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Synthesis, Spectral analysis and Biological Studies on Newly Derivatives of Amino salicylic acid

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ABSTRACT

In the present investigation Syntheses and Biological studies on some new derivatives of 5 – Amino Salicylic acid. Methyl, 5 – Amino Salicylic acid and Ethyl 5 – Amino Salicylic acid derivatives were synthesized by 5 – Amino Salicylic acid and methanol and ethanol under- reflux method. The resulting crude precipitates were recrystallized from the absolute ethanol. The compounds were Characterized using Elemental Analysis, Infrared spectra, Proton and 13C NMR spectroscopic. UV - spectroscopic. This compound has been screened for their antimicrobial activities and fungi.

Keywords : Synthesis, Spectral analysis, Biological and 5 -ASA.

I. INTRODUCTION

5 –Amino salicylic acid also known as mesalamine or mesalamine, is an anti-inflammatory drug used to treat inflammation of the digestive treat Ulcerative colitis [1]and mild – to – moderate Crohn's disease [2]. It is also recommended therapy for the induction and maintenance of remission of ulcerative colitis (UC) [3-4]. The drug acts topically at the colonic mucosa to reduce mucosal inflammation [5] yet because the active drug is rapidly absorbed in the stomach and small intestine [6] a number of oral formulations have been developed to deliver 5-ASA to the colon [5,7].

The most common side effects of 5-ASA are headache and flatulence. Hair loss and itching also may occur.

Infrequent side effects include increased hearth rate, Pancreatitis, back pain, fatigue, tremor, and ear pain and blood disorders.

The most important bimolecular, now a day with drastically different properties is required for various applications. Chelates of biologically important molecules are also being investigated for various requirements of human life. Organic molecules with

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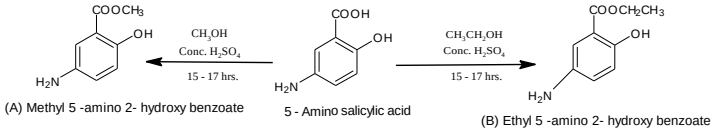
donor atoms like N, O etc. are very good examples that can form coordination compounds. They show important biological and chemical properties. The derivatives of 5 – Amino salicylic acid is used of medicinal purpose. Practically only few scientists have made attempt to study with 5 – Amino salicylic acid derivatives or biochemical formation and catalytic behavior of 5 –Amino salicylic acid derivatives. Looking to the literature survey carried out as well as the significance of the 5 – Amino salicylic acid derivatives as well as its coordination compounds, it is quite likely to give modified and improvised biochemical. Prompted by the above biological properties of 5 – Amino salicylic acid, it was contemplated to synthesize a novel series of 5 – Amino salicylic acid derivatives. Antibacterial and antifungal activities of the newly synthesized compounds are discussed in this paper.

II. EXPERIMENTAL

All chemicals used were of A.R. grade and used as such without further purification except for ethanol. 5 – Amino salicylic acid was obtained from S-d fine chemical company (Properties: White to pink crystals, dec ◦ 280° , Slightly soluble in cold water, more soluble in hot water, Empirical formula: $C_7H_7NO_3$, Mol. Wt. 153, Percent composition: (%) C- 54.90, H- 4.61, N- 9.15) [8].Melting points were determined in open capillary tubes and are uncorrected. IR spectra (4000 – 400 cm^{-1}) were recorded on Shimadzu Perkin – Elmer 8201 FT-IR with KBr pellets. The electronic spectra were recorded on Shimadzu- 1800 PTE Ltd. Japan. The ^{1}H-NMR spectra and ^{13}CMR spectra were recorded on BRUKER AVANCE II 400 MHz Spectrometer. Chemical shift values are reported as values in ppm relative to TMS (δ = 0) as internal standard in $CDCl_3$ solvent. Elemental analyses were performed on Vario MICRO C, H, N, S Elemental Analyzer system. Thermo gravimetric analysis was carried out under atmospheric condition with heating rate 50 – 1000 @ 10℃ min^{-1} on Mettler Toledo.

