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ANTIFUNGAL ACTIVITY STUDIES OF SCHIFF BASE COPPER COMPLEXES

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ABSTRACT

Schiff bases derived from an amino and carbonyl compound are an important class of ligands that coordinate to metal ions via azomethine nitrogen and have been studied extensively. The imine groups are present in various natural, natural-derived, and non-natural compounds. 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 were showed antifungal activity against pathogenic stains. We report here the antifungal activities of the Copper complexes with four Schiff base ligands derived from Vanilinethiosemicarbazone, Salicylaldenethiosemicarbazone, 2-Chlorobenzylidene-2-aminophenol, 4-Chlorobenzylidene- 2- aminophenol. The invitro biological screening effects of the prepared copper complexes were tested against three fungi by disc diffusion method. A comparative study of inhibition values of the Schiff base complexes were observed. Copper complexes derived from Salicylaldenethiosemicarbazone was found to be highly active against Candida albicans, Aspergillusniger and Vanilinethiosemicarbazone was found to be highly active against Trichodermaviride.

INTRODUCTION

Schiff bases continue to occupy an important position as ligands in coordination chemistry. Due to their great flexibility and diverse structural aspects, a wide range of Schiff bases have been synthesized conventionally and their complexation behavior was studied.Transition metals have a strong tendency to form co-ordination complexes 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 [1-4] 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. The development of the field of bioinorganic chemistry has increased the interest in Schiff base complexes, since it has been recognized that many of these complexes may serve as models for biologically important species and were investigated for antifungal, antimicrobial,antibacterial, anti-inflammatory,anti-convulsant,anticancer activities. [5].Aromaticaldehydes having a conjugation system and are making more stable ligands than aliphatic aldehydes. The azomethine group (-CH=N) is believed to be responsible for the biological activity of these complexes [6-8]. Several azomethine has been reported to possess remarkable antibacterial, antifungal, anticancer and antimalarial activities and make it as an extensively useful in various purposes. [9-14]. 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 [15-19]. Several reports have indicated that copper complexes are more biological important metal among the transition metal series. 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 study we synthesizedSalicylaldenethiosemicarbazone (SALTSC), Vanilinethiosemicarbazone (VALTSC), 2- Chlorobenzylidene-2-aminophenol (2-CAP), 4-Chlorobenzylidene-2- aminophenol (4-CAP), and their Cu (II) complexes. The complexes were tested for their antifungal activity.

MATERIALS AND METHODS

Preparation of CopperComplexes[20-23]

Ligands were prepared by usingThiosemicarbazide, 2-aminophenol as amine and Vaniline,Salicylaldehyde,2-chlorobenzaldehyde,4-chlorobenzaldehyde are used as aldehyde.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.

Antifungal Testing[24]

Preparation of inoculum

Stock cultures were maintained at 4°C on Sabouraud Dextrose agar Slant. Active cultures for experiments were prepared by transferring a loop full of culture from the stock cultures into the test tubes containing Sabouraud Dextrose broth , that were incubated at 48hrs at 37ºC.

Agar disc diffusion method

Antifungal of extracts was determined by disc diffusion method on Sabouraud Dextrose agar (SDA) medium. Sabouraud Dextrose agar (SDA) medium is poured in to the petriplate. After the medium was solidified, the inoculums were spread on the solid plates with sterile swab moistened with the fungal suspension. The discs were placed in SDA plates and add 20 µl of sample were placed in the disc .The plates were incubated at 37ºC for 1-7 days. The inhibition zones formed on media were measured with a zone reader in millimeters.

RESULTS

The structure of the synthesized ligands and its metal complexes were established with the help ofspectral techniques. The IRspectra of four ligands have been compared with the spectra of synthesized 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[25].

In 2-CAP and 4-CAP, the spectrum shows bands at the range of 3350-3400cm^{-1}. This confirms the presence of phenolic group. 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}	νOHCm^{-1}	νC-S Cm^{-1}	νNH cm^{-1}	νC-O Cm^{-1}
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

