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Synthesis, Spectral analysis and Antimicrobial Activity of Some Newly Derivatives of 5 – amino Salicylic Acid.

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ABSTRACT
In the present investigation Synthesis, Spectral analysis and antimicrobial studies on some newly synthesized 5 -amino salicylic acid derivatives. All the newly derivatives were Synthes-
-sized by reflux method. The resulting crude precipitates were recrystallized from theproper solvent. The compoundwase analysed using CHNS Analysis, IR spectra, ^{1}H and^{13}C NMR spectroscopic. These derivatives have been screened for their antimicrobial activities and antifungal.
Key words: Synthesis, Spectral analysis, Antimicrobial and5-ASA Derivatives.

I. INTRODCTION

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 Cronh´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 reducemucosal 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- amino salicylic acid to the colon[5,7]. The most common side effect of 5- amino salicylic acid are headache and flatulence. Hair loss anditching also may occur. Infrequent side effects include increased hearth rate, Pancreatitis backpain fatigue, tremor. and ear pain and blood disorders.

The most important bimolecular, now a day with drastically different properties is required forisvarious applications Chelates of biologically important molecules are also being investigated forvarious requirements of human life. Organic molecules with donor atoms like N, O etc. are very good examples that can form coordination compounds. They show important biological andchemical 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 acidderivatives or biochemical formation and catalytic behaviours of 5 -amino salicylic acidderivatives.

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 givemodified and improvised biochemical. Prompted by the above biological properties of5- amino salicylic acid, it was contemplated to synthesize a newly series of 5 - amino salicylicacid derivatives. Antibacterial activities of the newly synthesized derivatives arediscussed in this paper.The derivative of 5-amino salicylic acid contains – COOH, -OH (Phenolic) and-NH_2 groups.

EXPERIMENTAL

All chemicals used were of A.R grade and used & as such without further purification except for ethanol. 5- amino salicylic acid wasobtained from s-d fine chemical company. Melting point were determined in open capillary tubes and are uncorrected, IR spectra (4000-400 cm^{-}) were recorded on Shimadzu Pekin Elmer 8201 ET-IR with KBr pellets. The ^{1}H-NMR spectra and ^{13}CMR spectra yere recorded on BRUKER AVANCE II 400 MHZSpectrometer.

Chemical shift values are reported as values in ppm relative to TMS ($\delta = 0$) asinternal standard in CDCI solvent. Elemental analysiswas performed on Vario MICRO C, H, N,S Elemental Analyzer system.

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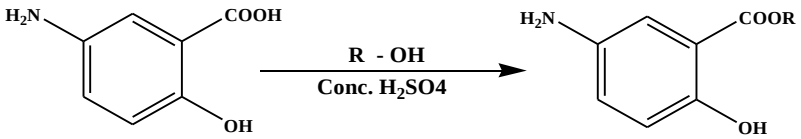
Synthesis of Derivatives:



5 -amino salicylic acid **Derivatives**

R = -CH_3, -C_2H_5, -$CH_2CH_2CH_3$, -CH (-CH_3)$_2$

(A) Methyl Derivatives:

A solution of 5 - amino salicylic acid (10.0 gm, 65.3 mmol) and sulfuric acid in methanolwas heated under reflux in water bath. After addition of $NaHCO_3$ (until the evolution of CO_2 gas) the reaction mixture was filtrate. The filtrate was poured into water and extracted with ether. The combine organic layers were dried over Magnesium sulphate and the solvent was removed [8-9].

(B) Ethyl Derivatives:

A solution of 5 - amino salicylic acid (10.0 gm, 65.3 mmol) and sulfuric acid in ethanol was heated under reflux in water bath. After addition of $NaHCO_3$ (until the evolution of CO_2 gas) the reaction mixture was filtrate. The filtrate was poured into water and extracted with ether. The combine organic layers were dried over Magnesium sulphate and the solvent was removed [8-9].

(C)Propyl Derivatives:

A solution of 5 - amino salicylic acid (10.0 gm, 65.3 mmol) and sulfuric acid in n-propyl alcohol was heated under reflux in water bath. After addition of $NaHCO_3$ (until the evolution of CO_2 gas) the reaction mixture was filtrate. The filtrate was poured into water and extracted with petroleum ether. The combine organic layers were dried over Magnesium sulphate and the solvent was removed [8-9].

(D) Iso propyl Derivatives:

A solution of 5 - amino salicylic acid (10.0 gm, 65.3 mmol) and sulfuric acid in iso propyl alcohol was heated under reflux in water bath. After addition of $NaHCO_3$ (until the evolution of CO_2 gas) the reaction mixture was filtrate. The filtrate was poured into water and extracted with petroleum ether. The combine organic layers were dried over Magnesium sulphate and the solvent was removed [8-9].

SPECTRAL ANALYSIS DATA

5- Amino Salicylic acid: **^{1}H-NMR**: δ =8.585(Singlet 1H, -COOH),δ = 8.077(1H, -OH phenolic) δ = 2.412 (Singlet, 2H, (NH_2 Primary amine), δ = 6.431 -7.531 (Multiple 6H, Aromatic H).**IR Spectra:** (KBr) 3090 (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).

(A) Methyl Derivatives:^{1}H-NMR: δ = 10.226 (Singlet 1H, -OH), δ = 3.075 (Singlet, 2H, (-NH_2) Primary amine), δ= 6.831- 7279 (Multiple 6H, Ar-H), δ= 3.937 (Singlet 3H, -CH_3).