Synthesis of 5 – ASA derivatives:



(A) Methyl 5 -amino 2- hydroxy benzoate — 5 - Amino salicylic acid — (B) Ethyl 5 -amino 2- hydroxy benzoate

Methyl 5 – amino – 2 – hydroxy benzoate

A solution of 5 – Amino salicylic acid (10.0 gm, 65.3 mmol) and sulfuric acid (14ml) in methanol (200ml) was heated under reflux for 15 –17 hours in water bath. After addition of $NaHCO_3$ (until the evolution of CO_2 gas) the reaction mixture was filtered. The filtrate was poured into water and extracted with ether. The combine organic layers were dried over Magnesium sulphate and the solvent was removed [9-10]. See spectral data.

(B) Ethyl 5 – amino – 2 – hydroxy benzoate

A solution of 5 – Amino salicylic acid (10.0 gm 65.3 mmol) and sulfuric acid (14ml) in Ethanol (200 ml) was heated under reflux for 15 – 17 hours in water bath. After addition of $NaHCO_3$ (Until the evolution of CO_2 gas) the reaction mixture was filtered. The filtrate was Poured into water and extracted with ether. The combine organic layers were dried over Magnesium Sulphate and the solvent were removed [9-10]. See spectral data.

SPECTRAL ANALYSIS DATA

5 – Amino Salicylic acid:

^{1}H-NMR: δ =8.585 (Singlet 1H, - COOH), δ =8.077(Singlet 1H, -OH), δ = 2.412 (Singlet, 2H, ($-NH_2$) Primary amine), δ = 6.431 – 7.531 (Multiple 6H, Ar – H**), IR Spectra:** (KBr) 3100 (N-H), 3160 (O-H), 2850 (C-H), 1650 (C=O), 1370 - 1600 (C=C & C-N)**^{13}C-NMR:** (Solvent $CDCl_3$) δ = 176.05(-COOH) , δ = 112.10 – 138.27 (Ar – C), and δ = 170.01 (-C=O)

Methyl 5 – amino – 2 – hydroxy benzoate

^{1}H-NMR: δ =10.226(Singlet 1H, -OH), δ =3.075 (Singlet, 2H, ($-NH_2$)Primary amine), δ = 6.831– 7.279 (Multiple 6H, Ar – H), δ = 3.937 (Singlet 3H, $-CH_3$)

^{13}C-NMR: (Solvent $CDCl_3$) δ = 17.19 (-CH_3), δ = 112.10 – 154.10 (Ar – C), and δ = 170.01 (-C=O) **IR Spectra:** (KBr)3300 (N-H), 3200 (O-H), 2880 – 2920 (C-H), 1760 (C=O), 1240(C-O), 1600, 1620, 1580 (C=C & C-N)

Ethyl 5 – amino – 2 – hydroxy benzoate:

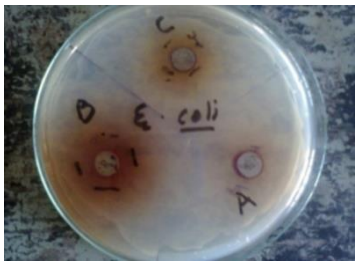
^{1}H-NMR: δ =10.310 (Singlet 1H, -OH) , δ=3.457 (Singlet, 2H, (-NH_2)Primary amine), δ =6.823– 7.281 (Multiple 6H , Ar – H), δ = 4.370 – 4.424 (Quartet 2H, -CH_2) δ = 1.400 – 1.436 (Triplet 3H, -CH_3) **^{13}C-NMR:** (Solvent CDCl3)δ = 14.21 (-CH_3), δ = 61.31 (-CH_2) , δ = 112.42 – 154.81 (Ar – C), δ = 170.01 (-C=O) **IR Spectra:** (KBr)3320 (N-H), 3210 (O-H), 2880 – 2920 (C-H), 1880 (C=O), 1280 (C-O),1620, 1680, (C=C & C-N)

