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Synthesis and biological evaluation of some new amides of 5-sulphosalicylic acid

Mishra Anjali [1], Singh R.K.[1], Singh S.[1], Mishra A.[1], Kumar M.[3], Kant Ravi [2],Thakur R.S.[1]*
[*1]Research Laboratory, Department of Chemistry, D.B.S.P.G. College, Kanpur
[2]Department of Applied Chemistry, Prabhat Engineering College, Kanpur
[3]Department of Applied Chemistry, Vidya Bhawan Engineering College, Kanpur
**Corresponding Author: profrsthakur@gmail.com*

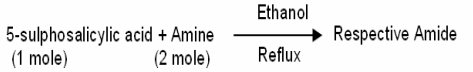
Abstract- Some new amides of 5-Sulphosalicylic acid were synthesized by the reaction of suitable amines with 5-sulphosalicylic acid in 2:1 ratio. The compounds are novel and first time screened for their complete biological evaluation along with general characterization with the help of elemental and IR spectral analysis. These compounds showed higher to moderate biological activity against different pathogenic microbial strains.
Keywords: 5-Sulphosalicylic acid, amines, antifungal, antibacterial and insecticidal activities

Introduction

It is well known in literature that nitrogen and sulphur containing compounds are essentially used in medicinal purpose for the treatment of different kinds of fungal, bacterial infections along with treatment of gastric ulcer and cancer[1-3].The introduction of nitrogen and sulphur atom in organic moiety resulting towards higher efficacy against various diseases[4-6].Since sulphur is capable of forming both σ and π bonds therefore the studies of their binding interaction with receptor moiety was also an interesting field of research during last few years[7-10].It is also revealed in literature that amines and amino compounds plays excellent role in controlling of various pathogenic diseases[11].The present communication deals with the synthesis of some novel amides of sulphosalicylic acid along with their antimicrobial activity against pathogenic microbial strains.

Results and Discussion

The amides of 5-sulphosalicylic acid were synthesized by the general procedure as shown below:



All the compounds were crystalline solids and quite stable at room temperature with good yield (70-75%). The compounds were soluble in polar solvents. They have sharp melting points. The compounds were also characterized on the basis of elemental analysis and IR spectra.

I.R. Spectra:

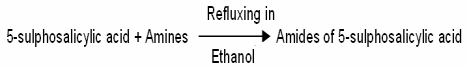
The solid state FTIR spectra of all these compounds were recorded in the spectra range of 4000-400 cm^{-1} and significant frequencies were observed in this region. The IR spectra of the entire compound shows absorption band due to phenyl group of 5-sulphosalicylic acid. The absorption frequencies of carbonyl group in the amide derivative have been assigned. Clearly, confirming the proximal geometrical arrangement.

Antimicrobial activity

The amides of 5-sulphosalicylic acid were tested for antibacterial activity against three pathogenic bacterial strains viz. *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Klebsiella pneumoniae*, using 10 µg/ml concentration of the compound. The compounds show positive antibacterial activity against these bacterial strains.The variations on activity was found in case of all these compound due to presence of different kinds of amines group. The activity of compound 1 was found higher against *Pseudomonas aeruginosa* while compound 3 show higher efficacy against *Staphylococcus aureus* and *Klebsiella pneumoniae* respectively. The efficacy of compound 6 against *Klebsiella pneumoniae* was also found higher. The biological activity of all these compound generally occurs due to presence of nitrogen and sulphur contents in the molecule, presence of hydrogen bonding in 5-sulphosalcylic acid, presence of polar OH group increases the water solubility. These compounds generally reacted with some groups of bacterial cell wall and damage it in such a manner that the aromatic ring gets entered inside the cell wall followed by death of bacterial cell.

Experimental

Synthesize of amides of 5-sulphosalicyclic acid was carried out by following method.



(Amines: *p*-methoxyaniline, 2-aminopyridine, aniline, *α*-naphthylamine, *p*-chloroaniline, hydrazine).

The amines were purified by crystallization before use. Molecular weights of the compounds were determined cryoscopically. The infra red spectra (FTIR) of new compounds were recorded in a Perkin-Elmer spectrophotometer in 4000-200 cm^{-1} range. The further characterization of these compounds is in progress. The method of preparation of some representative compounds is given below.

Reaction of 5-sulphosalicylic acid with p-methoxy aniline (1)

An ethanolic solution of 5-suphosalicylic acid (2.5 gm; 1 mole) and p-methoxy aniline (2.46 gm; 2 m mol) was refluxed together at room temperature for 6-7 hrs, followed by their evaporation and concentration in vacuum gives a crystalline solid which was recrystallized in ethanol to give respective amide of 5-sulphosalicylic acid.

