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Synthesis and antimicrobial studies on therapeutically significant Schiff bases of Salicaldehyde and sulfonamides

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ABSTRACT

A number of new Schiff bases have been synthesized from Salicaldehyde and sulfonamides and screened for antibacterial activity.

Keywords: Salicaldehyde, sulfonamides, Schiff reaction, antibacterial activity.

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INTRODUCTION

Sulfonamides form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications [1-5].Salicaldehyde has been proved to be a powerful medicinal agent[6].The chemistry of the carbon-nitrogen double bond plays a vital role in the progresses of chemistry science[7]. Schiff-base compounds have been used as antioxidant,antimicrobial and anti-HIV active agents[8-10] . By observation it is found that Schiff bases occupied an important place in medicinal chemistry as they show a verity of diverse biological activity,we have elevated a series of Schiff bases of Glutarimide by following the procedures of M. M. Sprung[11], Yasuo et al [12] and James B. Davis [13].Based on these studies, we have taken up the compounds for synthesis and evaluated for antibacterial activity. The structural assignments of the products were based on their UV, IR and ^{1}HNMR data. The title compounds were screened for their antibacterial activity.

MATERIALS AND METHODS

All the m.p. are uncorrected and were determined using Thomas Hoover capillary melting point apparatus. The ^{1}H NMR spectra in DMSO and $CDCl_3$ solvent were recorded on a Bruker DRX-300 FT NMR Spectrometer. The IR spectra were recorded on a Schimadzu 820 IPC FTIR spectrophotometer using KBr pellets. The UV spectra were recorded on a Schimadzu UV-160A, UV-vis. spectrophotometer. Single spot ascertained the purity of the compounds during TLC where mobile phase was chloroform/methanol mixture (90:10) and stationary phase was silica gel-G (chromatographic grade). The antimicrobial screening was performed using paper disc method [14]. Mullar Hinton Agar was taken as media for cultivation of bacteria. The inhibitory effect of the samples and their corresponding sulfonamides were measured against the bacteria after incubation for 24 h at 37^{o}C. The experiments were run in triplicate and the mean of readings were recorded.

All substituted sulfonamides were obtained as pure samples from the reputed pharmaceutical concern. Solvents used were distilled before use.

Experimental

Synthesis of Schiff bases from salicaldehyde. To the ethanol solution containing few drops of glacial acetic acid , 0.003 mol of Salicaldehyde were added to 0.003 mol of sulphonamide slowly with constant stirring. The reaction mixture then refluxed on water bath for ½ hrs. When crystallized product was obtained, recrystallise with 99.5% ethanol. Analogous members were prepared by the same procedure.

RESULTS AND DISCUSSION

The synthetic approach to the sulfonamide Schiff base is outlined in Scheme 1.

The newly prepared Schiff bases were characterized by elemental analysis and spectral data (UV, IR and ^{1}HNMR). The absorption bands of novel Schiff bases are totally agree with the anticipated structure. The physical characterization and spectral data are presented in Tables 1 and 2.

The Schiff bases were screened for the biological significance. The antimicrobial screening of duly characterized Schiff bases was performed using paper disc method against some pathogenic strains of *Salmonella entritidis* and *Staphylococcus aureus*. Table 3 revealed significant results of Schiff bases against S.*enteritidis*. Studying interaction of concentration level on zone of inhibition in each compound, it revealed Schiff bases 3c and 3d were significantly active at 40 mg/ml against this pathogen rather at 30 mg/ml. All the novel Schiff bases gave excellent response against *S. aureus* at all chosen concentration.

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With this much background, it will be interesting to compare changes in the antimicrobial activity of Schiff bases with the changes in their structure. In all cases, a change in structure occurred with the substitution of hydrogen (s) of the $–NH_2$ group attached at SO_2 position. The comparative study (Table 4) showed that all Schiff bases are significantly superior in their antibacterial activity over their parent sulfonamides. In case of (3b) and (3d), their corresponding sulfonamide fails to show any activity against *S. enteritidis* at this arbitrarily chosen concentration. This means that substitution of one of the hydrogen atom of the $–NH_2$ resulted in the decrease of antimicrobial activity. It further, indicates that sulfonamides fail to show any activity against *S. aureus*.

A perusal of Table 3 exhibits the following trend of antibacterial activity:

(i) *S. enteritidis*: 3d>3a>3c>3e>3b;

(ii) *S. aureus*: 3d>3a>3e>3c>3b.