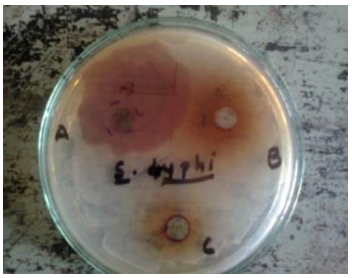
Table – 1. Analytical Data and Some physical parameters of Compounds

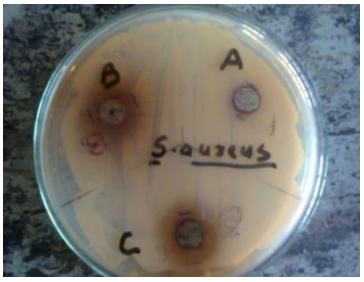
Molecular formula of compounds	Name of compounds	Color	Molecular weight	Yield %	Analysis (%) found / (%) calculated			M.P.
					C	H	N	
$C_7H_7NO_3$	5 - ASA	Light pink	153	----	--- 54.90	----- 4.61	------ 9.15	151
$C_8H_9NO_3$	A	Reddish Brown	167	77.70	56.64 57.48	5.34 5.38	7.90 8.38	96
$C_9H_{11}NO_3$	B	Reddish Brown	181	72.37	58.45 59.66	6.02 6.07	7.49 7.73	114

BIOLOGICAL ACTIVITY

The newly synthesized compounds A and B were screened for their antimicrobial and antifungal activity by Agar diffusion method [11]. Both the synthesized new titled compounds were evaluated for antimicrobial activity by E.coli, S. aureus, B. subtilis and S. typhi by measuring the zone of inhibition in mm. The activities were performed at a conc. of 50 µg / ml. Streptomycin sulphate (20 µg / ml.) was used as a standard drug for antimicrobial and antifungal activity respectively. Alcohol was used as solvent control for antimicrobial activity.







For the biochemical activity both the compounds show antibacterial activity and show maximum inhibitory activity against E.coli. Results of sensitivity against S. aureus of compound –B is maximum while compound –A did not show any activity against it. S. typhi was highly sensitive to compound – B while compound – A showed very poor inhibition against it. B. subtilis was found good sensitive to compound – A. This organism was not influenced by compound – B. Compound – A showed poor inhibition of bacteria except for B. subtilis. Compound –B showed inhibition of both positive and negative gram bacteria but could not inhibit sporulation bacteria.

The assay of bacterial sensitivity was conducted under standard conditions of antibacterial assay technique (Methods in microbiology, A/P, 1978). The results were averaged from the duplicate plates of the concerned set of experiment.

Table – 2
Antimicrobial activity data

Compounds	Diameter of zone of inhibition in (mm)			
	Escherichia Coli	Staphylococcus Aureus	Bacillus subtilis	Salmonella Typhi
A	11	11	15	12
B	18	15	----	17
Streptomycin sulphate (std. drug)	11	11	11	11

III. RESULT AND DISCUSSION

A novel series of 5 – amino salicylic acid derivatives were reported in this paper. The target compounds were synthesized by reflux method. The structures of the newly synthesized compounds have been elucidated on the basis of Elemental, 1H-NMR, ^{13}C-NMR, IR Spectra,
UV – visible, TGA and biochemical activities. See spectral analysis.

ACKNOWLEDGEMENT

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SPECTRAL ANALYSIS SKETCH OF COMPOUNDS

