sources is critical for addressing a wide range of challenges related to energy, the environment, and socioeconomic development.

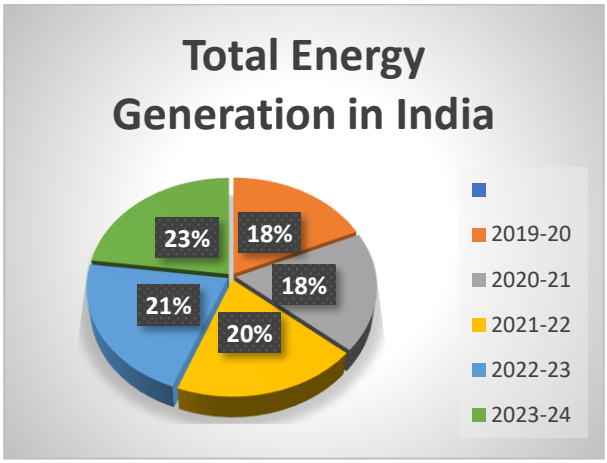

Figure 1 : Total energy generation in India last five years

III.ENERGY CONVERSION MECHANISMS

Energy conversion mechanisms refer to the chemical processes involved in the conversion of energy from one form to another in various renewable energy technologies. The most common forms of energy that are

converted in renewable energy systems include solar energy, wind energy, and chemical energy stored in fuels such as hydrogen. Here are some examples of energy conversion mechanisms.

3.1. Photovoltaic Cells:

Photovoltaic cells, also known as solar cells, convert sunlight directly into electricity through a process called the photovoltaic effect. When sunlight strikes the semiconductor material of the cell, it creates an electric field that separates positively charged holes and negatively charged electrons. The electrons are then collected by a circuit and used to power electrical devices.

3.2. Wind Turbines:

Wind turbines convert the kinetic energy of wind into mechanical energy, which is then converted into electricity. The blades of the wind turbine capture the energy of the wind and rotate a rotor connected to a generator, which produces electrical power. The conversion of kinetic energy to mechanical energy is achieved through a complex set of aerodynamic principles, including lift and drag.

3.3. Fuel Cells:

Fuel cells convert chemical energy stored in fuels such as hydrogen and oxygen into electrical energy. In a typical hydrogen fuel cell, hydrogen gas is fed into one side of a cell, while oxygen gas is fed into the other side. The hydrogen molecules are broken down into positively charged hydrogen ions and electrons, which travel through an electrolyte membrane. The electrons are then collected by a circuit and used to power electrical devices, while the hydrogen ions combine with oxygen to form water.

3.4. Geothermal Power Plants:

Geothermal power plants convert heat from the earth's interior into electrical energy. Hot water or steam from deep beneath the earth's surface is used to drive a turbine, which is connected to a generator that produces electricity. The conversion of heat energy to mechanical energy is achieved through the use of a heat exchanger and a working fluid.

3.5. Perovskite Solar Cells:

Perovskite solar cells are a promising new technology that offer higher efficiencies and lower costs than traditional silicon-based solar cells. In recent years, researchers have made significant progress in improving the stability and durability of perovskite solar cells, as well as reducing the toxicity of the materials used.

3.6. Floating Wind Turbines:

Floating wind turbines are designed to harness the strong winds found offshore, where wind speeds are generally higher and more consistent than on land. Recent advancements in floating wind turbine technology have made it possible to build larger and more efficient turbines that can be deployed in deeper waters.

3.7. Solid-State Batteries:

Solid-state batteries are a new type of battery that use a solid electrolyte instead of a liquid electrolyte. They offer higher energy densities and faster charging times than traditional lithium-ion batteries, as well as improved safety and longer lifetimes. Recent advancements in solid-state battery technology have improved their performance and made them more practical for commercial applications. However, there are still challenges in scaling up production and reducing costs.

3.8. Hydrogen Fuel Cells:

Hydrogen fuel cells are being developed as a zero-emissions alternative to fossil fuels in transportation and other applications. Recent advancements in fuel cell technology have improved their efficiency, durability, and

cost-effectiveness. There is significant potential for commercialization of hydrogen fuel cells in the automotive and transportation industries, but there are still technical and economic challenges that need to be addressed, such as the production and distribution of hydrogen fuel.

3.9. Organic Rankine Cycle (ORC) Systems:

ORC systems are used to convert low-grade waste heat into electricity, making them a promising technology for waste heat recovery in industrial processes. Recent advancements in ORC technology have improved their efficiency and reduced their costs, making them more practical for commercial applications.

3.10. Nuclear Energy:

Energy can be prepared with the help of nuclear reaction of Urenium and other radioactive elements, nuclear fission chemical reaction can produce huge energy at a very small place as compared to all other resources available. The water steam is used to spin large turbines that generate electricity. Nuclear power plants use heat produced during nuclear fission to heat water. In nuclear fission, atoms are split apart to form smaller atoms which results releasing energy. One fission event can results in the release of approximately 200 MeV of energy, or about 3.2×10^{-11} watt-seconds.

Overall, these recent advancements in renewable energy technologies have significant potential for commercialization, with the potential to reduce greenhouse gas emissions and improve energy efficiency on a large scale. However, further research and development is needed to optimize their performance and reduce costs, and there are still technical and economic challenges that need to be addressed in order to fully realize their potential.

Sr. No	Types of Energy	2023	2022
1	Wind Power	44.5	44.63
2	Solar Power	72.3	56.95
3	Biomass	10.2	8.28
4	Small Hydro Power	4.98	49.86
5	Waste To Energy	0.57	0.33
6	Large Hydro	46.88	46.85

Table No.1 Renewable Energy Production in India

IV.SCOPE IN THE FIELD

4.1. Materials design and synthesis:

Researchers can develop new materials using advanced materials science and engineering principles. This includes the use of computational modelling and simulation to design new materials with improved properties. Sustainable materials can be produced using environmentally friendly processes such as biomimetic synthesis, green chemistry, and low-energy routes to synthesis.

4.2. Sustainable manufacturing processes:

To address the environmental impact of renewable energy production, there is a need for more sustainable manufacturing processes. This includes the use of renewable energy sources such as solar and wind power in the manufacturing process. Other strategies that can be employed include reducing waste and emissions, optimizing production processes, and implementing circular economy practices.

4.3. Cost-effective storage technologies:

Researchers can develop new battery technologies that are more efficient, durable, and cost-effective. This includes the development of new materials and chemistries for batteries, such as solid-state batteries and lithium-sulphur batteries. In addition, the integration of energy storage technologies with smart grids can improve the efficiency of the energy system.

4.4. Policy and regulatory framework:

Governments can implement policies and regulatory frameworks that support the development and deployment of renewable energy technologies. This includes the use of feed-in tariffs and renewable energy mandates to incentivize the development of renewable energy. Governments can also invest in research and development of renewable energy technologies and provide support for small and medium-sized enterprises to enter the renewable energy market. Integration with existing energy systems: Smart grids can be used to integrate renewable energy sources with existing energy systems. This includes the use of energy storage technologies and demand-side management to balance energy supply and demand. In addition, the development of new business models such as peer-to-peer energy trading can enable the integration of renewable energy sources with existing energy systems. In summary, addressing the challenges associated with the chemistry of renewable energy sources requires a combination of technological innovation, supportive policies and regulatory frameworks, and collaboration between stakeholders.

V. CONCLUSION

However, the review also highlights the major challenges associated with renewable energy, such as the need for improved materials design and synthesis, sustainable manufacturing processes, and the development of cost-effective storage technologies. These challenges must be addressed to ensure the efficient and effective use of renewable energy sources. The review article concludes that the future of renewable energy relies on a combination of technological innovation, supportive policies and regulatory frameworks, and collaboration between stakeholders. The development of new materials and chemistries, sustainable manufacturing processes, cost-effective storage technologies, and the integration of renewable energy sources with existing energy systems are all key factors that will shape the future of renewable energy. Overall, the review article emphasizes the importance of continued research and development to improve the efficiency and effectiveness of renewable energy sources.

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Analytical Method Development and Validation of Biguanide, Empagliflozin, and Linagliptin by RP HPLC

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ABSTRACT

Designing a comprehensive analytical method for the simultaneous estimation of multiple drugs within a complex composition poses a considerable challenge. In this study, we successfully addressed this challenge by developing a reverse phase HPLC method that is not only simple and rapid but also highly precise and reliable. Our focus was on separating and estimating three specific drugs Biguanide i.e. Metformin (MET), Empagliflozin (EPG), and Linagliptin (LNG) present in a bulk drug mixture as well as in pharmaceutical dosage forms.

The chromatographic separation was achieved using an Inertsil C18 ODS column (250 mm × 4.6 mm, 5µm) and a mobile phase comprising 20mM KH2PO4: Acetonitrile (pH 3.5 with OPA) in a 30:70v/v ratio. Detection was performed at 270 nm using ultraviolet spectroscopy, ensuring a reliable assessment of the drug components. The optimized conditions led to proper resolution of all three drugs with individual run times of 3.2 minutes for MET, 8.1 minutes for EPG, and 5.4 minutes for LNG.

To ensure the robustness and reliability of the developed method, a thorough validation process was conducted. This included assessments of precision, linearity, accuracy, ruggedness, and robustness, providing a comprehensive verification of the method's efficacy. The validated method was then successfully applied to analyze a commercially available pharmaceutical dosage form, yielding consistently excellent and reproducible results.

Keywords: Metformin, Empagliflozin, Linagliptin, RP HPLC, Validation.

I. INTRODUCTION

In the pursuit of advancing pharmaceutical research and ensuring the efficacy, safety, and quality of therapeutic agents, the development and validation of analytical methods play a pivotal role. The present research endeavors to address this imperative by focusing on the analytical method development and validation of three significant pharmaceutical compounds Biguanide, Empagliflozin, and Linagliptin utilizing Reverse Phase High-Performance Liquid Chromatography (RP-HPLC)[1].

Biguanides, a class of oral hypoglycemic agents, have gained widespread use in the treatment of type 2 diabetes. Empagliflozin, a sodium-glucose cotransporter 2(SGLT2) inhibitor, and Linagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, represent cutting-edge advancements in antidiabetic pharmacotherapy. The coexistence of these compounds in a single study reflects the contemporary trend towards combination therapies to enhance therapeutic outcomes[2].

The analytical method employed, RP-HPLC, is chosen for its inherent advantages in terms of sensitivity, selectivity, and reproducibility. This chromatographic technique leverages the differential interaction of analytes with a stationary phase and a mobile phase, allowing for precise separation and quantification. As the pharmaceutical landscape continues to evolve, the development of robust analytical methods becomes indispensable for ensuring the consistency and reliability of drug formulations.

The primary objectives of this research include the systematic optimization of RP-HPLC conditions for each compound, elucidation of the method's specificity, linearity, precision, accuracy, and robustness, and subsequent validation following the guidelines outlined by regulatory authorities. The validation process is pivotal for establishing the suitability of the method for routine analysis, ensuring the reliability of results across various conditions and laboratories.

This study aims to contribute to the scientific community by providing a comprehensive blueprint for the analytical characterization of Biguanides, Empagliflozin, and Linagliptin. The outcomes of this research are anticipated to facilitate the pharmaceutical industry, regulatory agencies, and researchers in ensuring the quality and safety of these essential therapeutic agents, ultimately contributing to improved patient outcomes in the realm of diabetes management.

II. METHODOLOGY

Method development and validation for the estimation of MET, EPG and LNG were carried out by using RP-HPLC.

Materials and Methods

MET, LNG and EPG were purchased from local drug provider. High-purity acetonitrile were from (Merck Pvt. Ltd, Worli, Mumbai); water was from a (Milli-Q system, Millipore); potassium dihydrogen phosphate and sodium dihydrogen phosphate were from (Merck Pvt. Ltd, Worli, Mumbai); and ortho phosphoric acid was from (Merck Pvt. Ltd, Worli, Mumbai). The formulation was provided by the Boehringer Ingelheim Pharmaceuticals.

Selection of mobile phase

Initially to estimate MET, LNG and EPG in fix dosage form number of mobile phase in different ratio were tried. Taking into consideration the system suitability parameter like RT, Tailing factor, No. of theoretical plates and HETP, the mobile phase found to be most suitable for analysis was 20mM KH_2PO_4: Acetonitrile (pH 3.5 with OPA) in the ratio of 30:70v/v. The mobile phase was filtered through a 0.45µ filter paper to remove particulate matter and then degassed by sonication. Flow rate employed for analysis was 1.0 ml/min.

Selection of Diluent

Diluents used for preparation of sample were compatible with mobile phase and no any significant affect retention and resolution of analyte. After various trials Acetonitrile was used as diluents.

Selection of separation variable

Table 4.4: Separation Variable

Variable	Condition
Column	250mm x 4.60mm x 45µ
Bonded Phase	C_{18} ODS
Mobile Phase	20mM KH_2PO_4: Acetonitrile (pH 3.5 with OPA) in the ratio of 30:70v/v
Diluent	Acetonitrile
Flow rate	1.0 ml/min
Temperature	Ambient
Sample Size	20 µl
UV Detection	270mm
Retention time	MET 3.256 ± 0.3min
	LNG 5.478 ± 0.3min
	EPG 8.125 ± 0.3min

Preparation of standard Stock solution

Accurately weighed 10 mg of MET, LNG and EPG was transferred into 10 ml volumetric flasks separately and dissolved in 5 ml of methanol and sonicate for 10 min., then volume was made up to 10 ml with Acetonitrile. Concentration of MET, LNG and EPG in methanol was 1000µg/ml. (stock- A).

Preparation of Sub Stock Solution

1 ml of solution was taken from stock-A of MET, LNG and EPG and transferred into 10 ml volumetric flask separately and diluted up to 10 ml with diluent (Acetonitrile) to give concentration of 100µg/ml (Stock-B).

Preparation of Different Solution

1.0ml, 2ml, 3ml, 4ml and 5ml of stock-B was taken separately in 10 ml volumetric flask and volume was made up to 10ml with (Acetonitrile). This gives the solutions of 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml for drug. In same manner 0.5µg/ml, 1.0µg/ml, 1.5µg/ml, 2.0µg/ml, 2.5µg/ml of LNG and2.0µg/ml, 4.0µg/ml, 6.0µg/ml, 0.8µg/ml, 10µg/ml EPG also prepared.

Linearity and Calibration Graph

To establish the linearity of analytical method, a series of dilution ranging from 10-50µg/ml for MET, 0.5-2.5µg/ml for LNG and 2-10µg/ml for EPG were prepared. All the solution were filtered through 0.2µm membrane filter and injected, chromatograms were recorded at 270nm and it was repeat for three times. A calibration graph was plotted between the mean peak area and respective concentration and regression equation was derived.

System suitability parameters

Separation variables were set and mobile phase was allowed to saturate the column at 1.00 ml/min. After complete saturation of column, three replicates of working standard of MET 10µg/ml and LNG4µg/ml and EPG 0.5µg/ml were injected separately. Peak report and column performance report were recorded for all chromatogram.

Laboratory sample analysis

The commercial tablets formulation of MET, LNG and EPG is available in the strength of 1000:5:25mg. Based on this different standard solutions were prepared for quantitative analysis, which gives satisfactory results.

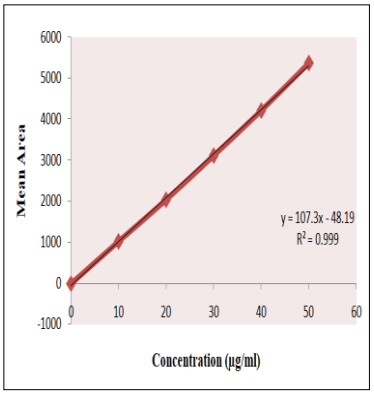
Stock solution was prepared in the same manner. Further dilutions were made to prepare the mixed standard of desired concentration.

Validation of HPLC method development[3,4]

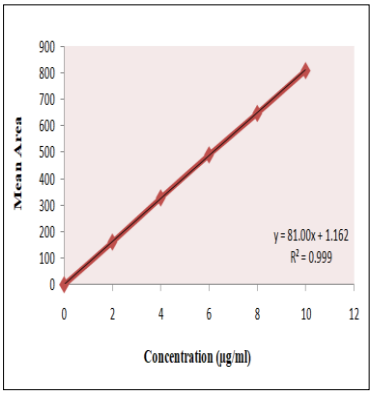
Linearity[5]

Linearity of both drugs was established by response ratios of drugs. Response ratio of the drug will be calculated by dividing the absorbance with respective concentration. Then a graph was plotted between concentration and response ratio.

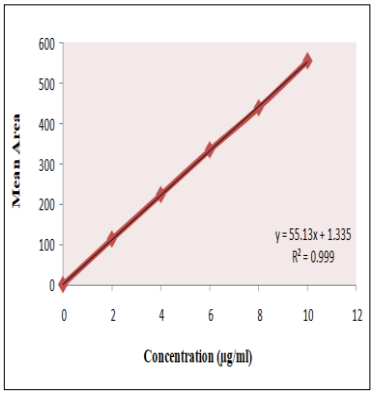
Parameter	MET	LNG	EPG
Concentration (µg/ml)	10-50	0.5-2.5	2-10
Correlation Coefficient (r^2)*	0.999	0.999	0.999
Slope (m)*	107.3	55.13	81.00
Intercept (c)*	- 48.19	1.335	1.162



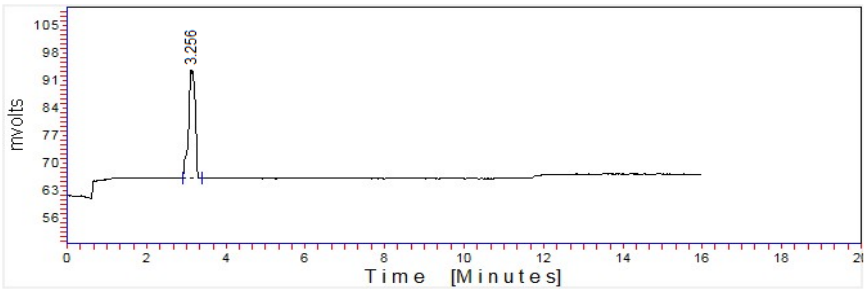
Calibration Curve of MET



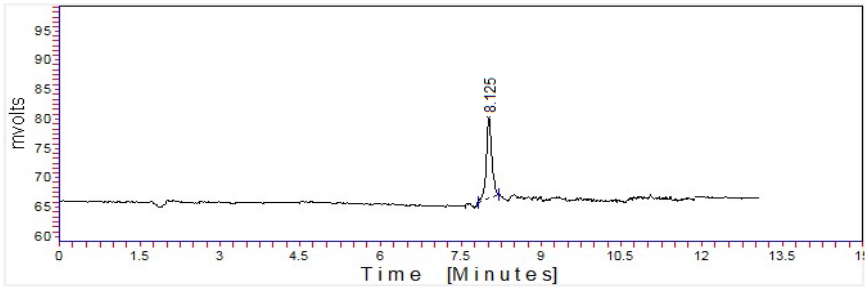
Calibration Curve of EPG



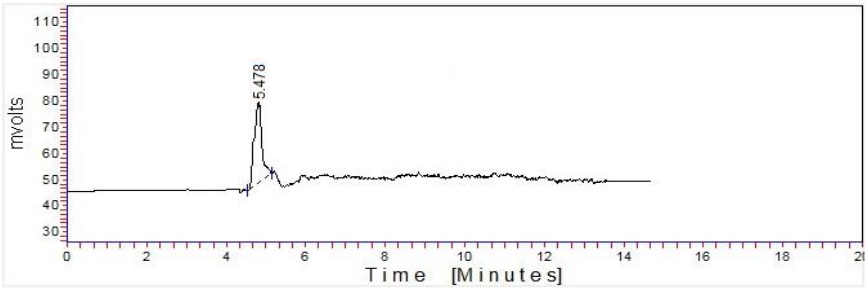
Calibration Curve of LN



Chromatogram of MET



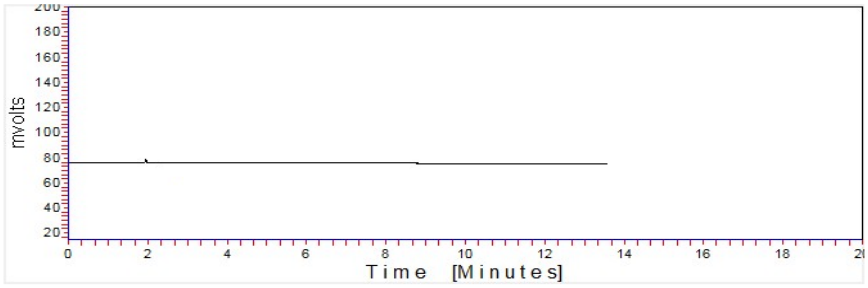
Chromatogram of EPG



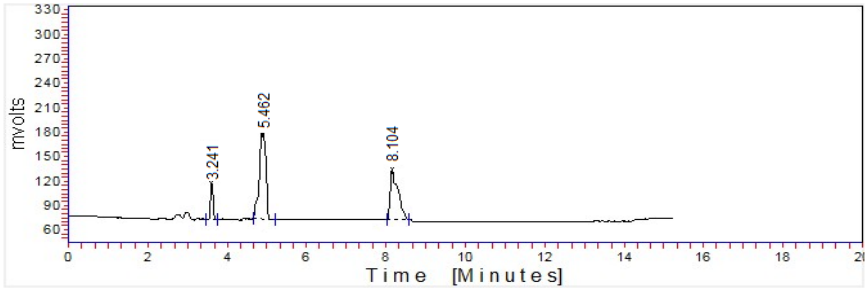
Chromatogram of LNG

Specificity[6]

Specificity of the method was carried out to assess unequivocally the analyte presence of the components that might be expected to be present, such as impurities, degradation products and matrix components.



Chromatogram of Blank



Chromatogram of MET, LNG, EPG

Accuracy[7]

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The recovery studies were carried out by adding known amount of standard solution of MET, LNG and EPG to reanalyzed tablets powder. The resulting solutions were then reanalyzed by proposed methods. Whole analysis procedure was repeated to find out the recovery of the added drug sample. This recovery analysis was repeated at 3 replicate of 5 concentrations levels.

% Level	% MEAN±SD*		
	MET	LNG	EPG
80%	99.02±0.245	98.06±0.422	99.26±0.271
100%	99.49±0.305	97.76±1.325	97.92±1.565
120%	99.15±0.705	97.79±0.513	99.04±0.840

Precision[8,9]

Precision of the methods was studied at three level as at repeatability, intermediate precision (Day to day and analyst to analyst) and reproducibility. Repeatability was performed by analyzing same concentration of drugs for five times. Day to day was performed by analyzing 5 different concentration of the drug for three days in a week.

Parameter	% MEAN±SD*		
	MET	LNG	EPG
Repeatability	99.285±0.090	97.678±0.013	98.280±0.060
Intermediate precision			
Day to day precision	98.76±0.200	97.35±0.020	97.40±0.092
Analyst-to-Analyst	99.34±0.242	97.81±0.014	98.34±0.048
Reproducibility	97.93± 0.983	97.45±0.024	98.16±0.077

Detection Limit and Quantitation Limit[10,12]

The LOD and LOQ of developed method were calculated based on the standard deviation of response and slope of the linearity curve.

Name	LOD (µg/ml)	LOQ (µg/ml)
MET	0.45	1.35
LNG	0.10	0.30
EPG	0.30	0.90

Analysis of tablets formulation

Tablet powder were weighed and ground to a fine powder; amount equal to 100mg of MET (2.5mg EPG and 0.5 mg LNG) was taken in 10 ml volumetric flask. Then 5ml of Acetonitrile was added and the flask was sonicated for about 10 min to solubilize the drug present in tablet powder and the volume was made up to the mark with acetonitrile. After sonication filtration was donethrough0.45µ membrane filter. Filtrate was collected and further diluted with methanol to get the final concentrations of drugs in the working range. The mean area of final dilutions was observed the concentrations were obtained from calibration curve method. The procedure was repeated for five times.

Replicate	% Concentration Found		
	MET	LNG	EPG
Replicate 1	98.92	97.52	95.20
Replicate 2	99.43	98.88	96.80
Average	99.18	98.20	96.00
S. D.	0.361	0.962	1.131
% RSD	0.364	0.979	1.179

III.CONCLUSION

The developed method was validated and applied to the bulk drug estimation and drug formulation and cleaning samples. All the results obtained with this method were accurate and precise. To summarize, this study has effectively developed and validated an RP-HPLC method for the simultaneous analysis of biguanides, empagliflozin, and linagliptin.

In conclusion, the developed RP-HPLC method provides a reliable and sensitive approach for the simultaneous determination of biguanides, empagliflozin, and linagliptin in pharmaceutical formulations. Its successful validation and demonstrated specificity position it as a valuable tool for routine quality control analysis in the pharmaceutical industry.

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Versatility of Azo Dyes : A Short Review

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ABSTRACT
Azo dyes are of synthetic organic compounds commonly used as colorants in various industries, including textiles, cosmetics, food, and pharmaceuticals. The process of conversion of primary amines into its Diazonium salt is called diazotization. Azo dyes are the largest group of dyes, having different classes, such as based on their application and based on their elemental composition. They are widely used to treat textiles, leather articles, and food items. Azo pigments are similar in chemical structure to azo dyes, but they lack solubilizing groups. Because they are insoluble in virtually all media, they are not readily purified and thus require highly purified precursors. However, certain azo dyes have been associated with health and environment concerns. In this review, we will be trying to give details of azo dyes along with their usage to substrates.
Key words: Cosmetics, Food, Leather, Solubilizing groups, Pharmaceuticals, Textiles.

I. INTRODUCTION

In early age natural dyes were used for caves painting. There are also some natural dyes they are still in use, such as indigo, henna, keser and turmeric etc. Due to limitations of natural dyes synthetic dyes were developed. William Henry Perkin's accidental discovery of the purple dye known as mauve or mauveine in 1856, is widely regarded as the birth of the synthetic dye industry. In 1858, Peter Griess, which laid the groundwork for the advancement of the chemistry of azo dyes and pigments, was responsible for the most important discovery in colour chemistry.[1-3] Most commonly, Diazonium salts are prepared by treatment of aromatic amines with nitrous acid and mineral acids.

$$ArNH_2 + HNO_2 + HX \longrightarrow [ArN_2]^+X^- + 2H_2O$$

Mechanism of Diazotizations:

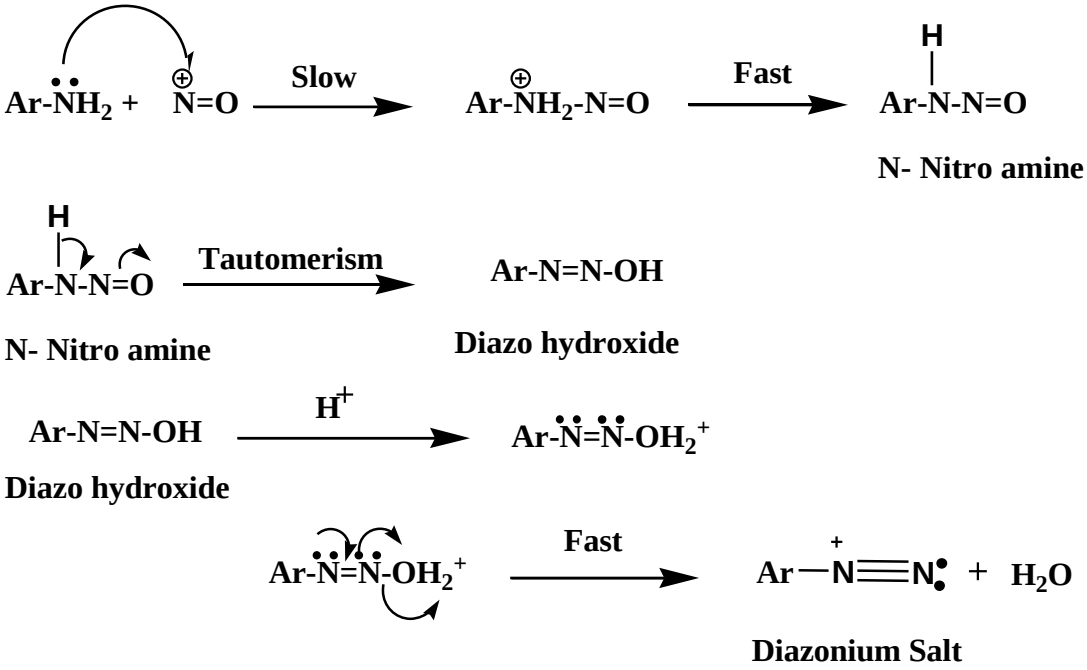
Due to some factors, the exact mechanism of diazotization is not yet settled. So reported mechanism will be as given below.

$$NaNO_2 + HCl \longrightarrow HNO_2 + NaCl$$

Nitrous acid

$$HO\text{-}N{=}O + H \longrightarrow H_2\overset{\oplus}{O}\text{-}N{=}O \longrightarrow H_2O + \overset{\oplus}{N}{=}O$$

Nitrosonium Ion



Diazonium salts are important synthetic intermediates that can undergo coupling reactions to form azo dyes. Azo dyes are organic compounds bearing the functional group R-N=N-R', in which R and R' are usually aryl. They are frequently included as the primary scaffold in many of organic compounds with emerging commercially and biological properties. The Diazonium salts react with aromatic amines, phenols etc. to yield products, having general formula Ar-N=N-Ar, called azo compounds or dyes. Temperature is one of the factors which affect on process of diazotization because diazotization is carried out between the temperatures of 0-5°C temperature. If temperature is increased, the Diazonium salt decomposes. Other factors like acidic concentration and pH of sodium nitrite also plays a vital role in diazotization.

The chemical structure of an azo dye is represented by a backbone, the Auxochrome groups, the chromophoric groups and the solubilizing groups. The colour of the azo dyes is determined by the azo bonds and their associated chromophore and Auxochrome. Azo dyes with particular colours allow absorption of light in the visible region.

The discovery of the first azo dye, Bismarck brown, is credited to the German chemist Johann Peter Griess in 1862. Griess synthesized this dye by combining diazotized sulphanilic acid with aniline. This chemical reaction formed a compound with the distinctive azo (-N=N-) linkage, which became the basis for numerous subsequent azo dyes. This discovery of Bismarck brown marked a significant milestone in the field of dye chemistry. Azo dyes like Bismarck brown played a crucial role in the development of the dye industry and paved the way for the synthesis of various colored compounds used in textiles, foods, pharmaceuticals, and other applications.

The azo group (-N=N-) is characterized by its ability to impart vibrant and diverse color to compound, making azo dyes one of the largest and most versatile classes of synthetic dyes known in chemistry. The discovery of Bismarck brown laid the foundation for the subsequent exploration and synthesis of numerous azo compounds with different colors and properties.

Then in 1864 structure of second azo dye Congo red was discovered. Chloride salts of Diazonium cation, prepared from the aniline, sodium nitrite, and hydrochloric acid, are unstable at room temperature and are classically prepared at 0-5°C. The major application of Diazonium compounds remains in the dye and pigment industry [4]. The most widely used reaction of Diazonium salts remain is azo coupled, which is used in the synthesis of azo dyes. [5] The coupling reaction can take place when an alkyl-substituted aromatic derivative

which is the Nucleophilic reagent, in which case the electrophile must contain an electron-withdrawing substituent. The Nitro group increases the electron deficit of the Diazonium group. This allows the coupling of 2,4,6-trinitroaniline with 1,3,5- tri-methyl benzene, 1,2,3,5 tetra-methyl benzene or Penta-methyl benzene [6, 7]. Typically, the freshly prepared Diazonium salt is immediately subjected to the coupling reaction, because after separation and drying becomes explosive [8]

Azo dyes are the most used dyes and account for more than 60% of total dyes [9,10] approximately 70% of all the dyes used in the industry are also dyes [11,12]. These compounds are characterized by the functional group (-N=N-) uniting two symmetrical and asymmetrical or non-azo alkyl or aryl radicals [13]. There are five strategies for the synthesis of azo dyes based on the diazotization and coupling reaction. Each strategy has certain restrictions associated with the availability of substrates. When the same compound is used for the preparation of azo compounds then the symmetrical compound is obtained and if two different compounds are used in the preparation of the compound two symmetrical and one asymmetric compound is obtained.

The oxidizing coupling reaction of two amines used can be carried out by oxygen in the presence of a catalyst CuCl/Pyridine [14] under photo-catalytic conditions promoted by TiO2 [15], Fe_2O_3 [16], HgO [17], or oxidizing agents such as $KMnO_4$ [18], MnO_2[19], $NaBO_3$[20], KO_2 [21], K_2FeO_4 [22], etc. Azo dyes are the most important synthetic colorants which have been widely used in textile, printing, paper manufacturing, etc. [23]

There are two categories of azo dyes in literature: direct dyes and reactive dyes. Also direct dyes have been found to be carcinogenic Mutagenic and have negative reproductive effects, whereas also reactive dyes have been linked to increasingly active allergy risk. Both of these types of diets are non-biodegradable and harmful to the environment as they accumulate in the oceans and affect marine life. Along with Diazonium salt dyes are prepared by Gewalds reaction [24]. Gewalds reaction is the condensation of ketone or an aldehyde (except lower derivative) with an α- cyano ester to give poly-substituted 2-aminothiophene. The 2-aminothiophene is a key intermediate for the diazotization reaction or the synthesis of azo dyes.

