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SYNTHESIS AND ANTIBACTERIAL PROPERTIES OF SCHIFF BASES

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ABSTRACT
Schiff bases have been synthesized by condensing salicyaldehyde with substituted aromatic amines. The structure of the Schiff base has been established on the bases of analytical and spectral data. The Schiff base was employed to study the antimicrobial activity against two gram-positive and two gram-negative strains of cultured organisms such as *Streptococcus mutans, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae*. The results of antibacterial activities of the Schiff bases were compared with ciprofloxacin as standard to reveal their potency. It is found that, the Schiff bases obtained shows nearly 10-30 % antibacterial activity against the tested bacterial species as compared to ciprofloxacin.

INTRODUCTION

The interest of studying Schiff bases arouse because of their preparative convenience, versatile nature in chemical permutation and wide range of application in catalysts , Photochromic properties , complexing ability towards toxic metal and broad range of biological activities (Dhar and Taploo, 1982; Przybylski *et al.,* 2009; Malik *et al.,* 2011; Djebbar-Sid and Benali-Baitich, 1998). They can be synthesized through simple methods by condensing carbonyl compounds with amines in presence of dehydrating agents. (Taguchi *et al.*, 1971). Several studies reveals that the presence of a lone pair of electron in an sp2 hybridized orbital of nitrogen atom of azomethine group is of considerable chemical and biological importance (Sreenivasolu, 2012). Schiff bases have been proved as promising antibacterial agents. For example, N-(salicylidene)-2-hydroxyaniline is effective against Mycobacterium tuberculosis H37Rv, exhibiting an MIC value of 8 lg/mL (de Souza *et al*., 2007). The synthesis and antimicrobial activity of a series of Schiff bases derived from the condensation of 5-chloro-salicylaldehyde and primary amines has recently been reported (Shi *et al*. 2007). The major causes of human death and disease is directly related to bacteria that exhibit multiple resistances to antibiotics. Thus the development of new antibacterial agents with potential effects against pathogenic bacteria is definitely an urgent medical need (Rice, 2006).

Metal complexes of a novel Schiff base derived from condensation of sulphametrole and varelaldehyde were screened against bacterial species (E. coli and S. aureus). The newly prepared Schiff base and its metal complexes showed a higher effect on E. coli (Gram-negative bacteria) and S. aureus (Gram-positive bacteria) (Mohamed *et al.,* 2010). It is known that the membrane of Gram-negative bacteria is surrounded by an outer membrane containing lipopolysaccharides. The synthesized Schiff base and its metal complexes seem to be able to combine with the lipophilic layer in order to enhance the membrane permeability of the Gram-negative bacteria. The lipid membrane surrounding the cell favours the passage of only lipid soluble materials; thus the lipophilicity is an important factor that controls the antimicrobial activity. Also the increase in lipophilicity enhances the penetration of Schiff base and its metal complexes into the lipid membranes and thus restricts further growth of the organism (Tumer *et al.,* 1999; Raman *et al.,* 2009). The Schiff base and its metal complexes are more toxic on *S. aureus* than on *E. coli*, probably due to the sulphonic OH, OCH_3, S and CH_3 CH_2 CH groups, which might interact with the double membrane (Mohamed *et al.,* 2010). This activity is related to the nature and structure of the complexes

The present investigation deals with the synthesis of two Schiff bases and the synthesized Schiff base compounds are screened *in-vitro* for their antibacterial properties against two gram-positive and two gram-negative strains of cultured organisms such as *Streptococcus mutans, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae* respectively.

MATERIALS AND METHODS

The starting materials *p*-anisidine and p- nitroaniline was obtained from Aldrich (USA). The salicyaldehyde, (Merck/ BDH, India, AnalR grade) were used as received. The agar used for preparation of agar plate for antibacterial study was obtained from Merck, Germany.

A PerkinElmer Spectrum-2000 (FTIR) spectrophotometer was used to obtain the IR spectra between 400 and 4000 cm^{-1}. The ^1H NMR spectra were recorded by Bruker 200 MHz spectrometer instruments

Synthesis of schiff bases

Preparation of 2-[(4-methoxyphenylimino)methyl]phenol (SB-1)

To 10ml of methanol, 1.23gm (0.01mole) of *p*-anisidine was dissolved and 0.73 ml (0.01mole) Salicylaldehyde was added drop wise. Now this reaction mixture was allowed to stir for 13 hrs. A yellow precipitate was formed, filtered, dried and recrystalised from methanol. Yield 38 %, MP-95 ^{o}C. FTIR (KBr) ν/cm^{-1}1614 cm^{-1}(C=N str., 1597 (C=C str.), 3084 (-OH str.) ^{1}H NMR (200 MHz, $CDCl_3$): ä8.6 (s, 1H, CH), 7.3-7.4 (m, 4H, Ar-H), 6.8-7.1 (m, 4H, Ar-H), 13.2 (br, Ar-OH).

Preparation of 2-[(4-nitrophenylimino)methyl]phenol (SB-2)

p-nitroaniline 1.38 gm (0.01 mole) was dissolved in 10 ml ethanol. To this solution 0.73 ml (0.01 mole) Salicylaldehyde was added drop wise. The reaction mixture was allowed to stir for 6hrs. The resulting solution was kept in refrigerator overnight. The resulting precipitate was filtered, dried and recrystalised from methanol. Yield 31%, MP- 145 ^{o}C.

