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SYNTHESIS AND COMPARATIVE ANTIBACTERIAL ACTIVITY STUDIES OF SCHIFF BASE COPPER COMPLEXES

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ABSTRACT

Azomethine linkage has a property to make various changes in microbial studies of Schiff bases and its complexes. A large number of Schiff bases have been synthesized and used as ligands. Most of these ligands and its complexes wereshowed antibacterial activity against pathogenic stains. Coppercomplexes derived from Vanilinethiosemicarbazone, Salicylaldene thiosemicarbazone,2-Chlorobenzylidene-2-aminophenol, 4-Chlorobenzylidene- 2- aminophenol were synthesized and characterized by spectral method.The *invitro* biological screening effects of the prepared copper complexes were tested against three gram negative bacteria Salmonella typhimurium, Vibrio cholera, Aeromonas hydrophila, and one gram-positive bacteria Bacillus subtilis by disc diffusion method. Among these complexes Salicylaldene thiosemicarbazone was found to be highly active against Aeromonashydrophila,Vibriocholera, Bacillus subtilis,and Vaniline thiosemicarbazone was found to be highly active against Salmonellatyphimurium.

INTRODUCTION

Aromatic aldehydes having a conjugation system and are making more stable ligands than aliphatic aldehydes.Several azomethine has been reported to possess remarkable antibacterial, antifungal, anticancer and antimalarial activities [1-5]. Theantibacterial, antifungal, anticancer and antimalarial activities of Schiff base make it as an extensively useful in various purposes [6, 7]. The biological activity of chelating ligands having N,S and O as a donor atoms are attracting attention due to their versatile nature of metal binding mode.The metal ions may alter or enhance the activity of biological active compounds [8-13].Transition metals have a strong tendency to form co-ordination complex due to small size, high charge densities and vacant (n-1) d orbitals. A large number of ligands with transition metals have been reported so far and their catalytic and biological properties have been studied intensively [14-16].Among these complexes copper attracts much more attention because of its biological relevance and its own interesting co-ordination chemistry such as geometry, flexible redox property and oxidation state.Several reports have indicated that copper complexes are more biological important metal among the transition metal series.The azomethine group (-CH=N) is believed to be responsible for the biological activity of these complexes [17-19]. The compounds having antibacterial activity may act either by killing the microbe or by inhibiting multiplication of microbe by blocking their active sites. In the present paperSalicylaldehyde thiosemicarbazone (SALTSC), Vaniline thiosemicarbazone (VALTSC)2-Chlorobenzylidene-2-aminophenol(2-CAP)4-Chlorobenzylidene2-aminophenol (4-CAP), and their Cu (II)complexes were synthesized andtested for their antibacterial activity.

MATERIALS AND METHODS

Preparation of Vaniline thiosemicarbazone (VALTSC)

Thiosemicarbazide(0.01 mole) in hotethanol was added to an ethanolic solution of vaniline (0.01mole). Themixture was refluxed for about 2 hours on a water bath till a clear solution was obtained. It was allowed to cool and the ligand was separated, filtered, washed with ethanol and dried for 6hours[20].

Preparation of Salicylaldenethiosemicarbazone (SALTSC)

0.01 mole of salicylaldehyde dissolved in ethanol. To this ethanolic solution of 0.01 mole ofthiosemicarbazide wasadded mixed well and refluxed for two hours. The precipitate was then filtered, washed with ethanol and dried for 4 hours [21, 22].

Preparation of 2- Chlorobenzylidene-2-aminophenol (2- CAP)

0.01mole of 2-aminophenol was mixed with equivalent amount of 2 -chlorobenzaldehyde in 25 ml of ethanol. The resulting mixture was left under reflux for 2 hours and the solid product formed was separated by filtration, washed with ethanol, and then dried.

Preparation of 4- Chlorobenzylidene-2-aminophenol(4-CAP)

0.01 mole of 2-aminophenol was mixed with equivalent amount of 4 -chlorobenzaldehyde in 25 ml of ethanol. The resulting mixture was left under reflux for 2 hours and the solid product formed was separated by filtration, washed with ethanol, and then dried.

Synthesis of metal complexes

To an ethanolic solution of the ligands were taken in a RB flask an ethanolic solution of copper nitrate was added in a molar ratio (1:1). The resulting solution was refluxed for two hours.Sodium acetate was added to control the pH.The refluxed solution was cooled and the precipitated complexes were filtered. Complexes were washed with ethanol and dried over anhydrous calcium chloride.