Azo dyes have many uses and that is the reason, which they consist of an average-70% of the world's commercial dyes. It is assumed that approximately 2000 azo dyes are presently present in the market even though many countries have banned on azo dyes. These dyes are especially effective for the health of children and infants and their exposure causes various problems for them. The harmful effects of azo compounds are not very known. It was found that these compounds can be carcinogenic, have reproductive toxins, and have cellular and neurological toxicants, irritants, allergens, environmental hazards, and developmental toxicants. The majorly used dyes belong to the class of azo compounds, some of which are known for their toxic and genotoxic properties. They are used in great quantities in textile industries and are of environmental concern because of their discharge into water. Azo dyes are used in tattoos, inks for printers, insecticides, pesticides, paints, varnishes, lacquers, and personal care products. In laboratory some azo dyes are used as indicators for acid base titrations, redox titration, complexometric titrations & precipitation titrations. Methyl orange is a pH indicator that is mostly used in titrations of acid base neutralization reactions. The pKa value of methyl orange is 3.47. Methyl red, an azo dye is used as a pH indicator for acid-base titration. It shows different colours at different pH. The pKa values of methyl redis 5.1. Congo red contains two azo groups. it is used as a pH indicator for titrations. It changes colour with a change in pH.

Complexometric indicators are an azo dye that undergoes a change in colour in the presence of metal ions. During these titrations they form a weak complex with metal ions. Eriochrome black –T used for titrations of Cd, Zn, Mg, Al, and Ca where as fast sulphon-black with ethylene diamine tetra acetic acid (EDTA) used for titrations of Cupper metal ion.

Azo dyes are the most diverse group of synthetic dyes. They are widely used in the pharmaceutical industry for colouring pharmaceutical agents. They are used for the treatment of insomnia. Azo groups containing cyclized-cyanine derivatives are used in two-photon photodynamic cancer therapy. They are used in cosmetics, paper, plastics, and food colours.

Tertrazine is one of the azo dye abundantly used as food colour. In addition to their use as colorants in over 50% of all commercial dyes, they have been employed in many applications, such as in inkjet printing, thermal transfer printing, photography, colour additives, the biomedical area, molecular recognition, light-controlled polymers, and in the liquid crystal industry. [25]

A variety of biological and pharmacological applications were probe for azo dyes that contain heterocycles. [26, 27] Heterocycles are important components of the azo dyes and play an important role in increasing their pharmacological and medicinal properties, such as antibacterial [28], antioxidant [29], anticancer and antitumor [30], and anti-inflammatory activities [31].

II. CONCLUSION:

After referring to various data about Azo dyes in literature, it's realized that azo dyes are very important precursors. Even Though it was banned in some countries, it is still in use. Leather industries use the majority of Azo dyes. It is found that other than the colorant properties of azo dyes have some pharmacological properties. They show positive anti-microbial properties.

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Significance of Study of Physicochemical Properties of Drug

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ABSTRACT
Drugs are a class of organic compounds which is vital to every living cell. Drugs play an immense role in body chemistry in living beings. They are needed to perform task for easy regulation and metabolism in bio-chemical reactions in the human body. Drugs are required to regulate and protect body chemistry. The volumetric, ultrasonic, and transport properties of drugs in aqueous/mixed solvents provide important information about solute–solute and solute–solvent interactions. This paper discusses about the thermodynamics concerned with the behavior of complex structure of drugs with the different kinds of co-solutes such as drugs, sugars, salts etc. This will help in better understanding of the molecular interactions of drugs. Many researchers are interested in the study of different kinds of physicochemical properties of drugs and their effect in the better absorption enhancing their effect.

Keywords – drug , volumetric physicochemical measurements, solute-solvent interactions.

I. INTRODUCTION

Characterization of physicochemical properties gained strong interest in the pharmaceutical research area and is now a standard method. One of the key challenges is to develop a pharmaceutical active ingredient into a drug, which combines biological activity with an appropriate physicochemical profile. Poor solubility in aqueous media is one of the major hurdles in the drug development process. Study of physicochemical properties of drug solutions helps us to understand the nature of interactions of drugs in biochemical processes.

Physicochemical Properties:

The branch of physical chemistry termed as solution chemistry investigate the solubility of substance and how it is affected by chemical nature of both solute and solvent. The study of thermodynamic properties gives significant information about molecular interactions present in the components of the solution. They can be satisfactorily described using experimental volumetric, ultrasonic, viscometric data on hydration of amino acids/drug solution. The trends in these properties with changes in temperature and composition offer qualitative assessment of the solution behavior in the composition range studied.

The studies on physicochemical properties of biomolecules such as amino acids, sugars and drugs in aqueous solution provide useful information which helps in understanding the complex mechanism of molecular interactions. Thermodynamic and physicochemical measurements are useful in understanding solute-solvent

and solute-solute interactions in solution. Solution studies of amino acids with their surrounding environment play important role in conformational characteristics of proteins. These properties help us in many ways to study drug interactions thoroughly. This paper we will discuss about the volumetric properties of drug solution and their significance.

Volumetric physicochemical properties

Volumetric properties of solution are believed to be sensitive to the nature of hydration. Density which is defined as mass per unit volume is a fundamental property of matter. Density is the fundamental physical property associated with some derived properties such as these properties helps in understanding the volume changes in the solution which is related with the intermolecular forces in solution.

II. METHODS AND MATERIALS

The solution density can be measured by using calibrated and standardized single capillary pcynometer (made of borosil glass). now a days researcher are using more advanced and sensitive instruments like Anton paar DSA500 which is able to measure density and speed of sound simultaneously. The experimental densities are reported for the various concentration ranges of amino acids. These density values are studied with respect to different concentrations of amino acids and also studied with respect to temperature. Depending upon the nature of solute-solvent, solute- solute interactions developed in the solution under study we find a particular trend in the experimental values of densities of the solution range under study. The trend may be either increasing or decreasing. These trends of densities for the system under study indicate molecular interactions existing between solute and solvent molecules. Densities of a specific composition of amino acid solutions are measured at different temperatures.

These experimental densities are further used to calculate the other derived thermodynamic volumetric properties of system under study which are as.

- Apparent molar volume
- Standard molar volume.
- Transfer volume etc

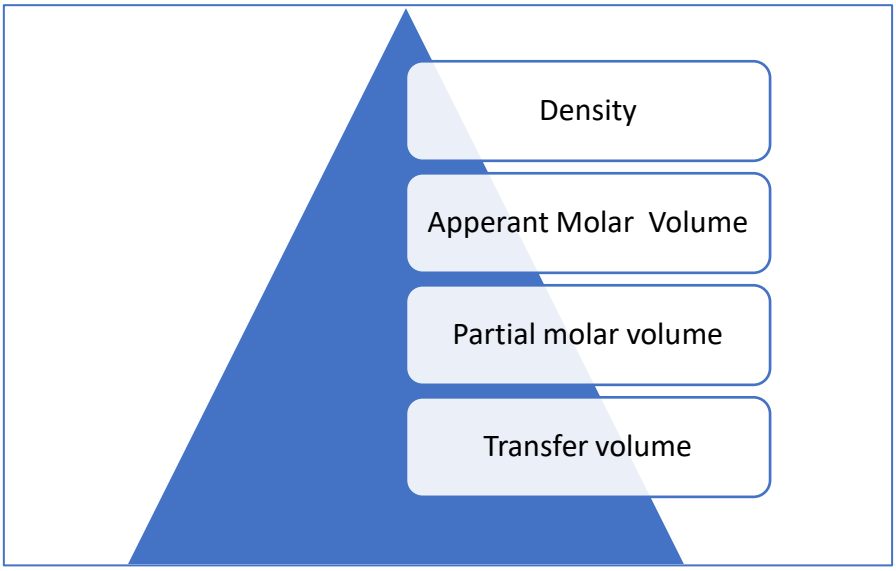

Fig: pictorial representation of volumetric physicochemical properties.

1) Apparent Molar Volume

Apparent molar volume is a function of composition of solution at given temperature and pressure and for infinite dilution it represents PMV, Φ^0v. It is important thermodynamic property which gives idea about physicochemical behavior of solution and intermolecular forces in drug solution.

Solution containing n_1 moles of component 1 and n_2 moles of component 2,we can write:

$$V_1 = \left(\frac{\delta V}{\delta n1}\right)_{T, P, n2} \quad (3)$$

Change in volume this solution after adding of the one of the component at constant T and P is:

$$V = (n_1 V_1 + n_2 V_2)_{T, P,} \quad (4)$$

Appearent molal volume is given by:

$$\Phi v = \frac{V - n1\, V01}{n2} \quad (5)$$

Where,

V^0_1 =Volume of one mole of pure solvent at constant T and P. Rearranging above equation

$$V = n2\Phi v + n1V01 \quad (6)$$

Differentiate this equation(6) with respect to n_2,we get

$$V_2=\left(\frac{\delta V}{\delta n2}\right)_{T, P, n1} = \varphi + n2 \left(\frac{\delta \Phi v}{\delta n2}\right)_{T, P, n1} \quad (7)$$

from equation (5)

$$V1 = \frac{V - n2V2}{n1} \quad (8)$$

Combining equation (6) to (8) we get

$$V_1 = \frac{1}{n1}\left[n_2 \Phi v + n1V^0_1 - n2\, \Phi v - n_2\left(\frac{\delta \Phi v}{\delta n2}\right)_{T, P, n1}\right] \quad (9)$$

Now, if M_1 and M_2 are molar masses of component 1 and 2 and ρ is experimental density of solution, then

$$V = \frac{n1M1 + n2M2}{\rho} \quad (10)$$

Adding (10) in (5) :

$$\Phi v = \frac{1}{n2}\left[\frac{n1M1 + n2M2}{\rho} - n_1 V^0{}_1 \right] \quad (11)$$

In terms of molal concentration scale, $n_2 = m_2$ and $n_1 = 1000/m_1$. then ,

$$\Phi v = \frac{1}{m}\left[\frac{1000 + mM2}{\rho} - \frac{1000V01}{M1}\right] \quad (12)$$

Also, $M_1/V^O{}_1 = \rho^0{}_1$ = density of the pure solvent at given T and P therefore, for AMV we write :

$$\Phi v = \frac{M2}{\rho} + \frac{1000}{m\rho\rho0} (\rho_0 - \rho) \quad (13)$$

Or for molar concentration (c) of the solute :

$$\Phi v = \frac{M2}{\rho} + \frac{1000}{c\rho0} (\rho_0 - \rho) \quad (14)$$

Where ,

Φv = Appearent molar volume

ρ_0 = Density of solvent (component 1) in which solution are prepared ($g.cm^3$)

ρ = Density of experimental solution. ($g.cm^3$)

M_2 = Molar mass of solute (component 1) ($g.cm^3$)

C = Molar concentration of solution ($mol.dm^3$)

Using equation (14) the AMV of the drug in different solutions can be calculated.

The calculated values of apparent molar volume studied for the solutions at different temperatures are used to calculate partial molar volume.

2) Partial Molar Volume:

The concentration dependence of AMV (Φv) is fitted to the following different equations:

$$\Phi v = \varphi_v^0 + S_V \times c \quad (15)$$

$$\Phi v = \varphi_v^0 + S_V \times \sqrt{c} \quad (16)$$

$$\Phi v = \varphi_v^0 + a_0 \times c + a_1 \times c^2 \quad (17)$$

Where,

C = concentration of CPT solution

φ_v^0 = Limiting infinite dilution apparent molal volume (PMV)

S_V = Experimental slope which represents solute –solute interactions.

Equation (16) is a Massons linear relation.

Partial molal volume is an important thermodynamics property gives an idea regarding volume changes with concentrationof drug and solute –solvent interactions .It has applications in different fields of the science such as biochemistry, pharmaceutical sciences, oceanography ,aquatic environmental science etc.

3) Transfer Volume

Partial molar volume of transfer (standard transfer volume of drug $\Delta_{tr}\ \varphi_v^0$) which gives information regarding solute –co- solute is calculated (8-12) using Equation (18):

$$\Delta_{tr}\ \varphi_v^0 = \varphi_v^0\ (Aq.) - \varphi_v^0\ (W) \quad (18)$$

Where,

$\Delta_{tr}\ \varphi_v^0$ = Partial molar volume of transfer

φ_v^0 (Aq.) = PMV in aqueous-alcoholic /aqueous β-Cyd solution.

φ_v^0 (W) = PMV in water.

III.RESULTS AND DISCUSSIONS

The following factors are found to be involved in drug related solution as

- **Molecular weight and size**

There is a clear relationship between the diffusion coefficient (D) and molecular weight (Mr): $D(Mr)^{-½} \approx$ constant. Molecular size is believed to play a role in the permeation process.There appears to be an inverse relationship between the absorption rate and molecular weight. Generally, an increase in the molecular volume is associated with the hydrophobic surface area and this leads to enhanced permeability through a lipid membrane. Conversely, larger molecules diffuse more slowly because they require more 'space' to be created in the medium, and this in turn leads to diminished permeability.Small molecules penetrate more rapidly than large, but within a narrow range of molecular size, there is little correlation between size and penetration rate.

Since the diffusion of molecules through liquids is inversely proportional to the square root of their molecular weight and the dependency is generally not much higher for diffusion through a membrane, one might expect higher permeability coefficients to be associated with drugs of low molecular weight.

❖ **Volumetric properties**

a) Solute-solvent interactions are to be confirmed with positive values of apparent molar volume.

b) Partial molal volume is an important thermodynamics property gives an idea regarding volume changes with concentration of drug and solute –solvent interactions

c) Partial molar volume of transfer (standard transfer volume of drug $\Delta_{tr}\ \varphi_v^0$) gives information regarding solute –co- solute interactions.

IV.CONCLUSION

study of the elaborate relationship of physicochemical properties stands as a essential factor influencing the balance between a drug's pharmacokinetic and pharmacodynamic profile. These properties emerge as a keystone in understanding the bioavailability of drug in biological system. This all summarizes that these basic and derived thermodynamic physicochemical volumetric properties of drug solution helps us in a great way to understand the thermodynamics of the solution behavior under study. The results obtained from this data have importance in many fields such as immunology, biosynthesis, medicine, pharmacology. In our body drug-protein interactions play vital role in metabolic pathway. Thus properties of aqueous drug solutions are essential for understanding the chemistry of biological systems. This data is useful in pharmaceutical and medicinal chemistry

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Comparative Study of Catalytic Effect of Metal Salt on Alcohol Fermentation

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ABSTRACT
Fermentation has been widely used for the production of a wide variety of substances that are highly beneficial to individuals and industries. Ethanol is one of the most useful products which obtained in fermentation reaction. A microorganism Saccharomyces Cerevisiae is used. Healthy micro-organism can increase the production of alcohol. There are metal and metal salts which affect the physiology of Saccharomyces cerevisiae. And act as the catalyst. In present work different metal salts are used to study the catalytic effect of metal salt.
Key word- Saccharomyces Cerevisiae, Metal, Metal salt.

I. INTRODUCTION

Absolute alcohol, rectified spirit, and denaturated alcohol are used as solvents and as liquid fuel. Ethyl alcohol is also used as source of ethylene and butadiene. It also used to make ether, Chloroform, Iodoform, glacial acetic acid etc. It is used as disinfectant for making various tinctures used in medicine. Alcohols are also used to prepare alcoholic beverages.

Ethyl alcohol is prepared by fermentation process. Fermentation is a process in which complex organic substance is converted into simpler organic substance by the action of enzymes secreted by the microorganisms. Alcoholic fermentation is the process in which reducing sugar i.e. glucose and fructose are converted into ethyl alcohol and carbon dioxide by the action of enzymes invertase and zymase secreted by microorganism.

$$C_{12}H_{22}O_{11} + H2O \xrightarrow{\text{Invertage}} C_6H_{12}O_6 + C_6H_{12}O_6$$

$$C_6H_{12}O_6 \xrightarrow{\text{Invertage}} 2C_2H_5OH + 2CO_2$$

In fermentation process the role of yeast is very important. It is said that healthy yeast can increase the fermentation yields and profitability. References indicate that additional nutrients are important for yeast growth. Yeast must multiply many times over to reach critical mass.

Important nutrient required for the growth of yeast are, nitrogen, sterols and unsaturated fatty acid, Vitamins and minerals. The free amino acid provides nitrogen to yeast in fermentation process. The yeast cells needs vitamins in small quantities for enhance structure and function, minerals for enzyme stability and metabolism. Many of the micronutrients also increases activity of enzymes. Known micronutrient are Mn, Zn, Ca, Cu each micronutrient have important function in yeast growth and better fermentation.

Mn insulates the cell against stress factor of temperature. Alcohol and osmotic pressure.Ca, helps stimulate cell growth and cell wall permissibility. Cu assists with cell internal enzymes production. K assists with storage of ATP inside the cell. Vitamins also causes the fermentation action of yeast like Biotin help in carboxylation and decarboxylation reaction. Thiamin helps amino acid biosynthesis, Niacin helps in redox reaction. Riboflavin also help in redox reaction.

The role of microelements in metabolism of higher organism and yeast has recently become very interesting field of research work.(Jones 1990.), References also indicate that Zn, Cu, Cr, Fe, Mn, etc. have important physiological role in the action of yeast.

During the alcohol fermentation addition of microelement into yeast cell is of particular interest. The trivalent Cr is useful in carbohydrate mechanism of yeast.

The number of studies of the process involved in the uptake of trace metal by the yeast Saccharomyces Cerevisieae has increased considerably in recent years. The yeast has become model microorganism for studying metal transports and their accumulation in the cell. However excess amount of the same metal ion toxic and cause the damage to the function.

Zinc, Copper and Manganese ions are very interesting because they have a positive effect on the respiratory activity and growth rate of Saccharomyces Cerevisieae. Thus impact of these ions on the yeast growth and fermentation activity have been reviewed.

Zn^{++} ions is essential as catalytic cofactor of many enzymes including alcohol dehydrogenase .Copper is also a vital divalent cation in yeast cell acting as cofactor of some enzymes such as cytochrome , oxidase, lactase and Cu. Zn superoxide dismutase . The optimal concentration of Cu^{+2} ions in the nutritive medium for the yeast growth and fermentation activity are in the range 1-10 μM. the specific growth rate of Saccharomyces cerevisiae was higher in continuous batch culture *(11) if Mn^{+2} ions were present in optimal concentration in the medium.

The aim of the present work is to study effect of Cr, Mn, Fe, Co, Ni, Cu metal ion Salt. The fermentation were carried out with Saccharomyces Cerevisieae on standard substrate molasses.

II. MATERIAL AND METHODS.

Microorganism - Yeast used in the study was Saccharomyces cerevisiae collected from local market. The culture was mainted on solid yeast medium.

Molasses.- The molasses were obtained from Bhaurao Co.op. sugar industries, Laxmi Nagar, Nanded.

Batch process is adopted in fermentation.

The % of reducing sugar is about 40% the molasses were diluted to prepare different concentration of sugars. The production medium is supplemented with nitrogen and Phosphate. The pH of medium was adjusted to 5.

Media composition.

KH2PO4-	0.1%
(NH4)2SO4	0.5%
MgSO4 7H2O	0.05%
Yeast extract	0.1%
pH	5

The ph of medium was adjusted by putting drop by drop dil. sulphuric acid.

The fermentation flasks were arranged and they were labeled along with yeast catalyst. Metal salt were added. pH were adjusted.

III.EXPERIMENTAL

To study the effect of the metal ions different experiment were carried out. All the fermentation flask were sterilized. All solution which are used for the experiment were also sterilized. 7 fermentation flask (sterilized) were arranged and they were labeled from 1 to 7.

Fermentation flask no.1 is used as control, Fermentation flask no. 2 is used to study the effect $CrCl_3$Salt which is 0.5 gm.Added in conical flask no. 3 $MnCl_2$0.5 gm. wereadded and conical flask no. 4, 5, 6 and 7,$FeCl_3$,$CoCl_2$,$CuCl_2$,$NiCl_2$respectively 0.5gm. were added.

The solution like 0.05 % $KHSO_4$, 0.5% $(NH_4)_2SO_4$, 0.05 % $MgSO_4 7H_2O$ and as mentioned above different metal ion were added. the pH of the experiment is adjusted by putting drop by drop dil. H_2SO_4. The fermentation reaction were carried out for 24 hours. In each fermentation flask 10 ml 1% molasses solution and media

Estimation of biomass:-

The quantity of biomass depends upon yeast growth takes place.

The dry biomass were measured by transferring the content of conical flask through the filter paper. The residue of biomass which is collected on the filter paper is dried by keeping it in oven at 100°C. The mass of biomass were recorded and it is given in the table.

Estimation of ethyl alcohol: -

Spectroscopic method is used to determine the alcohol generated in the fermentation process. Fermented wash were taken in distillation flask. 15 ml distillate were collected in the conical flask. 5 ml $K_2Cr_2O_7$(0.1N) in 0.1N H_2SO_4 solution were added it is warmed at 60°C. The color obtained. The optical density of solution was measured from standard graph. The ethanol generated during fermentation was determined.

Table no.1-Effect of metal chloride on fermentation

Sr. No	Flask No.	Compounds	%wt. of biomass	% Alcohol
1	**1**	Control	1.09	2.05
2	**2**	$CrCl_3$	1.21	2.60
3	**3**	$MnCl_2$	1.19	2.25
4	**4**	$FeCl_3$	1.15	2.27
5	**5**	$CoCl_2$	1.13	2.13
6	**6**	$CuCl_2$	1.15	2.19
7	**7**	$NiCl_2$	1.18	2.20

IV.RESULT AND DISCUSSION

References indicate that some microelement affects growth of yeast. To study the effect of Cr^{+2},Mn^{+2}, Fe^{+3},Co^{+2},Ni^{+2},Cu^{+2} metal Chloride were used in fermentation process. The table no. 1 gives information regarding effect of metal ion

Observation table indicate that $Crcl_3$ gives yield 1.21 % biomass and it generate 2.60% alcohol. Indicating the this salt enhance the fermentation more among other metal salt where as $Cocl_2$ give yield 1.13 % biomass and it generate 2.13 % alcohol. $Mncl_2$ is second one effective metal salt which produces 1.19 % biomass and 2.25% alcohol. $Nicl_2$ goes on third number it gives 1.18 % biomass and generate 2.20% alcohol. If we compare $Fecl_3$ and $Cucl_2$ both gives same biomass yield 1.13% but $Fecl_3$ generate more alcohol 2.27% while $Cucl_2$ generate 2.19% alcohols.

V. CONCLUSION

the results of fermentation experiments indicates that certain metal chloride which are used in this experiment accelerates the biomass formation also generation of alcohol.

Conclusion can be drawn from the results observed from different experiments carried in the study Cr^{+2},Mn^{+2}, Fe^{+3},Co^{+2},Ni^{+2},Cu^{+2}metal ion were added in the fermentation process to see their comparative effect on fermentation. The results indicate that Cr^{+2}, Co^{+2} increase the formation of biomass and generation of alcohol.

The molasses was the main substrate for yeast and ethanol production. Our results indicates that chromium metal ion enhance cell growth. The recent studies indicate that certain microelement act biologically important.Certain references indicate that the Cu^{+2} ion increases the rate of fermentation because their helpful in metal binding. Copper induces the result indicate that the metal ion enhance the formation of yeast biomass Mn^{+2} metal ion increases biomass formation of yeast and alcohol generation.

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Synthesis and Characterization of {2,6-Dichloro-4- [(Phenyl Thio) Methyl] Pyridine-3-Yl}-(Phenyl)Methanone and Its Derivatives

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ABSTRACT
The importance of the benzo[b]furan motif becomes evident in the remarkable results of numerous biological investigations, establishing its potential as a robust therapeutic option. This research paper present invention relates to a Synthesis and characterization of {2,6-Dichloro-4- [(phenyl thio) methyl] pyridine-3-yl} methanone derivatives, to processes for its preparation and to its use in agrochemical preparations.
Keywords: synthesis, Isobenzofuran, Pyridine, Characterization.

I. INTRODUCTION

Isobenzofurans which is represented by benzofuran served as an interesting class of reactive intermediates in organic synthesis. Isobenzofuran is a bicyclic heterocycle consisting of fused cyclohexa-1,3-diene and furan rings. It is isomeric with benzofuran.Isobenzofuran is highly reactive and rapidly polymerizes however it is identified [1]and prepared by thermolysis of suitable precursors and trapped at low temperature.[2] Though isobenzofuran itself is not stable, it is the parent of related stable compounds with more complex structures, [3] such as the hindered analogue 1,3-diphenylisobenzofuran.
As functional analogues of o-xylylenes, they take partbin both inter- and intramolecular Diels-Alder reactions leading to a variety of polycyclic ring systems including natural products of biological significance [4-6]. In comparision heteroanalogoues of isobenzofurans have received lesser attention, although this situation is changing in reecent year [7,8]. Isobenzofuran is a hetero cyclic compond consisting of fused benzene and furan rings. They take part in diff type of reactions leading to a variety of polycyclic ring systems including natural products of biological significance [9].

II. MATERIALS AND METHOD

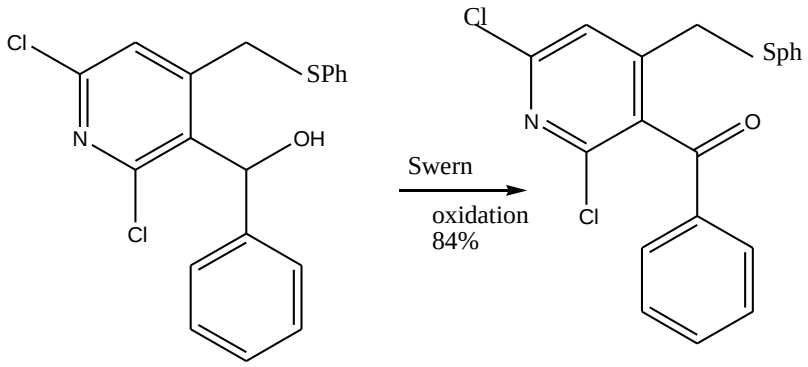
All chemicals used were of high purity analytical grade. 2,6-dichloro-4-ethylpyridin-3-yl(p-tolyl)methanol Synthesized in laboratory starting from aldehyde, to dry CH2Cl2, PCC etc. The synthesized product then concentrated under reduced pressure and purified by chromatography (EtOAc:Petrolium ether 5:95). Melting

point of product is taken on digital melting point apparatus. IR spectra of synthesized product is taken in the range of 4000-400 cm^{-1}

III.EXPERIMENTAL DETAILS

A] Preparation of {2,6-Dichloro-4-[(phenyl thio)methyl]pyridine-3-yl}-(phenyl)methanone

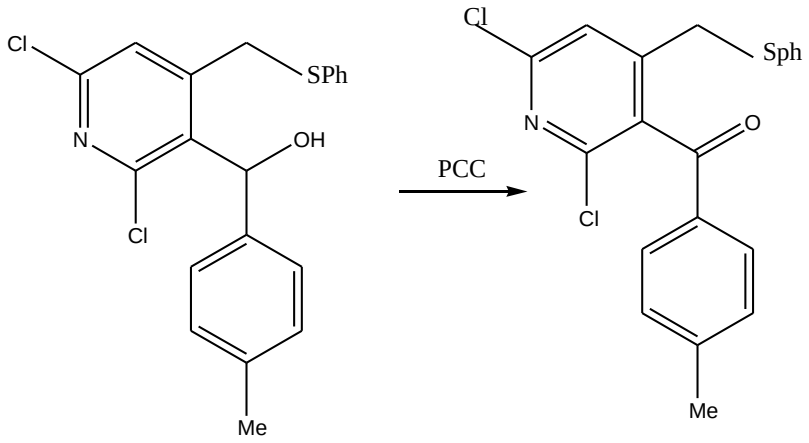
To a stirred solution of oxalyl chloride (0.278 ml, 3.13 mm0l) in 10ml of CH_2Cl_2 cooled at -60^{0}c was added DMSO (0.453 ml, 6.39 mmol) in 5ml of CH_2Cl_2 drop wise via dropping funnel in 15 min under argon atmosphere. The mix was stirred for 30 min followed by addition of 119 (800 mg, 2.13 mmol) in 10 ml CH_2Cl_2 over a period of 10 min. After 30 min of stirring Et3N (1.5 ml, 10.65 mmol) was added and the reaction mixture was allowed to attain room temperature and stirred for 1 hour. Then 100 ml cold H_2O was added to the mixture. The organic layer was separated and washed with 1% HCl and brine. Finally the organic fraction was concentrated in vacuo and purified by chromatography (EtOAc:petroleum ether 5:95) to give 670 mg of the product in 84% yield.



IR (KBr) 1666, 1602, 1555, 1332 cm^{-1} ^{1}H NMR (200MHz, $CDCl_3$: CCl_4 7:3), 3.90 (s, 2H), 7.00-7.85 (m, 11H). ^{13}C NMR (50 MHz, $CDCl_3$:CCl_4 7:3) δ 35.7 (t), 123.7 (d), 127.6 (d), 128.9 (d), 129.2(d), 129.6 (d), 130.9(d), 132.7 (s), 133.5 (s), 134.5 (d), 135.8 (s), 146.7 (s), 150.8 (s), 151.1 (s), 192.5 (s).

B] Preparation of {2,6-Dichloro-4-[(phenyl thio)methyl]pyridine-3-yl}-(4-methylphenyl)methanone

To a stirred solution of 2,6-dichloro-4-ethylpyridin-3-yl(p- tolyl)methanol (2 g, 5.12 mmol) in 20 ml of dry CH_2Cl_2 was added PCC (1.7 g, 7.7 mmol) at room temperature. After 1.5 h of stirring the solution was filtered over a short celite pad. The yellow solution was then concentrated under reduced pressure and purified by chromatography (EtOAC: petroleum ether 5.95) to give 1.55 g (78%) of 123 as a white solid: mp 105 -107^0 C.

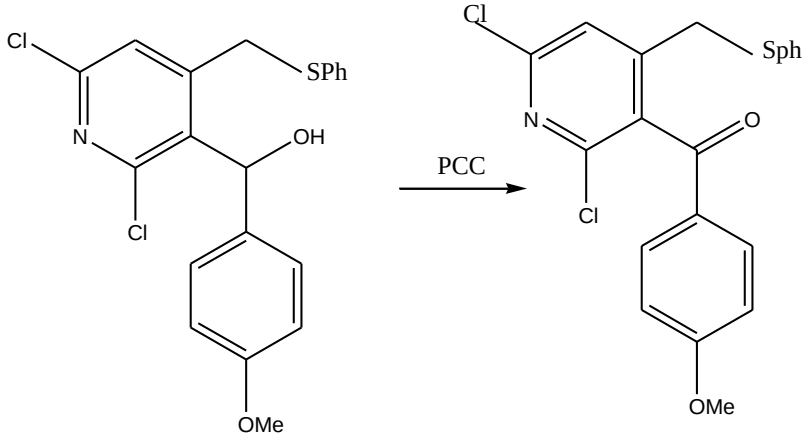


IR (KBr) 1658, 1602, 1565, 1325 cm^{-1} ^{1}H NMR (200MHz, $CDCl_3$: CCl_4 7:3) δ 2.42 (s, 3H), 3.90 (s, 2H), 7.05-7.35 (m, 8H), 76.4 (d, 2H, J= 8.0 Hz). ^{13}C NMR (50 MHz, $CDCl_3$:CCl_4 7:3) δ 21.9 (q), 35.6 (t), 123.6 (d), 127.5 (d), 129.1(d), 129.7 (d), 129.8 (d), 130.8 (d), 133.0 (s), 133.4 (s), 133.6 (s), 145.7 (s), 146.7 (s), 150.6 (s), 150.9 (s), 192.0 (s)

C] Preparation of {2,6-Dichloro-4-[(phenyl thio)methyl]pyridine-3-yl}-(4-methoxyphenyl)methanone

(2,6-dichloro-4-ethylpyridin-3-yl)(4-methoxyphenyl)methanone was obtained by the PCC oxidation of alcohol in the (2,6-dichloro-4-ethylpyridin-3-yl)(4-methoxyphenyl)methanol (400 mg, 0.98 mmol) in 96% yield as a yellow oil.

IR (KBr) 1660, 1595, 1564, 1343 cm^{-1} ^{1}H NMR (200MHz, $CDCl_3$: CCl_4 7:3) δ 3.88 (s, 3H), 3.90 (s, 2H), 6.90 (d, 2H, J = 9.1 Hz), 7.12-7.28 (m, 6H), 7.70 (d, 2H, J= 8.6 Hz). ^{13}C NMR (50 MHz, $CDCl_3$:CCl_4 70:30) δ 35.6 (t), 55.4 (q), 114.2 (d), 123.4 (d), 127.5 (d), 128.9 (s), 129.1 (d), 130.8 (d), 132.0 (d), 133.0 (s), 133.7 (s), 146.7 (s), 150.5 (s), 150.7 (s), 164.6 (s), 190.7 (s).



IV.CONCLUSION

In conclusion we have developed potent system for the oxidative trans position readily accessible aromatic alcohol to exclusively yield the product 2,6-Dichloro-4-[(phenyl thio)methyl]pyridine-3-yl}methanone in average to excellent yields.

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Recent Advancements in Manganese Pincer Complexes for Catalytic N-Methylation of Amines Using Methanol as C1 Source

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ABSTRACT

N-Methylamines are an essential class of amines with growing uses in the material, agrochemical, essential fine and bulk chemicals and pharmaceutical sectors. Hence, N-methylations represent a significant class of chemical processes or reactions in the synthesis of organic compounds and drug discovery, providing access to sophisticated molecules, medications, biomolecules, and agricultural chemicals. For N-methylation processes, valuable late transition metal catalysts have been used in past few decades. The early transition metals are gaining a lot of interest lately because of their overall sustainability, reduced cast and reduced environmental impact. There are multiple applications in academia and industry for catalytic hydrogen methodology reactions in the synthesis of various molecular scaffolds. As an effective substitute in this context, manganese the third most common transition metal in crust of the earth - has developed. But the multifunctional ligand design of selection of suitable auxiliary ligands, which enable them to replicate the activities of noble metals, are crucial to the effectiveness of such manganese-based complexes. As methanol is utilized as a common solvent, cost effective reagents and sustainable feed stock for value added chemical, medicines and materials. Among its numerous uses, chemical synthesis of drug development still relies heavily on the use of methanol as a C1 source for the synthesis of carbon-carbon, carbon-nitrogen and carbon oxygen bonds. Additionally, methanol is less hazardous and in methylation processes yields only water as a by-product. The objective of the current investigation is to present the most recent development in the catalytic N-methylation of amines using methanol a major C1 source of CH3, from 2016 to 2023. In particular, the synthesis of N-methylamines via borrowing hydrogen methodology.