FTIR (KBr) ν/cm^{-1} 1598 cm^{-1}(C=N str.), 1585 cm^{-1}(C=C str.), 3018 cm^{-1}(-OH str.) and 1566 cm^{-1}(Ar-NO_2 str.) ^{1}H NMR (200 MHz, $CDCl_3$) ä8.6 (s, 1H, CH), 7.3-7.5 (m, 4H, Ar-H), 6.8-7.0 (m, 4H, Ar-H), 13.5 (br, Ar-OH).

Antibacterial studies

Both the synthesized Schiff bases were screened for the antibacterial activity against the pathogenic bacterial strains of *Streptococcus mutans, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae* and the result was compared with ciprofloxacin taken as standard. For the study paper disc diffusion method was adopted. The Schiff bases (20 μg) in DMSO (0.1 mL) were applied on a paper disc (prepared from blotting paper 5 mm diameter) with help of the micropipette. The discs were put in a vacuum incubator for 48 h at 37^{o}C and then applied on the bacteria grown agar plates. For the preparation of the agar plate for bacterial species, 12g of agar was soaked in 200 ml of distilled water for 15 minutes and then boiled in water bath until the agar was completely dissolved. This was autoclaved for 15 minutes at 120^{o}C, then poured into sterilized Petri dishes, and stored at a temperature of 40^{o}C for inoculation. Platinum wire loop was used for inoculation. Platinum wire loop was made red hot in a flame, cooled and used for the application of bacterial strains. The paper discs were applied to the inoculated agar plates with the help of sterilized forceps. After the application of the discs, they were incubated at 37^{o}C for 24h. The diameter of the inhibition zone was measured.

RESULTS AND DISCUSSION

Schiff bases were synthesized by condensing salicyladehyde with different aromatic and amines as per Scheme-1.

In order to compare the activity of Schiff bases, two Schiff bases (SB1 and SB2) are chosen which are differed by the kind of substituents. In SB1 the OCH_3 group is a electron donating group whereas in SB2, NO_2 is a electron withdrawing group. In the FTIR spectra of the Schiff bases, several characteristic absorption of starting materials vanished and new absorption bands appeared. The stretching frequency of carbonyl group of salicyaldehyde appear at 1666 cm^{-1} vanished and instead new peaks were appeared in the range of 1598-1680 cm^{-1} which were ascribed to the C = N stretching along with C = C stretching and -OH stretching at 3084 cm^{-1} are also observed for all the Schiff bases. These FTIR data provides ample evidence for the formation of Schiff bases.

The ^{1}H NMR Spectra of the above Schiff base was taken, which provided direct evidence for formation of the Schiff bases. In the Schiff bases the characteristics aldehydic proton peak at 10.3 ppm vanished and new peak around 8.6 appeared, which are attributed to azomethine proton (C*H* = N) peak. A complex set of multiplets between 6.8 - 7.1 and 7.2-7.5 ppm were due to coupling of the aromatic ring protons (Hafi *et al*.). Both FTIR data and NMR data support the formation of Schiff bases.

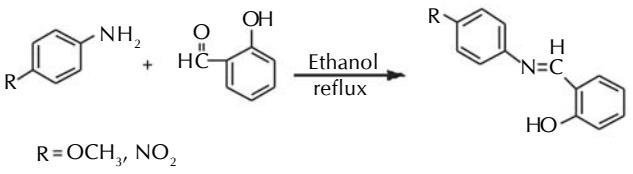
Antibacterial studies

Both the Schiff bases were evaluated for the *in-vitro* antibacterial activity against two gram-positive and two gram-negative strains of cultured organisms such as *Streptococcus mutans, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae* respectively. (Table-1). The antimicrobial activity was performed by paper disc diffusion method at the concentration level of 200¼g/ml in DMSO solvent. Ciprofloxacin (S) was used as standard drug at a concentration of 200ìg/ml and pure solvent DMSO is used as blank sample. The antibacterial activities of the Schiff bases were compared against the standard (S) sample and Blank (B) Sample. The zone of inhibition was maximum (25-28 mm) in the standard sample while it was zero in the blank sample. The Schiff base SB-1 shows 20-30% antibacterial activity while the Schiff's base SB-2 shows 10-20% antibacterial activity in comparison to the standard (S) sample. This is probably due to the effect of electron donating (-OCH_3) and Electron withdrawing (-NO_2) group. Electron donating group increases the anti bacterial activity while withdrawing group reduces it.

Antibacterial activities of the synthesized Schiff base were done in comparison with ciprofloxacin as standard to reveal the potency of synthesized derivatives. All the 4 selected strains of bacteria namely *Streptococcus mutans, Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae* showed sensitivity to both the Schiff bases. Schiff's base SB-1 shows better anti bacterial activities than the Schiff's base SB-2.This may be due to the effect of electron withdrawing and electron donating groups present in them. Schiff base chelating resins

Table 1: Antibacterial activity of the synthesized Schiff base compounds

Sl. No	Name and symbol of the Schiff base	Zone of inhibition (in mm)			
		S. mutans	*S. aureus*	*E. coli*	*K pneumoniae*
1	2-[(4-methoxyphenylimino)methyl]phenol (SB-1)	5-8	5-7	6-8	4-7
2	2-[(4-nitrophenylimino)methyl]phenol (SB-2).	Negligible (d″4)	Negligible (d″4)	Negligible (d″4)	Negligible (d″4)
3	Ciprofloxacin(standard) (S)	26-28	25-26	27-28	25-26
4	DMSO(Blank) (B)	0	0	0	0



Scheme 1: synthetic route to Schiff bases.

have wide range of applications. In future work we will synthesize resins from these Schiff bases, which can be used for purification of drinking water.

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