Reaction of 5-sulphosalicylic acid with α-naphthylamine (4)

An ethanolic solution of 5-sulphosalicylic acid (2.5 gm; 1 m mole) and □-naphthalamine (2.86 gm; 2 m mole) was refluxed together at room temperature for 6-7 hrs, followed by their evaporation and concentration in vacuum afforded a crystalline solid mass which was further recrystallized in ethanol to gives respective amides.

Reaction of 5-sulphosalicylic acid with hydrazine (6)

An ethanolic solution of 5-salphosalicylic acid (2.5 gm; 1 m mole) and hydrazine (0.64 gm; 2 m mole) was refluxed together at room temperature for 6 hrs, followed by evaporation and concentration in vacuum afforded a crystalline solid which was further recrystallized in ethanol to give respective amides.

Antibacterial Activity

The antibacterial activity of these compound was carried out by disc diffusion method [12], using Gentamycin as standard. In this technique the filter paper (Whatmann No.1) sterile disc of 5 mm diameter, impregnated with the test compounds (10 □g/ml of ethanol) along with standard were placed on the nutrient agar plate at 37°C for 24 hrs in BOD incubator. The inhibition around dried impregnated disc was measured after 24 hrs. The bacterial activity was classifieds as highly active (dia = > 15 mm), moderately active (dia = 10-15 mm) and partially active (dia = 5-10 mm).

Conclusion

The newly synthesized amides of 5-sulphosalicyclic acid have great potential as antibacterial agents, and therefore can be explore further for the development of new drugs for treatment of bacterial diseases.

Acknowledgment

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Table 1 : Analytical data of complexes (1:2) of 5-Sulphosalicylic acid

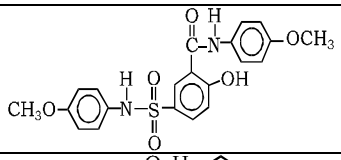
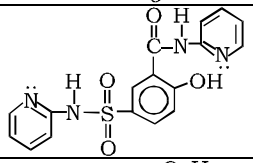
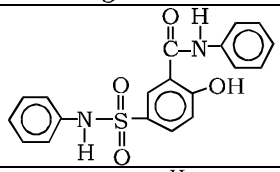
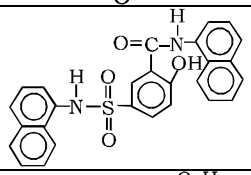
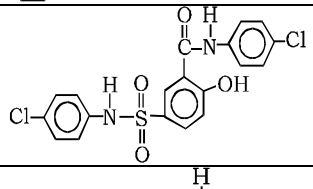
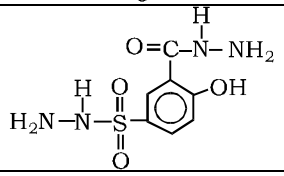
S.N.	Compound	Formula of compound	Formula wt.	Melting point	Yield (%)	Elemental Analysis (%)			Solvent for Extraction
						C	H	N	
1.		$C_{21}H_{20}N_2O_6S$	460	127	70	54.78	4.34	6.08	Ethanol
2.		$C_{17}H_{14}N_2O_4S$	374	122	70	54.54	3.74	7.48	Ethanol
3.		$C_{18}H_{16}N_4O_4S$	388	116	65	55.67	4.12	7.21	Ethanol
4.		$C_{27}H_{20}N_2O_4S$	500	112	70	64.80	4.00	5.60	Ethanol
5.		$C_{19}H_{14}N_2O_4SCl$	433.5	131	60	52.59	3.22	6.45	Ethanol
6.		$C_7H_{10}N_4O_4S$	278	102-104	75	30.21	3.59	20.14	Ethanol

Table 2: Antibacterial Activity

S.N.	Compound	Control	*P. aeuruginosa*	*S. aureus*	*K. pneumoniae*
1.	$C_{21}H_{20}N_2O_6S$	-	+++	++	++
2.	$C_{17}H_{14}N_2O_4S$	-	++	++	++
3.	$C_{18}H_{16}N_4O_4S$	-	++	+++	+++
4.	$C_{27}H_{20}N_2O_4S$	-	++	++	++
5.	$C_{19}H_{14}N_2O_4SCl$	-	++	++	++
6.	$C_7H_{10}N_4O_4S$	-	++	++	+++

++ = (10-15 mm dia), +++ = (>15 mm dia), (-) = Control