Keywords: N-methylamines, borrowing hydrogen methodology, homogeneous catalysis, methanol, manganese, pincer complexes, amines, aniline

I. INTRODUCTION

In organic chemistry, molecules that contain nitrogen are preferred and most abundant structures for instance, among the thousands of small molecules pharmaceuticals that have received FDA approval, over 80% compound have at least one nitrogen atom, with an average of 2.3 nitrogen's per drug.[1] Among different amines, *N*-methylamine including aniline functionalities are valuable class of amines, that are often

encountered in commercial pharmaceuticals, essential fine and bulk chemicals widely used in organic synthesis and often employed in drug discovery process (Fig.1).[2-8] Notably, *N*-methylamines are crucial precursors and intermediates that are widely employed in academic as well as industrial applications to create specialized chemicals, biomolecules, medication, agrochemicals and materials. Indeed, out of the 55 FDA approved medications in 2023 two that had *N*-methyl functionality [9] and more than 10 of the top 200 pharmaceuticals by retail sale between 2019 to 2023 contains an *N*-methyl moiety (Fig.2.).[10]

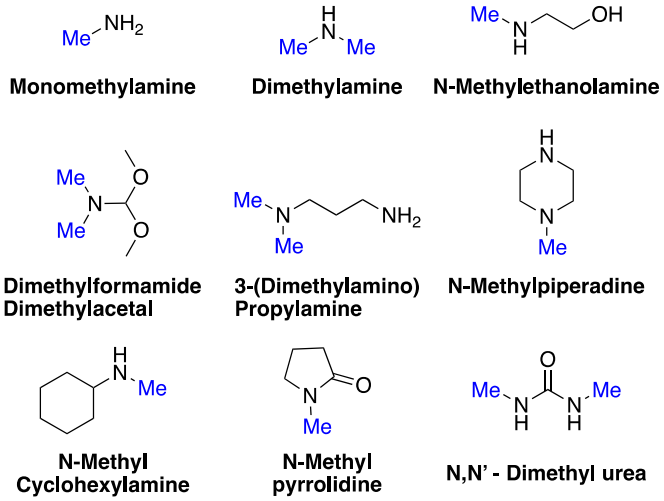


Fig. 1. Examples of *N*-methylated molecules as essential building blocks that are potentially valuable in the chemical industries.

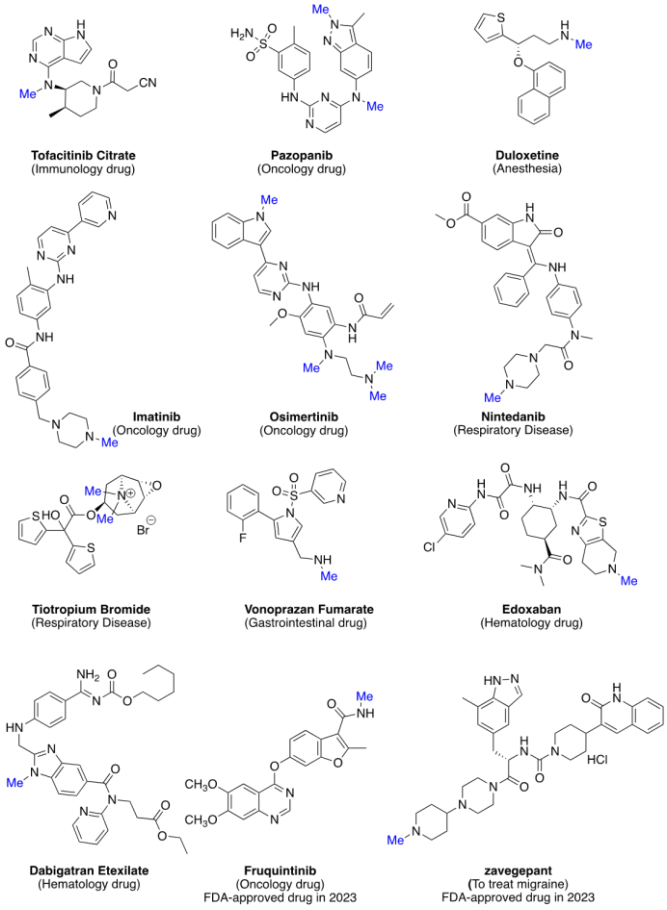


Fig. 2. Representative best-selling medications and newly FDA-approved medications with an *N*-methyl moiety.

In addition to these, *N*-methylamines functionality also present in pincer ligands complexes as tridented ligand as well as bidented ligand in organometallic chemistry and catalysis.[11] Despite being a straightforward chemical change, the *N*-methylation process is a potent toll for controlling the physicochemical characteristics and bioactivities of drug and biomolecules.[12] *N*-Methylation of peptides and DNA, for instance, increases these molecules hydrophobicity, bioavailability, and metabolic stability. It also plays crucial role in epigenetic modifications to gene expression and cellular phenotype.[13] Moreover, pharmacokinetics, the transport of drugs, enzyme activity and antibody activity are all regulated by *N*-methyl functionality. [13,14] Therefore, adding mono and dimethyl unit to peptides, DNA or amine-based compounds has proven to be a powerful method for adjusting their functions and researching the structure function relationship, which aids in the development of novel molecules for use in life science application. Considering the simplest and smallest methylation as a late-stage modification in bioactive compounds have the most profound impact on altering the biological properties of molecules.[15,16] This phenomenon is well-known as the "magic methyl effect".[17]

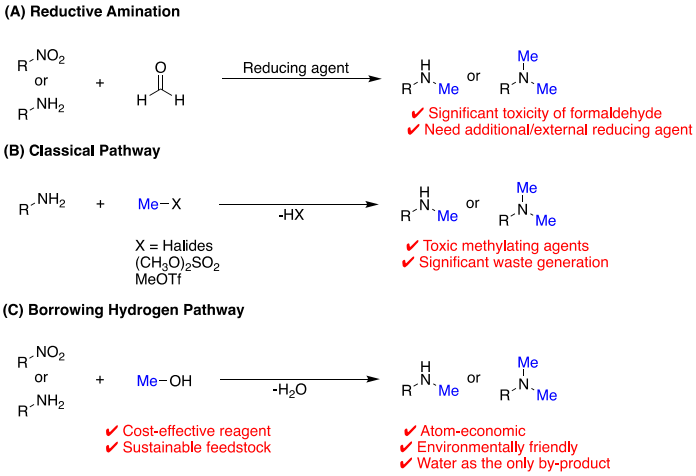


Fig. 3. Methodologies for the synthesis of *N*-methylamines.

Hence, new synthetic methodology for efficient, environmentally benign friendly and selective mono- and di-*N*-methylamines and their derivatives are of great interest. However, major challenges with these specific transformations need to considered first, A well-known traditional technique in the chemical and pharmaceutical industries for constructing *N*-methylamines is the Eschweiler-clarke reaction. this technique uses their formic acid or $NaBH_4$ as a reducing agent with formaldehyde.[18,19] Although formaldehyde is widely applicable affordable, abundant, its substantial toxicity and instability represent a risk and are recognized as carcinogens for humans. Conversely, methylating agents like methyl iodine (MeI), diazomethane (CH_2N_2), Methyl triflate (MeOTf) and dimethyl sulphate (DMS) are typically used in drug development to carry out *N*-methylation reaction.[13,20-22] However, some of these activated methylating agents are poisonous low atom-efficient and they should be used excessively and produced stoichiometric amount of inorganic wastes.[22-23] compared to these two approaches catalytic methylation reaction employing methanol as a possible C1 source of CH_3 are more environmentally benign, atom-economic and more sustainable because (a) methanol is an inexpensive, and bulk chemical that is globally produced in large quantities 171.84 million metric tonnes in 2022, The globally methanol production capacity expected to grow by more than 80% between 2021 and 2030.[24] (b) The only by product of this reaction is water, which is produced by the catalytic borrowing process. (c) Methanol act as both the source of C1 and H_2 and no extra reducing agents or pressurized apparatus is required for this reaction (Fig. 3).

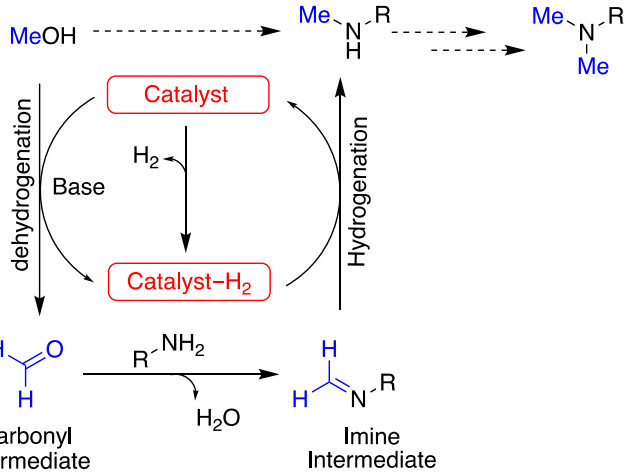
The synthesis of various *N*-methylamines is receiving a lot of attention due to the operational simplicity of MeOH and its prospective benefits in organic transformations [25] and energy technologies.[26] Using methanol as the methylating agents for selective mono-*N*-methylamines enabled by the borrowing hydrogen methodology.[27,28] The reaction of methanol with various amines have been performed to access divers mono- and di-*N*-methylamines product. Catalyst that are both homogeneous and heterogeneous were developed and utilized to accomplish these reactions. [25,27] Over the past few decades, noble-metal catalysts were employed for these reactions.[29] The early transition metals have recently gained much attention due to their lower cost, less toxicity, and overall sustainability. In this regards, manganese is the third most abundant base metal, cheep, non-toxic metal and environmentally benign and most suitable for given organic transformation.[30] Given the considered amount of research articles, few methodologies of *N*-methylation are reviewed in the past.[29,31-33]

Nonetheless, a more thorough evaluation of the recent advancement in manganese pincer complexes for catalytic *N*-methylation of amine using methanol as C1 source is missing in this systematic and in-depth analysis. Thus, we go into more comprehensively in this review of recent developments from (2016 to 2023) in the employing of MeOH as a methylation source to prepare *N*-methylamines that are simple, functionalized and structurally diverse. These amines can be synthesized by starting with amines and utilizing various manganese pincer complexes via borrowing hydrogen methodology.

II. REACTIVITIES, AND STRUCTURE OF MANGANESE PINCER COMPLEXES

N-Methylation of amines and/ or nitro compounds with methanol using Manganese based homogeneous catalysts

Based on the borrowing hydrogen approach, or hydrogen auto-transfer amines are catalytically *N*-methylated using methanol as methylating agents. [34,35] The following reaction stages are involved in this process. (1) Methanol is first dehydrogenated to formaldehyde in the presence of a catalyst with liberation of molecular hydrogen in the process. (2) The formaldehyde produced in situ then condenses with



Scheme-1: Reaction mechanism of *N*-methylation of amine via borrowing hydrogen methodology

amine to produces the equivalent imines as an intermediate. (3) Lastly, the desired mono-*N*-methylamine is produced by catalytic reduction of the imine with hydrogen that is liberated from methanol. Subsequently, the

already formed mono-*N*-methylamine is reduced to make *N,N*-dimethylated amine, and condensation with another formaldehyde molecules produces iminium ions (Scheme-1). [36]

III.CATALYSIS

N-Methylation of amines and/or Nitro Compounds with Methanol Using Homogeneous Manganese-Based Catalysts

Manganese catalyzed selective mono *N*-methylation of aniline with methanol

The selective mono methylation of amines with methanol is most challenging reaction as formation of side products such as *N,N*-dimethylated amines is in competition. Mono-*N*-methylated amine functionalities are valuable motifs, which play vital roles in the properties and activities of essential fine and bulk chemicals, molecule used in life science applications such as drug molecules and natural products. [31] In 2016, Beller and co-workers were described pioneering reports dealing with the mono-*N*-alkylation of amines using methanol in the presence of homogeneous catalyst (Fig. 4.).

Beller and coworkers performed the synthesis of mono-*N*-methylated derivatives in the presence of 3 mol% PNP manganese complex **Mn-1** As shown in **fig. 4.**, a series of aniline derivative. Efficient mono *N*-methylation of aniline by methanol occurred when toluene solution of reaction mixture containing *t*-BuOK (1 equiv., 1 mmol), anilines derivative (1 mmol) methanol (1 ml) and **PNP Mn-1** (3 mol%) was stirred at 100°C in closed condition for 24h. Reaction is highly selective as only mono-*N*-methylation of anilines has been observed.

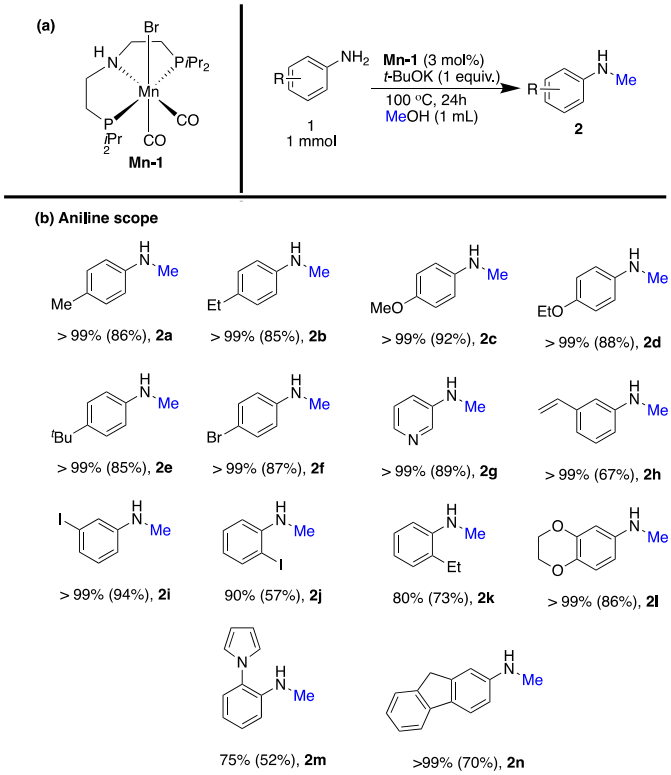


Fig. 4. *N*-methylation of primary anilines using methanol. (a) General reaction conditions: aniline derivative (1 mmol), Mn-1 (3 mol%), *t*-BuOK (1 equiv.), and toluene (2 ml) 100°C, 24h (b) Conversion was determined by GC (Isolated yield in parantheses) traces of reduction of double bond. 15% dehalogenation was observed.

Aniline **1a-1k** bearing alkyl substituent such as 4-Me (**1a**), 4-MeO (**1c**), 4-EtO (**1d**), 4tBu (**1e**), halogen substituent such as 4-Br (**1f**) and 3-I (**1i**) were reacted with methanol to gave the mono-*N*-methylated products in good to excellent isolated yields (**2a-2k**: 52% to 94%). In most cases the **PNP Mn-1** catalyst showed very good selectivity vide supra and even Br- and I- substituents were well tolerated (**2f**, **2i**), albeit in the case of sterically hindered 2-iodo *N*-methyl aniline **2j** some dehalogenation was observed. Again, aromatic (1n) and hetero aromatic substituted anilines (1m) were selectively monomethylated to the corresponding secondary *N*-methylaniline derivative (**2m**, **2n**) in good isolated yield (52-70%). In all the cases they didn't observed any traces of dialkylation products.

Mono-*N*-Methylation Of Anilines With Methanol Catalyzed By A Manganese Pincer Complex

In 2017, Sortais and co-workers described the PN3 P Mn(I)-2 catalysed *N*-methylation of anilines via the borrowing hydrogen approach. [37] Employing **PN³ P Mn (I)-2** pincer precatalyst (5 mol%), *t*-BuOK (20 mol%), MeOH (1 ml) and toluene (1 ml) as solvent a variety of electron rich arylamines undergo *N*-methylation at 120°C for 24h with methanol giving the corresponding mono-*N*-methylated arylamine product in high yield (Fig. 5.).

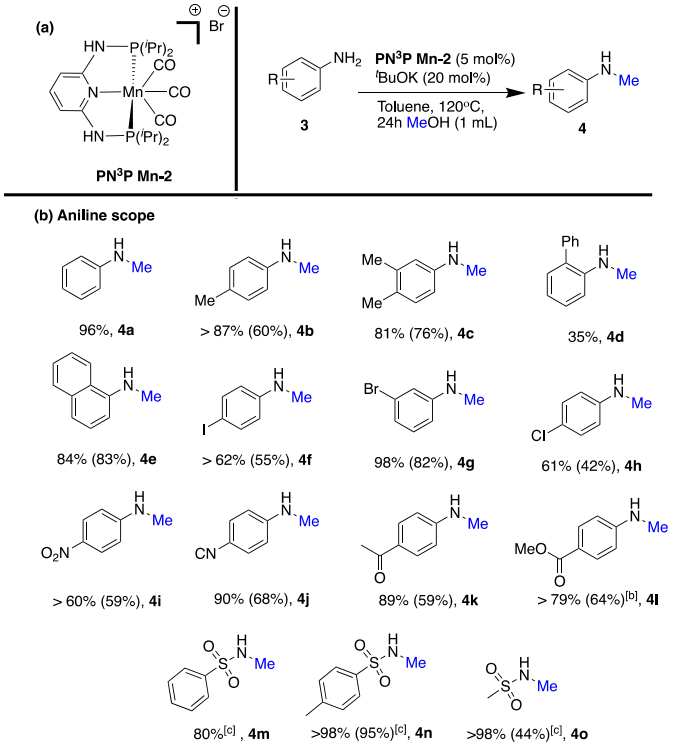


Fig. 5. *N*-methylation of primary anilines to give *N*-methyl-anilines under the catalysis of **PN³P Mn(I)-2**. Using methanol. (a) General reaction conditions: aniline (0.5 mmol), methanol (1 ml), toluene (1 ml), catalyst **PN³P Mn(I)-2** (5 mol %), and *t*-BuOK (20 mol %) were mixed in this order and heated in a closed Schlenk tube in an oil bath. Conversion determined by ^{1}H NMR (isolated yield in parantheses); [b] starting from ethyl 4-aminobenzoate **3l**, methyl 4-*N*-methylaminobenzoate **4l** was obtained; [c] 1.2 euiv. *t*-BuOK, 60h.

Aniline **3a-3h** bearing alkyl or halide substituent such as 4-Me (**3b**), 3,4 $(Me)_2$ (**3c**), naphthyl (**3e**) were reacted with methanol giving 81% to 96% conversion to the corresponding mono-*N*-methylaryl amines product in good isolated yield. (**4a-4e**; 62% to 96%). However, this catalytic system was sensitive to steric hindrance as 2-phenylaniline was methylated with only 35% conversion. The presence of halide substituents such as 4-I (**3f**),

3-Br (**3g**) and 4-Cl (**3h**) were methylated using methanol giving 61% to 98% conversion to the corresponding mono-*N*-methylarylamines product in moderate yield (4f-4h; 42% to 82%). Interestingly, this catalytic system was tolerant to several reducible or reactive functional group such as nitro (**4i**), cyno (**4j**), acetal (**4k**) and ester (**4l**) could be also be methylated in satisfactory yield. Furthermore, sulfonamides (**4m-4o**), which are common moieties in biologically active compounds, could be also be methylated under optimized reaction condition with excellent yields, although under harsher conditions for longer reaction time (1.2 equiv. of base for 60h).

Manganese- Catalyzed one-pot Conversion of Nitroarenes into *N*-Methylarylamine Using Methanol

In 2020, Morrill and coworkers reported bench stable **PN³P Mn(I)-3** pincer precatalyst for the *N*-methyl aryl amine from nitroarenes and methanol starting materials. [38] Using **PN³P Mn(I)-3** (5 mol%) as catalyst and KOH (2 equiv.) as base with methanol as a methylating agent as well as solvent, a variety of Nitroarenes react with methanol, accessing the corresponding *N*-methylated product in good yields (Fig. 6.). The reaction is highly selective as only monomethylation of Nitroarenes has been observed.

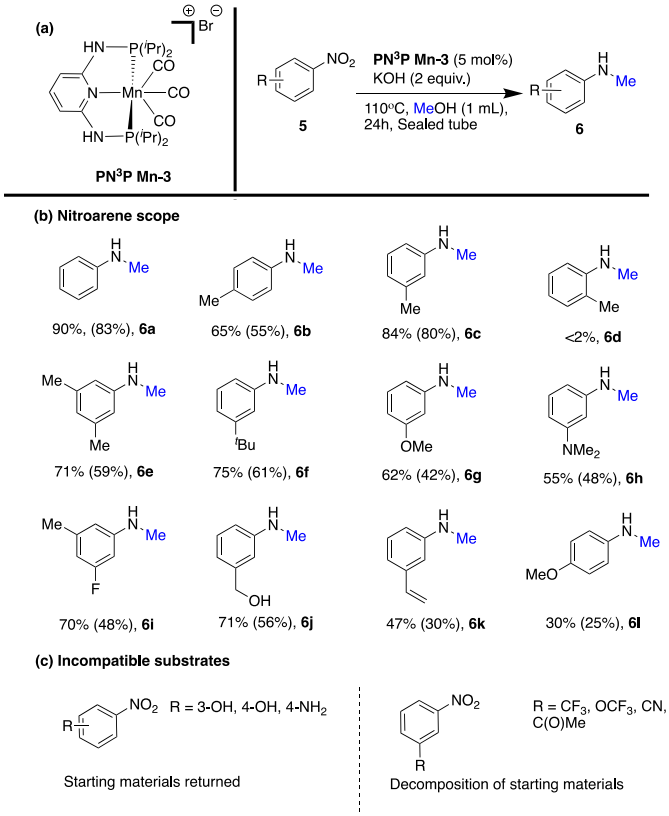
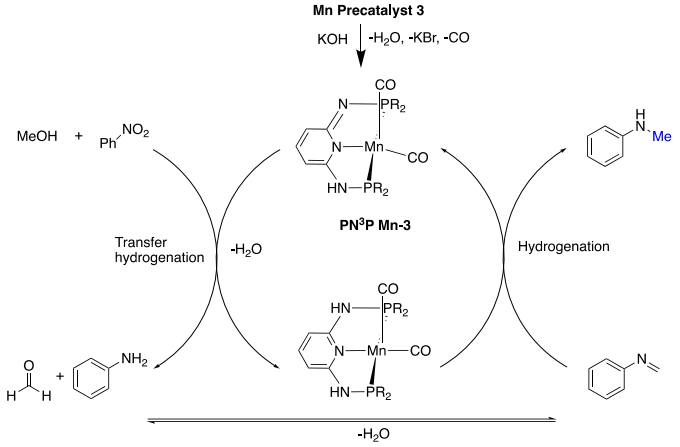


Fig. 6. *N*-methylation of nitroarenes to give *N*-methyl-anilines under the catalysis of **PN³P Mn(I)-3**. Using methanol. (a) General reaction conditions: nitroarenes (0.5 mmol), methanol (1 ml), toluene (1 ml), catalyst **PN³P Mn(I)-3** (5 mol %), and KOH (2 equiv.) were mixed in this order and heated in a closed Schlenk tube in an oil bath. Yields as determined by ^{1}H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard. (isolated yield in parentheses)

Nitroarenes (**5a-5i**) bearing alkyl substituent such as 4-Me (**5b**), 3-Me (**5c**), 3,5-Me (**5e**), 3-tBu (**5f**), 3-MeO (**5g**), 3-N(Me)$_2$ (**5h**), 3-F,5-Me (**5i**) were reacted with methanol giving 55% to 90% conversion to the corresponding product in moderate to good isolated yields (**6a-6i** ; 42% to 83%). Nevertheless, adding a 2-methyl substituent to the nitroarene caused the starting material to fully recover after a 16h reaction period. This could be related to the nitro functionalities increased steric shielding, which inhibited the transfer hydrogenation step.

Furthermore, more nitroarenes embedded functional groups that can undergo, dehydrogenation, including alcohols (**5i**) and alkenes (**5k**) can be present within the nitroarene and are preserved within *N*-methylarylamines (**6i** and **6k**) respectively. Under optimized reaction condition, 1-methoxy-4-nitrobenzene was reduced to 6% NMR yield; this climbed to 30% when the reaction temperature was raised to 130°C. A variety of nitroarenes containing hydroxyl or amino functionalities were unreactive with starting material returned. Moreover, Nitroarenes containing various electron with drawing groups at 3-position, such as CF_3, OCF_3, CN, and C(O)Me decomposition of starting materials was observed.



Scheme-2. Mechanistic studies of **PN³P Mn(I)-3** determined by ^1H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard.

A plausible reaction mechanism initiates with activation of **PN³P Mn(I)-3** (pre-catalyst) with KOH to form the active manganese complex Subsequent transfer hydrogenation converts nitrobenzene and methanol into aniline and formaldehyde, which can undergo a condensation reaction to form *N*-phenylmethanimine. Further, hydrogenation of *N*-phenylmethanimine with the manganese hydride provides access to the *N*-methylated product *N*-methylaniline with regeneration of the catalytically active species (Scheme-2).

IV. CONCLUSION AND OUTLOOK

Methanol's "ideal" characteristics such as cost-effective reagent, environmentally benign and sustainable feedstock for value-added chemicals make it crucial to valorize it in chemical synthesis to obtain the required chemicals. The borrowing hydrogen technique has been used to synthesis a variety of *N*-methylamines, with methanol used as $-CH_3$ source for the synthesis of medicines and biomolecules over the past few years. Due to the widespread applications of the resultant products in pharmaceuticals, and the materials sciences, the synthesis of *N*-methylated molecules using methanol via borrowing hydrogen methodology is remarkable. The use of homogeneous and heterogeneous catalysis based on noble and nonnoble metals is essential to the effectiveness of these *N*-methylation procedures. Although much progress has been made in catalytic *N*-methylamines reactions using MeOH, there are still certain obstacles to overcome. Most catalysts available today have a hard-working environment, have problems with selectivity, and need noble transition metal catalyst. Therefore, the creation of extremely active base metal catalysts that should function in extremely mild circumstances to selectively and highly efficiently synthesized *N*-methylamines is essential yet difficult. It is particularly desirable to generate mono- or di-*N*-methylation selectively under mild conditions with a high degree of functional group tolerance, as this is necessary to meet the needs of the pharmaceutical industry. The

application of MeOH assisted *N*-methylation processes for the selective insertion of -CH_3 moieties in peptides, DNA, and other biomolecules needs to be improved, and that is more crucial. Highlights of this synthesis include producing *N*-methylated products in an atom-efficient and sustainable way by using easily available anilines or nitroarenes and methanol. We think that scientists working in academic research labs and enterprises will find this review fascinating and helpful, given the growing significance of *N*-methylation reactions in organic synthesis, medicinal and biological chemistry.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGMENT

M. S. P. Mandal Aurangabad.

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A Recent Review On Synthesis and Pharmacological Applications of Schiff Bases and Their Transition Metal Complexes

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ABSTRACT

The Schiff base is a versatile compound containing azomethine group and prepared by condensation of primary amine with aldehyde or ketone. Schiff base transition metal complex is a unique class of compound that has a wide range of applications in coordination chemistry, analytical chemistry, catalysis, pharmaceutical chemistry, etc. The medicinal study of Schiff base transition metal complexes shows that they are effective against various strains of microorganisms. Schiff base and their transition metal complexes show pharmaceutical applications due to their biological activity like anticancer, antifungal, antibacterial, anti-inflammatory, antiviral, and antidiabetic activity. This review summarizes the synthesis and pharmacological applications of Schiff bases transition metal complexes.

Keywords: Schiff bases, Metal complexes, Pharmacological applications.

I. INTRODUCTION

The Schiff base is a compound with the general formula ($R_2C{=}NR_1$), where R_1 represents an alkyl/aryl group but not hydrogen, and it contains the azomethine functional group[1]. Hugo Schiff noted that it is normally produced by condensing primary amine with aldehyde or ketone while eliminating one water molecule.

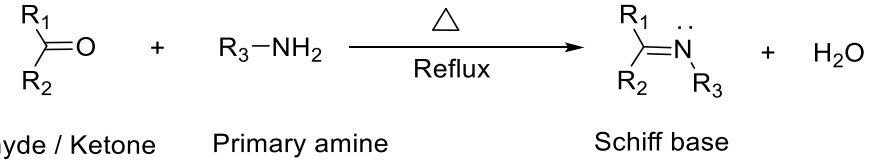

Fig. 1: Synthesis of Schiff base by condensation reaction.

The presence of a single pair of electrons on nitrogen atoms of the azomethine group (-C=N-) illustrates Schiff bases' higher chelating activity, particularly if paired with one or more donor atoms such as -OH, -COOH, C=S, and -SH nearby to the azomethine group[2]. Schiff bases are an important type of ligands in coordination chemistry, and they interact with metal ions through azomethine nitrogen[3]. Schiff base ligands have been

extensively studied in coordination chemistry, owing primarily to their ease of synthesis and electrical characteristics. Schiff-base coordination chemistry has grown more attractive as a result of its potential applications in metallurgy, organic synthesis, metal refining, analytical chemistry, electroplating, and photography[4–6]. Schiff-base transition metal complexes have been used in medicine to treat infections caused by viruses. The (-C=N-) moiety is crucial for biological activity in Schiff base compounds. Schiff base transition metal complexes have medical and pharmaceutical applications comprising antifungal, anticancer, antibacterial, antioxidant, anti-inflammatory, disorders of the nervous system, and diuretic abilities[7–20]. Schiff bases are additionally applied as catalysts, organic synthesis intermediates, dyes, pigments, polymer stabilizers, and corrosion inhibitors[21,22]. This article presents an overview of the synthetic techniques used to synthesize Schiff bases and also addresses antibacterial, antifungal, and anticancer Schiff bases.

I. Biological importance of Schiff base transition metal complexes

Transition metals have varying oxidation states, which allows them to interact with ligands to form complexes, making them valuable for the manufacturing of metal-based medicines with promising pharmacological uses. Schiff base metal complexes have an essential role in medical biochemistry due to their anti-cancer, antibacterial, antifungal, antiviral, anti-inflammatory, and anti-diabetic properties.

II. Pharmacological activity of Schiff base transition metal complexes

Lotfi M. Aroua et al., 2023 synthesized Schiff base ligand by condensation of (1H-benzimidazole-2-yl)methanamine, with 2-hydroxynaphthaldehyde. Furthermore, synthesized metal complexes of Zn(II), Cr(III), and Mn(II). Synthesized metal complexes show promising activity against *E. coli* and *Bacillus subtilis*, as well as modest activity against *Aspergillus niger*. The diffusion method was used in the microbiology area to carry out these tests. *E. coli* and *Bacillus subtilis* were utilized to assess antibacterial activity. The antifungal activity of the DMSO solution was tested using *Aspergillus niger*. As a control, an empty poured disc was used. The extent to which the chemical solutions inhibited the growth of microbes was determined for the 10^{-3} M drugs studied. To compare inhibition, tetracycline, and nystatin were used as positive controls for antibacterial and antifungal activity. Bacterial and fungal growth inhibitions were found in millimeter-sized regions near the holes[23].

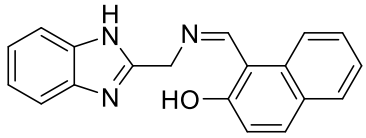

Fig.2: (Z)-1-((((1H-benzo[d]imidazol-2-yl)methyl)imino)methyl)naphthalen-2-ol

Priyanka Devi et al,.2023 synthesized 5-methyl-3-((5-bromosalicylidene) amino)-pyrazole Schiff base by condensation of of methanolic solutions of 3-amino-5-methylpyrazole and 5-bromo- salicylaldehyde for five hours in the presence of 3-4 drops glacial acetic acid. The synthesized Schiff base and its metal complexes have been examined for antibacterial properties with three Gram- positive and two Gram-negative bacteria using the well diffusion method.

The compounds were tested against foodborne pathogens such as *Staphylococcus aureus*, *sub.aureus*, *Clostridium perfringens*, *Listeria monocytogenes*, *E. coli, Pseudomonas aeruginosa* , and fungi *Aspergillus fumig atus, Aspergillus niger, and Candida albicans*. The complexes were discovered to have greater biological impacts on distinct organisms than the newly developed Schiff base[24]

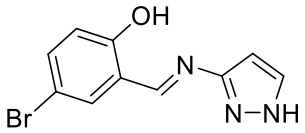

Fig. 3: (E)-2-(((1H-pyrazol-3-yl)imino)methyl)-4-bromophenol

In 2023, K. Jagadesh Babu et al. synthesized a Schiff base ligand by refluxing a methanolic solutions of 5-cyclohexyl-2-methoxyaniline and salicylaldehyde in a 1:1 mole ratio, and thereafter, synthesized its metal complexes. The agar well diffusion method was used to test the antibacterial activity of synthesized compounds and the standard drug Gentamycin sulfate against Gram-positive *Staphylococcus aureus* and *Bacillus subtilis*, and Gram-negative *E. coli* and *Klebsiella pneumonia* bacterial stains. Inhibition zones were measured in mm and compared to standard drug zones. The Agarwell diffusion method was used to evaluate the antifungal activity of produced compounds against *Aspergillus niger* and *Candida albicans*. A one-week-old fungal culture was employed as an inoculum. Nystatin was utilized as the reference antifungal medication. Compounds' antifungal activity was measured based on their inhibition zone. In-vitro investigations reveal that the complexes exceed the parent ligand in terms of antibacterial and antioxidant activity. Complexes exhibited higher cytotoxicity against A549 and MCF7 cell lines compared to their parent ligand [25].