IR Spectra:(KBr) 3320 (N-H), 3200 (O-H), 2880-2920 (C-H), 1760 (C=O), 1240(C-O), 1600, 1620,1550 (C=C&C-N).**^{13}C-NMR:**δ= 59.60 (-CH_3), δ = 112.10- 154.10 (Ar-C), and δ = 170.01(-C= O).

(B)Ethyl Derivatives:^{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= 4.424 (Quartet 2H, -CH_2) δ = 1.400 1.436 (Triplet 3H,CH_3).**IR Spectra:**(KBr) 3320 (N-H), 3210 (O-H), 2880 - 2920 (C-H), 1880 (C=O), 1280 (C-O),1620,1550 (C = C& C-N).**^{13}C-NMR**:δ = 14.21 (CH_3), δ = 61.31 (-CH_2), δ = 112.42- 154.10 (Ar-C),δ= 170.01(-C=O).

© N- Propyl Derivatives: ^{1}H-NMR:δ=10.315(Singlet 1H, -OH) δ=3.484(Singlet, 2H, (NH_2 Primary amine), δ = 6.820-7.279 (Multiple 6H Ar- H), δ = 4.277- 4.309(Triplet 2H, -CH_2), δ = 1.764- 1.851 (Multiple 2H, -CH_2) and δ = 1.024- 1,061(Triplet 3H, -CH_3). **IR Spectra**:(KBr) 3360(N-H), 3230 (O-H), 2890–2930(C-H),1870 (C=O), 1295 (C-O),1640,1690 (C=C & C-N) and 725 – 720(C-C-C).**^{13}C-NMR**: δ =10.49(CH_3), δ =21.97(-CH_2),δ = 66.81 (-CH_2) δ =112.45- 154.87(Ar-C), δ =170.06 (-C=O).

(D) Iso Propyl Derivatives:^{1}H-NMR:δ=10.387(Singlet 1H, -OH) δ = 3.484 (Singlet, 2H, (-NH_2)), δ = 6.790 - 7.279 (Multiple6H, Aromatic H),δ = 5.205-5.298(Multiple 1H, >CH) and δ = 1.359-1.375

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(Doublet 6H, -CH_3). **IR Spectra**: (KBr)3360 (N-H),3230 (O-H), 2900-2940 (C-H stretch Ar -C),1340-1360 (C-H),1880(C=O),1300 (C-O),1640-1690(C=C & C-N),1280 - 1700 (C-C_v) and 1360-1340(C-H_b).**^{13}C-NMR**: δ = 21.84 (-CH_3), δ= 69.05 (-CH) δ =112.75 – 154.81 (Ar-C), δ = 169.56 (-C=O).

Table -1
Analytical Data and Some Physical Parameters of Compounds

Molecular formula of Derivatives	Name of Derivatives	Colour	Molecular weight	Yield %	Analysis (found/%calculated)			M.P.
					%C	%H	%N	
$C_7H_7NO_3$	5-amino salicylic acid	Light pink	153	--	--- 54.90	-- 4.61	-- 9.15	151
$C_8H_9NO_3$	Methyl Derivative	Reddish brown	167	77.70	56.64 57.48	5.34 5.38	7.90 8.38	96
$C_9H_{11}NO_3$	Ethyl Derivative	Reddish brown	181	72.37	58.45 59.66	6.02 6.07	7.49 7.73	114
$C_{10}H_{13}NO_3$	N- propyl Derivative	Reddish black	195	68.75	60.50 61.53	6.17 6.72	6.98 7.17	---
$C_{10}H_{13}NO_3$	Iso-propyl Derivative	Reddish black	195	62.55	60.50 61.53	6.17 6.72	6.98 7.17	---

ANTIMICROBIAL ACTIVITY

The newly Synthesized compounds A. B, C and D were screened for their antimicrobial activity by Agar diffusion method [10]. All the synthesized new titled derivatives were evaluated for the antimicrobial activityby E.coli, S. aureus, B. subtilis and S.typhi by measuring the zone of inhibition in mm. The activities were performed at a concentrate of 50µg / ml. Streptomycin sulphate (20µg/ml) was used as a standard drug for antimicrobial activity respectively. Alcohol was used as solvent control for antimicrobial activities. For antimicrobial activity both the derivatives (C & D)show antibacterial activity and show maximum inhibitory activity againstE.coli. Result of sensitivity against S.aureus of derivative - D is maximum while derivative - A show poor activity. S. typhi was highly sensitive to derivative -D while derivative - A showed very poor inhibition against it. B. subtilis was found good sensitive to derivative - D. This organism was not influenced by derivative -B. Derivative – A showed very poor inhibition of bacteria except for B. subtilis. Derivative – 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 of derivatives.

Derivatives	Diameter of zone of inhibition in mm.			
	E. coli	S. aureus	B. subtilis	S. Typhi
Methyl derivative	**11**	**11**	**15**	**12**
Ethyl derivative	**18**	**15**	**----**	**17**
N- propyl derivative	**19**	**20**	**18**	**17**
Iso-propyl derivative	**20**	**22**	**16**	**18**
Streptomycin sulphate (std. drug)	**11**	**11**	**11**	**11**

II. RESULT AND DISCUSSION:

A newly series of 5 - amino salicylic acid derivatives were reported in this paper. The target derivatives compounds were synthesized by reflux method, The structure of the newly synthesized derivatives compounds have been elucidated on the

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basis of Elemental, ^{1}H-NMR, ^{13}C-NMR,IR-Spectraand antimicrobial activities.

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