Furthermore, the data presented in Table 4 reveal that:

1. All the five sulfonamides used are inactive against bacteria viz. *S. aureus* , while the Schiff bases derived from them exhibit pronounced antibacterial activity against this bacteria;

2. In case of *S. enteritidis*, two of the five sulfonamides used viz. are inactive and in these cases the antibacterial activity of sulfonamide is much smaller than that of the Schiff bases derived from them.

CONCLUSIONS

In conclusion, some of the compounds of the sulfonamide series proved to be promising antimicrobial agents. The sulfa guanidine is considered to play a significant role in antimicrobial activity. Further pharmacological investigation is needed in this area.

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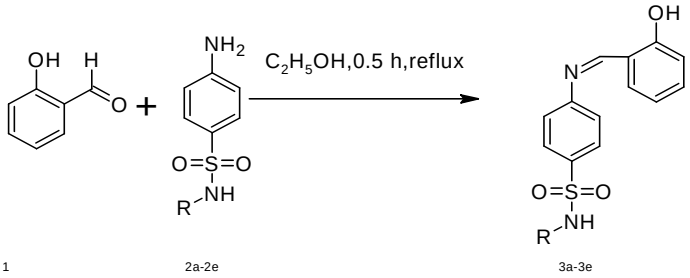
The authors wish to express gratitude Director, CDRI Lucknow, for recording elemental analysis and ^1H NMR spectra of the compounds.

Scheme 1. Synthesis of Schiff bases (3a-3e)



1 2a-2e 3a-3e

where R =

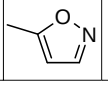
CN	a	b	c	d	e
R			H	C=NH.NH_2	C=O.CH3

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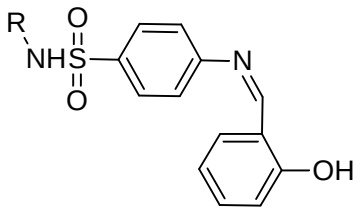
Table 1. Physical characterisation data of the synthesised compounds



Compound No	Compounds	Molecular formula	M.P. (^{o}C)	Elemental Analysis (found (calcd.) %)		
				C	H	N
3a	4-{[(1*E*)-(2-hydroxyphenyl)methylidene]amino}-*N*-pyrimidin-2-ylbenzenesulfonamide e	$C_{17}H_{14}N_4O_3S$	198-199	57.64 (57.62)	3.94 (3.98)	15.80 (15.81)
3b	4-{[(1*E*)-(2-hydroxyphenyl)methylidene]amino}-*N*-(5-methylisoxazol-3-yl)benzenesulfonamide	$C_{17}H_{15}N_3O_4S$	146-147	57.12 (57.13)	4.18 (4.23)	11.68 (11.76)
3c	4-{[(1*Z*)-(2-hydroxyphenyl)methylidene]amino}benzenesulfonamide	$C_{13}H_{12}N_2O_3S$	152-154	56.49 (56.51)	4.36 (4.38)	10.12 (10.14)
3d	*N*-carbamimidoyl-4-{[(1*E*)-(2-hydroxyphenyl)methylidene]amino}benzenesulfonamide	$C_{14}H_{14}N_4O_3S$	164-165	52.80 (52.82)	4.42 (4.43)	17.58 (17.60)
3e	*N*-[(4-{[(1*Z*)-(2-hydroxyphenyl)methylidene]amino}phenyl)sulfonyl]acetamide	$C_{15}H_{14}N_2O_4S$	132-134	56.58 (56.59)	4.42 (4.43)	8.78 (8.80)

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Table 2. Spectral Data of prepared compounds