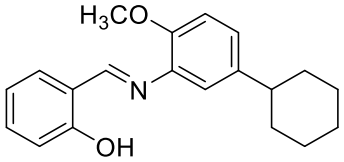

Fig. 4: (E)-2-(((5-cyclohexyl-2-methoxyphenyl)imino)methyl)phenol

In 2023, Bushra Mohan and Naser Shaalan prepared a tetradentate Schiff base by condensation of 2-Hydroxy naphthaldehyde with 2-amine benzhydrazide and subsequently synthesized its novel Mn(II), Co(II), Ni(II), Cu(II), and Zn(II) complexes. Schiff base and its metal complexes were examined and assessed for antibacterial and antifungal activities using the etch-diffusion technique. Two species of pathogenic bacteria, Gram-negative Klebsiella pneumonia, Gram-positive Staphylococcus aureus, and Candida albicans, were chosen to test at 24 hours under aerobic conditions at 37°C. Bacteria and fungi were preserved in nutrients, and the Schiff's base and its metal complex tests were positive. Zinc complex was more effective against gram-positive bacteria, whereas cobalt and copper complexes were most effective against gram-negative bacteria. Copper was particularly effective against Candida albicans [26].

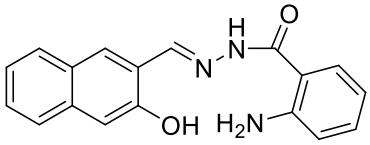

Fig. 5: (E)-2-amino-N'-((3-hydroxynaphthalen-2-yl)methylene)benzohydrazide

Dipti D. Gharat et al., 2023 synthesized the Schiff base ligand by condensation of 2-amino-6-chloro benzothiazoles and 2, 4-dihydroxybenzaldehyde in a 1:1 molar ratio, followed by the formation of bivalent complexes with metals of Fe, Cu, Co, Ni, Pd, and Zn. Using the disc diffusion method, two Gram-positive bacterial strains *B. subtilis* and *S. aureus,* two Gram-negative bacterial strains *E. coli* and *P. aeruginosa*, and two fungal strains *C. albicans* and *A. cerevisiae* were used to test all of the synthesized compounds for antibacterial and antifungal activity in vitro. The in vitro cytotoxicity effects of the ligand and its metal complexes against Artemia salina were also examined using the brine shrimp bioassay. The results confirmed that the ligand's biological functioning expanded during complexation [27].

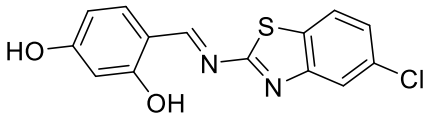

Fig. 6: (E)-4-(((5-chlorobenzo[d]thiazol-2-yl)imino)methyl)benzene-1,3-diol

In 2023, Onder Idil et al. synthesized Schiff bases of 5-bromo-3-nitro salicylaldehyde utilizing varying sulfonamide group compounds and their Cu(II) complexes. The antimicrobial activity of ligands and developed complexes has been studied in vitro against Gram-negative and Gram-positive bacteria, as well as yeast Candida albicans. The microdilution method has been applied to investigate the influence of antimicrobial compounds on bacterial colony formation and time-killing kinetics. Copper complexes exhibit stronger antibacterial activity than their equivalent ligands. It had stronger effects on *Staphylococcus aureus* and *Pseudomonas aeruginosa* compared to *E. coli, L. monocytogenes,* and *C. albicans*[28].

Nuha Ayad Abd AL Qadir et al., 2023 synthesized the Schiff ligand by refluxing (Z)-3-hydrazineylideneindolin-2-one and hexane-2,5-dione in the presence of glacial acetic acid for four hours. It subsequently generated metal complexes of Ni(II), Mn(II), Zn(II), and Cu(II). The synthesized Schiff base and its complexes have been studied on positive bacteria *Staphylococcus aureus* and negative bacteria *Escherichia coli*, with 0.001M DMSO as a control. The results demonstrate that the Schiff base ligand and the Nickel complex have a negative inhibitory effect on *Staphylococcus aureus* bacteria [29].

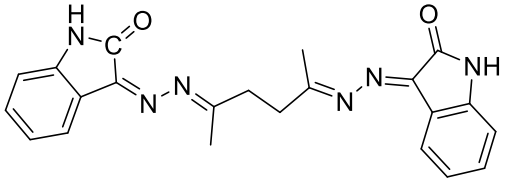

Fig. 7: (3Z,3'E)-3,3'-(((2E,5E)-hexane-2,5-diylidene)bis(hydrazine-2,1-diylidene))bis(indolin-2-one)

In 2023, Khalidah Hamil Manati Al Furaiji et al. synthesized Schiff base (4-((3-mercapto-5-(naphthalene-1-ylmethyl)-4H-1,2,4-triazole-4-yl)imino)methyl)methoxy) by stirring a methanolic solution of (4-amino-5(naphthalene-1-ylmethyl)-4H-1,2,4-triazole-3-thiol(thione)) with a methanolic solution of 4-methoxy benzaldehyde in the presence of 2-3 drops of glacial acetic acid for 24 hours. Then synthesized its metal complex of Cr(III), Mn(II), and VO(IV). In vitro study of *P. aeruginosa* and *B. subtilis* strains revealed that Schiff base has antibacterial action against both Gram-positive and Gram-negative pathogens. Metal complexes outperform the Schiff base against both types of bacteria [30].

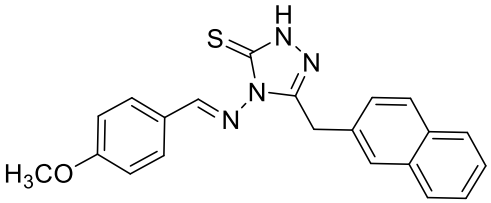

Fig. 8: (E)-4-((4-methoxybenzylidene)amino)-5-(naphthalen-2-ylmethyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione

Riaz Hussain et al. (2023) synthesized two hydrazone ligands: 4-chloro-2-((4-isopropylphenyl)-hydrazono)methylphenol and 4-(2-(5-chloro-2 hydroxybenzylidene) hydrazinyl)benzonitrile, as well as their Cu(II), Ni(II), and Co(II) complexes. utilizing a disk diffusion approach, synthesized Schiff base ligands and metal complexes were tested on Gram-positive strains *Bacillus halodurans* and *Micrococcus luteus*, Gram-negative strains *E. coli* and *Salmonella*, and fungal strains *Aspergillus flavus* and *Aspergillus niger*. The results proved that the ligands were more efficient than the metal complexes against pathogenic bacteria.The Schiff

base ligand 4-chloro-2-((4-isopropylphenyl)-hydrazono)methylphenol has a maximum inhibition against *E. coli* and *B. halodurans* bacterial strains, with lower activity. The second Schiff base 4-(2-(5-chloro-2 hydroxybenzylidene) hydrazinyl)benzonitrile has a 15 mm zone of inhibition against *the E. coli* bacterium strain. Ni(II) Complex of the second ligand has the strongest activity against *E. coli*, *B. halodurans*, and *M. luteus*, with inhibition zones measuring 13, 18, and 14 mm, respectively [31].

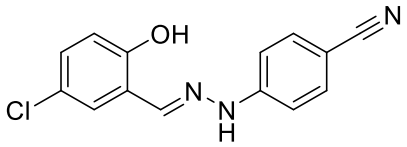

Fig. 9((E)-4-(2-(5-chloro-2-hydroxybenzylidene)hydrazinyl)benzonitrile

Haruna A. et al., 2023 synthesized the Schiff base ligand 4[(4,6-Dimethylamino-2-hydroxybenzylidene)amino]-N-thiazole-2-ylbenzenesulphonamide was produced by refluxing an ethanolic solution of sulphathiazole and 4-diethylaminosalycyaldehyde for 4 hours, followed by the synthesis of its Mn(II) complex. The antibacterial activity of the ligand and its complexes has been investigated against two Gram-positive bacteria *Bacillus subtilis* and *Staphylococcus aureus*, as well as two Gram-negative bacteria *E. coli* and *Klebsiella pneumoniae*, using the paper disk diffusion technique. The antifungal susceptibility of Schiff base ligand and its Mn(II)complex was determined using the disk diffusion method with the fungi pathogens *Aspergillus niger* and *Candida albicans*. The antimicrobial assessment results demonstrated that metal (II) complexes had more antibacterial effects than the free Schiff base ligand [32].

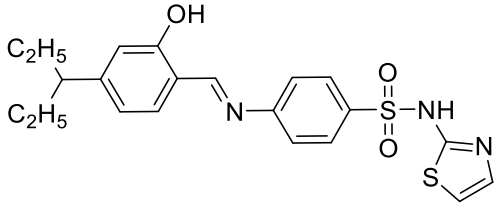

Fig. 10: (E)-4-((2-hydroxy-4-(pentan-3-yl)benzylidene)amino)-N-(thiazol-2-yl)benzenesulfonamide

Laila H. Abdel Rahman et al. (2023) synthesized two Schiff bases. 4-bromo-2-[(E)-{[4-(2-hydroxyethyl)phenyl]imino{methyl]phenol and 2-[(E)-{[4-(2-hydroxyethyl)phenyl]imino}methyl]-4-methoxyphenol by refluxing 1 mmol ethanolic solution of 2-(4-aminophenyl)ethan-1-ol with an ethanolic solution of 1mmol 5-methoxy salicylaldehyde and 1 mmol of 5-bromo salicylaldehyde, respectively. Then their metal complexes with Cr(III), Mn(II) and Fe(III). The newly synthesized compounds were tested against various bacterial species, including *Staphylococci aureus*, *Escherichia coli* , *Bacillus subtilis , Pseudomonas vulgaris, A. Albicans, and A. fumigatus*. The cytotoxicity for both ligands and their Mn(II), Fe(III), and Cr(III) complexes was tested on the Hep-G2 liver carcinoma and MCF7 breast cancer cell lines. All compounds did better activity relative to free ligands. The Mn(II) complex demonstrated the highest activity [33].

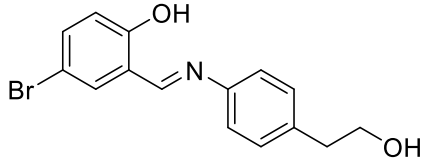

Fig. 11: (E)-4-bromo-2-(((4-(2-hydroxyethyl)phenyl)imino)methyl)pheno

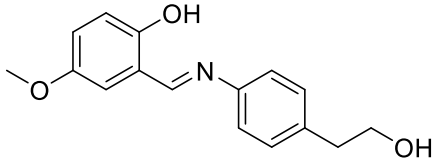

Fig. 12: (E)-2-(((4-(2-hydroxyethyl)phenyl)imino)methyl)-4-methoxyphenol

Isyaky A. et al. (2023) synthesized a Schiff base by condensing an ethanolic solution of isatin and thiosemicarbazide in a 1:1 molar ratio in the presence of acetic acid for two hours. Then synthesized its Ni(II) and Co(II) complexes. The ligand and its Co(II) and Ni(II) complexes was examined in vitro against *E. coli, Salmonella Typhimurium, and Staphylococcus aureus*. The Schiff base and its metal complexes were additionally examined against the *Mucor, Aspergillus flavus,* and *Aspergillus niger* fungal organisms species. The complexes outperformed the ligand against bacteria species, except *E. coli*, where the ligand outperformed the Co(II) complex at 300 and 400 µg/disc, respectively. At all doses, Co(II) and Ni(II) complexes outperformed the Schiff base against *Mucus* and *Aspergillus flavus* fungal isolates. However, against *Aspergillus niger,* the Schiff base outperformed the metal complexes. The Schiff base and Co(II) combination have no efficacy against *Aspergillus flavus* [34].

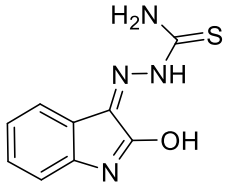

Fig. 13. (Z)-2-(2-hydroxy-3H-indol-3-ylidene)hydrazine-1-carbothioamide

In 2023, Doaa A. Nassar et al. synthesized Schiff base ligands by stirring Pyridine-2,6-diamine with 5-methyl-2-carboxaldehyde-thiophene for 6-7 hours, followed by metal complexes. The biological effects of Schiff base and its metal complexes were studied on two fungi and four bacteria. The Schiff base ligand has little effectiveness against *E. coli, A. flavus, and C. albicans*, but moderate activity against *S. aureus, B. subtilis,* and *P. vulgaris*. The Co, Ni, and Cu complexes exhibited higher activity than the ligand. The agar dilution method was used to determine the minimum inhibitory concentration (MIC) of the highly active Cd(II) complex against *S. aureus, B. subtilis,* and *E. coli* [35].

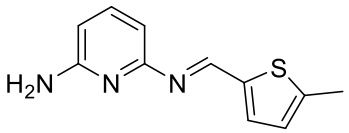

Fig. 14 (E)-6-(((5-methylthiophen-2-yl)methylene)amino)pyridin-2-amine

In 2023 Jyoti C. Ajbani et. Al., Synthesized Schiff base ligand Gabapentin - 2-hydroxy naphthaldehyde by Microwave method. Microwave irradiation of a methanolic solution containing 0.03M Gabapentin and 0.03M 2-hydroxy naphthaldehyde at 110 watts for one minute with a 30-second pulse and the reaction progress monitored by TLC. The antibacterial activity of Schiff bases and complexes was investigated in vitro against *E. coli* and *Salmonella enteric*. The well diffusion method was applied to isolate *Klebsiella pneumoniae*, *Staphylococcus aureus, Streptococcus agalactiae, Aspergillus niger,* and *Aspergillus flavus*. The culture media were Muller Hinton agar and Potato dextrose agar. Some metal complexes had considerable antibacterial and antifungal action [36].

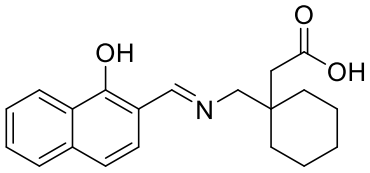

Fig. 15: Gabapentin-2-hydroxynaphthaldehyde

Binesh Kumar et. Al., 2023 synthesized the hydrazone ligands by refluxing a methanolic solution of 3,5-bis(trifluoromethyl)benzohydrazide for 5-6 hours with 2-methoxy-1-napthaldehyde or 3-bromo-5-ethoxy-4-

hydroxybenzaldehyde in the presence of 2 drops of glacial acetic acid. The metal complexes were then produced using Co(II), Ni(II), Cu(II), and Zn(II) acetate salt. In vitro, the synthesized compounds were tested for anti-TB activity against Mycobacterium tuberculosis H37Rv strain utilizing a microplate alamar blue procedure in triplicate, using streptomycin as the standard. Cu(II) and Zn(II) metal complexes have the most potential to prevent tuberculosis deformity. In comparison to streptomycin, the Zn(II) combination has roughly four times the potency to suppress tuberculosis. The Zn(II)complex had higher antibacterial and anti-inflammatory activity, with lower MIC and IC50 values [37].

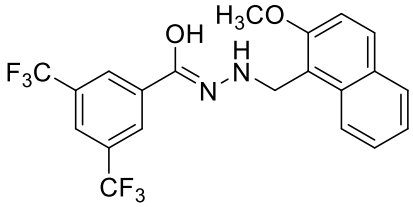

Fig. 16: (Z)-N-((2-methoxynaphthalen-1-yl)methyl)-3,5-bis(trifluoromethyl)benzohydrazonic acid

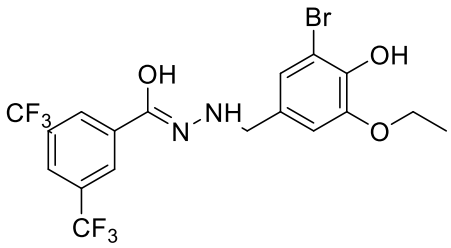

Fig. 17: (Z)-N-(3-bromo-5-ethoxy-4-hydroxybenzyl)-3,5-bis(trifluoromethyl)benzohydrazonic acid

In 2023 Emam M. Komyha et. Al., Schiff base ligand was synthesized by condensing an ethanolic solution of benzohydrazide and (E)-1-(2-(p-tolyl)hydrazono)propan-2-one in a 1:1 molar ratio for 4 hours. The metal complexes were then synthesized of Cr(III), Mn(II), Co(II), Ni(II), and Cu(II). The disc diffusion technique was utilized to evaluate the antibacterial and antifungal characteristics of gentamycin, ampicillin, and amphotericin B, which were used as positive controls for Gram-positive, Gram-negative, and fungi, respectively. Bacteria employed included Gram-positive *Bacillus subtilis, Bacillus cereus, and Staphylococcus aureus*, Gram-negative *E. coli, Pseudomonas aeruginosa*, and *Neisseria gonorrhoeae*, and fungal *Candida albicans and Aspergillus flavus*. The complexes demonstrated better efficacy against the tested strains than the synthetic Schiff base ligand. The Skehan and Storeng approach was used to assess the cytotoxicity of synthetic substances. The Mn(II) compound showed promising effectiveness against HepG2 cells, with a low IC50 of 1.537 μg/ml [38] .

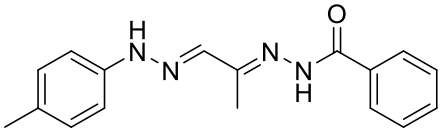

Fig. 18: N'-((1E,2E)-1-(2-(p-tolyl)hydrazono)propan-2-ylidene)benzohydrazide

Abhay Bagul et al. (2023) synthesized the Schiff base ligand 4-[2-(2-chlorobenzylidene)Hydrazinyl]-7H-pyrrolo[2,3-d]pyrimidine refluxing a hot solution of 2-chlorobenzaldehyde with a solution of pyrolopyrimidinehydrazide for 7 hours and then synthesized its metal complexes Cr(III), Fe(II), Co(II), Ni(II), and Cu(II). The synthesized Schiff base ligand 4-[2-(2-chlorobenzylidene)hydrazinyl]-7H-pyrrolo[2,3-d]Pyrimidine and its metal complexes have been studied for antibacterial properties against Gram-positive bacteria *Staphylococcus aureus* and *Bacillus subtilis*, Gram-negative bacteria *E. coli* and *Pseudomonas aeruginosa,* and fungi *Aspergillus niger, Aspergillus flavous, and Fusarium* species, as well as cytotoxic studies

against Artemia salina. Metal complexes were found to be more potent against bacteria and fungus in antibacterial and cytotoxic tests compared to the Schiff base ligand [39].

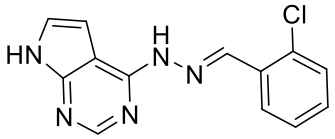

Fig. 19: (E)-4-(2-(2-chlorobenzylidene)hydrazinyl)-7H-pyrrolo[2,3-d]pyrimidine

Hawraa M Alabidia et al., 2023 synthesized Schif base ((E)-4-((4-hydroxy-3-methoxybenzylidene) amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one) by refluxing a solution of vanillin (4-hydroxy-3-methoxy benzaldehyde) and 1 ml glacial acetic acid with an ethanolic solution of 4-Amino antipyrine for 5 hours. Then Azo-Schiff derivative (4-((E)-3-((E)-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-4-hydroxy-5-methoxybenzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one) was synthesized utilizing an azo compound 1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazole-4-diazonium chloride . Azo-Schiff at a concentration of 200 mg/ml, exhibits significant antibacterial effects against Staphylococcus aureus (S. aureus) and Pseudomonas aeruginosa (P. aeruginosa), with inhibition zones of 16.11 ± 0.1035 mm and 13.21 ± 0.4044, respectively. Thereafter, new Schiff base complex with Cu(II) and Ni(II) metal was prepared [40].

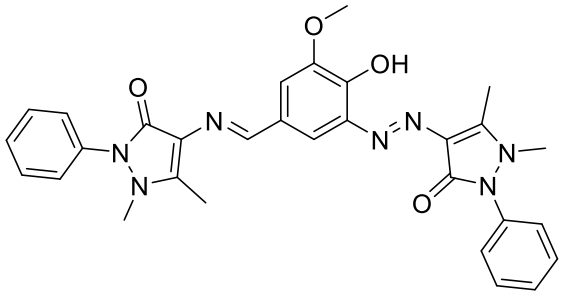

Fig. 20: 4-(((E)-3-((E)-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-4-hydroxy-5-methoxybenzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one

Ilonwa Ifeanyichukwu et al. (2023), synthesized Schiff base 4-[(3-hydroxybenzalidene)amino]antipyrine by condensing an ethanolic solution of 4-aminoantipyrine and 4-hydroxybenzaldehyde in a 1:1 molar ratio for two hours. Cu(II) metal complex was then synthesized. The disc diffusion method was applied to evaluate the antibacterial effects of both the ligand and the complex. Additionally, the minimum inhibitory concentrations (MIC) were determined using the broth dilution method. The MIC data showed that the copper complex had greater antibacterial action than the Schiff base against the examined microorganisms [41].

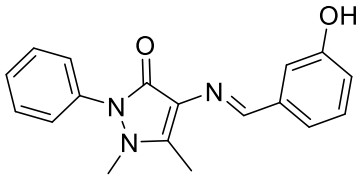

Fig. 21: (E)-4-((3-hydroxybenzylidene)amino)-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one

In 2023, Nagesh Gunavanthrao Yernale et al. synthesized a novel Schiff base ligand, 3-chloro-N'-(4-(diethylamino)-2-hydroxybenzylidene)-benzo[b]thiophene-2-carbohydrazide is by the condensation of 3-chlorobenzo[b]thiophene-2-carbohydrazide and 4-(diethylamino) salicylaldehyde. After that, Cu(II), Co(II), Ni(II), and Zn(II) complexes were produced. The antimicrobial activity investigation demonstrated that complex formation increased the activity of the free ligand, and the Cu(II) complex may be considered a prospective antibacterial agent, while the Ni(II) and Zn(II) complexes are promising antifungal agents. Cu(II)

and Zn(II) metal complexes have displayed promising anti-tuberculosis behavior against M. tuberculosis. Furthermore, the benzo[b]thiophene-based ligand and its metal complexes were examined for in vitro antioxidant activity [42].

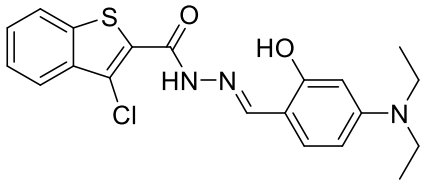

Fig. 22: (E)-3-chloro-N'-(4-(diethylamino)-2-hydroxybenzylidene)benzo[b]thiophene-2-carbohydrazide

In 2023, Noor S. Hassan and Waleed K. Mahdi synthesized a novel Schiff base ligand, N-(4-Bromo-2-methylphenyl)-1-(furan-2-yl) methenamine, by condensation of ethanolic solution of furfural and 4-Bromo-2-methylaniline in a 1:1 molar ratio in the presence of 2-3 drops of glacial acetic acid for five hours. They additionally synthesized metal complexes with VO(II), Cr(III), Mn(II), Co(II), Ni(II), Cu(II), Zn(II), and Cd(II). The antibacterial effects of the synthesized Schiff base ligand and its complexes were investigated against Gram-positive bacteria Staphylococcus aureus, Gram-negative bacteria E. coli, and fungal strains Candida albicans were shown to be the most effective biologically active. The Cd(II) and Co(II) complexes are more efficient against the bacteria Staphylococcus aureus, but the Cd(II) and Ni(II) complexes inhibit the bacteria E. coli with greater efficacy. Cu(II) and Cd(II) complexes were more effective at inhibiting fungi [43].

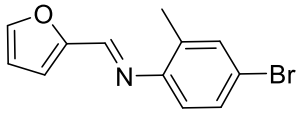

Fig. 23: (E)-N-(4-bromo-2-methylphenyl)-1-(furan-2-yl)methanimine

In 2023, Rehab Ghalib Hammoda and Naser Shaalan synthesized a novel Schiff base ligand by refluxing a 1:2 molar mixture of pyridine carboxaldehyde and Malonic acid dihydrazide in the presence of two drops of anhydrous acetic acid for four hours in an inert atmosphere. Furthermore, new complexes have been established of nickel (II), copper (II), and zinc (II). The ligand's antibacterial activity in vitro was investigated using both Gram-negative *Staph* and *E. coli* and Gram-positive *Bacillus* and *Pseudomonas* bacteria. The synthesized Schiff base ligand experienced the highest activity among its complexes against all tested bacterial species, with the Cu(II) complex showing the most activity against *Bacillus* and the Zn(II) complex showing the highest activity against *Staph* germs. Antifungal activity against several fungus strains was also assessed for the synthesized Schiff base ligand and its complexes. The synthesized Schiff base ligand has the highest action against *Candida* than its complexes [44].

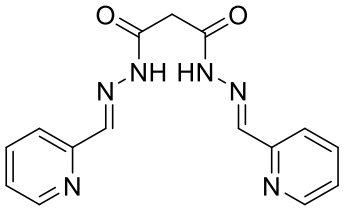

Fig. 24: N'1,N'3-bis((E)-pyridin-2-ylmethylene)malonohydrazide

I. Wazirie et. al., 2023 produced the Zn(II) complex of (Z)-4-((4-nitrophenyl)amino)pent-3-en-2-one. The Schiff base ligand (Z)-4-((4-nitrophenyl)amino)pent-3-en-2-one was produced by stirring a hot methanolic solution of 4-nitroaniline and hot acetylacetone in a 1:1 molar ratio, with five drops of formic acid, at room temperature for 6 hours. The Schiff base ligand itself and its complex were examined for antimicrobial efficacy against *Staphylococcus aureus, Streptococcus pyrogens, E. coli,* and *Klebsiella pneumoniae*, among others

by using a modified disc agar diffusion technique. The broth microdilution method was used to determine the MIC of each drug. The antimicrobial investigation revealed that the Zn(II) complex has stronger antibacterial activity than the Schiff base ligand and the control Streptomycin [45].

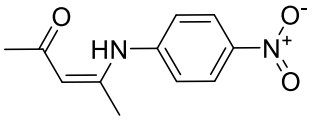

Fig. 25: (Z)-4-((4-nitrophenyl)amino)pent-3-en-2-one

In 2023, Elham S. Aazam and Maryam A. Majrashi synthesized a novel Schiff base ((E)-2-ethoxy-6((pyren-1-ylimino)methyl)phenol) and its metal complexes (Zn(II), Cu(II), Co(II), Cr(III), and Fe(III). The cytotoxic effects of the Schiff base ligand and its synthesized metal complexes were investigated on human breast cancer (MCF-7) cells. Cu(II) and Zn(II) complexes were found to be more effective than fluorouracil cancer drug against the tested cell line, particularly MCF-7 cells[46].

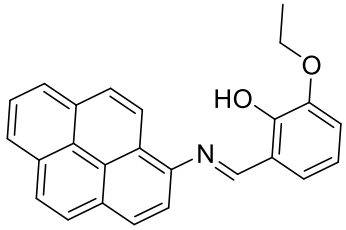

Fig. 26: (E)-2-ethoxy-6-((pyren-1-ylimino)methyl)phenol

In 2024, Kavita Poonia et. Al., synthesized a Schiff base ligand (Z)-2-(2-methyl-1-phenylpropylidene)hydrazine-1-carbothioamide by adding a hot absolute methanolic solution of isobutyrophenone to a hot methanolic solution of thiosemicarbazide in an equimolar ratio (1:1:1) along with three drops of HCl with constant stirring on a magnetic stirrer and then in micro oven for 7 minutes. The Co(II) and Mn(II) complexes were then prepared. The Schiff ligand and its metal derivatives have been tested for antibacterial, antitubercular, and anticancer properties.The antibacterial activity of the named compounds against E. coli (3 ATCC25922) and S. aureus (ATCC25923) was assessed using Muller Hinton Agar medium and the Disc diffusion procedure.The antifungal activity of the named compounds was evaluated using Sabouraud dextrose agar medium and the disc diffusion method, which is analogous to antibacterial action testing. The fungus strains employed in this investigation were Aspergillus fumigatus and Candida albicans. The fast culture - MGITTM DST method was used to perform automated antibacterial susceptibility testing of several drugs against M. tuberculosis bacteria. The metal complexes were found to be more effective antibacterial agents than the ligands, notably Mn(II) complexes against Staphylococcus aureus[47].

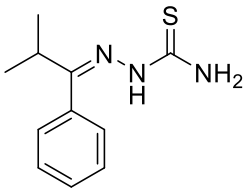

Fig. 27: (Z)-2-(2-methyl-1-phenylpropylidene)hydrazine-1-carbothioamide

In 2024, S. Sindhu et. Al., synthesized the Schiff base Ni(II) complex by condensing bis(2-hydroxy-3-methoxybenzaldehyde) nickel (II) and n-propylamine in methanol. The synthesized Ni(II) complex has been investigated for antibacterial activity by the Agar well diffusion method. Three DMSO doses (100 µg/ml, 200 µg/ml, and 300 µg/ml) were tested for their effect on the growth of Staphylococcus aureus and Escher using the well diffusion method. The results reveal significant antibacterial action against Escherichia coli and

Staphylococcus aureus when the concentration approaches 200 μg/mL. The antifungal study demonstrates substantial suppression using imidazole as a positive control (PC). Small values of MIC and MBC/MIC show that less complex is required to inhibit the growth of microorganisms[48].

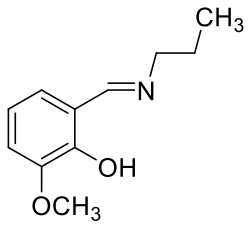

Fig. 28: Schiff base (E)-2-methoxy-6-((propylimino)methyl)phenol

II. CONCLUSION

This review article discusses current advances in Schiff bases and transition metal complexes, including synthesis, structure, and biological applications. Schiff base ligands and metal complexes play a vital role in medical domains. In the medical field, they are commonly employed as antibacterial, antifungal, and antiviral medications. Schiff bases and their complexes are extremely powerful chemotherapeutic medicines for treating a variety of malignancies. These Schiff base transiton complex actions are extremely diverse. There is a pressing need for more effective antibacterial and antifungal medicines due to high death rates from bacterial and fungal infections, as well as an increase in multidrug-resistant strains.

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Physicochemical Assessment of Groundwater Around Osmanabad Industrial Area, Maharashtra, India

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ABSTRACT
Groundwater quality around Osmanabad industrial zone was studied for a period of six months during June 2022 to January 2023. During the study groundwater samples were collected from 10 sampling sites and various physico-chemical parameters like temperature, pH, conductivity, salinity, total hardness, TDS and chloride were analyzed and the results were compared with WHO and BIS standards.
Keywords: Groundwater, Industry, Physicochemical, Tubewell, water quality.

I. INTRODUCTION

Water scarcity is going to be a big problem for the world in the future as water scarcity is increasing globally[1]. With increasing population, there is increasing pressure on the existing water bodies due to increasing demand from various sectors like domestic, agricultural and industrial, hydropower etc. Available surface water resources are insufficient to meet increasing human demand; therefore, dependence on groundwater sources is increasing in various parts of the world. India is the largest user of groundwater. In India, 56% of metropolitan cities are partially or fully dependent on groundwater.2 Moreover, the overall dependence on groundwater for urban water supply in India is very high. Groundwater quality has been seriously polluted due to discharges from industrial areas, sewage infiltration, seepage, waste disposal, mining activities and sometimes agricultural nutrient overload. Once groundwater is contaminated, it is very difficult to restore it to original water quality, so it is better to protect it first rather than relying on new technologies to clean up the source of contamination.3

Osmanabad district is an administrative district in the Marathwada division of the state of Maharashtra. The district lies between 17°37' and 18°42' north latitude and 75°16' and 76°47' east longitude. The total area of the district is 7569 sq. km and is about 600 meters above sea level. It is bounded by Solapur district on the south-west, Ahmednagar district on the north-west, Beed district on the north and Latur district on the east.

Due to increasing urbanization and industrialization, Osmanabad city and surrounding area is growing rapidly, along with the industrial area, the area of slums is also increasing. Many problems such as lack of sanitation facilities, poor drainage system, and inadequate waste management facilities are seen in this area. People are using large quantities of groundwater for various purposes, but this groundwater has been found to be

contaminated by industrial effluents and sewage. Thus, it is important to assess the groundwater quality of such areas. Herein, an attempt has been made to know the quality of groundwater around Osmanabad Industrial Area.

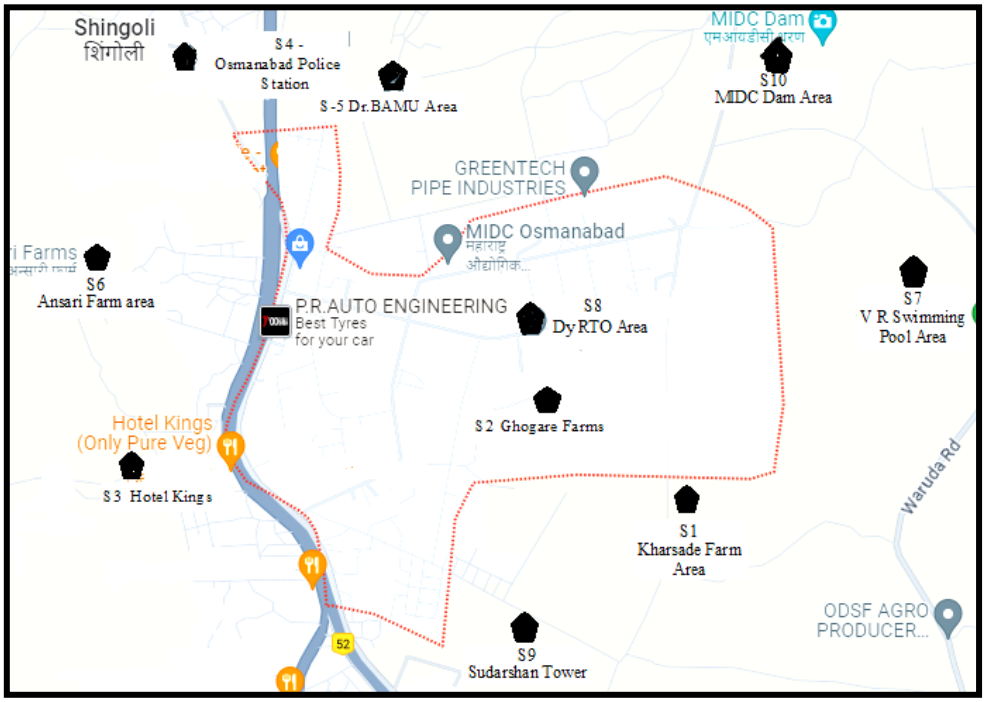

Fig. 1 Sampling sites in MIDC Osmanabad area.