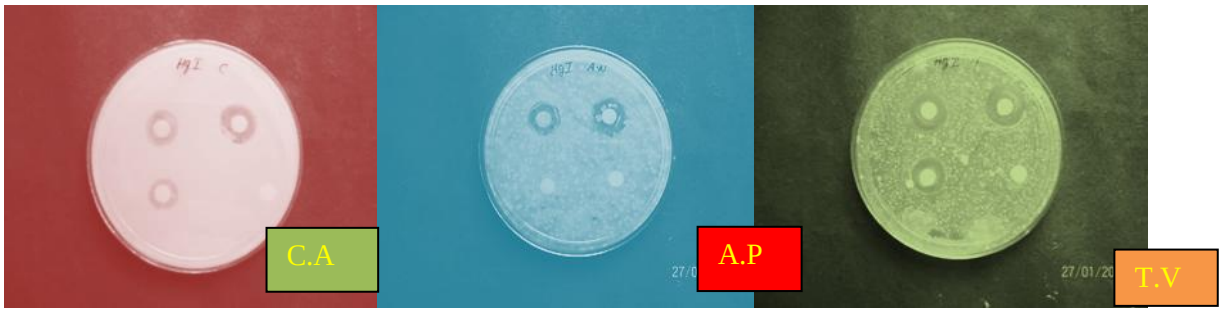


Figure 1 Antifungal activity of Vanilinethiosemicarbazone (VALTSC)

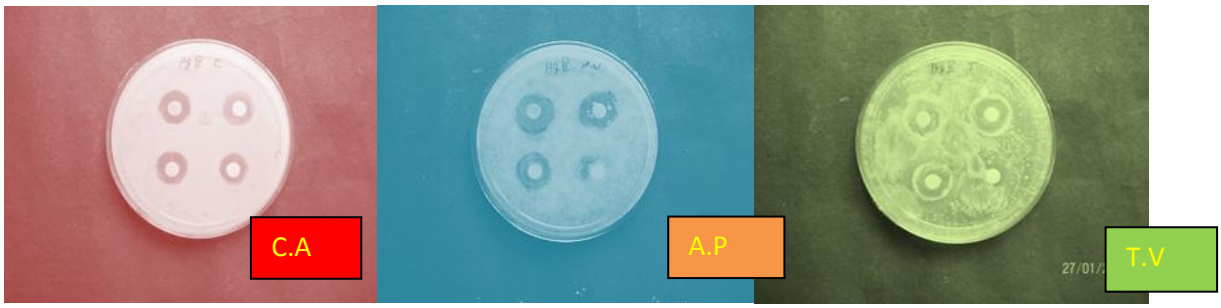


Figure2 Antifungal activity of Salicylaldenethiosemicarbazone (SALTSC)

Figure3Antifungal activity of 2- Chlorobenzylidene-2-aminophenol (2- CAP)

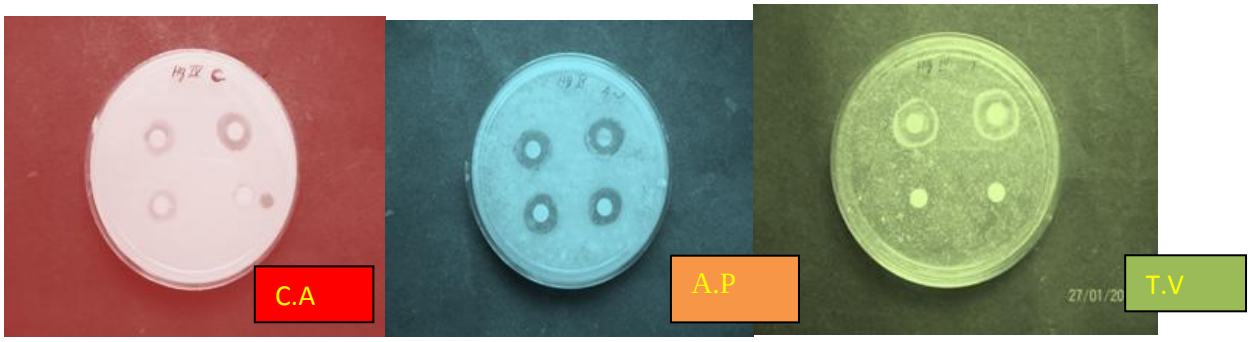


Figure 4 Antifungal activity of 4- Chlorobenzylidene-2-aminophenol (4-CAP)

Abbreviations

C.A-Candida albicans, A.P-Aspergillusniger, T.V-Trichodermaviride

Table 2 The antifungal activity of the complexes

Complexes	Candida albicans			Aspergillusniger			Trichodermaviride		
	1000 µg/ml	750 µg/ml	500 µg/ml	1000 µg/ml	750 µg/ml	500 µg/ml	1000 µg/ml	750 µg/ml	500 µg/ml
Cu-VATSC	+++	++	++	+++	+	_	+++	++	++
Cu-SALTSC	+++	++	++	+++	+++	+	++	++	+
Cu-2-CAP	++	_	_	+++	+	_	+++	++	++
Cu-4-CAP	++	++	++	+++	++	++	+++	+	_