Fig: 1 (a) ^{1}HNMR Spectrum of 5 – amino salicylic acid

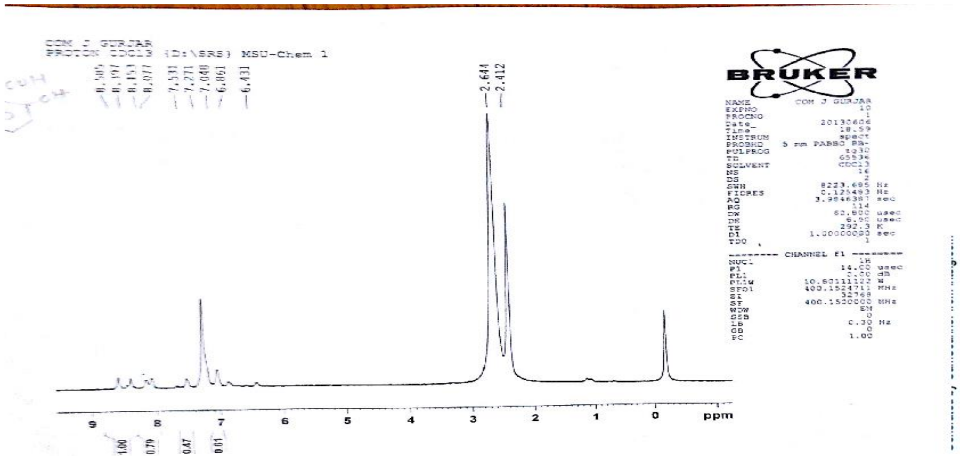

Fig: 1 (b) ^{1}HNMR Spectrum of Methyl - 5 - amino - 2 – Hydroxy benzoate

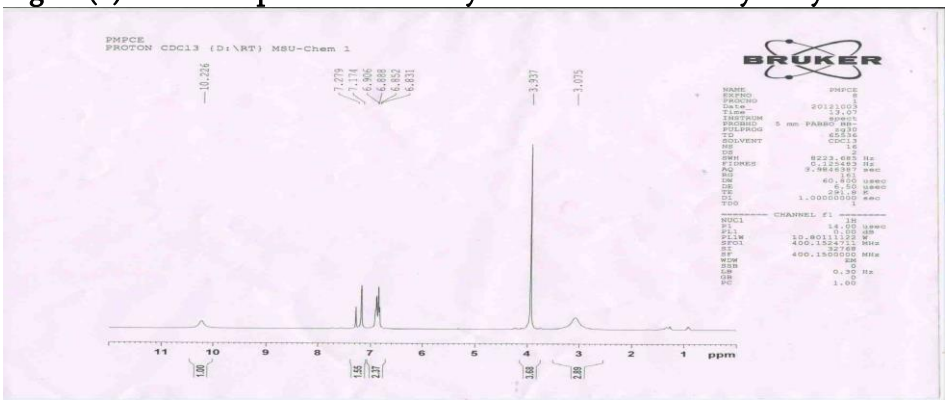

Fig: 1 (c) ^{1}HNMR Spectrum of Ethyl - 5 - amino - 2 – Hydroxy benzoate

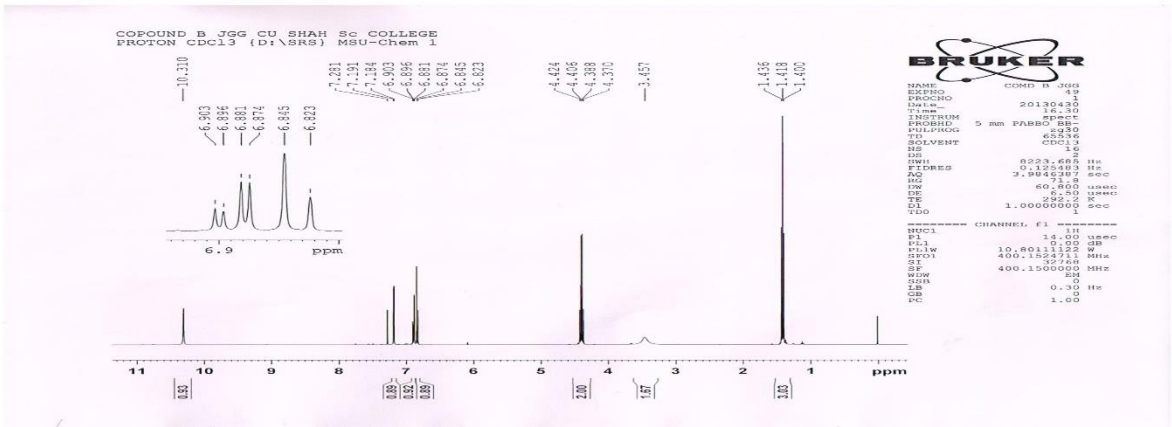