II. METHODS AND MATERIAL

Osmanabad Industrial Area is east of Osmanabad-Aurangabad Highway and due to unhygienic conditions, lack of planning and increasing population there is a need to monitor groundwater in this area from time to time. Therefore, the area around the industrial area was selected for the study and water samples were collected from selected locations (Table. 1) during June 2022 to January 2023.

Table. 1 Sampling Sites

Sampling Site	Station No.
Kharsade Farm area Tubewell	S-1
Ghogare Farm Tubewell	S-2
Hotel Kings	S-3
Osmanabad Gramin Police Station	S-4
Dr. BAMU Area Tubewell	S-5
Ansari Farm Area	S-6
VR Swimming Pool	S-7
Dy RTO area	S-8
Sudarshan Tower	S-9
MIDC Dam	S-10

Groundwater samples were collected in clean polythene bottles of 2 liter capacity. The bottles were washed with groundwater before sampling and then the samples were collected, tightly closed and labelled. The collected samples were analyzed for temperature, pH, conductivity, alkalinity, total hardness, chloride and TDS parameters by using methods of physicochemical analysis.4 Temperature and pH of water samples was determined on site using a thermometer and portable pH meter, respectively. Conductivity measured by conductivity meter, total alkalinity was determined by visual titration method using methyl orange and phenolphthalein as indicators. Total hardness was measured by EDTA titration method using EBT indicator. Chloride content was measured by argentometric method using potassium chromate, while TDS was determined by standard method. The groundwater quality has been assessed by comparing each parameter with standard desirable limits set by BIS and WHO.

III.RESULTS AND DISCUSSION

After analysis obtained results are shown in table no. 3 and 4, and further it was compared with the BIS and WHO standards from table no. 2.

Table 4 Drinking water standards

Sr. No.	Parameters	BIS (IS 10500-91)		WHO
		Desirable Limit	Max. Permissible Limit	
1	pH	6.5 - 8.5	No relaxation	6.5–8.5
2	Conductivity (µS/cm)	-	300	-
3	Total dissolved solids (mg/l)	500	2000	1000
4	Total hardness as $CaCO_3$ (mg/l)	200	600	500
5	Alkalinity (mg/l)	200	600	200
6	Chloride (mg/l)	250	1000	250

Table 3 - Mean value of parameter for Monsoon Season (June 2022 - September 2022)

Station No.	Temp. °C	pH	Conductance (µS/cm)	Alkalinity mg/l	Total Hardness (mg/l)	Chloride (mg/l)	TDS (mg/l)
S-1	25.05	7.12	376.2	212	213.5	120.01	172.6
S-2	24.68	7.81	366.7	159.5	167.5	111.13	155.9
S-3	24.80	7.67	773.4	161.5	172.5	131.01	356.9
S-4	25.05	7.96	432.4	168	217	121.78	165.4
S-5	24.45	7.70	336.2	167	166	113.62	165.6
S-6	25.18	7.50	286.7	195	163	124.27	158.2
S-7	25.02	7.10	371.2	207.5	219.5	117.81	179.2
S-8	24.80	7.61	381.9	166.5	172.0	123.21	169.2
S-9	24.5	7.71	339.8	162.5	207	113.8	161.8
S-10	25.20	7.50	407.3	199.5	227	122.9	186.2

Table 4 - Mean value of parameter for winter Season (October 2022 - January2023)

Station No.	Temp. °C	pH	Conductance (µS/cm)	Alkalinity mg/l	Total Hardness (mg/l)	Chloride (mg/l)	TDS (mg/l)
S-1	23.8	7.59	399.4	225	221	109.36	166.1
S-2	23.6	7.96	359.9	169.5	173.5	105.45	153.1
S-3	23.98	7.91	805.7	173.5	177.5	120.36	355.4
S-4	23.88	7.97	416.2	183	230.5	109.36	161.9
S-5	23.7	7.99	381.9	180.5	173	101.9	170.6
S-6	23.88	7.54	299.7	205	203.5	109.36	148.1
S-7	23.52	7.48	403.2	226.0	242.0	108.32	174.7
S-8	23.30	7.63	416.1	184.5	201.5	112.23	163.2
S-9	23.6	7.83	371.7	179.0	224.5	106.58	156.5
S-10	23.70	7.77	422.5	206.5	244.0	116.16	173.8

Table 4 Drinking water standards

Sr. No.	Parameters	BIS (IS 10500-91)		WHO
		Desirable Limit	Max. Permissible Limit	
1	pH	6.5 - 8.5	No relaxation	6.5–8.5
2	Conductivity (µS/cm)	-	300	-
3	Total dissolved solids (mg/l)	500	2000	1000
4	Total hardness as $CaCO_3$ (mg/l	200	600	500
5	Alkalinity (mg/l)	200	600	200
6	Chloride (mg/l)	250	1000	250

Temperature

During the study period, the temperature of groundwater samples ranged from 23.3 ºC to 25.20 ºC, monsoon temperature ranged from 23.30 ºC to 25.20 ºC (Table. 3) and winter temperature ranged from 23.30 ºC to 23.98 ºC (Table. 4). Due to changes in the atmosphere, the temperature value naturally decreases during the winter season as compared to the rainy season.

pH

pH ranged from 7.12 to 7.99 over the two-season study period. The pH ranges between 7.12 to 7.96 in monsoon and 7.48 to 7.99 in winter. Groundwater samples from station number S1 showed the lowest pH during rainy season and station number S5 showed the highest pH during winter. All the samples were found to be within the desirable limits given by BIS and WHO (Table. 2). Exposure to air, temperature changes, and biological activity can cause pH to change greatly over time. In natural waters, pH varies daily and seasonally due to changes in photosynthetic activity, increasing pH as CO2 is consumed in the process.5

Conductance

The conductivity ranges from 306.7 to 773.4 μS/cm in the rainy season and from 299.7 to 805.7 μS/cm in the winter season. Station number S3 showed the highest conductivity in both seasons. Except station number S6, all the samples were found above BIS permissible limits (Table. 2). The salts present in it increase electrical conductivity, the more electrolyte there is in water, the higher will be its electrical conductivity. Conductivity is proportional to the amount of dissolved solids. Both showed similar trends in seasonal variation.6

Total Alkalinity

Total alkalinity ranges from 159.5 to 212 mg/litre during monsoon and 169.5 to 226 mg/litre during winter. A slight increase in alkalinity was observed during the winter season. Highest alkalinity was observed at station numbers S1 and S7 during monsoon and winter respectively. All the samples were found to be within the permissible limits given by BIS and WHO for total salinity. Natural water is mostly found in alkaline form due to sufficient amount of carbonate, hydroxide and bicarbonate. Alkalinity itself is not harmful to human beings.7

Total Hardness

Total hardness ranges from 163 to 227 mg/litre in monsoon and 173 to 244 mg/litre in winter. Ground water of station number S1, S4, S7 and S10 found hardness above 200 mg/liter almost at all places during monsoon and winter. But all the samples were within the permissible limits given by BIS and WHO for total hardness. Hardness is caused by various dissolved polyvalent metallic ions, mainly calcium magnesium and barium cations, other cations such as iron, manganese, strontium and zinc also contribute too. High concentrations of total hardness in water samples may be due to dissolution, leaching, and leaching of polyvalent metal ions from sedimentary rocks.6

Chloride

The chloride concentration in the study area ranged from 111.13 to 131.01 mg/litre during monsoon and 101.9 to 116.6 mg/litre during winter season. In both the seasons, maximum chloride was found at station number S3. All types of natural water contain chloride but high concentrations are considered a sign of pollution. All samples during the study period were found to be within the desirable limits given by BIS and WHO for chloride.8

Total Dissolved Solids (TDS)

In monsoon season, Total Dissolved Solids (TDS) was found to be between 155.9 to 356.9 mg/liter and in winter season it was found to be between 148.1 to 355.4 mg/liter. TDS at station number S3 was found to be highest in both the seasons. High total dissolved solids in groundwater can be seen due to groundwater pollution. When waste water from residential and dying units is released into ponds, lagoons, pits; such water reaches the ground water level and pollutes the ground water. TDS during both the seasons was found to be between the desirable limits given by BIS and WHO.9

IV.CONCLUSION

All groundwater samples collected around Osmanabad industrial area were found within permissible limits for different parameters by BIS and WHO except conductivity parameters. In case of sample of S3, S4 and S10 i.e. Hotel Kings, Osmanabad Gramin Police Station and MIDC Dam show highest conductivity in both seasons, indicates the high concentration of dissolved solids, due to industrial effluents. Physicochemical analysis of ground water samples of Osmanabad industrial area shows that ground water of all locations is suitable for drinking but some preliminary treatment is required to reduce conductivity and total hardness.

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Microwave Mediated Synthesis of Pyrrole Derivatives Promoted by ([EMIm][BH3CN]) Ionic Liquid

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ABSTRACT

The solvent-free synthesis of substituted pyrroles with high yields has been elucidated, employing 1-ethyl-3-methylimidazolium cyanoborohydride ([EMIm][BH3CN]) as an environmentally friendly catalyst. This green catalyst demonstrates notable efficacy in facilitating a multicomponent protocol, encompassing the reaction of aldehydes, amines, 1,3-dicarbonyl compounds, and nitromethane. The utilization of [EMIm][BH3CN] as a biodegradable, environmentally benign, and readily available catalyst, coupled with its exceptional activity in a four-component reaction (4CR), establishes this method as an efficient and sustainable alternative pathway for synthesizing substituted pyrroles. The synthesized compounds were subjected to rigorous spectral characterization through techniques such as IR, 1H NMR, 13C NMR, and mass spectrometry, thereby confirming their structural integrity and composition. This innovative approach not only offers a green and efficient synthetic route but also contributes to the advancement of sustainable practices in chemical synthesis.

Keywords: 1-ethyl-3-methylimidazolium cyanoborohydride ([EMIm][BH3CN]), Green synthesis, Pyrrole, Microwave.

I. INTRODUCTION

The pyrrole and its derivatives represent a crucial group of heterocyclic aromatic compounds, serving as fundamental building blocks in various synthetic pharmaceuticals and natural substances.[1] They exhibit significant biological properties, including antitumor,[2] antibacterial,[3] antioxidant,[4], and antifungal activities.[5] Pyrroles form the core structure of intricate macrocycles such as heme porphyrins, bacteriochlorins, chlorophyll, and porphyrinogens.[6] Additionally, pyrroles find extensive applications in materials science, leading to the development of numerous synthetic methods for their construction.

Several established methods for pyrrole synthesis, such as Hantzsch,[7] Knorr, and Paal-Knorr,[8] are widely used despite their drawbacks, including multistep operations, harsh reaction conditions, and limited scope. To address these issues, alternative approaches like the use of transition metal catalysts[9] and multicomponent reactions (MCR)[10] have been introduced. MCRs, involving more than two reactions in a sequential manner from accessible precursors, provide an efficient means to access polysubstituted pyrroles in a single synthetic step. Recent advancements in substituted pyrrole synthesis through MCR methods have employed various catalysts like FeCl3,[11] gluconic acid,[12] NiCl2.6H2O,[13], CeCl3.7H2O,[14] and p-toluenesulfonic acid doped polystyrene (PS-PTSA).[15]. However, these catalysts often suffer from limitations such as low product yields, recyclability challenges, and extended reaction times.

An emerging class of catalysts gaining attention is derived from bioresources. Notably, chitosan (Scheme 1) stands out as an attractive catalyst due to its low cost, reusability, and environmentally friendly nature. Chitosan has demonstrated efficacy in various reactions, including asymmetric aldol condensation,[17] aldol and Knoevenagel reactions,[18] Henri condensation,[19], and metal-supported forms in diverse reactions like the preparation of Hantzsch esters,[20] hydrogenation of ethyl cinnamate,[21], Suzuki and Heck cross-coupling reactions,[22–24], hydration of nitriles to amides in water,[25], and allylic substitution of (E)-cinnamyl ethyl carbonate by morpholine.[26].

In this report, we present a novel synthesis of substituted pyrroles using chitosan as a green, environmentally benign, recyclable, and cost-effective catalyst in a four-component reaction (4CR) involving an amine, an aldehyde, a 1,3-dicarbonyl compound, and nitromethane (Scheme 2). Notably, this represents the first instance of utilizing chitosan in its native form in a 4CR. Additionally, we have significantly reduced reaction times by employing microwave irradiation (MW), leveraging the well-established role of MW in organic synthesis.[27].

II. EXPERIMENTAL

General

All chemical substances used in this study were sourced from Fluka, Aldrich, and Merck chemical companies and were applied without undergoing any additional purification steps. The melting points of the substrates were determined using an Electrothermal-9100 apparatus, and the values were recorded without correction. Fourier transform infrared (FT-IR) spectra were acquired using a PerkinElmer PXI spectrometer on KBr wafers. X-ray diffraction (XRD) patterns of the samples were obtained using a Siemens D-5000 X-ray diffractometer (Germany) with Cu Kα radiation. Magnetic susceptibility measurements were conducted with a vibrating sample magnetometry (VSM; Lake Shore 7200 at 300 kVsm). Thermogravimetric analysis was performed using a PerkinElmer instrument under a nitrogen atmosphere at a heating rate of 10 °C min^–1. Scanning electron microscope (SEM) images were captured with a SEM-LEO 1430VP instrument. The chemical composition of the synthesized nanoparticles was determined using energy dispersive X-ray spectroscopy (EDX) on an Environmental Scanning Electron Microscope (ESEM, Philips, and XL30).

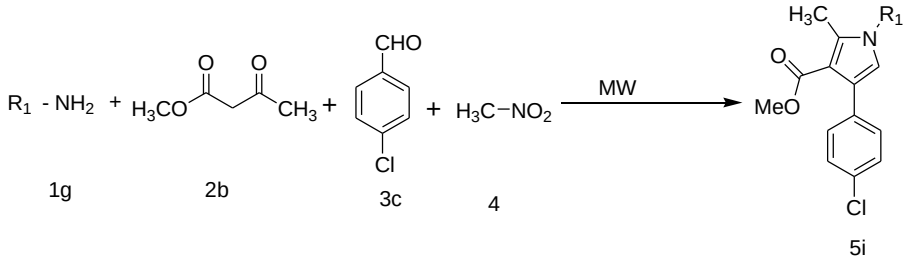
III.EXPERIMENTAL SECTION

Materials. NMR studies were conducted using a Bruker Avance 300 spectrometer in $CDCl_3$, with chemical shifts reported in ppm relative to external TMS. The reaction mixtures were analyzed on a Trace GC Shimadzu chromatograph equipped with an FID detector. GC parameters for capillary columns TG-5MS (30 m × 0.25 mm) were set as follows: injector, 230°C; detector, 200°C; oven, 40°C for 2 min, followed by a ramp of 40°C min^–1 until 280°C for 12 min; column pressure, 42.9 kPa; gas flow, 20 mL min^–1. The mass spectrum of the products was obtained by ionization on an ISQ LT single quadruple mass spectrometer in positive EI mode, utilizing a mass scan range of 50 to 400 da.Liquid chromatography was carried out on silica gel (Merck 60, 220–440 mesh). All reagents and solvents used in the experiments were procured from commercial sources (Aldrich, Acros) and employed without undergoing further purification.

IV.RESULTS AND DISCUSSION

To identify optimal reaction conditions, initial investigations were conducted using benzylamine (1 mmol), 4-chlorobenzaldehyde (1 mmol), methyl acetoacetate (1 mmol), and nitromethane (1 mL) as model substrates. The reaction did not proceed in the absence of a catalyst at ambient temperature and reflux (Table 1, entries 1 and 2). When 30 mg of chitosan was introduced, the corresponding product was obtained in reasonably good yields but required extended reaction times (Table 1, entries 3, 4). However, under microwave irradiation, the reaction yield increased to 91%, and the reaction time significantly decreased from several hours to only 4 minutes (compare entries 3, 4 with 7). Using 10 mg of the catalyst resulted in a longer reaction time (6 min) and decreased product yield (Table 1, entry 5). Both 30 and 40 mg of the catalyst yielded similar results (entries 7, 8); therefore, 30 mg of catalyst was chosen as the optimal amount. The model reaction was also explored in ethanol and toluene, but the use of a solvent did not improve the product yield (Table 1, entries 9, 10).

Table 1. Screening the different reaction conditions on model reaction.



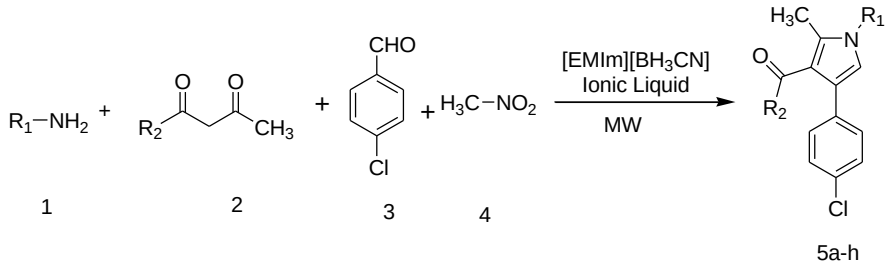
1g 2b 3c 4 5i

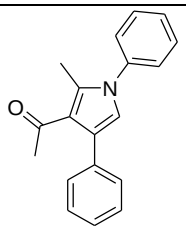
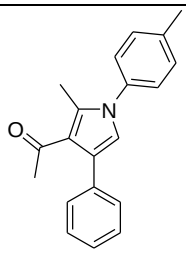
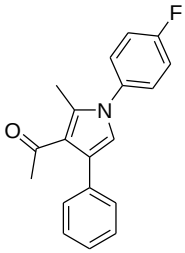
Entry	Ionic Liquid(mg)	Solvent	Reaction Conditions	Time	Yield
1.	-	-	RT	22h	Trace
2.	-	-	Reflux	22h	Trace
3.	30	-	RT	11h	82
4.	30	-	Reflux	4h	84
5.	10	-	MW	5 mim	86
6.	20	-	MW	4mim	71
7.	30	-	MW	4 mim	85

8.	40	-	MW	4 mim	82
9.	30	Ethanol	MW	5 mim	88
10.	30	Toluene	MW	5 mim	71

To assess the generality of the method, various pyrrole derivatives were synthesized under optimized conditions (Table 2). Benzylamine and aniline derivatives produced corresponding pyrroles in high yields (up to 91%). Additionally, different benzaldehyde derivatives showed no significant impact on pyrrole production yield or reaction time.

Table 2. Synthesis of different substituted pyrroles catalyzed by [EMIm][BH_3CN] and promoted by microwave irradiation.



Entry	R^1	R^2	R^3	Time (min)	Product	Isolated yield (%)	Melting point (8C)
1	C_6H_5 1a	Me 2a	C_6H_5 3a			81	104–106
2	4-Me–C_6H_4 1b	2a	3a	4		85	112–114
3	4-F-C_6H_4	2a	3a	7		80	127–131

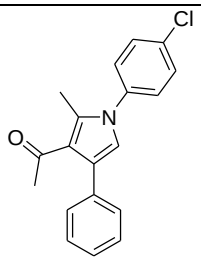
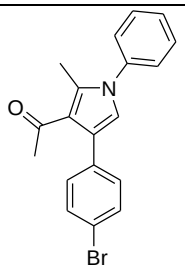
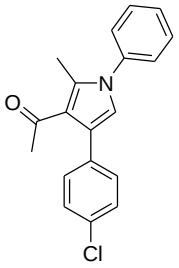
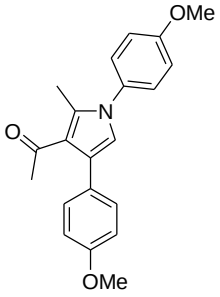
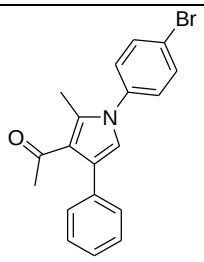
4	4-Cl–C_6H_4	2a	3a	5		82	125–129
5	1a	2a	4-Br-C_6H_4 3b	5		80	92–94
6	1a	2a	4-Cl–C_6H_4 3c	4		80	105–107
7	4-OMe-C_6H_4 1e	2a	4-OMe-C_6H_4 3d	5		85	132–136
8	4-Br-C_6H_4 4f	2a	3a	7		72	142–144

Table 3. Comparison of the catalytic activity of chitosan with some other catalysts in the synthesis of substituted pyrroles.

Entry	Catalyst	Reaction condition	Time	Yield (%)
1	$NiFe_2O_4$ (5 mol %)	reflux	3-4 h	80–96
2	Silica gel-supported tungstic acid (10 mol %)	reflux	4.5 h	85
3	$NiCl_2.6H_2O$ (10 mol %)	reflux	10 h	78
4	$FeCl_3$ (10 mol %)	reflux	5–16 h	44–85
5	**[EMIm][BH_3CN] (30 mg) (this work)**	**MW**	**4–7 min**	**78–92**

6	PS-PTSA (5 mg)	MW	51–76 min	78–93
7	$Y(OAc)_3.H_2O$ (5 mol%)	MW	120–150 min	42–48
8	[bmim]HSO_4 (20 mol%)	reflux	4–5 h	80–90

V. CONCLUSION

In conclusion, this study introduces a novel, cost-effective, and environmentally friendly approach for synthesizing highly substituted pyrroles. The method involves a one-pot four-component reaction utilizing amines, aldehydes, 1,3-dicarbonyl compounds, and nitromethane, with chitosan serving as a sustainable and bioavailable catalyst. Notably, the chitosan catalyst exhibits efficient performance and can be easily recycled multiple times without significant loss of activity. Through the incorporation of microwave acceleration, the reaction times have been substantially reduced from several hours, as observed in alternative methods, to just a few minutes in our study. This innovative methodology not only streamlines the synthetic process but also aligns with green chemistry principles, showcasing the potential for sustainable and efficient synthesis of pyrroles.

Spectral Data;

Representative spectral data for pyrroles:

1-(2-Methyl-4-phenyl-1-(p-tolyl)-1H-pyrrol-3-yl) ethanone (5b). White solid (0.24 g, 85%); mp: 112–114 °C; 1H NMR (500 MHz, CDCl3) δ 2.06 (s, 3H, CH3), 2.38 (s, 3H, COOCH3), 2.41 (s, 3H, CH3), 6.65 (s, 1H, CH), 7.21 (d, J=8.4 Hz, 2H, Ar), 7.29 (d, J= 8.4 Hz, 2H, Ar), 7.32 (q, J= 5.0 Hz, 1H, Ar); IR (KBr) (cm-1): 3110, 3033, 2920, 1643, 1516, 1502, 1407, 1230, 821, 767, 702 cm1.

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Advances in pH Metric Studies of Transition Metal Complexes: Insights into Equilibrium Constants, Molecular Interactions, and Applications

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ABSTRACT

Transition metal complexes represent a fascinating and versatile class of compounds with profound implications across diverse scientific disciplines. Over the years, pH-metric studies have emerged as a powerful tool for investigating the formation, stability, and behaviour of transition metal complexes. This review comprehensively surveys recent advances in pH-metric studies of transition metal complexes, providing an in-depth analysis of the methodologies, insights gained, and applications in various fields.

The review begins with an overview of the principles underlying pH-metric titrations and their application to transition metal complex systems. It explores the factors influencing the choice of ligands and metal ions, emphasizing the impact of ligand design and metal coordination geometry on complex stability. Case studies featuring transition metal ions such as Fe(III), Cu(II), Zn(II), Mn(II), and Ni(II) are highlighted to exemplify the versatility and applicability of pH-metric studies across different systems.

Furthermore, this review explores the implications of pH-metric studies in catalysis, medicinal chemistry, and environmental science. Insights into metal-ligand interactions gleaned from pH-metric investigations contribute to the design of more efficient catalysts, inform drug development strategies, and enhance our understanding of metal speciation in natural systems.

The evolving landscape of pH-metric studies in transition metal complexes is critically assessed, and future directions in this dynamic field are outlined. As the demand for a deeper understanding of metal-ligand interactions grows, this review aims to serve as a comprehensive resource for researchers and practitioners, fostering advancements at the intersection of coordination chemistry and applied sciences.

Keywords: pH-metric studies, transition metal complexes, equilibrium constants, ligand-metal interactions, coordination chemistry, applications

I. INTRODUCTION

Transition metal complexes, characterized by the coordination of metal ions with various ligands, stand at the forefront of interdisciplinary research due to their diverse applications in fields such as catalysis, medicinal chemistry, and environmental science. The precise understanding of the thermodynamics governing the formation and stability of these complexes is pivotal for harnessing their potential in these applications. pH-metric studies have emerged as a powerful and versatile approach, providing unique insights into the intricacies of metal-ligand interactions.

The exploration of metal-ligand equilibria through pH-metric titrations has evolved into a sophisticated methodology, allowing researchers to probe the nuances of complex formation under controlled pH conditions. This approach not only provides a comprehensive understanding of the equilibrium constants governing these interactions but also sheds light on the molecular dynamics that underpin the stability of these complexes.

In this review, we embark on a comprehensive examination of recent advances in pH-metric studies of transition metal complexes. We delve into the principles of pH-metric titrations, exploring their application to a myriad of transition metal ions, including but not limited to Fe(III), Cu(II), Zn(II), Mn(II), and Ni(II). The discussion encompasses the diverse ligands employed, emphasizing the influence of ligand structure on complex stability and the ensuing implications for catalytic processes and medicinal applications.

The analytical techniques and methodologies employed in pH-metric investigations have witnessed significant advancements. From state-of-the-art instrumentation to sophisticated computational methods, researchers have leveraged cutting-edge tools to extract precise information about the equilibrium constants and molecular interactions governing these complex systems. Notably, advancements in data analysis, including global fitting approaches and statistical validation, contribute to the robustness of the obtained results.

Beyond the fundamental insights gained, this review explores the practical implications of pH-metric studies in catalysis, medicinal chemistry, and environmental science. The impact of metal-ligand interactions on catalytic efficiency, drug development, and environmental metal speciation is discussed, highlighting the translational potential of pH-metric studies in addressing real-world challenges.

As we navigate through the exciting developments in pH-metric studies of transition metal complexes, this review aims to serve as a valuable resource for researchers and practitioners, fostering a deeper understanding of coordination chemistry and its applications across scientific domains. The subsequent sections will delve into specific aspects of methodology, case studies, and emerging trends, providing a comprehensive overview of the evolving landscape in this dynamic field.

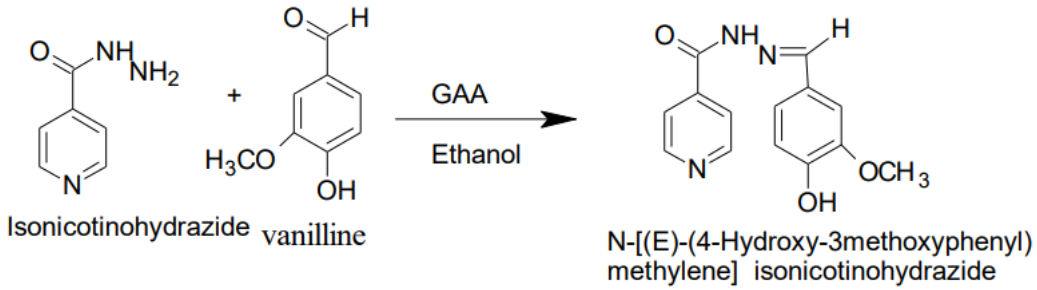
II. LITERATURE SURVEY

In this study by Tanaji N. Bansode, the pH-metric method was employed to investigate the stability constants of promazine (PMZ) complexes with Fe(III), Cd(II), Pb(II), Cu(II), and Zn(II) metal ions in aqueous medium at temperatures of 298 K and 308 K and 0.1 M ionic strength. The potentiometric titration technique facilitated the determination of proton-ligand and metal-ligand stability constants, while computational methods were utilized to derive metal-ligand stability constants. Thermodynamic parameters, including ΔG, ΔH, and ΔS, were determined potentiometrically. The study demonstrated that stability constants decreased with an increase in temperature, suggesting a temperature-dependent influence on the formation of stable complexes. Additionally, the thermodynamic analysis revealed the exothermic nature of the reaction process, with entropy and enthalpy

factors favoring complexation. Overall, this comprehensive investigation provides valuable insights into the thermodynamics and molecular interactions governing the formation of promazine-metal complexes, contributing to the understanding of metal-ligand interactions in aqueous environments.

Zamzam Taher Omar et al. conducted a pH-metric study on transition metal complexes with the pharmacologicallyactive ligandN-[(E)-(4-Hydroxy-3-methoxyphenyl)methylene]isonicotinohydrazide. They explored the interactions of Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) metal ions with the synthesized ligand in a 70% ethanol–water medium. The ligand, obtained through the condensation of an anti-mycobacterial agent with an aromatic aldehyde, was characterized using various spectroscopic techniques. The study revealed a distinct order of stability for the binary complexes: Cu (II) > Co (II) > Mn (II) > Ni (II) > Zn (II). The research contributes insights into the pH-dependent behavior of transition metal complexes and their potential pharmacological applications, showcasing a systematic approach from synthesis to comprehensive analysis.

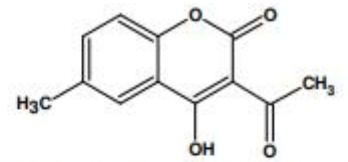
Synthesis Pathway for Organic Ligands :



Isonicotinohydrazide vanilline

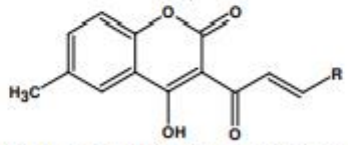
N-[(E)-(4-Hydroxy-3methoxyphenyl) methylene] isonicotinohydrazide

In this study by M. V. Hathi et al., novel metal complexes of first transition metal ions with a chromene derivative as ligands were synthesized and characterized through elemental analysis. The ligand, 3-[{3-(9'-anthryl)}-prop-2-enoyl]-4-hydroxy-6-methyl-2H-chromen-2-one, was examined for its interaction with M (II) ions (M = Mn, Cu, Ni, Co) using pH measurements and Irving-Rossotti titration technique. The research delves into factors influencing the formation and stability of metal complexes. The coupling of transition metals with coumarin derivatives is noteworthy for potential applications, given the distinct physiological activities exhibited by certain coumarins. The study provides valuable insights into the chelating characteristics of the synthesized ligand and its metal complexes, offering a foundation for further exploration in analytical chemistry and potential biomedical applications.



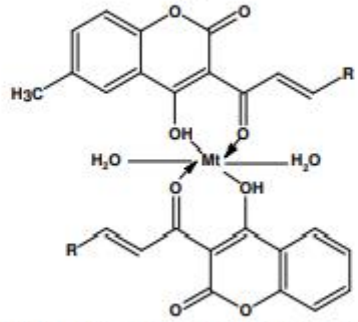
3-Acetyl - 4-hydroxy -6-methylcoumarin (I)

3-Chloro benzaldehyde



3-[{3-(3'-Chloro phenyl)}-prop-2-enoyl]-4-hydroxy-6-methyl-2*H*-chromen-2-one
[Where R = 3'-Chloro phenyl]

Metal Salt



Bis -(3-[{3-(3'-Chloro phenyl)}-prop-2-enoyl]-4-hydroxy-6-methyl-2*H*-chromen-2-one)
Mt^{+2}Complex(II).

The study by Praneeta V. Susatkar explores the complex formation between Cu(II), Ni(II), Co(II), and Fe(III) metal ions and two 2-hydroxy-4-substituted phenyl-6-substituted phenyl pyrimidines, namely [H4AHBP] (L1) and [H4CHBP] (L2). Conducted at 0.1 M ionic strength in a 70% dioxane-water mixture, the investigation employs the Bjerrum method as adopted by Calvin and Wilson. The research reveals that Cu(II), Ni(II), Co(II), and Fe(III) metal ions form 1:1 and 1:2 complexes with ligands L1 and L2. The proton-ligand and metal-ligand stability constants (pK and log k) are estimated and compared, shedding light on the impact of substituents on these values. The work adds valuable insights to the field of metal-ligand interactions, particularly focusing on the physiochemical properties and stability of complexes in various solvent systems, providing a foundation for potential analytical applications.

The paper by A.B. Patil investigates the pH-metric behavior of ternary complexes formed by Mn (II), Co (II), Ni (II), Cu (II), and Zn (II) metal ions with primary ligands aspartic acid (ASP) and glutamic acid (GLU), and secondary ligands nicotinic acid (NA) and ascorbic acid (AA). The study, conducted in aqueous medium at 302 ± 0.5 K and 0.1 M ionic strength, employs pH-metric techniques to determine proton-ligand and metal-ligand stability constants. The results reveal the formation of 1:1:1 mixed ligand complexes, and the obtained stability constants exhibit the Irving-Williams order. The systematic investigation sheds light on the intricate interactions within these ternary complexes, providing valuable insights into the coordination chemistry of transition metal ions with biologically relevant ligands.