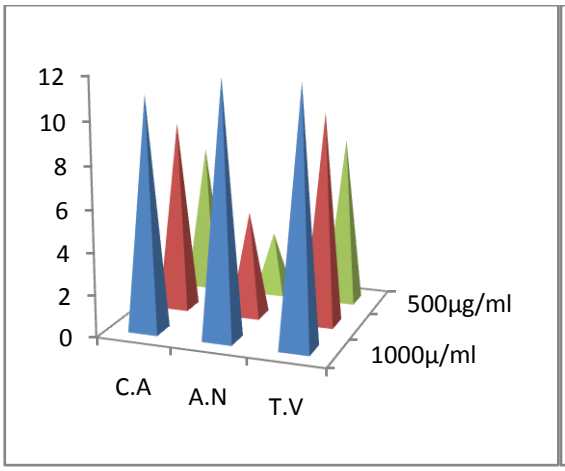
Key to symbols:

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

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

Slightly active = + (inhibition zone4-6 mm)

Inactive = – (inhibition zone <4mm)



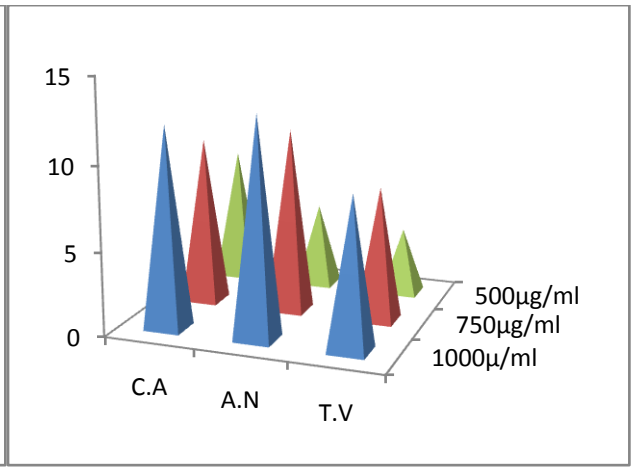
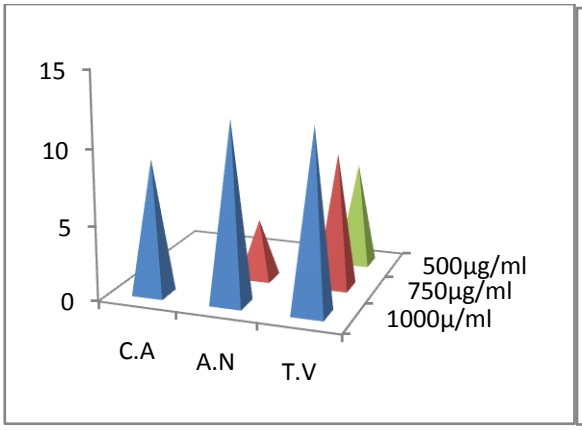


Figure 5 Cu VANTSCFigure 6 CU SALTSC



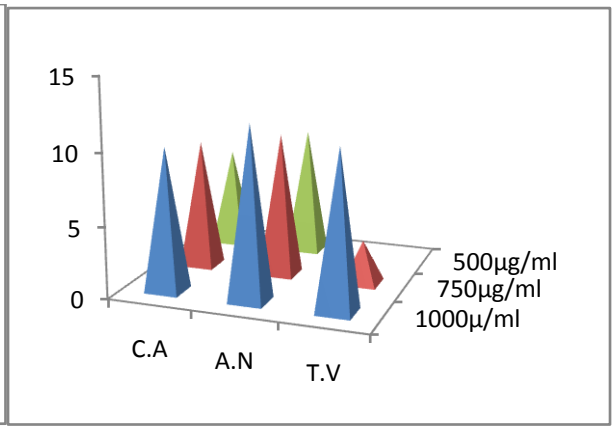


Figure 7 Cu 2-CAPFigure 8 Cu 4-CAP

DISCUSSION

Comparative studies in invitro antifungal activity of the prepared Cu (II) complexes were carried out against three pathogens by using disc diffusion method. In all the above samples DMSO was used as control. From Table 2 comparative study of inhibition values of the Schiff base complexes indicates copper complexes derived from Salicylaldenethiosemicarbazone was found to be highly active against Candida albicans and Aspergillusniger. Vanilinethiosemicarbazone was found to be highly active against Trichodermaviride.

It was observed from the above data that antifungal 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 antifungal activity due to the killing microbes or inhibiting their multiplication by blocking their active site .From the above complexes Cu2-CAP and Cu4-CAP also showed activity. All the synthesized compounds have been investigated for their antifungal activities. Therefore, these compounds may be used as new drugs after performing further research work with advanced technology.

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