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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.

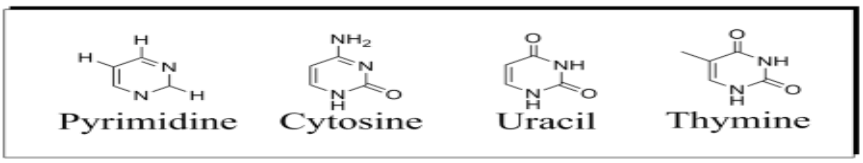

fig (1) pyrimidine and different isomeric forms

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].

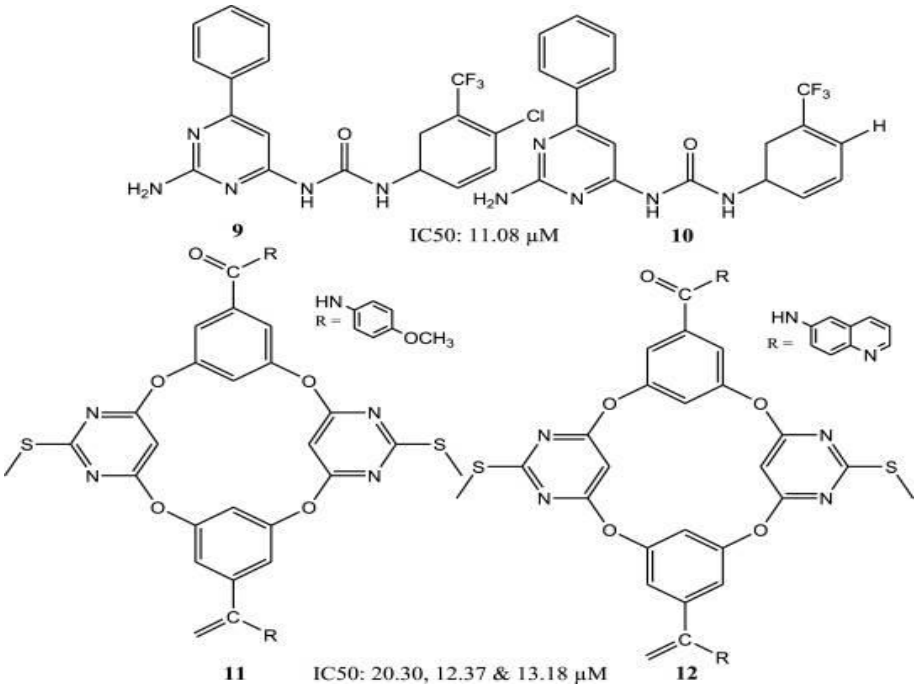

Fig (2) Pyrimidines nucleus as an anti-cancer Agent.

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].

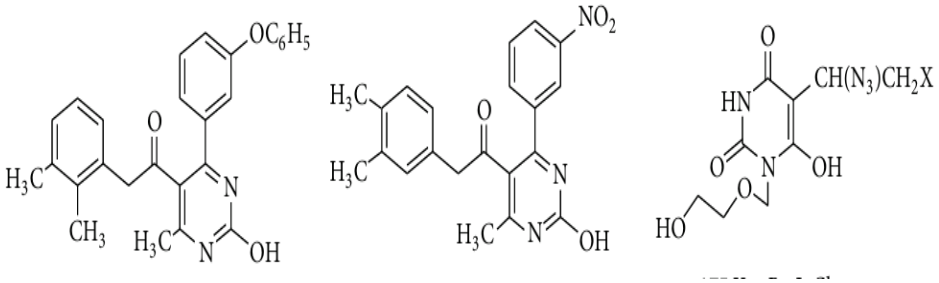

Fig 3:- Tetrasubstituted Pyrimidine Derivatives of Antibacterial and Antifungal Activities

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

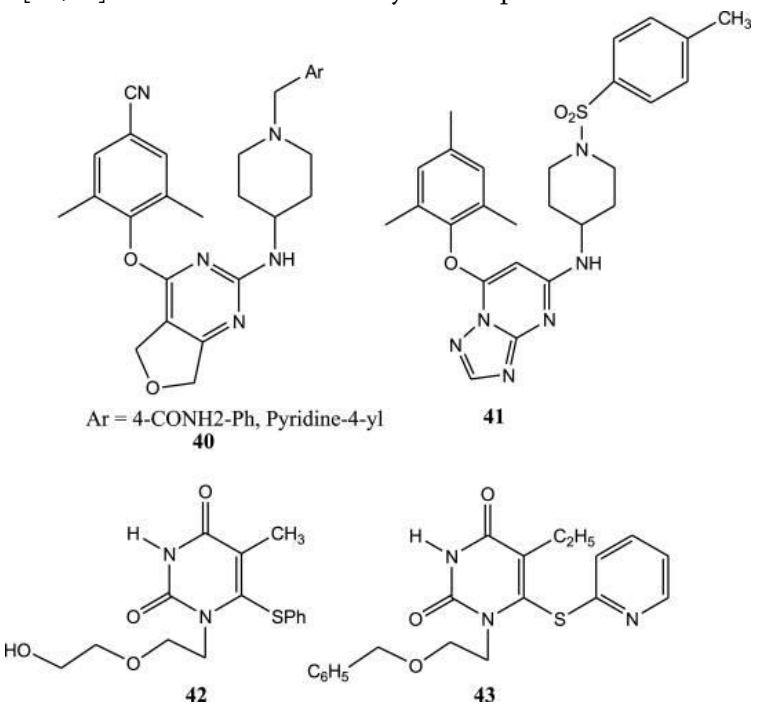

Fig 4:- anti- HIV agent

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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