The study by J.P. Nehete and team investigates the interaction between transition metal ions and the substituted heterocyclic drug Clarithromycin in a 70% ethanol-water mixture. Using pH-metric methods, the research explores proton-ligand and metal-ligand stability constants at 0.02 M ionic strength. Results indicate

the formation of 1:1 and 1:2 complexes with the drug. The work provides a comprehensive review of relevant literature, emphasizing the significance of stability constant studies in diverse applications. The systematic approach and detailed experimental procedures enhance our understanding of metal-ligand interactions, contributing valuable insights to coordination chemistry.

The study conducted by S.A. Olagboye explores the pH-metric behavior of transition metal complexes with azole-based ligands, specifically benzimidazole and 1,2,3-triazole, in a water-methanol medium. The research investigates metal-ligand complexation through pH-metric titrations at different temperatures, revealing stability constants and thermodynamic stabilities. The findings suggest that the metal complexes are exothermically favorable, and their spontaneity is supported by negative Gibbs free energy values. The study highlights the influence of temperature on the stability of the complexes, with the optimum formation observed at 35°C. The results contribute to understanding the coordination chemistry of these azole-based ligands with Fe(III), Ni(II), and Zn(II) ions.

The research conducted by D. D. Kayande and colleagues focuses on the stability constant study of ternary complexes involving transition metal elements (Fe, Co, Ni, Cu, Zn) with pharmacologically active ligands, nicotinamide, and alanine. The study, employing pH-metric techniques at 25±0.1°C, investigates the formation and stability of these complexes in a 70% ethanol-water medium at 0.1M ionic strength. The stability constants were determined using potentiometric pH titrations, and the order of stability was found to be Co (II) > Fe (II) > Cu (II) > Ni (II) > Zn (II). The results suggest potential applications in the drug industry, emphasizing the importance of understanding the impact of biologically active ligands on complex stability. The study provides valuable insights into the interactions between transition metals and pharmacologically relevant ligands, contributing to the broader field of coordination chemistry.

Dr. S. A. Quazi conducted a pH-metric study investigating the complexation of para-aminobenzoic acid (PABA) with transition metal ions (Co, Cu, Fe, Ni, Zn, Cd) in aqueous solutions at 27°C with a 1N $NaNO_3$ ionic strength. Using the Irving Rossoti titration method and computer calculations with the SCOGS program, the protonation constant and formation constants of metal complexes (1:2 metal-to-ligand ratio) were determined. PABA, a water-soluble compound relevant to sulfonamide antibiotics and folic acid synthesis, was selected due to its limited literature coverage and potential pharmaceutical importance. The study reveals the order of stability constants: Co (II) > Cu (II) > Fe (III) > Ni (II) > Zn (II) > Cd (II), indicating varying metal affinities for complex formation. The research contributes to understanding ligand-metal interactions in drug development and coordination chemistry, offering valuable insights into PABA-metal interactions for potential pharmaceutical applications. The study's methodology, including computer-assisted equilibrium constant calculations, enhances its robustness.

The study by K. B. Vyas, G. R. Jani, and M. V. Hathi investigates the formation constants of binary complexes between d10 metal ions (Cu(II), Ni(II), Co(II), and Mn(II)) and a substituted coumarin derivative. The ligand's chelating characteristics were explored for potential analytical reagent applications. pH-metric titrations, employing the Irving-Rossotti method at 30±1 °C and ionic strength μ=0.1 M $NaNO_3$, revealed varying stability orders for different metal ions. The research contributes insights into ligand-metal interactions, particularly in biochemical reactions and analytical contexts. The computer-assisted equilibrium constant calculations enhance the reliability of the findings.

III.CONCLUSION

In summary, the comprehensive review of various studies on transition metal complexes and ligands highlights the intricate nature of coordination chemistry. Investigations employing pH-metric methods, potentiometric titrations, and computational analyses reveal temperature-dependent influences, stability orders, and the impact of ligand substituents on complex formations. From the dynamic behavior of promazine complexes to the systematic exploration of binary and ternary systems, each study contributes valuable insights into the thermodynamics and molecular interactions governing metal-ligand coordination. These findings extend our understanding of diverse applications, including potential pharmacological uses and analytical chemistry. Collectively, these studies significantly enrich the field of coordination chemistry, paving the way for further exploration in interdisciplinary scientific research

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Green Approach – Solvent free Synthesis and Its Advantage

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ABSTRACT

Issues in the past decade demonstrate several methodologies that protect human health and the environment in an economically beneficial manner that is green chemistry. The introduction of green chemistry is often considered a response to the need to reduce environmental damage caused by manufactured materials and their production processes. In this study, our main attention is drawn to the use of green chemistry concepts in daily life, work, laboratory and education. A brief introduction and prospects for green chemistry are also presented. Green chemistry is a new approach to the synthesis, processing and usage of chemicals, thereby reducing harm to human health and environmental pollution. Anastas has prepared twelve important points of green chemistry that can help prevent environmental pollution and ensure environmental friendliness. During laboratory studies, turning off fume hoods when not in use, conducting micro-experiments to reduce waste, etc. In this review Some of the important green tools used in medicine and drug synthesis are described such as microwave-assisted synthesis, organic synthesis in a dry environment, use of computer-aided drug design, ionic liquid and water mediated reactions, use of green catalysts, etc.

Keywords: Green chemistry, Eco-friendly, Microwave synthesis, Green Solvents.

I. INTRODUCTION

The term "green chemistry" was first introduced by Anastas in 1991 as a specific guideline created by the U.S. Environmental Protection Agency (EPA) to promote the development of chemistry and chemical technology.[1,2] Green chemistry includes new methods for synthesizing, processing and using chemicals that will minimize harm to human health and environmental pollution. [3] Green chemistry can be an important tool in promoting new technologies that reduce or eliminate the use or production of hazardous substances in the design, manufacture and use of chemical products.[4] Advances in science and technology in the second half of the twentieth century led to economic growth and improvements in infrastructure in the world.[5] Many forward-thinking companies are adopting green practices not only to protect the environment and create good public relations, but also because they are often beneficial to the bottom line. Based on available data, it is estimated that the US economy spends between $100 and $150 billion annually to comply with environmental

regulations. The greatest success of green chemistry is in the petrochemical and pharmaceutical industries. However, these industries are often accused of polluting the environment. The challenge for the pharmaceutical industry today is to continue to deliver the applications and health benefits available through green chemistry in an environmentally friendly manner.

II. PRINCIPLES OF GREEN CHEMISTRY

There are twelve principles contributing the green chemistry. These are elaborated as follows:

1. **Prevention:** It is better to prevent waste than to treat or clean up waste after it has been created.
2. **Atom Economy:** Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. **Less Hazardous Chemical Syntheses:** Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. **Designing Safer Chemicals:** Chemical products should be designed to affect their desired function while minimizing their toxicity.
5. **Safer Solvents and Auxiliaries:** The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.
6. **Design for Energy Efficiency:** Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.
7. **Use of Renewable Feed stocks:** A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.
8. **Reduce Derivatives:** Unnecessary derivatization (use of blocking groups, protection/ deprotection, temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.
9. **Catalysis:** Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. **Design for Degradation:** Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.
11. **Real-time analysis for Pollution Prevention:** Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12. **Inherently Safer Chemistry for Accident Prevention:** Substances and the form of a substance used in a chemical process should be chosen to minimize the potential for chemical accidents, including releases, explosions, and fires.

Green chemistry approach plays a vital role in:

- Pollution prevention can be improved operational practices by lowering energy consumption and improving yields.
- Development of greener processes to manufacture unchanged chemical products by avoiding the use of chlorinated compounds or solvents if chlorine is not in the final product.
- Use of alternative chemicals for the same application.
- Avoidance of chemicals and also use of chemistry for improved environmental performance by designing chemical sensors for better observation of environmental quality. Less hazardous chemical syntheses/inherently safer chemistry for accident prevention

The main goal of green chemistry is to make the environment safe not only for the peoples but also for production or laboratory workers through the use of safe materials and processes. Synthetic methods should be prepared and designed to ensure that the usage and production of chemicals are as non-toxic to human health and the environment as possible. The chemicals used in the chemical process must be carefully selected to reduce the risk of chemical injury/explosion and fire. Doctor's use poisons all the time because these substances form kinetically and thermodynamically favorable substances. It's easy to not worry about all the other "stuff" that goes into the glass and focus all our energy on the synthetic method that delivers the desired product. Toxic products will continue to increase unless new drugs and new synthetic methods are developed. Chemists must expand their horizons and try to use especially environmentally benign and less lethal materials for chemical reactions. Otherwise we need to to pay for the damage caused to the environment.

Green chemistry has many advantages like

1) Non toxic
2) Environment Friendly
3) Simple
4) Sustainable
5) Economical
6) Safe
7) Avoid Waste

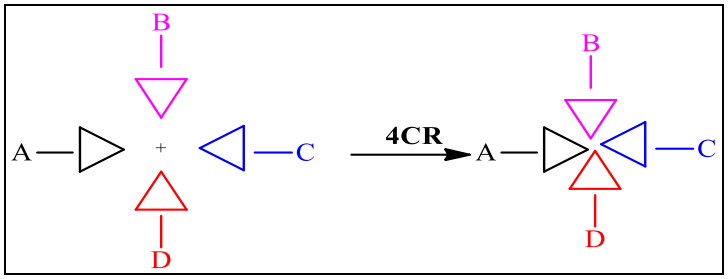
Research Methodology: The present studies especially involve the application of the following tools of Green Chemistry*:*

- **Reactions:** (i) Multi-component reactions
  (ii) One pot reaction
- **Catalysis:** (i) Biocatalysis
  (ii) Synergistic catalysis
- **Use of environmentally benign solvents:** Ionic liquids
- **Energy conservation:** Use of microwave irradiation as a energy source
- **Chemical feedstocks:** Use of readily available or renewable starting materials

Green synthesis of organic Compound by using different techniques

1) Multi-Component Reactions (MCR's)

Multicomponent reactions (MCRs) are convergent reactions, where three or more starting materials react to form a product and generally all or most of the atoms contribute to the newly formed product (Scheme 1).



Scheme 1

MCR strategies provide significant advantages over conventional syntheses in terms of diversity, speed and efficiency[6] The major challenge is to conduct MCR in such a way that the network of pre-equilibrated reactions channel into the main product without generation of side products. The outcome of MCR reactions are clearly dependent on the reaction conditions: temperature, solvent, concentration, catalyst, functional groups and the kind of starting materials. MCRs have great contribution in the synthesis of complex organic molecules starting from simple and readily available starting materials, paticularly heterocyclic scaffolds can be used for the creation of diverse chemical libraries of "drug-like" molecules for biological screening.

2) One-pot reactions:

It is generally said that chemists tend to clean up the organic synthesis utilizing one pot reactions. During one-pot synthesis all the reactants are subjected to successive chemical reactions in just one reactor. Organic synthesis involving the manufacturing of drugs and agrochemicals till date utilizes multi step synthesis. Some sophisticated multi-step reactions may require weeks to complete. And henceforth, it becomes an environmentally non-benign which besides generating the desired product produces tons of toxic waste. This is partially because each step requires different conditions of temperature, pressure, catalyst and solvent. And before next step, each step requires workup generating waste. But due to environmental concerns, the chemical industry are forced to look for cleaner methods

3) Green Solvent in Organic synthesis:

Green Solvents are easily biodegradable, having high boiling point, low miscibility in water and less or no toxicity. Here,we described the ionic liquid as green and environmentally benign sovents and their importance.
Ionic Liquid- Solvents are auxiliary materials that are used during chemical synthesis to facilitate mass transfer. However, the excessive use of offensive organic solvents like toluene, dichloromethane, benzene and chloroform etc for various organic reactions is a major concern in today's chemical processing industries due to their harmful impact on environment and human health. Due to above concern there is an urgent need to minimize the usage of organic solvents during a chemical synthesis or to find an alternate for halogenated toxic solvents which is one of the key concern of green chemistry. Some of the strategies include reactions on solid support, use of supercritical fluids or water as solvents etc. Recently, ionic liquid (IL) have attracted much attention [Anastas and Warner (1998) [7]
ILs generally refers to those salts, which have melting points below 100°C. "Room temperature ionic liquids" (RTILs) are the salts that melt at room temperature. This distinction of IL based on temperature does not have any physical or chemical significance and is just an indicator to differentiate the ILs from high-temperature molten salts. Generally, ILs consists of relatively large organic cation such as imidazolium based or pyridinium based cation, whereas anion can be organic as well as inorganic such as Br^-, Cl^-, PF_6^-, BF_4^-, NO_3^-, $[AcO]^-$, $[CF_3CO_2]^-$, $[N(CF_3SO_2)_2]^-$, $[CF_3SO_3]^-$ and $[SCN]^-$ etc Some of the commonly used cations and anions used for the synthesis of ILs are depicted in Figure 13.

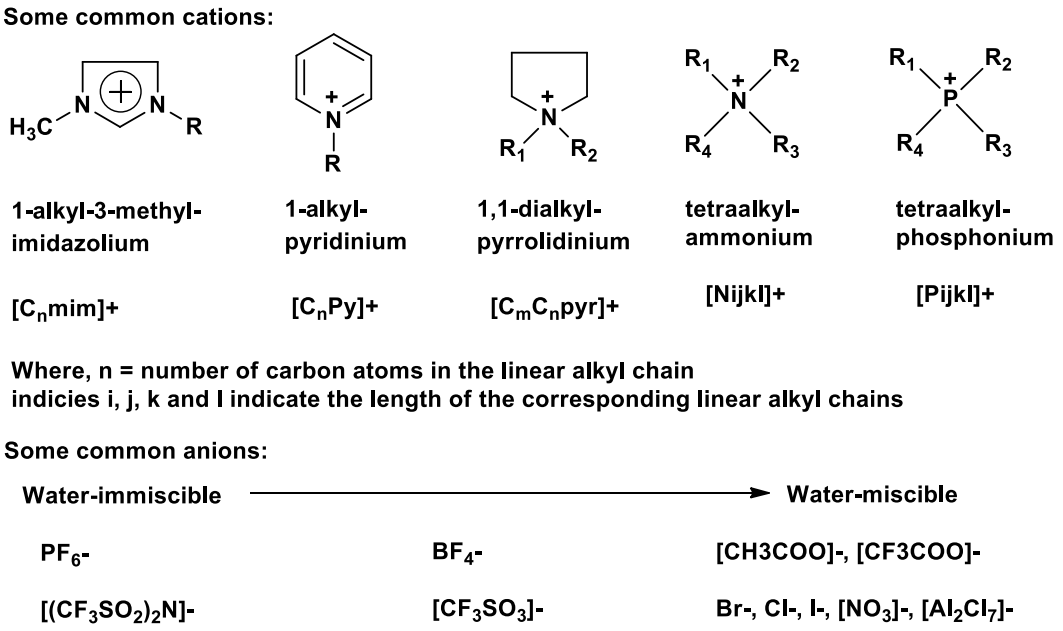


Figure 13 Examples of commonly used cations and anions of ionic liquids

4) Energy conservation:

Traditionally, in most commonly used heating sources such as oil bath, heating mantle, Bunsen burner, heater or electric plate heater, the transfer of heat energy into the reaction system depends on convection currents beside thermal conductivity of various materials of the reaction pot. Consequently, the temperature of the reaction vessel is always higher than that of the reaction mixture which in turn can lead to the decomposition of reactants, reagent or product due to development of temperature gradient. In the above context, microwave irradiation (MW) as a non conventional energy source has become very popular and useful technology in organic synthesis [Lidstrom *et al*[8]

5) Microwave (MW):

Microwaves are electromagnetic radiations which fall in the frequency range from 300 Hz to 30 GHz that corresponds to the wavelengths of 1m to 1cm. In order, to avoid the interference with radar and telecommunications, most of the MW appliances operate at fixed frequency of 2450 MHz. In contrast to traditional heating sources, MW irradiation couple directly with the component of reaction mixture[9]

5.1) Theory of Microwave:

Heat energy of MW is transferred to the reaction mixture by the following two mechanisms

(i) Dipolar polarization (ii) Ionic conduction

(i) Dipolar polarization:

In the dipolar polarization mechanism, electric field component of MW interacts with polar molecules of reaction mixture.

When a molecule possessing dipole moment is irradiated with MW it tends to align itself with the field by rotation (Figure 15). However, the frequency of the rotating dipole is not high enough to accurately follow the alternating electric field of MW. So as the dipole re-orients to align itself with the electric field, the field is already changing and generates a phase difference between the dipole and the orientation of the field which generates excess of friction which leads to intense internal heating.

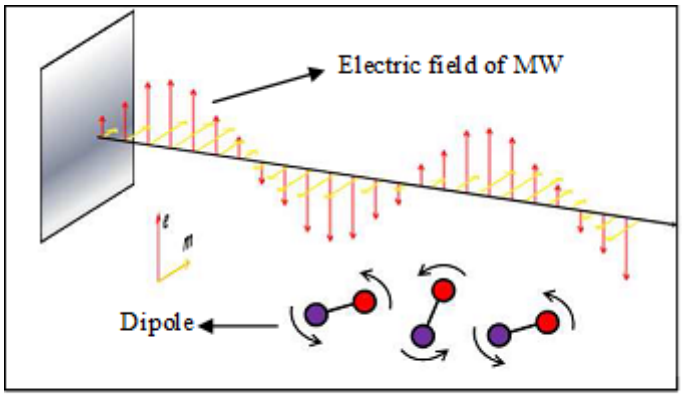


Figure 15. Interaction of the electric field of MW with dipole moment [Gagnon (2008)]

(ii) Ionic conduction:

According to the ionic conduction mechanism, the charged particles of the sample (usually ions) oscillate back and forth under the influence of electric component of MW irradiation and subsequently collide with their neighbouring molecules or atoms and resulting into agitation or motion, creating heat. The ionic conduction principle is a much stronger effect than the dipolar rotation mechanism with regard to the heat-generating capacity. That's why the media containing ions are heated more efficiently by MW than just polar solvents.

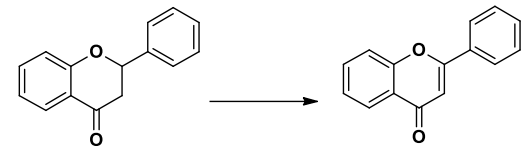
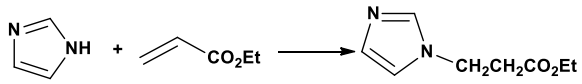
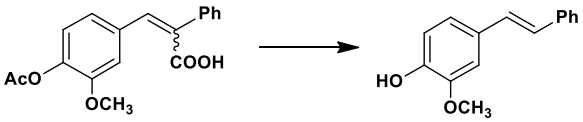
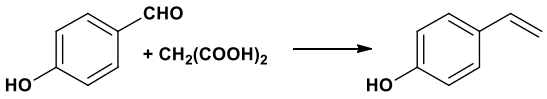
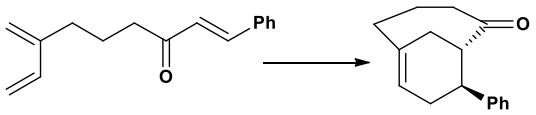
Since MW energy is imparted directly to the reaction medium rather than through the wall of reaction vessel, it is an efficient energy source compared with conventional steam wherein heating the entire furnace or oil bath consumes lot of time and energy.

Microwave-assisted organic synthesis [MAOS]:

MAOS is considered as an important approach towards green chemistry. The MAOS technique has been accepted to reduce the reaction time besides increasing yield of product compared to conventional synthesis since its first report in 1986. Additionally, MW heating in a pressurized system rapidly increases the reaction temperature far above the boiling point of the solvent and leads to a uniform energy transfer to the reactants of the chemical reaction.

Some of the examples of microwave-assisted organic reactions and their comparison with conventional methods are given in Table 1.

Table 1 Some examples of microwave-assisted reactions and their comparison with conventional conditions

Reaction	Activation mode	Time	Yield	Reference
	Conventional	16 h	61%	Zhou et al. (2006a)
	MW	10 min	88%	
	Conventional	5 min	27%	Martin-Aranda et al. (1997)
	MW	5 min	75 %	
	Conventional	16 h	62%	Kumar et al. (2007b)
	MW	20 min	87%	
	Conventional	6 h	12%	Sinha et al. (2007b)
	MW	5 min	61%	
	Conventional	10h	0%	Cleary et al. (2011)
	MW	1 h	73%	

Recent trends in microwave assisted organic synthesis (MAOS) are the use of environmentally benign ILs in conjunction with MW. This combination has been gaining momentum as ionic liquids being salts (feature polar and ionic character) interact more efficiently with MW irradiation through both polarization and ionic conduction energy transfer mechanisms. Thus, ILs are considered as an ideal solvents for MAOS..

6) Sonication in Organic Synthesis:

It brings out the chemical reaction by using sound energy. The ultrasound frequencies for chemical reaction ranges between 20 – 100 KHz. It accelerate the chemical reaction by acoustic cavitation phenomenon. It increases the reactivity of catalyst and reagent. Most of the chemical reaction done by sonication are at room temperature instead of conventional heating and time required under sonication to complete the reaction is very low as compared to classical processes. It is non-classical form of energy and eco-environmental technology in green synthesis.

7) Green Catalysis in Organic Synthesis:

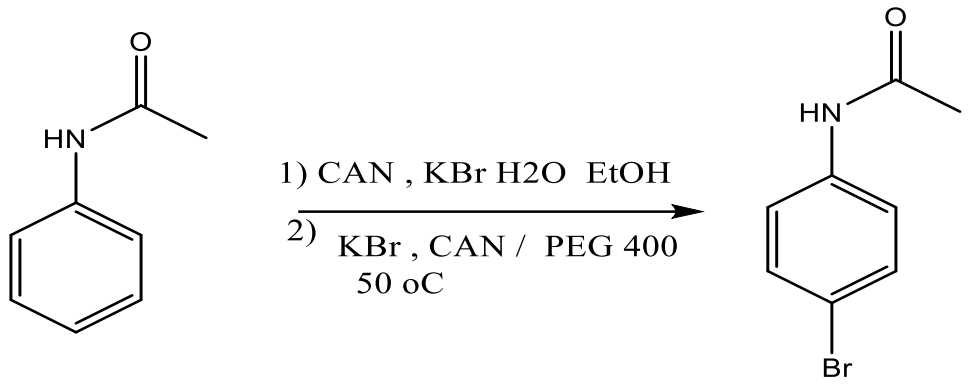
Use of catalyst in organic synthesis is a important part of green synthesis. Catalyst accelerates the reaction and lower the energy required to complete the reaction. Use of catalyst avoids the use of reagent in stoichiometric quantity. Green catalyst has high catalytic efficiency, environment friendly nature, such catalysts are Zeolites, Clays and biodegradable acids which may replaces the hazardous catalyst which are in use. Enzyme catalysis is example of homogenous green catalysis.

III.LITERATURE REVIEW

We, mention some of the reactions where toxic reagents have been replaced by environmentally friendly/safe reagents.

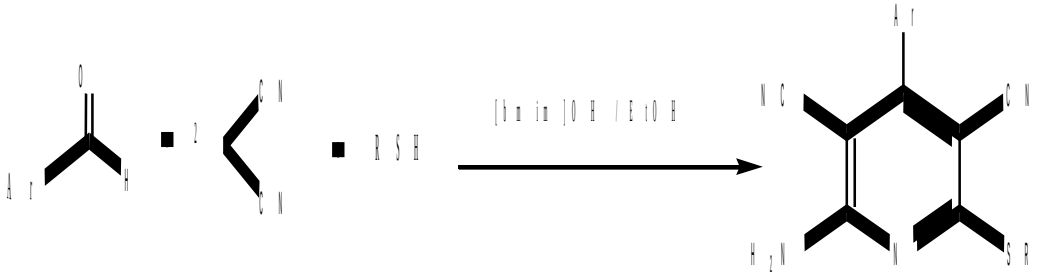
Bromination of acetanilide using ceric ammonium nitrate and potassium bromide

Traditional bromination processes involve the use of corrosive bromine, a chemical that can cause severe burns. Its use create serious problems in handling and disposal, especially in large and commercial sectors where it has been replaced by new bromination chemicals (ceric ammonium nitrate and potassium bromide).[10] It also has the following advantages: greater solubility in water, lower cost, environmental protection, easy handling, high reactivity and easy finishing. Additionally, bromination is done in green media.

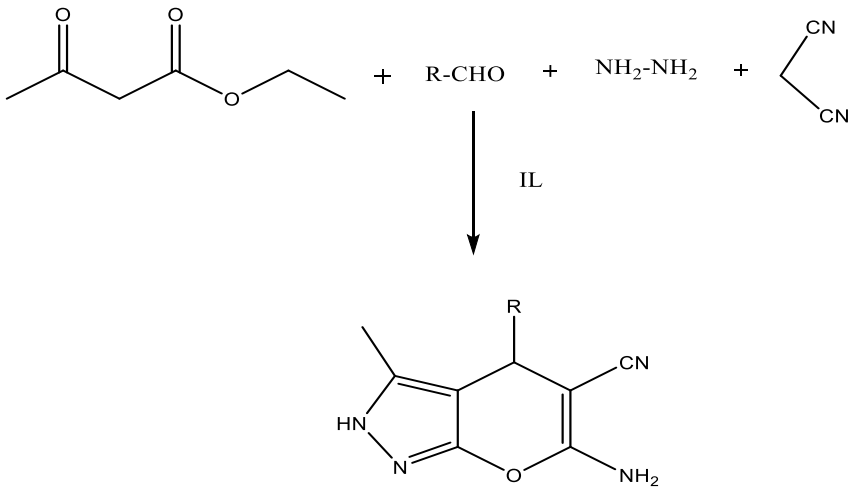


A rapid, environmentally friendly and regioselective bromination method for aromatics was developed, where ceric ammonium nitrate (CAN) was used as Lewis acid catalyst to produce Br + in situ from potassium bromide (KBr) in PEG-400 (polyethylene glycol) and the product was obtained at excellent yields without further purification.

A literature review shows that a number of heterocyclic compounds with a fused ring system have different types of physiological activities. Condensed triazolopyrimidines and N-benzylidene derivatives exhibit antifungal, anti-inflammatory, antibacterial, herbicides and anticancer effects. Recently, B. C. Ranu et al.[11] reported an improved and green protocol for the synthesis of highly substituted pyridines via the one-pot three-component condensation of aromatic aldehydes, malononitrile, and thiophenols using the basic ionic liquid [Bmim]OH at room temperature. This reaction does not involve any hazardous organic solvent and the toxic catalyst and ionic liquid are recovered and recycled for subsequent reactions.



S. M. Deshmukh et al. [12] Ionic liquid catalyzed one pot synthesis of pyranpyrazoles from hydrazine hydrate, ethyl acetoacetate and malano nitrile.



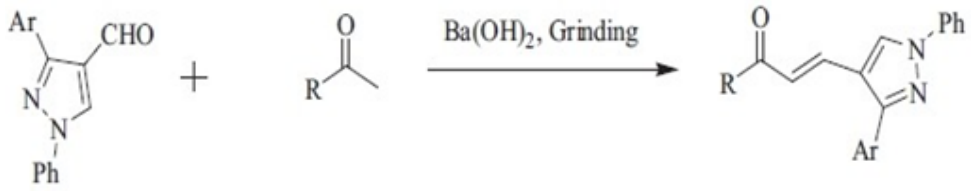
Synthesis of Pyrazoles compounds by green Approach

3 Solvent free method:

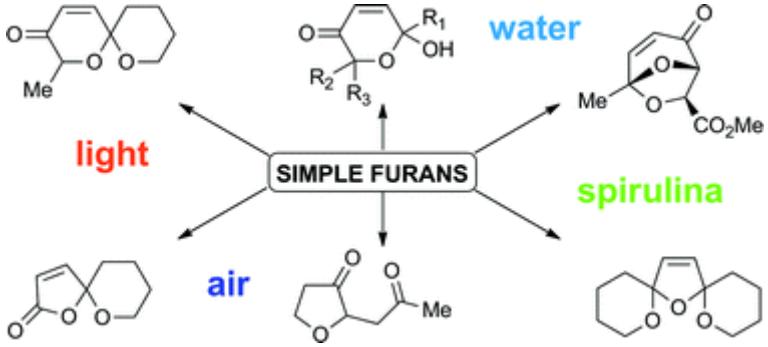
We described a few reports where no use of solvents for synthesis of compounds Generally, chalcones can be synthesized by Claisen Schmidt condensation between ketones & aryl halides using catalysts like alkali metal hydroxide or sodium ethoxide. It has disadvantages include use of harmful organic solvents & difficult extraction process.

Solvent free method

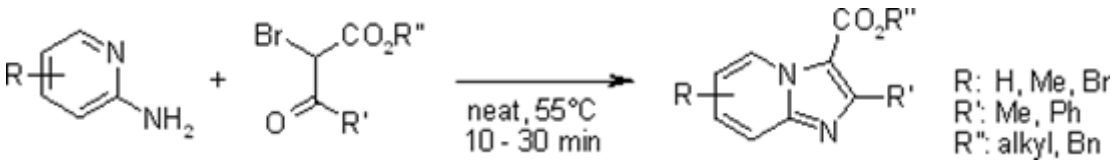
This process involves the grinding of a mixture of pyrazole aldehydes, acetophenones & activated barium hydroxide(C-200) in a mortar & pestle for 5-10mins in the absence of any solvent. It was proposed by P.Kumar et al. the advantages are less reaction time, high yield, reaction is carried out at room temperature & mild reaction conditions[13]



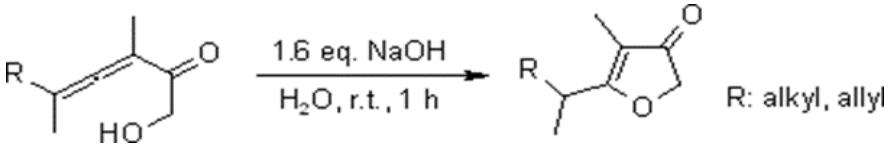
A greener way of utilizing air, sun light, water and spirulina to transform readily available furan derivatives into a wide range of synthetically useful polyoxygenated compounds which are commonly found in natural products is now possible with green chemistry[14].



Temperature Controlled microwave heating of aminopyridines and α-bromo-β-keto esters has been used for the synthesis of highly substituted imidazo[1,2-a]pyridines under solvent-free conditions. This method gives the highest yields of products in reaction times of less than two minutes compared to the traditional way of heating i.e. thermal heating[15].



A simple, cost efficient and effective method of synthesis of 3(2H)-furanones by cycloisomerization of allenic hydroxyketones has been carried out in water. This method eliminates the use of any expensive metal catalyst[16].

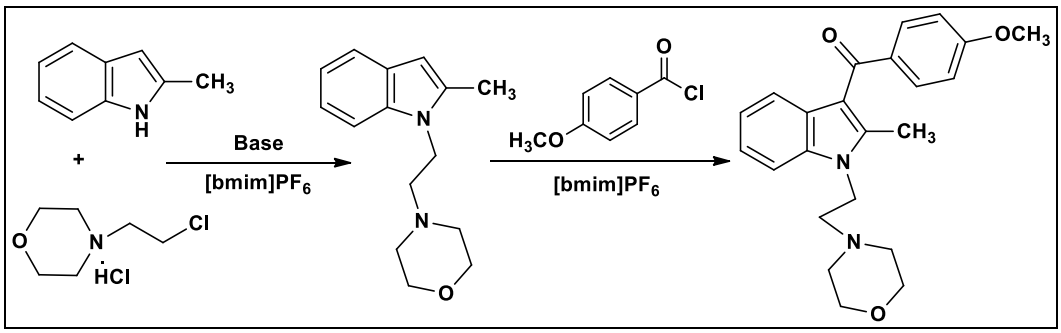


Application of ionic liquids:

In synthetic organic chemistry, ILs have successfully been explored for various reactions such as Diels-Alder, Knoevenagel, Mannich, Aldol condensation, Heck, Friedal-Craft reaction etc besides their applications in synthesis of pharmaceutical intermediates

For example,

Earle *et al*[17] synthesized Pravadoline, NSAID in ionic liquid [bmim]PF_6 without employing any Lewis acid (Scheme 25). The use of IL not only not only eliminated the waste disposal problems associated with conventional Friedal-Craft reaction but can also be recycled.



Scheme 25

In 2002, the first successful example of an industrial process utilizing IL technology, was the BASIL™ (Biphasic Acid Scavenging utilising Ionic Liquids) process [18]. The use of IL in BASIL process increased the yield of their alkoxyphenylphosphine (photoinitiator precursor) by a factor of 80000 compared with the conventional process Although, the research in the field of IL is expanding day by day, however there are certain restrictions pertaining to the use of ILs which needs to be resolved.

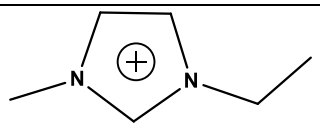
Application of ionic liquids in microwave assisted organic synthesis:

Many reports on the use of ILs as solvents, heating aid, co-solvents, additives and catalysts in MAOS has been furnished in literature. Some of the selected applications of ILs in MAOS are described below:

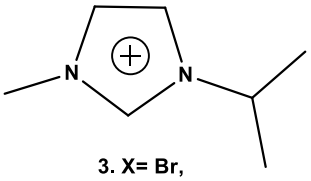
Ionic liquids as heating aid under microwave:

Leadbeater *et al.* investigated the role of ILs during MW heating of non polar solvents such as hexane, THF, toluene and dioxane etc [19] and found that such non polar solvents can be heated far above their boiling points with the help of small amount of an IL. Some of the investigated ILs in the study along with comparison of the attained temperature in the presence or absence of these ILs is depicted in Table 2.