Compound No	UV λ_{max} (nm)	IR (cm^{-1})	^{1}H NMR δ (ppm)
3a	208 (C=O), 219 (S=O), 230 (C=N=N), 250 (Ar. Ring), 261 (sulphonamide moiety), 305 (5-nitrofuran derivatives)	3320ν_{NH} of SO_2NH, 2911 ν_{as} C-H in CH_2, 2729 ν >CH_2N<, 1680 ν (C=O), 1540 ν_{as} N⁻O, 1338, ν_{as} S=O, 1249, ν(C-H) in 1,4 disubstituted benzene, 1087, ν_{as} C-O-C, 943 out of plane δ C-H in trisubstituted heteroaromatic ring	2.72 (d, 2H, *J* = 8.94, CH_2); 6.52 (d, =CH-CH ring protons, *J* = 9.2); 6.70 – 7.2 (m, ArH); 7.80 (s, 1H, =CH-N); 7.90 (s, 1H, =N-NH), 10.8 (s, 1H, SO_2NH)
3b	210 (C=O), 218 (S=O), 252 (Ar. Ring), 264 (sulphonamide moiety)	3350 ν_{NH} of SO_2NH, 2950 ν_{as} C-H in CH_2, 2805 ν >CH_2N<, 1340 ν_{as} S=O, 1240 δ C-H in 1:4 disubstituted benzene	2.90 (d, 2H, *J* = 8.94, CH_2); 5.30 (s, 1H, NH); 6.50 (d, =CH-CH ring protons, *J* = 9.2); 6.80 – 8.01 (m, ArH); 7.80 (s, 1H, =CH-N); 10.6 (s, 1H, SO_2NH)
3c	208 (C=O), 220 (S=O), 251 (Ar. Ring), 261 (Sulphonamide moiety)	3400 ν_{as} (NH) in sec amide, 3360 ν_{NH} of SO_2NH, 2910 ν C-H in CH_2, 2790 -CH_2N<, 1680 ν (C=O) in sec. amide, 1580 δ NH, 1540 ν_{as} N⁻O in $ArNO_2$, 1345, ν_{as} S=O, 1250 in plane δ C-H in 1:4 disubstituted benzene	2.55 (d, 2H, *J* = 8.94, CH_2); 5.40 (s, 1H, NH); 6.40 (d, =CH-CH ring protons, *J* = 9.2); 6.70 – 7.8 (m, ArH); 7.08 (s, 1H, CONH); 7.90 (s, 1H, =N-NH), 10.9 (s, 1H, SO_2NH)
3d	209 (C=O), 219 (S=O), 250 (Ar. Ring), 263 (sulphonamide moiety)	3300 ν_{NH} of SO_2NH, 2905 ν_{as} C-H in CH_2, 2805 vib. due to -CH_2N<, 1680 ν (C=O) in sec. Amide, 1540 ν_{as} N⁻O in $ArNO_2$, 1340, ν_{as} S=O, 1255 ν C-H in 1:4 disubstituted benzene	3.05 (d, 2H, J = 8.94, CH_2); 5.40 (s, 1H, NH); 6.40 (d, =CH-CH ring protons, *J* = 9.2); 6.65 – 8.0 (m, ArH); 10.7 (s, 1H, SO_2NH)
3e	210 (C=O), 218 (S=O), 251 (Ar. Ring), 260 (sulphonamide moiety)	3400 ν_{as} (NH) in sec amide, 3350 ν_{NH} of SO_2NH, 2900 ν_{as} C-H in CH_2, 2750 vib. due to -CH_2N<, 1685, 1660 ν (C=O) in sec. amide, 1342 ν_{as} S=O grp., 1250 δ C-H in 1:4 disubstituted benzene	2.60 (d, 2H, *J* = 8.94, CH_2); 5.30 (s, 1H, NH); 6.40 (d, =CH-CH ring protons, *J* = 9.2); 6.80 – 8.20 (m, ArH); 7.10 (s, 1H, CONH); 7.70 (s, 1H, =CH-N); 10.60 (s, 1H, SO_2NH)

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Table 3. Antibacterial screening of prepared Schiff bases
(Zone of inhibition in mm)

Compound No	*S. enteritidis* (mg/ml)				*S.aureus* (mg/ml)			
	20	30	40	avg	20	30	40	avg
3a	18.60	18.20	19.40	18.73	16.00	18.00	20.00	17.40
3b	17.06	17.40	18.60	17.55	12.20	13.04	14.00	13.20
3c	18.00	18.30	18.20	18.30	14.00	14.20	14.36	14.18
3d	20.02	21.06	20.20	20.76	18.06	18.24	18.60	18.30
3e	15.06	18.02	20.06	17.71	15.60	15.68	16.04	15.77
Avg. of conc.	17.74	18.59	19.29		15.17	15.83	16.60	

Table 4. Antibacterial activity of Schiff bases compared to reference sulfonamides
(Zone of inhibition in mm)

Compound No	*S. enteritidis* (mg/ml)				*S.aureus* (mg/ml)			
	20	30	40	avg.	20	30	40	avg.
3a	18.60	18.20	19.40	18.73	16.00	18.00	20.00	17.40
a	10.00	15.00	20.00	15.00	Nil	Nil	Nil	Nil
3b	17.06	17.40	18.60	17.55	12.20	13.04	14.00	13.20
b	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
3c	18.00	18.30	18.20	18.30	14.00	14.20	14.36	14.18
c	15.00	15.00	18.00	16.00	Nil	Nil	Nil	Nil
3d	20.02	21.06	20.20	20.76	18.06	18.24	18.60	18.30
d	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
3e	15.06	18.02	20.06	17.71	15.60	15.68	16.04	15.77
e	10.00	12.00	16.00	12.66	Nil	Nil	Nil	Nil

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