Antibacterial studies

Four pathogenic bacteria have been selected to study the antibacterial activity of the copper complexes. These were Gram- negative Vibriocholera,Salmonellatyphimurium, Aeromonas hydrophila and one Gram-positive Bacillus subtilis. Antibacterial activities of each copper complexes were evaluated by the agar disc diffusion method on Muller Hinton Agar [23-25]. Muller Hinton Agar (MHA) medium was poured in the petridish and kept at 45^0C. After the medium was solidified, bacterial suspension were spread on the solid plates with sterile swab. The appropriate antibiotic test discs were placed on MHA plates with sterilized forceps. The plates were incubated at 37ºC for 24 hrs. The antimicrobial activity was measured by using the diameter of zone of inhibition. Different concentration of the tested samples in DMSO solutions (125, 62.5, 31.2, 15.6, 7.8, 3.9µg/ml) were used for the determination of minimum inhibitory concentration (MIC). The highest concentrations which inhibit the growth have been recorded (125, 62.5, and 31.2µg/ml).

RESULTS

The structure of the synthesized ligands and its metal complexes were established with the help of spectral techniques. The IR spectra of four ligands have been compared with the spectra of synthesised complexes. It was observed that binding mode of ligands to metal ions which is precisely confirmed by change in the position of absorption peaks. A characteristic

band is observed in all the ligand due to the formation of azomethine linkage (1580-1610cm^{-1}). In copper complexes this band appears at a frequency lower than that of the free ligand.

In VALTSC and SALTSC the SH vibrations are absent in the region 2650-2500cm^{-1} indicate that the free ligand exist in the keto form in the solid state. However during the complex formation it might exist in the enol form.This is indicated by the absence of the band due to νC-S of the ligand in the complexes. In the complexes the bands are obtained at 3450-3400cm^{-1}for the copper complexes which exclude the possibility of hydrogen bonding.The bands due to νNH,νOH are retained in the case of complexes excludes any possible participation of the oxygen of the phenol group or nitrogen of the NH_2 in coordination [23]

In 2-CAP and 4-CAP,the spectrum showsbands at the range of 3350-3400cm^{-1}. This confirms the presence of phenolicgroup. But these characteristic bands are not present in the complexes.Whereas intense ligand band at about 1250cm^{-1}(phenolic C-O) shift to higher frequency in the complexes. Deprotonation of the phenolic –OH group on chelation with metal ion has been confirmed.

Table 1-The characteristic FT-IR frequencies of the ligand and complexes

Name of the compound	νCH=N cm^{-1}	νOH cm^{-1}	νC-S cm^{-1}	νNH cm^{-1}	νC-O
VALTSC	1599	3440	780	3276	1276
CuVALTSC	1580	3435	773	3255	1288
SALTSC	1610	3447	754	3171	-
CuSALTSC	1598	3439	789	3250	-
2-CAP	1618	3428	-	-	1250
Cu-2-CAP	1592	-	-	-	1278
4-CAP	1625	3431	-	-	1239
Cu-4-CAP	1582	-	-	-	1280

Table 2-The antibacterial activity of the complexes

Complexes	*B.S*			*V.C*			*S.T*			*A.H*		
	125 µg/ml	**62.5 µg/ml**	**31.2 µg/ml**	**125 µg/ml**	**62 .5 µg/ml.**	**31 .2 µg/ml**	**125 µg/ml**	**6 2.5 µg/ml**	**31.2 µg/ml**	**125 µg/ml**	**62.5 µg/ml**	**31.2 µg/ml**
CuVATSC	+++	++	-	-	-	-	+++	++	-	-	-	-
CuSALTSC	+++	+++	++	+++	+++	++	++	+	+	+++	++	+
Cu-2-CAP	+++	+++	++	-	-	-	++	++	+	+	+	-
Cu -4-CAP	+++	++	++	-	-	-	+	+	-	-	-	-

Key to symbols:

Highly active =+++ (inhibition zone>10mm)

Moderately active =++ (inhibition zone7-10 mm)

Slightly active =+ (inhibition zone4-6 mm)

Inactive =– (inhibition zone <4mm)

Abbreviations:

B.S=*Bacillus subtilis*

V.C=*Vibrio cholera*

S.T=*Salmonella typhimurium*

A.H=*Aeromonas hydrophila*

Figure 1: Antibacterial activity of Cu-VALTSC

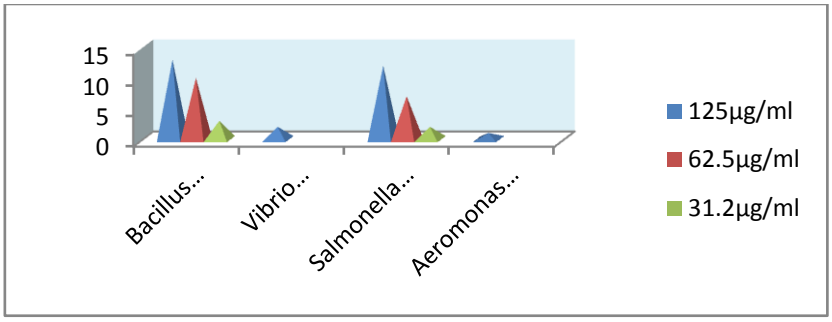


Figure 2: Antibacterial activity of Cu-SALTSC

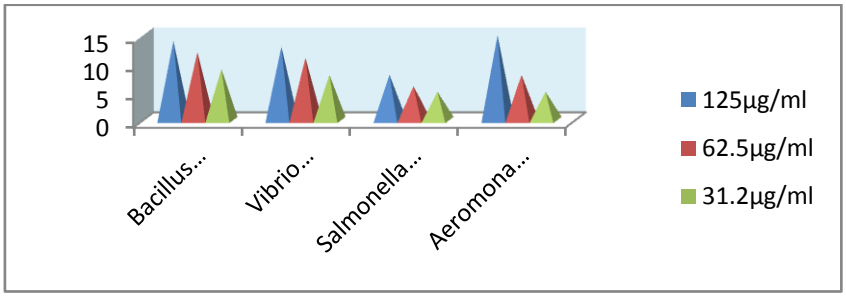


Figure 3: Antibacterial activity of Cu-2-CAP

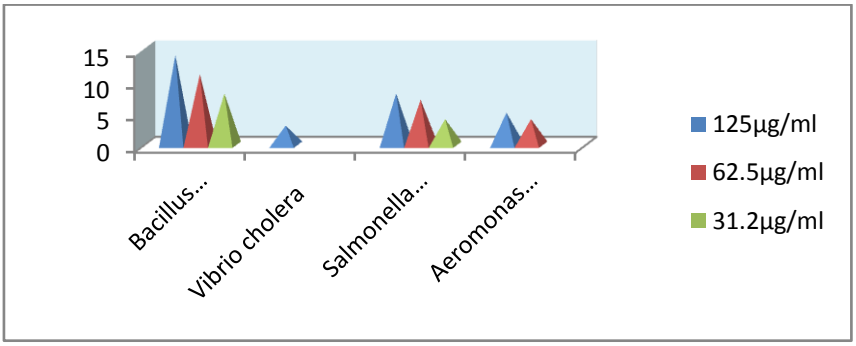
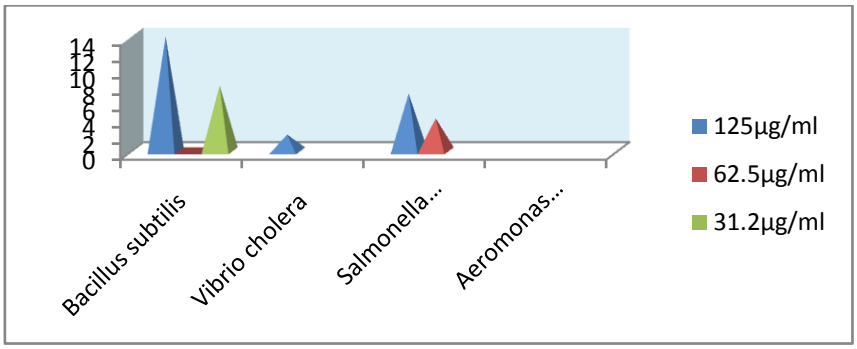


Figure 4: Antibacterial activity of Cu-4-CAP



Comparative studies in *in vitro* antibacterial activity of the prepared Cu(II)complexes were carried out against four pathogens by using disc diffusion method. In all the above samples DMSO was used as control.CuSALTSC has shown antibacterial activity against all gram negative and gram positive bacteria. Whereas CuVATSC and Cu -4-CAPhave antibacterial activity against only two organisms one gram-positive and one gram negative bacteria.

Cu-2-CAP showed activity against three organisms one positive and two negative bacteria.

DISCUSSION

It is observed from the above data that antibacterial activity of the prepared Cu(II) complexes have shown significant increase due to co-ordination. CuSALTSC has shown more activity than compared to other Copper complexes. In all the metal complexes as the concentration increases antibacterial activity also increases. Due to the presence of thiosemicarbazone group. CuSALTSC and CuVALTSC were showed good activity.The chloride ion in the complex can enhances the antibacterial activity due to the killing microbes or inhibiting their multiplication by blocking their active site .From the above complexesCu-2-CAP and Cu-4-CAP also showed activity.

All the synthesized compounds have been investigated for their antibacterial activities. Therefore, these compounds may be used as new antibacterial drugs after performing further research work with advanced technology.

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