Table 2:



1. X= I,
2. X= PF_6



3. X= Br,

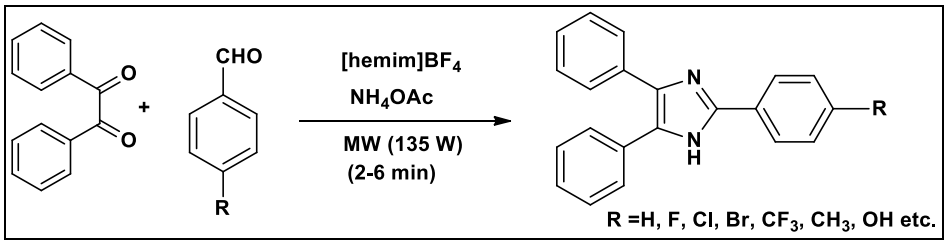
Solvent used	IL added	Temperature attained with IL (°C)	Time (S)	Temperature without IL (°C)	Boiling point (°C)
Hexane	**1**	217	10	46	69
	2	279	20		
	3	228	15		
Toluene	**1**	195	150	109	111
	2	280	60		
	3	234	130		
THF	**1**	268	70	112	66
	2	231	60		
	3	242	60		
Dioxane	**1**	264	90	76	101
	2	149	100		
	3	246	90		

1.3.5.1.3.2 Ionic liquids as benign reaction medium under microwave:

Some of the organic reactions wherein ILs have been used as reaction media are discussed below:

1.3.5.1.3.2.1 For synthesis of 2,4,5-trisubstituted imidazole derivatives:

Xia *et al.*[20] employed neutral ionic liquid, 1-methyl-3-heptylimidazolium tetrafluoroborate ([hemim]BF_4) under MW to carry out a three component synthesis of 2,4,5-trisubstituted imidazole derivatives (Scheme 27) .The reaction completed within 2-6 min of MW irradiation whereas conventional heating (oil bath) required 2 h for its completion besides the low yield product.



Scheme 27

Applications of ionic liquids and microwave combination for some of the organic name reactions:

The application of synergism of IL-MW technology for various name reactions is summarised in Table 4 [Palou (2010)].

Table 4. Applications of ionic liquids and microwave for some selected organic reactions

S.No.	Name of the reaction	Catalyst/IL-MW conditions	Reference
1	Diels-Alder cycloaddition	Organotungsten catalyst/[bmim]PF_6 Mineral supports/[hmim]BF_4	Chen *et al*. (2004) López *et al*. (2007)
2	Fisher esterification	[bmim]HSO_4	Arfan and Bazureau (2005)
3	Mannich condensation	CuCl/[*i*-ProMIM]PF_6	Leadbeater *et al*. (2003)
4	Knoevenagel condensation	[bmim]BF_4	Ma *et al*. (2006)
5	Biginelli	[bmim]HSO_4	Arfan *et al*. (2007)
6	Tsuji–Trost	$Pd(OAc)_2$/[emim]BF_4/H_2O	Liao *et al*. (2005)
7	Friedel–Craft (acylation)	Bis{(trifluoromethyl)sulfonyl}amine ($HNTf_2$) or BF_3-Et_2O/[bmim]BF_4	Hakala and Wahala (2006)
8	Pechmann	[bmim]HSO_4	Singh *et al*. (2005)
9	Beckmann Rearrangement	In(OTf)/[bdmim]PF_6	Sugamoto *et al*. (2011)
10	Morita–Baylis–Hillman	H_2O/DABCO/[bmim]PF_6	de Souza *et al*. (2008)
11	Heck coupling	Pd/C/[omim]BF_4	Xie *et al*. (2004)
12	Pictet–Spengler	[bmim]Cl–$AlCl_3$	Srinivasan and Ganesan (2003)

Microwave heating can have certain benefits over conventional heating:

- Drastic reduction in reaction times i.e. acceleration in rate of reaction
- Improved chemical yields
- Higher energy efficiency
- Possibility of solventless reactions
- Operational simplicity
- different reaction selectivities

Most ionic liquids are salts of organic cations with high temperatures above 100o C, chemical and thermal stability, inflammability and electrochemical ability. In general, ionic liquids act as organic solvents and catalysts. In this chemical process, not only desired products are produced, but also many undesirable and negative products in the form of solids, liquids and gases. They have become the most difficult thing that chemistry has to face. So we need to learn the problem and reduce the amount of chemicals. We have done a lot of work in this direction in the last decade. The aim is to develop drugs and chemical processes that are less harmful to human health and the environment. Chemists, scientists, and pharmaceutical companies should consider the principles of green chemistry when designing reaction mechanisms and selecting catalysts. With

the use of green chemistry, we can reduce waste, reduce chemical use, control the atomic industry and protect the environment, which is our future. This research focuses on the synthesis of heterocyclic compounds in ionic liquids and the characterization and evaluation of the biological activities of these heterocyclic derivatives.

IV.CONCLUSION

Green chemistry principles has gained much popularity. It is one of the best techniques in green chemistry by which many important compounds can be synthesized in an efficient & environment friendly manner.In that Solvent free synthesis, MW-assisted,ionic liquidcatalysed reactions,water mediated reactions plays a vital over the classical method of synthesis. Some of the important advantages are as follows -

1. Prevention of waste/by-products.
2. Designing of safer reactions.
3. Maximum incorporation of the reactant (startingmaterial & reagents) into the final products.
4. Prevention or minimization of hazardous products.
5. Products obtained are mostly biodegradable.
6. Energy requirement for such synthesis is minimum.
7. Prevention of harsh reaction conditions.
8. High yields of products.
9. Shorter reaction time.
10. High selectivity in many of the reactions.
11. Prevention of the use of harmful solvents.
12. Easy extraction process.

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Synthesis, Characterization and Biological Active Thiazolidinones Derivatives

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ABSTRACT

Thiazolidinone and its derivatives is measured as biologically crucial compound that possesses almost antibacterial and antifungal biological activities. Some new 1,3-thiazolidin-4-ones synthesized from Schiff bases by conventional method. Synthesized fully thiazolidinone compounds were analysed for their antibacterial and antifungal biological activities. The refereed organic reactions of heterocyclic compounds occur with good yields from aldehydes, amine and mercaptoacetic acid by this method. All the synthesized products were verified for their antibacterial and antifungal activities. The results of the assessments presented that some of the synthesized compounds are effective antibacterial as well as antifungal agents.

KEYWORDS: - Schiff bases, mercaptoacetic acid, Thiazolidinones derivatives.

I. INTRODUCTION

Thiazolidinones1-3 and its derivatives show many prominent biological activities such as bactericidal, anticonvulsant, antifungal, antituberculotic. The heterocyclic compounds are contents nitrogen and sulphur have basic elements they got vast importance in organic and medicinal chemistry4-7. A lot of research work on thiazolidinones has been done in the past. The thiazolidinones nucleus is wonder nucleus because it gives out different derivatives with all different types of biological activities8. They have been reported as novel inhibitors of the bacterial enzyme Mur B which is precursor acting during the biosynthesis of peptidoglycan as non-nucleoside inhibitors9-12 of HIV-RT, anti-histaminic agents, anticancer, antitumor, diuretics, anti-inflammatory, antidiabetic nematocidal, and anti-viral. Certain organic transformations which need some hours completed reactions. Thiazolidinone derivatives have varied therapeutic and pharmaceutical activities and are used in probe design12-14.. The novel synthesis of thiazolidine derivatives using various agents is debated with respect to yield, purity and pharmacokinetic activity. The accessible clinical applications in various biological areas are critically reviewed. These data provide useful information for designing next-generation drug candidates. Developing multifunctional drugs and improving their activity should be a focus of research. In view of these findings large number of thiazolidinones have been widely investigated from the aldimine source

however significant attention have not given when precursors are aldimines. This report prompted us to synthesize some novel 4-thiazolidinones from aldimines by using conventional method as good synthetic route and to judge their bio potential.

II. EXPERIMENTAL

Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a FTIR Perkin-Elmer spectrometer. 1HNMR spectra were recorded on Avance 300 MHz spectrometer in DMSO solvent. To enhance the results nitrogen was bubbled through the sample to remove the oxygen. Mass spectra were taken on Agilent 5973 N LC-MS. Nutrient agar was used as culture for antibacterial activity and potato dextrose agar was used as culture for antifungal activity and DMSO was used to dissolved compounds. All used substituted aldehydes, substituted anilines, gla. acetic acid, ethanol, mercaptoacetic acid, DMF solvent were purchased from SD fine Chemicals.

General Procedure for Synthesis of Thiazolidinones: -

Procedure for synthesis of thiazolidinones are two steps in first step synthesis of Schiff bases and second step formation of thiazolidinones.

Step:Ist

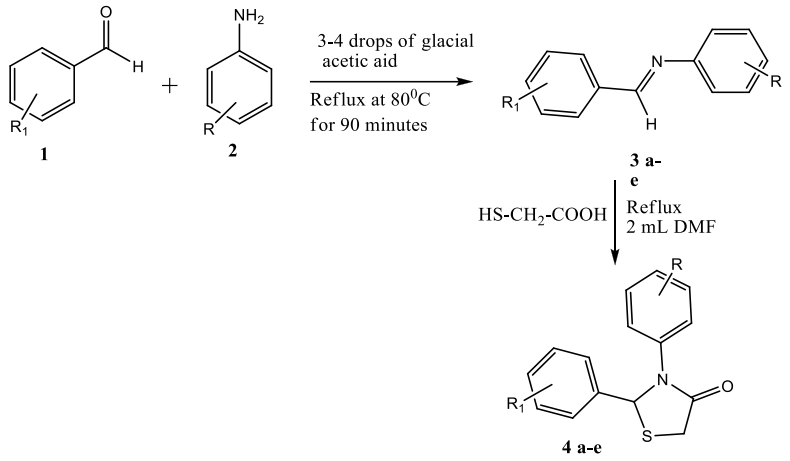
The equimolar amount of aldehyde (0.01mole) and aniline (0.01mole) with 3,4 drops of glacial acetic acid as a catalyst, 5 ml ethanol reflux 90 minutes in round bottom flask. The reaction mixture was poured on ice cubes, it was washed with 10% sodium bicarbonate followed by water. The obtained solid crystals were filtered, dried and recrystalized from ethanol to obtained pure crystals of Schiff bases. Completion of reaction monitored by TLC.

Step:IInd

This synthesised Schiff bases(0.01mole) dissolved in solvent DMF, freshly distilled mercaptoacetic acid (0.01mole) was added slowly to it. The mixture was stirred firstly few minutes and then refluxed them.It was poured on ice cubes, it was washed with 5% sodium bicarbonate (10ml) followed by water (25 ml). The obtained solid was filtered, dried and recrystalized from ethanol to obtained pure crystals of desired compounds 4(a-e).

III.RESULTS AND DISCUSSION

4-Thiazolidinones were synthesized from different Schiff bases (Scheme 1). Both analytical and spectroscopic data of all the synthesized compounds are in agreement with the proposed structures. Assignments of chosen characteristic of IR band positions provided significant sign for the formation of the thiazolidinones. Synthesized thiazolidinones shows absorption at 1687-1716 cm-1 for C=O confirms formation of thiazolidinone, which was supported by the absence of absorption bond at 1615-1636 cm-1 for C =N. Compound shows band near 660cm-1 due to C-S-C and 1455 cm-1 due to C-N. The band near 1455-1585 cm-1 is for C=C aromatic stretch, in addition, confirmation for the formation of thiazolidinone was obtained from the 1HNMR spectra, which provide indicative tools for the positional elucidation of the protons. Singlet appears at δ 3.6-4.25 due to S-CH2-conforming cyclization. The mass spectra of the synthesized compounds show the molecular ion peak confirming the molecular weight of the compounds.



3-(4-substitutedphenyl)-2-(4-substitutedphenyl) thiazolidin-4-one

Scheme 1: - Synthesis of 4-thiazolidinone from Schiff bases

4a:	**R=H**	**R_1=H**	**4b:**	**R=4-Cl**	**R_1=4-CH_3**
4c:	**R=H**	**R_1=4-OCH_3**	**4d:**	**R=4-Cl**	**R_1=4-Cl**
4e:	**R=4-NO_2**	**R_1= H**			

1) 2,3 diphenylthiazolidin-4-one (4a): Yield- 78%; M.P.-1380C, IR(KBr): 1682(C=O), 1545(C=C), 685(C-S) cm-1; 1HNMR(CDCl3): -δ3.55(s,2H, S-CH2), 3.74(s, 1H, S-CH-N, J=6.5 Hz),7.15-7.65 (m, 10H), ppm; M.S.- m/z-256M+, Anal. Caled for C15H13NOS; C,70.68; H, 5.16; N,5.54, S, 10. 43 Found: C, 70.80; H, 5.07; N, 5.13. S, 10.32.
2) 3-(4-Chloro-phenyl)-2-p-tolyl-thiazolidi-4-one (4f): - Yield-74%; M.P. -193OC IR (KBr) :1710(C=O), 1590 (C=C), 670 (C-S) cm-11HNMR (CDCl3) :- δ3.68 (s, 2H, S-CH2), 2.30 (s, 3H, p-totyl CH3), 3.60 (s, 1H, S-CH-N, J=6.50 Hz; 6.50-6.80 (m, 8H), ppm; M.S.- m/z -301 M+, Anal. Calcd for C16H14ClNOS: C, 64.69; H, 4.46; Cl, 11.61; N, 4.28; O, 5.12; S, 10.45. Found: C, 62.34; H, 4.20; N, 4.10; O, 4.95; S, 10.23.
3) 2-(4-methoxy-phenyl)-3-phenyl-thiazolidin-4-one (4c): -Yield - 68%; M.P.-1350C; IR(KBr) :1710(C=O), 1605(C=C), 690(C-S) cm-1 ;1HNMR (CDCL3) :- δ3.40 (S, 3H J=6.5 Hz), 7.30 (s, 5H), 7.43 (dd, 4H, J=8.0 Hz), 3.85(s, 1H), 3.55 (s, 2H, S-CH2), ppm; M.S.-m/z-284M+, Anal. Calcd for C16H15NO2S: C, 66.24; H, 5.20; N, 4,65; O,11.10;S,11.10. Found: C, 65.87; H, 4.75; N, 4.85; O, 10.85; S, 10.90.
4) 2,3-bis(4-Chloro-phenyl)-thiazolidin-4-one (4d): -Yield-71%, M.P.- 1230C; (KBr) IR: 1710 (C=O), 1590(C=C), 685(C-S) cm-1; 1HNMR (CDCl3):- 3.60 (s, 1H, S-CH-N, J=6.50 Hz), 7.33 (m 4H, J=8.5 Hz), 7.10(s, 4H, J=8.0 Hz), 3.80 (s, 2H, S-CH2), ppm; M.S.- m/z -319M+ , Anal. Calcd for C15H11Cl2NOS: C, 55.49; H, 3.47; Cl, 21.75; N, 4.28; O, 4.82; S, 9.82. Found: C, 55.98; H, 3.24; N, 4.31; O, 4.75; S, 9.73.
5) 3-(4-NO2-phenyl)-2-phenyl-thiazolidi-4-one (4g): - Yield-64%; M.P. -126OC IR (KBr) :1720(C=O), 1545 (C=C), 680 (C-S) cm-11HNMR (CDCl3) :- δ 4.10 (s, 1H, S-CH-N), 7.38 (d, 4H, J=8.3Hz, C-4H),7.18 (d, 5H, J=8.5 Hz,),3.48 (s, 2H, S-CH2)ppm; M.S.- m/z -302 M+, Anal. Calcd for C15H12N2O3S: C,58.52; H, 4.17; N, 9.22, O, 15.42; S, 10.21. Found: C, 54.20; H, 4.01; N, 9.88; O, 14.88; S, 9.94.

IV.CONCLUSION

Novel thiazolidinones were synthesized from Schiff bases using conventional methods which offers advantages such as improved yields of products and these above synthesized thiazolidinones shows good antibacterial and antifungal activities.

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Synthesis, Structural and Electro-Magnetic Properties of Nanocrystalline $Li_{0.5}Al_{0.5}Fe_2O_4$ Spinel Ferrite Prepared Via Sol-Gel Route

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ABSTRACT
An influence of Al3+ ions substitution on lithium ferrite of chemical formula Li0.5Al0.5Fe2O4 for its structural, electrical, and magnetic properties is presented here. The sample was synthesized by sol-gel route using nitrates as raw materials and citric acid as a fuel. The prepared powder was annealed at 500 0C for 4h for better crystallization. XRD pattern has confirmed the formation of spinel structure. Raman spectra were recorded in the range of 200-800 cm-1 at room temperature which supported the confirmation of formation of cubic structure. The DC electrical resistivity was carried out by standard two-probe technique as a function of temperature which exhibited the semiconducting nature. The activation energy, drift mobility, charge carrier concentration, diffusion coefficient and Curie temperature were obtained from the Arrhenius plot. The magnetic parameters deduced from M-H loops studied at room temperature representing a ferrimagnetic nature of the prepared sample.

Keywords: XRD pattern, Raman spectra, Arrhenius plot, M-H loop

I. INTRODUCTION

Ferrites composed of ferric oxide (Fe_2O_3) and metal oxide (MO) and are characterized by ferrimagnetic properties. These materials exhibit simultaneous electrical and magnetic properties, leading to their classification as magnetic semiconductors. There are three main types of ferrites based on their crystal structure: spinel ferrites, hexagonal ferrites, and garnets. Spinel ferrites represented by the general chemical formula MFe_2O_4, where M denotes a divalent or trivalent transition metal ion (e.g., Ni, Cu, Zn, Co, Al, Cr) with an average valency of two or three, form an interlocking network of positively charged metal ions and negatively charged divalent oxygen ions. The crystal structure of spinel ferrites involves relatively large oxygen anions arranging in a cubic close packing, occupying specific interstitial sites with metal ions.

Nanocrystalline spinel ferrites have gained significant attention for their unique properties and diverse technological applications, including phase shifters, circulators, gyrators, multi-layer chip inductors, targeted drug delivery, hyperthermia, cancer treatment, catalysts, and gas sensors [1-5]. The electrical and magnetic

properties of nano ferrites surpass their bulk counterparts, with grain boundaries playing a crucial role in their electrical transport properties.

Various synthesis methods, such as co-precipitation, micro-emulsion, hydrothermal, and sol-gel auto-combustion, have been developed for spinel ferrite nano particles preparation. The structural, electrical, dielectric, and magnetic properties are strongly influenced by synthesis parameters, including stoichiometric proportion, synthesis temperature, pH, sintering temperature, and sintering time. Sol-gel auto-combustion is a preferred technique due to its advantages, including controlled stoichiometry, fine particle size distribution, purity, homogeneity, ease of preparation, low cost, and simplicity.

Lithium ferrite [6], among spinel ferrites, is extensively studied for its relevance in constructing electromagnetic and microwave devices. The inverse cation distribution in bulk lithium ferrite contributes to ferrimagnetic ordering of magnetic moments, making it suitable for applications like isolators, gyrators, phase shifters, and circulators. Additionally, lithium ferrites play crucial roles in lithium batteries, microwave latching devices, magnetic switching circuits, and exhibit desirable properties such as high Curie temperature, temperature stability of saturation magnetization, ease of preparation, and cost-effectiveness.

The aim of the present work was to synthesize the nanoparticles of $Li_{0.5}Al_{0.5}Fe_2O_4$ using wet chemical synthesis route. Further, to study the structural, DC electrical resistivity, and magnetic properties.

II. METHODS AND MATERIAL

The synthesis of $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles was achieved through the sol-gel auto-combustion method at a remarkably low temperature. The raw materials employed in this process included lithium nitrate ($LiNO_3$), aluminum nitrate ($Al(NO_3)_3.9H_2O$), ferric nitrate ($Fe(NO_3)_2{\cdot}9H_2O$), citric acid ($C_6H_8O_7.H_2O$), and ammonia (NH_3), all of high purity (99% pure, AR Grade). The synthesis procedure involved dissolving the metal nitrates and citric acid in distilled water, with a stoichiometric proportion of 1:3 between metal nitrates and fuel. The mixture was stirred until a homogeneous solution was obtained. Subsequently, drop-by-drop ammonia solution was added to adjust the pH to 7. The solution was continuously stirred and heated to 100 °C on a hot plate with magnetic stirring. Upon the formation of a sol-gel, a highly viscous gel, the temperature was further increased to 120°C, initiating gel ignition and resulting in loose powder formation. The as-burnt powder was ground using an Agate Mortar and Pestle, and for enhanced crystallization, it was sintered at 500 °C in a muffle furnace under ambient air conditions for 4 hours, followed by cooling to room temperature.

Characterizations:

$Li_{0.5}Al_{0.5}Fe_2O_4$ was synthesized using the sol-gel auto-combustion method, and their properties were analyzed through various characterization techniques. The sintered $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles underwent crystalline phase examination using powder X-ray diffraction (XRD) with Cu-Kα radiation (λ=1.540 Å). The XRD scans were conducted at room temperature, scanning in the range of 10° to 80° with steps of 0.04°/Sec. Raman spectra in the range of 200 cm^{-1} to 800 cm^{-1} were recorded using Raman spectrometer. The excitation laser source employed in the system was He-Ne 632.8 nm. To assess the electrical and magnetic properties, the synthesized powders were pelletized by adding 2% polyvinyl alcohol (PVA) as a binder, forming circular pellets with a diameter of 13 mm and thickness of 2 mm. These pellets were then sintered at 500 ˚C for 4 hours in an air environment to eliminate the PVA. Silver paste was applied on both sides of the pellet to ensure good ohmic contact. DC resistivity measurements were performed on each sample using the standard two-probe method

within a temperature range of 300-850 K. The magnetization behavior was studied through the pulse field hysteresis loop tracer technique at room temperature.

III.RESULTS AND DISCUSSIONS

XRD

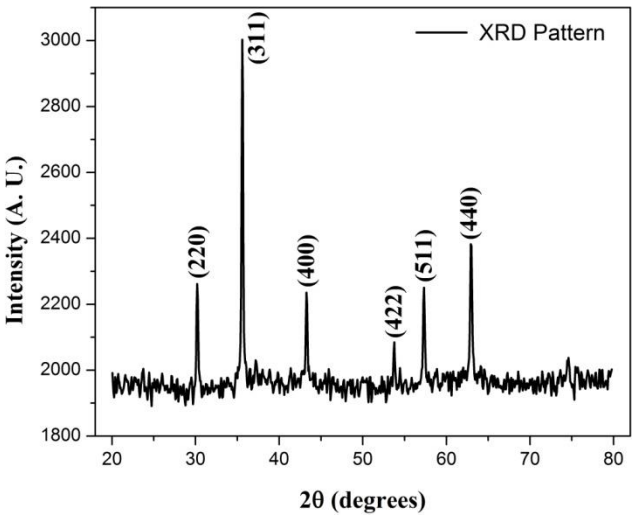

Fig. 1: XRD pattern of $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles

Figure 1 displays the XRD pattern of $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles. XRD pattern exhibits distinct reflections indicative of a cubic spinel structure. The reflections at planes (220), (311), (400), (422), (511), and (440) were identified using Bragg's law, confirming the cubic spinel structure for all samples. Notably, the reflection peaks are intense and sharp, with no impurity peaks observed, confirming the single-phase nature of the samples. The intensity of the (311) plane is maximum among the reflections. Using standard formulae [7, 8] various structural parameters were obtained using XRD data.

Lattice Parameter:

$$a = d\sqrt{h^2 + k^2 + l^2} \quad \text{Å} \qquad \ldots\ldots (1)$$

Lattice parameter, calculated using formula (1) is 8.316 Å, showing a decrease in 'a' with the substitution of Al^{3+} ions compared to its parent sample (8.331 Å). This aligns with the smaller ionic radius of Al^{3+} compared to Fe^{3+}, resulting in lattice shrinkage.

Crystallite size:

$$t = \frac{0.94\lambda}{\beta \cos\theta} \quad \text{nm} \qquad \ldots\ldots (2)$$

The crystallite size, determined using the Debye Scherrer formula (2), was of the order of 19 nm.

X-ray density: The X-ray density of the prepared samples was calculated using the relation (3)

$$d_x = \frac{nM}{a^3 N} \quad \text{g/cm3} \qquad \ldots\ldots (3)$$

X-ray density (4.448 gm/cm^3), decreased on Al^{3+} substitution compared to parent sample (4.760 gm/cm^3), possibly due to the combined effects of decreasing molecular weight and lattice parameter. This is supported by the decrease in both molecular weight and lattice parameter with Al^{3+} substitution.

Experimental density

Experimental density (4), obtained through Archimedes principle, also decreases with Al^{3+} substitution.

$$d_E = \frac{Wt\ of\ \text{the sample in air}}{Wt\ of\ \text{the sample in air} - Wt\ of\ \text{the sample in xylene}} \times Density\ of\ Xylene$$

gm/cm^3.... (4)

Porosity

Porosity, calculated using the experimental density (d_E) and X-ray density (d_X) values, was of the order of 8.7%.

$$p = 1 - \frac{d_E}{d_x} \quad \% \quad \ldots (5)$$

Raman Spectroscopy

Raman spectroscopy [9] proves highly sensitive to material disorder and serves as a valuable tool for investigating the structural characteristics of various materials. In Figure 2, Raman spectra for $Li_{0.5}Al_{0.5}Fe_2O_4$, are presented across the 200-800 cm^{-1} range at room temperature. The recorded Raman spectra exhibit three first-order Raman active modes: A_{1g}, E_g, and T_{2g}. These modes correspond to specific structural phenomena, where A_{1g} and E_g result from the symmetric stretching of oxygen atoms along Fe-O bonds and the bending of oxygen in relation to Fe, respectively. The T_{2g} mode arises from the asymmetric stretching of Fe. The Raman spectrum depicted in Figure 2 aligns with the findings reported [10].

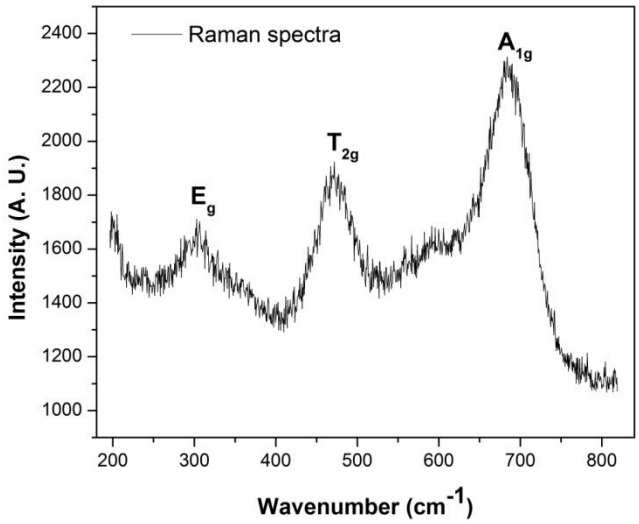

Fig. 2: Raman spectra of $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles

DC Electrical resistivity

DC electrical resistivity measurements of $Li_{0.5}Al_{0.5}Fe_2O_4$ were performed over a temperature range of 300-950 K using the standard two-probe method. Figure 3 illustrates the variation of the logarithm of resistivity against the reciprocal of temperature. The resistivity plot clearly indicates that the electrical resistivity of lithium spinel ferrite sample decreases with the temperature. This behavior aligns with semiconductor characteristics, following the well-established Arrhenius relation.

)

$$\rho_{DC} = \rho_o \exp\left(\frac{\Delta E}{kT}\right) \quad \ldots\ldots (6)$$

where, ΔE represents the activation energy, k is the Boltzmann constant and T denotes the absolute temperature. The DC electrical resistivity plot depicted in Figure 3 reveals two distinct regions with varying slopes. These regions are identified as the ferrimagnetic and paramagnetic regions. Utilizing equation (6) and

the slope values obtained from the resistivity plot, activation energies corresponding to the ferrimagnetic and paramagnetic regions were determined.

Table 1 provides the values of activation energies for both the paramagnetic and ferrimagnetic regions. Notably, higher activation energy value is observed for the paramagnetic region compared to the ferrimagnetic region, suggesting a correlation with disordered states. The low activation energy in this case suggests that the conduction mechanism is attributed to electron hopping ($Fe^{3+} \leftrightarrow Fe^{2+}$). During the sintering process, some Fe^{2+} ions transform into Fe^{3+} ions, generating electrons that participate in the conduction mechanism.

The coexistence of Fe^{2+} and Fe^{3+} ions on equivalent lattice sites (octahedral B-site) may contribute to the low resistivity observed. Figure 3 also indicates a change in slope at a certain point, potentially related to exchange interactions determining the Curie temperature for that composition. The Curie temperature, as obtained from the DC resistivity plot is 510 °C.

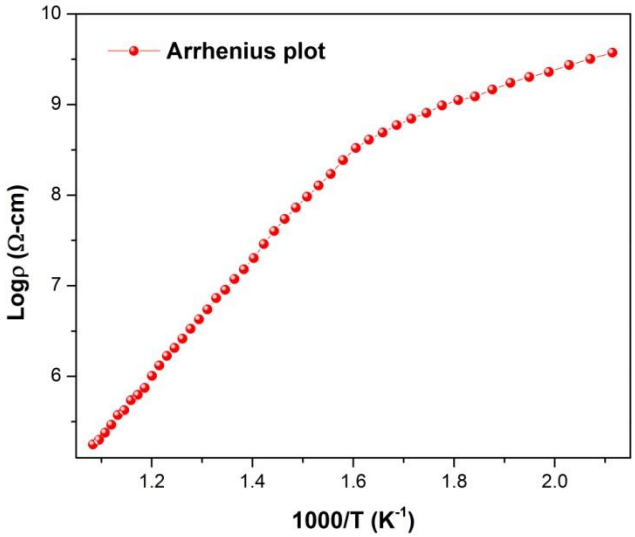

Fig. 3: Arrhenius plot of $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles

Table 1: Activation energy in paramagnetic (E_p) region, ferrimagnetic (E_f) region, change in energies (ΔE), Curie temperature and charge carrier concentration (CCC), diffusion coefficient

E_p (eV)	E_f (eV)	ΔE (eV)	Tc (°C)	CCC (10^{23}/atoms)	Diffusion coefficient	
					At 473k	At 973k
0.374	0.098	0.276	510	1.095	9.53×10^{-8}	4.52×10^{-7}

Drift mobility, charge carrier concentration and the diffusion coefficient

The drift mobility, charge carrier concentration, and diffusion coefficient for $Li_{0.5}Al_{0.5}Fe_2O_4$ was calculated using the provided relations [11].

$$\mu_d = \frac{1}{ne\rho} \quad \ldots\ldots. (7)$$

$$n = \frac{N_A d_B P_{Fe}}{M} \quad \ldots\ldots. (8)$$

$$D = \frac{\sigma k_B T}{Ne^2} \quad \ldots\ldots. (9)$$

Here, PFe represents the number of iron atoms, and all other symbols retain their conventional meanings. Figure 4 illustrates the mobility of $Li_{0.5}Al_{0.5}Fe_2O_4$ spinel ferrite, calculated using relation 7. As depicted in Figure

4, the mobility exhibits an increasing trend with rising temperature. This behavior aligns with the observed decrease in resistivity with elevated temperature. The charge carrier concentration, determined through relation 8 is presented in Table 1. Notably, the charge carrier concentration is 1.095×10^{23}/atoms. The observed increase in charge carrier concentration can be attributed to a reduction in molecular weight. The diffusion coefficient, obtained using relation 9, exhibits an upward trend with rising temperature. This inverse correlation with resistivity and direct relationship with conductivity elucidate the increase in the diffusion coefficient. Additionally, the potential reduction in oxygen vacancies in the sublattice due to Al^{3+} substitution contributes to the observed increase in the diffusion coefficient.

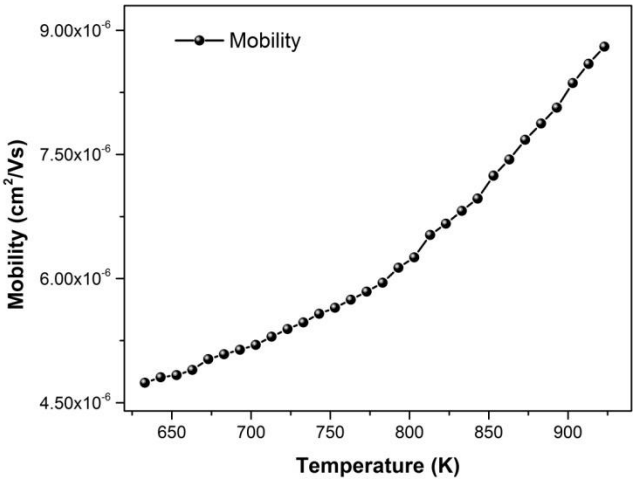

Fig. 4: Mobility of $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles

Magnetic Properties

Table 2 illustrates the magnetic parameters obtained from M-H curve for $Li_{0.5}Al_{0.5}Fe_2O_4$ utilizing the pulse field hysteresis loop tracer technique at room temperature.

Table 2: Saturation magnetization (M_s), remenance magnetization ((M_s), coercivity (H_c), magneton number (), anisotropy constant (), and anisotropy field ()

M_s (emu/gm)	M_r (emu/gm)	H_c (Oe)	η_B (μ_B)	K (emu/gm)	H_k (emu/gm)
38.88	13.46	144.93	1.416	5750.03	295.78

Lithium spinel ferrite is known for displaying square hysteresis loop, and in this study, the observed hysteresis loop closely resemble that reported by [12]. The magnetic parameters, including saturation magnetization, remanence magnetization, and coercivity, were derived from the M-H plot and are presented in Table 2. The observed magnetization pattern in this study can be elucidated based on Neel's model of magnetization for ferrimagnetic ferrites. According to Neel's model, the magneton number can be determined using the following relation.

$$\eta_B^N = M_B - M_A \quad \ldots\ldots. (10)$$

Where M_B represents the magnetic moment on the B-site, and M_A denotes the magnetic moment on the A-site. The observed increase in saturation magnetization with Al^{3+} substitution may be attributed to a reduction in the magnetic moment in sublattice (A), leading to an increase in the net magnetic moment. It is noteworthy that coercivity values up to 200 Oe suggest single-domain behavior, indicating a crystallite size in the nanometer range.