Fig: 2 (a) Electronic Spectrum of Methyl - 5 - amino - 2 – Hydroxy benzoate

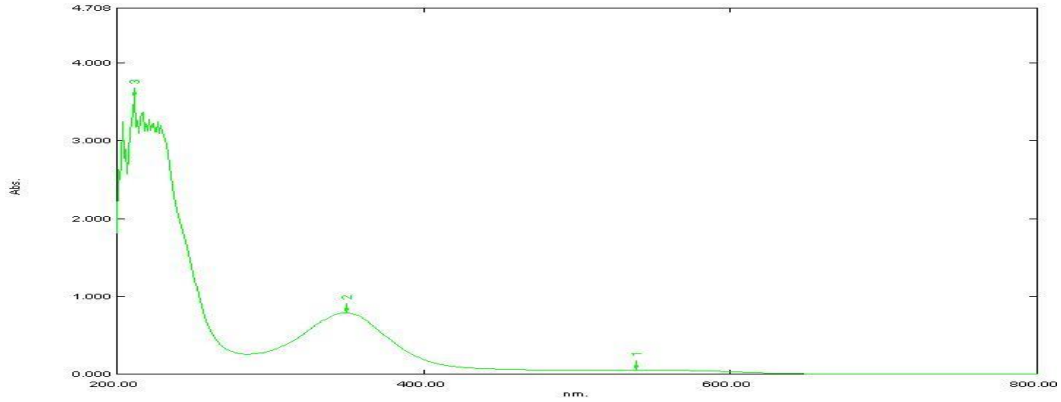

Fig: 2 (b) Electronic Spectrum of Ethyl - 5 - amino - 2 – Hydroxy benzoate

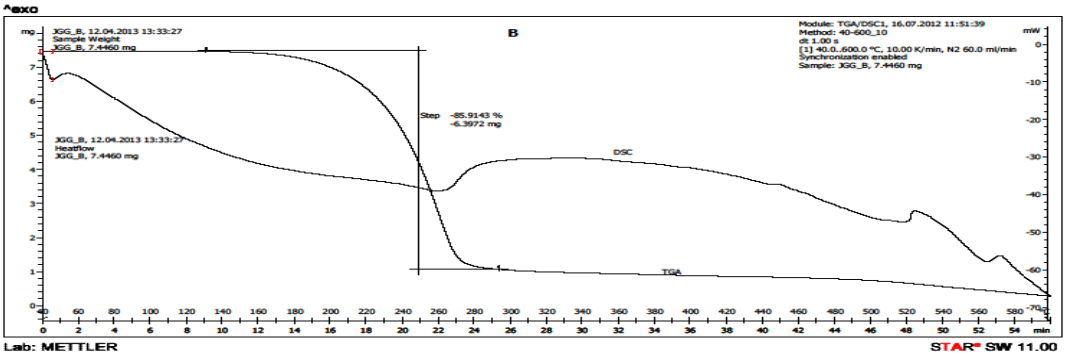

fig : 4 (a) IR Spectra of o5 – amino salicylic acid

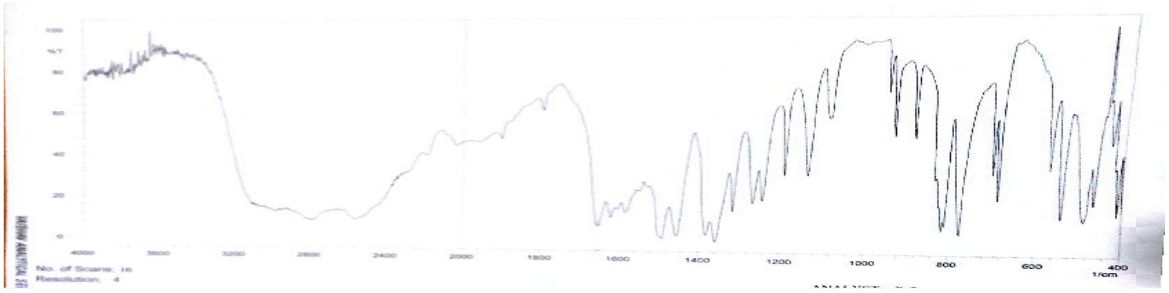