The anisotropy constant and anisotropy field were determined using the provided relations [13].

$$K = \frac{M_s \times H_c}{0.98} \text{ ..... (11)}$$

$$H_K = \frac{2K_1}{M_s} \text{ ..... (12)}$$

Where all the symbols maintain their usual meanings, the computed values of anisotropy constant and anisotropy are presented in Table 2. Notably, the anisotropy constant displays an increase which can be attributed to the rise in saturation magnetization and coercivity values.

IV.CONCLUSION

The utilization of the sol-gel auto-combustion method with citric acid as a fuel proved successful in synthesizing $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles. Both XRD and Raman techniques validated the formation of spinel ferrite. $Li_{0.5}Al_{0.5}Fe_2O_4$ ferrite displayed a semiconducting nature. The DC resistivity exhibited a downward trend with increasing temperature. M-H curve exhibit the ferrimagnetic nature of $Li_{0.5}Al_{0.5}Fe_2O_4$ nanoparticles.

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An Overview On Some Cyclooxygenase-2 Inhibitor Drugs Used in Management of Pain and Inflammation

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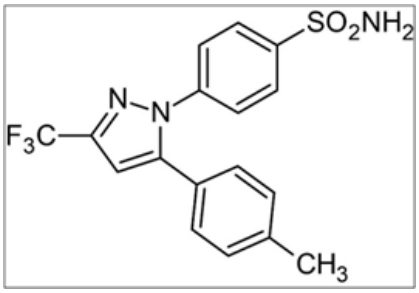
ABSTRACT
Cyclooxygenase-2 (COX-2) inhibitors are widely used in management of pain, fever and inflammation belongs to the class of non-steroidal anti-inflammatory drug (NSAID). It is one of the important class of NSAIDs used in management of pain, fever and inflammation. In present review we have collected information of Celecoxib, Etoricoxib, Rofecoxib, Valdecoxib regarding their uses, absorption, half-life, mechanism of action, adverse effects, drug interaction etc.
Key words: Celecoxib, Etoricoxib, Rofecoxib, Valdecoxib

I. INTRODUCTION

COX-2 enzymes produces prostaglandins that are mainly involved in inflammation. COX-2 inhibitors extensively block inflammation. Cyclooxygenase-2 (COX-2) inhibitors are a type of NSAID's (nonsteroidal anti-inflammatory drugs) that selectively blocks COX-2 enzymes. Nonsteroidal anti-inflammatory agents are one of the group of medicines that are significantly used in management of pain, fever and inflammation. [1,2,3].
COX-2 inhibitors directly target cyclooxygenase-2which reduces the risk of peptic ulceration. Clinical trials showed that COX-2 inhibitors caused a remarkable increase in heart strokes and attacks. Due this Rofecoxib was taken off the market in2004 and celecoxib marked with warnings on lable. Number of COX-2 selective inhibitors have been removed from the US market. Though celecoxib is permitted to use in US and etoricoxib is permitted to use in European Union. Some selective COX-2 inhibitors are used as a single dose in post-operative pain. [4,5]. Celecoxib shows pharmacological action as functional as ibuprofen [6].

Celecoxib:



Uses: It is used in treatment of mild to moderate pain, stiffness, inflammation and swelling associated with osteoarthritis, rheumatoid arthritis etc. Also used in treatment of ankylosing spondylitis, acute migraine headaches with or without aura. [7]

Absorption: By oral administration it is rapidly absorbed.

Metabolism: In liver, very low concentration less than 3% eliminated as unchanged. It is metabolized mainly by cytochrome P450 (CYP) 2C9 isoenzyme [8].

Excretion: Through feces and urine [9].

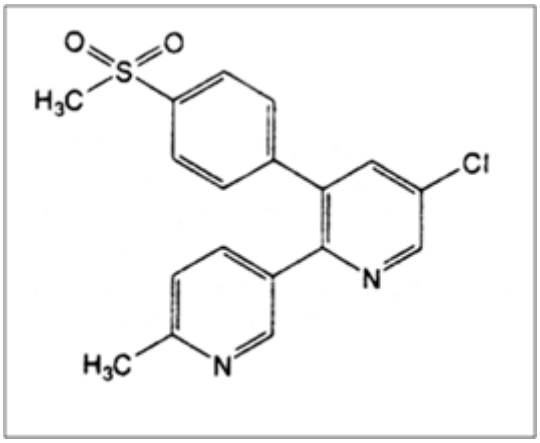
Half-life: For healthy individualsits elimination half-life is about 11 hours.

Mechanism of action: It acts by selective inhibition of cyclooxygenase-2 (COX-2) responsible for prostaglandin synthesis.

Adverse effects: nausea, vomiting, heartburn, dizziness, swelling, headache, skin rash, stomach pain, diarrhea, constipation etc.

Drug interactions: It interacts with warfarin, digoxin, blood pressure medications.

Etoricoxib:



Uses: It is used to reduce the pain and inflammation of muscles and joints in rheumatoid arthritis osteoarthritis etc.

Absorption: moderate absorption when given orally and intravenous doses. [10]

Metabolism: It is metabolized primarily by the cytochrome P450 (CYP) 3A4 isoenzyme [10].

Excretion: It is eliminated in urine and faeces after biotransformation to glucuronide and carboxylic acid metabolites [10].

Half-life: Its elimination half-life is approximately 22 hours.

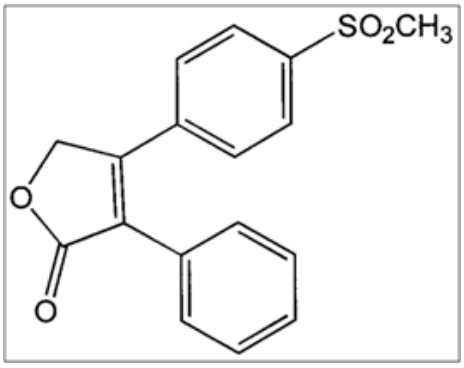
Mechanism of action: It selectively inhibits the isoform 2 of cyclo-oxigenase enzyme (COX-2) and prevents the production of prostaglandins from arachidonic acid. [11]

Adverse effects: nausea, dyspepsia, increased blood pressure, stomach pain, dizziness, palpitations, constipation etc.

Drug interactions:

It may interact with warfarin, aspirin, rifampicin, methotrexate, enalapril, ramipril, losartan, valsartan, minoxidil, diuretics, digoxin, salbutamol etc. It is used with caution in patients with liver diseases, stomach ulcers, colitis, severe kidney disease, heart problems. [12]

Rofecoxib:



Uses: It is used in the treatment of rheumatoid arthritis, osteoarthritis, primary dysmenorrhea, acute pain in adults, migraine attacks etc.

Absorption: Its bioavailability is 93% after oral administration.

Metabolism: In the liver.

Excretion: Primarily excreted through urine.

Half-life: 17 hours after oral administration.

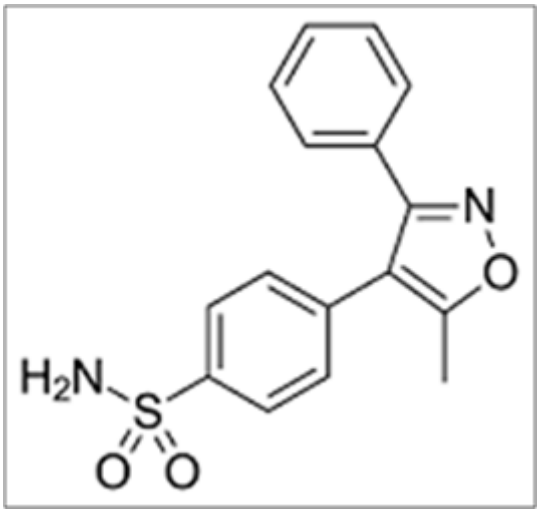
Mechanism of action: It involves inhibition of cyclooxygenase [13].

Adverse effects: dyspepsia, headache, diarrhea, dizziness, abdominal discomfort, hypersensitivity reactions etc.

Drug interactions: It interacts with alendronic acid, alfentanil, aliskiren etc.

Rofecoxib is withdrawn from market from 2004 due to increased risk of heart attacks after long term use.

Valdecoxib:



Uses: It is used in the treatment of rheumatoid arthritis, osteoarthritis, painful menstrual symptoms etc.

Absorption: After oral administration bioavailability is 83%.

Metabolism: In hepatic system.

Excretion: In urine and feces.

Half-life: Its elimination half-life varies from 8-11 hours. [13].

Mechanism of action: It involves the inhibition of prostaglandin synthesis mainly through inhibition of cyclooxygenase-2.

Adverse effects: swelling of the feet, fingers, face, legs, severe stomach pain, unusual weight gain, skin rash etc. [14]

Drug interactions: It may interact with medications including warfarin, digoxin, blood pressure medications etc.

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A Review of the Oxidative Behavior of Potassium Permanganate for Organic Compounds

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ABSTRACT

Permanganate has a long and illustrious history of usage in organic chemistry as an efficient oxidant. Industrial applications have recently become more environmentally appealing due to the advent of a technology for recovering manganese dioxide, a byproduct of these reactions. Permanganate technology is now more environmentally friendly and meets Brundtland Commission standards for sustainability owing to this recycling strategy. An overview of certain upcoming technologies is included along with a discussion of some possible and current industrial applications of permanganate oxidations. In this review, we also provide a summary of KMnO4 synthesis, characteristics, and reactive species. For the first time, the current review covers all aspects of KMnO4 as an oxidizing agent for the oxidation of organic molecules.

Keywords: Potassium Permanganate, Oxidation, Kinetics, Organic compounds.

I. INTRODUCTION

One of the most significant and frequently employed reactions in the synthesis of complex organic molecules is the oxidation process. As a result, scientists have created a vast array of oxidants with distinct functions. One of these, permanganate, is a general-purpose reagent that is adaptable, widely used and frequently cited.[1, 2]

Permanganate was a common oxidant utilized by early organic chemists, particularly for the oxidation of molecules with carbon-carbon double bonds. Kekule[3] and Wagner both documented its application for the *cis*-dihydroxylation of substances like fumaric and maleic acids more than a century ago.[1] Since then, a variety of oxidative reactions using permanganate have been revealed to be possible under certain conditions.[4-10]

Apart from its significance as a reagent for researchers, permanganate finds commercial application in the synthesis of numerous chemical molecules.[11-14] **Table 1** includes examples of substances that are made in large quantities with this oxidant in industry. The following article lists some of the applications for permanganate that are now in use, provides an overview of recent research findings and showcases innovative "green" technology that is being used to reduce harmful environmental effects.

Table 1. Industrially manufactured compounds derived from permanganate oxidations.

Sr. No.	Compounds	CAS no.
1.	Algestone Acetophenide	24356-94-3
2.	Acipimox	51037-30-0
3.	Finasteride	98319-26-7
4.	Cicloxilic Acid	57808-63-6
5.	Cetirizine	83881-51-0
6.	Dinicotinic Acid	499-81-0
7.	2-acetamidobenzoic acid	89-52-1
8.	Isocinchomeronic Acid	100-26-5
9.	Flumazenil	78755-81-4
10.	Metolazone	17560-51-9
11.	2,3-pyrazinedicarboxylic Acid	89-01-0
12.	Isonicotinic Acid	55-22-1
13.	Chlormezanone	80-77-3
14.	Trimethylpyruvic Acid	815-17-8
15.	Pyrazinamide	98-96-4
16.	2,6-pyridinedicarboxylic Acid	499-83-2
17.	Pyrazinoic Acid	98-97-5
18.	4-sulfobenzoic Acid	636-78-2
19.	Sulbactam	69388-84-7

1. Synthesis of $KMnO_4$

The Carus Chemical Company, a significant permanganate manufacturer has declared that it can now recycle manganese dioxide, a byproduct that arises when permanganate oxidizes organic substances. It helps to know that manganese dioxide ore is oxidized twice to form permanganate, which helps explain how this can be done economically.[15] As shown in Scheme 1, it is first oxidized by oxygen in a concentrated potassium hydroxide solution to potassium manganate (VI) and then it is electrochemically converted to potassium permanganate.

Scheme 1

$$MnO_2 \xrightarrow[KOH]{O_2} K_2MnO_4 \xrightarrow[\text{Electrochemical}]{-e^-} KMnO_4$$

Manganese dioxide, which is produced during the reduction of permanganate, can be recycled into permanganate or used for other purposes by following a similar procedure.[16] Currently, Carus recycles over 90% (several million pounds) of the manganese dioxide that results from organic oxides along with its permanganate on a yearly basis. The amount of solid waste generated during the production of permanganate is also decreased by roughly 20% when recovered manganese dioxide is used instead of ore.

Manganese dioxide was often disposed away in landfills as a waste product until Carus decided to recycle it. Nevertheless, the new strategy promotes the universal advantages of sustainable development as outlined by the Brundtland Commission because it is perpetually recyclable.[17]

2. Properties of $KMnO_4$

In media that are neutral, alkaline, or acidic, $KMnO_4$ is an extremely powerful oxidizing agent. The following equations illustrate oxidation in these media:

In acidic medium

$2KMnO_4 + H_2SO_4 \rightarrow K_2SO_4 + 2MnSO_4 + 3H_2O + 5\,[O]$ $MnO_4^- + 8H^+ 5e^- \rightarrow Mn^{2+} + 4H_2O$

In neutral and alkaline conditions

$2KMnO_4 + H_2O \rightarrow 2KOH + 2MnO_2 + 3\,[O]$ $MnO_4^- + 2H_2O + 3e^- \rightarrow MnO_2 + 4OH^-$

II. OVERVIEW OF EARLIER WORK DONE

3.1. Oxidation of organic compounds by $KMnO_4$

Potassium permanganate, or $KMnO_4$, is arguably the most often used oxidizing agent among all those covered in organic chemistry. Many different organic compounds can be oxidized with $KMnO_4$, as will be demonstrated below. The end products are frequently carboxylic acids because $KMnO_4$ is such a potent oxidizing agent. However, the compounds that are formed can vary depending on the conditions.

Under acidic conditions, Mn(VII) is reduced to Mn(IV) or Mn(II) in accordance with the half-reactions described below, with the indicated cell potentials.

$MnO_4^- + 4H^+ + 3e^- \rightarrow MnO_2 + 2H_2O$ $E^o = 1.68V$ (1)

$MnO_4^- + 8H^+ + 5e^- \rightarrow Mn^{2+} + 4H_2O$ $E^o = 1.5V$ (2)

$MnO_4^- + 2H_2O + 3e^- \rightarrow Mn^{2+} + 4OH^-$ $E^o = 0.6V$ (3)

Overall Reactivity with Organic Substances

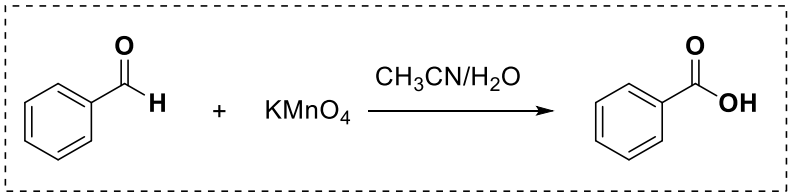
If carbon atoms have weak bonds $KMnO_4$ can oxidize them. Examples of such weak bonds include

1. Alkenes and alkynes, which contain carbon atoms bound by π bonds
2. Weak carbon-hydrogen bonds,
   - Those seen in substituted aromatic rings' alpha locations
   - C-H bonds in carbon atoms found in alcohols and aldehydes, which also contain C-O bonds
3. Particularly weak carbon-carbon bonds like those in a glycol molecule or carbon-carbon bonds next to both an oxygen atom and an aromatic ring

Reactions to Particular Functional Groups

We anticipate $KMnO_4$ to react with alcohols, aldehydes, alkynes, alkenes and aromatic side chains based on the previously mentioned principles. Below are some examples. Starting at the top is the easiest.

Aldehydes

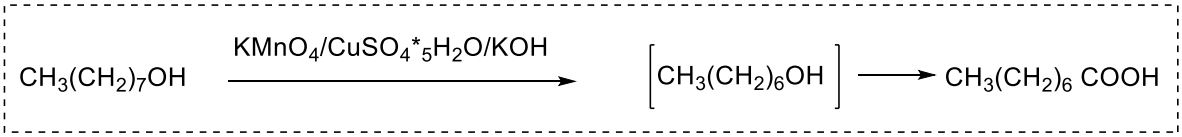


Carboxylic acids can be easily formed from aldehydes RCHO.

Under basic conditions, $KMnO_4$ oxidations likely to occur unless considerable care is taken to maintain a neutral pH. The ideal setup for $KMnO_4$ to oxidize aldehydes is actually t-butanol as the solvent combined with a NaH_2PO_4 buffer.[18] The aforementioned reactions are purposefully unbalanced equations. In order to balance the reactions, half reactions would be needed for each process, following the procedures covered in general chemistry.

Alcohols

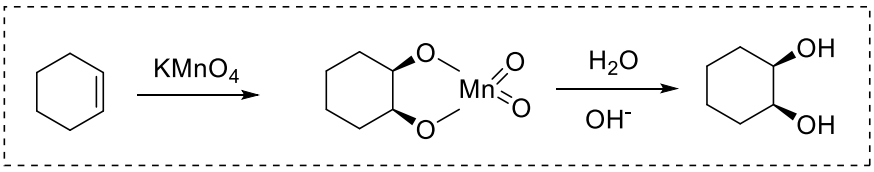
When basic copper salts are present, $KMnO_4$ can effectively oxidize primary alcohols such octan-1-ol.[19] Nevertheless, due to over oxidation the product is mostly octanoic acid with very little aldehyde.



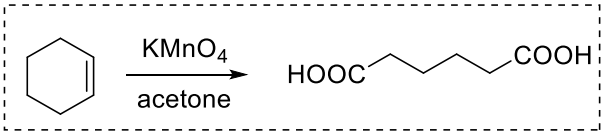
While secondary alcohols provide less of a risk for over oxidation, $KMnO_4$ is still not thought to be a good choice for converting alcohols to aldehydes or ketones.

Alkenes

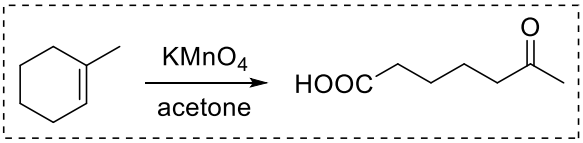
Potassium permanganate can convert alkenes[20] to glycols in mild circumstances. However, it can further oxidize the glycol by cleaving the carbon-carbon bond, so the reaction conditions must be carefully controlled. In the process of these oxidations, a cyclic manganese diester is created, leading to the formation of glycols through syn addition.



The C-C bond can be broken by further oxidizing the glycol with the addition of heat or more concentrated $KMnO_4$.



There will be more substituted olefins that end at the ketone.

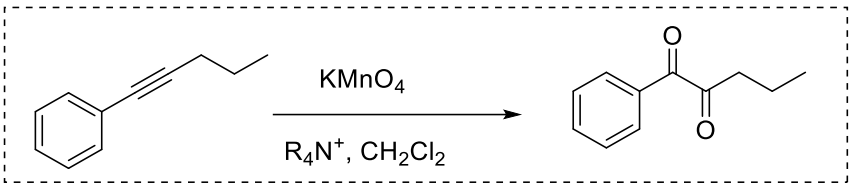


IO_4 can be used as an oxidant to more gently carry out the oxidative cleavage of the diol.

The location of double bonds in organic compounds can be ascertained by observing the breakdown of alkenes into ketones or carboxylic acids.[21]

Alkyne

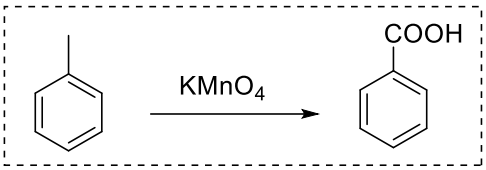
Diones are first formed when alkynes undergo permanganate oxidation, as instead of bis-hydroxylation, which happens with alkenes.



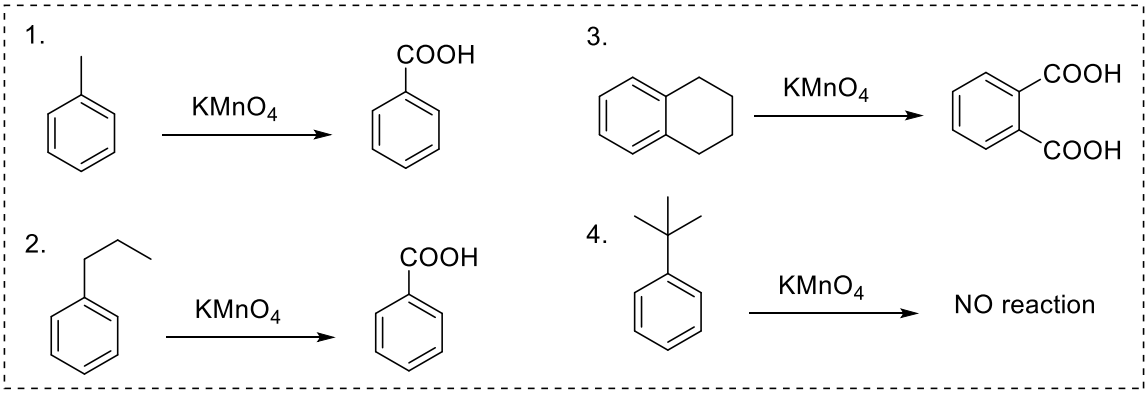
The Dione cleaves to generate two carboxylic acids in harsher circumstances.

Aromatic side-chains[6]

Benzoic acid is produced when potassium permanganate is applied to an alkylbenzene causing oxidation.



Only when the carbon has at least one hydrogen bonded to it can then proceed. On the other hand, the oxidation process continues till the carboxylic acid if there is at least one hydrogen present.



Take note that case 2's excess carbons cleave to produce the same result as example 1's. Additionally, two benzoic acids are produced in case 3. Lastly, no reaction takes place if there are no hydrogen atoms on the benzylic carbon (example 4).

In the past, qualitative analysis has been used to identify the locations of alkyl groups in substituted aromatic systems through the oxidation of alkyl side-chains to generate benzoic acids.

III.FACTORS AFFECTING OXIDATION OF ORGANIC COMPOUNDS BY KMNO4

3.2. Effect of concentration

The study of the reaction was conducted under different initial concentrations of the oxidant, but with constant sugar initial concentrations (sugars), constant temperature and constant pH ionic strength. The slopes of the plot of the logarithm of absorbance vs time have been used to calculate the first-order rate constants (k_{obs}) for different initial concentrations of $KMnO_4$. As the concentration of the $KMnO_4$ solution reaction increases, the first-order rate constants demonstrate a continuous increase as indicated by the result shown in Table 1. This is entirely reliant on the concentration of $KMnO_4$.

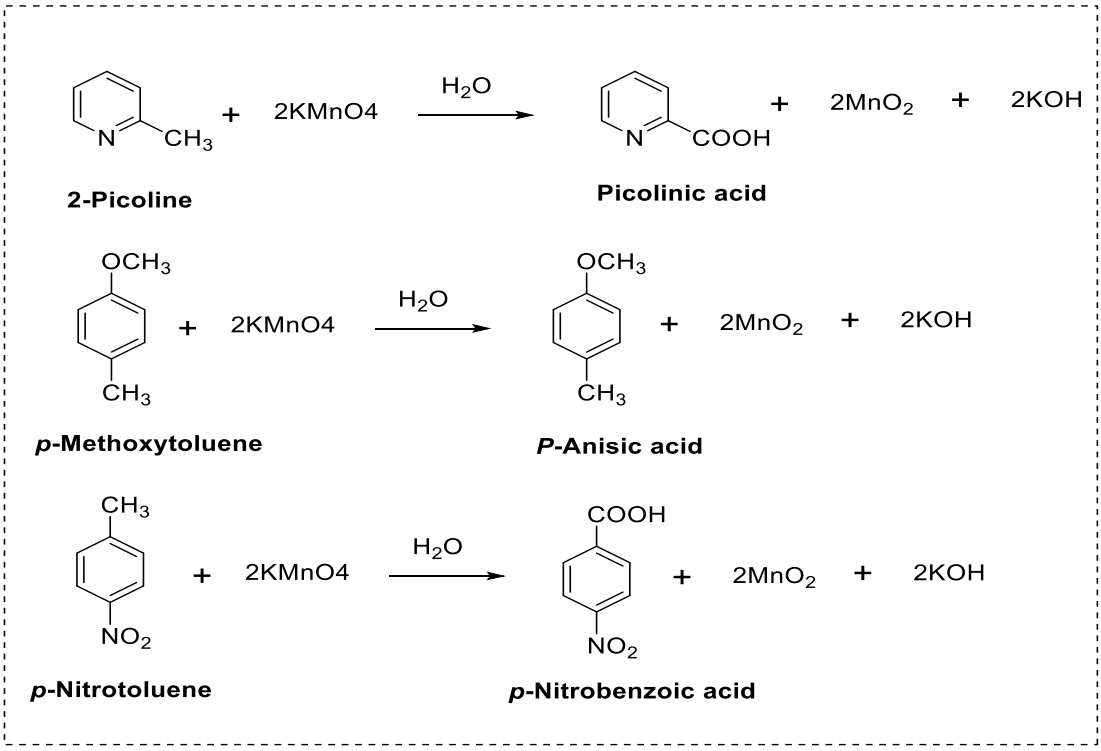
Table 2. Variation of rate constant with $KMnO_4$ concentration at t = 35°C, pH = 11.0, [KNO_3] = 0.2 M, [Sugar] = 0.005 M.

($KMnO_4$) X 10^{-4} M	GLUCOSE k_{obs}X 10^2 S^{-1}	FRUCTOSE k_{obs}X 10^2 S^{-1}	SUCROSE k_{obs}X 10^2 S^{-1}	MALTOSE k_{obs}X 10^2 S^{-1}	MANNITOL k_{obs}X 10^2 S^{-1}	SORBITOL k_{obs}X 10^2 S^{-1}
1.	-	11.70	1.20	2.20	9.00	2.43
2.	17.20	13.80	3.00	2.50	-	2.85
3.	22.70	16.20	3.50	2.60	15.00	2.94
4.	-	18.00	3.60	2.83	16.00	-
5.	23.70	18.20	3.70	-	17.00	3.05
6.	-	18.50	3.80	-	18.00	3.15
7.	-	19.00	3.90	3.00	20.00	3.83

3.3. Effect of solvent

The oxidant and the reductant must both be at least somewhat miscible in the solvent for a selective reaction to take place. For industrial uses an aqueous solutions are favored because permanganate is easily soluble in water. Compared to less concentrated potassium permanganate solutions, LIQUOX, a 40% solution of sodium permanganate, has numerous processing benefits. Since both base and acid can catalyze permanganate reactions in aqueous solutions, adjusting the pH can typically easily regulate the rate of reaction. Scheme 2 is a summary of common industrial operations that are conducted in aqueous solvents.

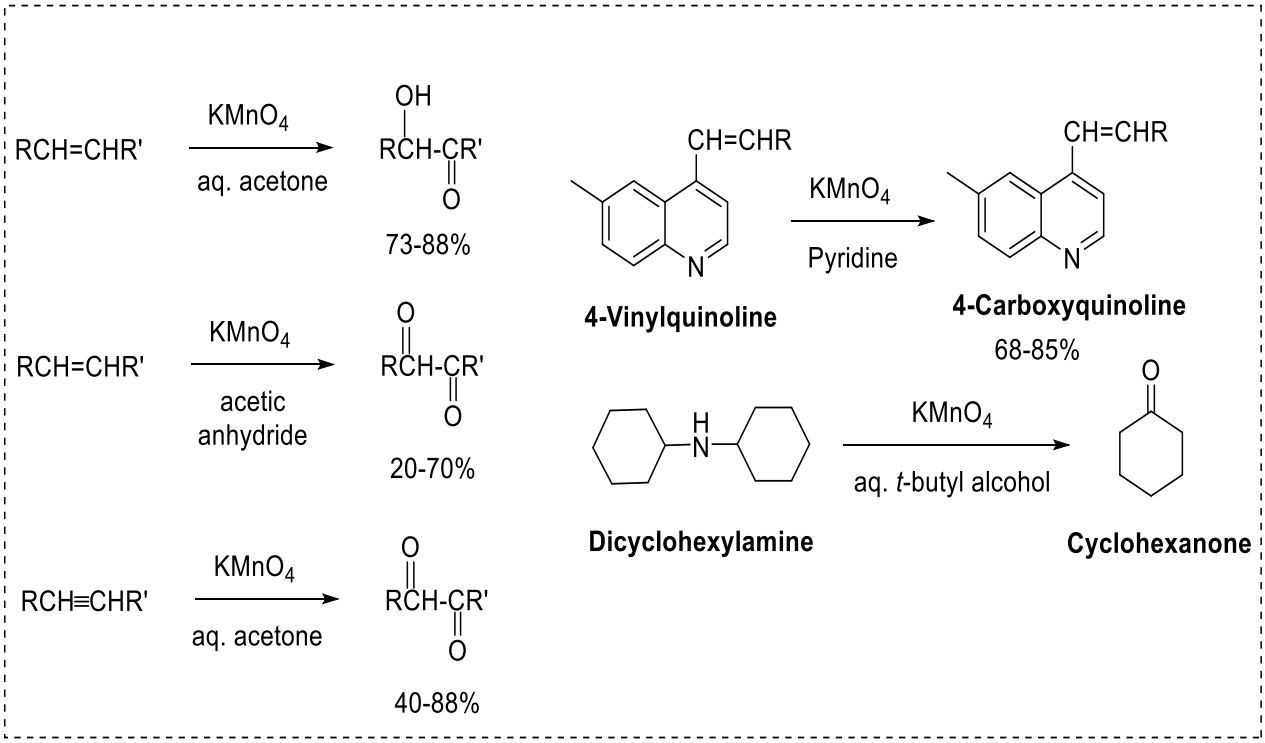
Scheme 2. Common oxidation processes in water-based solutions.[1]



Limitations that arise when an organic chemical is insoluble in aqueous solutions can be addressed by use a polar organic solvent, such as acetone, pyridine, or tert-butyl alcohol, whereby the reductant and oxidant are at least somewhat soluble. Because ethanol and 2-propanol can reduce permanganate at a pace that could compete

with the targeted reductant, other polar organic solvents like these are less helpful. Examples of reactions conducted in polar organic solvents or in mixes of aqueous and organic solvents are shown in Scheme 3.

Scheme 3. Common oxidation processes in polar organic solvents.[1]



Recently, it has been noted that Lewis's acids like boron trifluoride, ferric chloride, and zinc chloride catalyze permanganate oxidations in certain polar organic solvents. Scheme 4 contains typical instances of reactions that have been conducted under these circumstances.

It should be noted that in the third scenario, the sulfoxide sulfurs are oxidized preferentially, resulting in the sulfide and disulfide sulfurs being excluded.

3.4. Effect of Temperature

The sugars were oxidized at a range of temperatures, from 30 to 60°C, while keeping the concentrations of KNO_3 (0.2 M), $KMnO_4$ (0.005 M), substrates (0.1 M), and pH (11.00) constant. As the data in Table 2 demonstrate, the first order rate constant rises as temperature rises. The logarithmic plot of the second order rate constant as a function of the temperature in Kelvin was used to derive the Arrehenius parameters (i.e., Ea and A). Based on the slope of the linear plots, the Arrenhenius activation energy (Ea) values for the oxidation of glucose, fructose, mannitol, sorbitol, sucrose, and maltose are 80.77, 60.00, 42.86, 60.00, 60.78, and 46.59 kJ/ mole respectively, demonstrating the equivalent activation energy of fructose and sorbitol.

Table 3. Variation of rate constants with the KNO_3 concentration; T = 35 °C, pH = 11.0, $[KMnO_4]$ = 2.5 X 10^{-3} M, [Sugar] = 5.0 X 10^{-3} M

Sr. No.	(KNO_3) M	GLUCOSE $k_{obs}X10^2$ S^{-1}	FRUCTOSE $k_{obs}X$ 10^2 S^{-1}	SUCROSE $k_{obs}X$ 10^2 S^{-1}	MALTOSE $k_{obs}X$ 10^2 S^{-1}	MANNITOL $k_{obs}X$ 10^2 S^{-1}	SORBITOL $k_{obs}X$ 10^2 S^{-1}
1.	0.40	98.20	40.10	2.00	-	11.00	2.90
2.	0.30	-	36.10	1.90	2.95	4.00	2.40
3.	0.25	95.30	30.70	1.80	2.77	3.00	2.20
4.	0.20	89.50	23.30	1.60	2.42	-	-
5.	0.15	59.26	15.20	1.40	2.40	2.30	2.18
6.	0.10	40.56	12.85	1,20	2.38	2.00	2.10

IV.ECONOMICS OF THE PROCESS

Following the oxidation of organic molecules, $KMnO_4$ produced the non-toxic compounds, which can be separated and used in a subsequent reaction. It is also an environmentally friendly substance. We can lower the cost of the reaction if we employ catalyst and apply $KMnO_4$ carefully and cautiously. The aforementioned investigation also showed that no expensive chemicals or equipment were needed for these processes.

V. CONCLUSION

Permanganate has been used in novel and sophisticated processes for more than a century due to its shown efficacy as an oxidant in organic chemistry. These days, industrial uses that once required thousands of tons of potassium permanganate per year can be completed without having a negative effect on the environment. The introduction of recycling technologies has made these operations more ecologically friendly and sustainable. This reagent's application in both current and emerging technologies suggests that it will probably remain a significant industrial oxidant for a very long time.

VI.CONFLICT OF INTEREST

The authors have no conflicts of interest.

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