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Fig : 4 (a) IR Spectra of Methyl - 5 - amino - 2 – Hydroxy benzoate

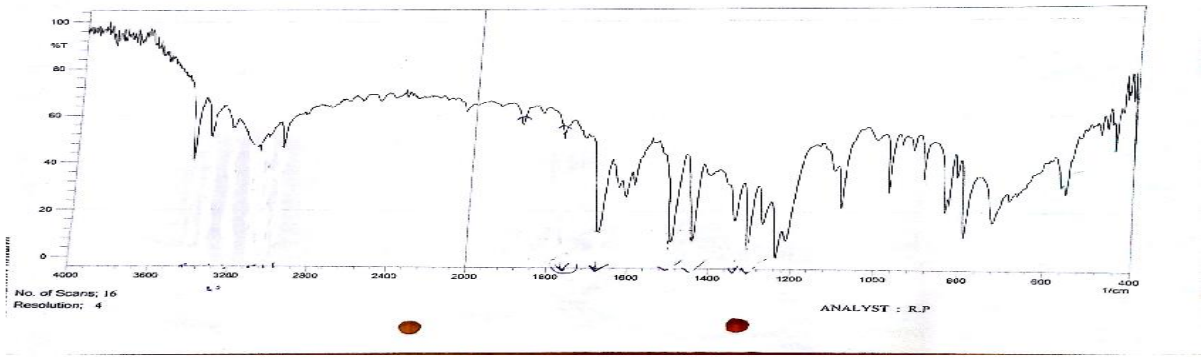

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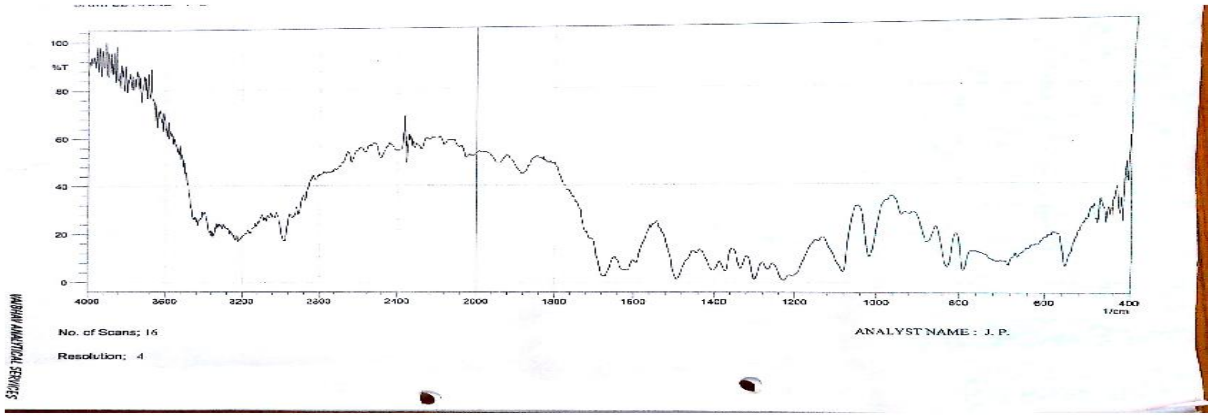
Fig : 4 (b) IR Spectra of Ethyl - 5 - amino - 2 – Hydroxy benzoate



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