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Research Article

Antifungal Activity of Some Mixed Ligand Complexes Incorporating Schiff Bases

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Abstract

The Schiff base (HL1), namely; [(S,Z)-2-((2-hydroxy-1-phenylethylidene) amino)-3-(4-hydroxyphenyl)propanoic acid] was synthesized by the condensation of 2-hydroxyacetophenone and L-Tyrosine Whereas, the other Schiff base (HL2), namely; (E)-4-((2-(2,4-dinitrophenyl)hydrazono)methyl)-N,N-dimethylaniline] was synthesized by refluxing 4-dimethylaminobenzaldehyde and 2,4-dinitrophenylhydrazine. The first Schiff base (HL1) is used as primary ligand, whereas, the second Schiff base (HL2) is used as secondary ligand to prepare five mixed ligand complexes with Co(II), Ni(II), Cu(II), Zn(II) and Fe(III) ions. These synthesized mixed ligand complexes were characterized by using several spectroanalytical techniques. The data reveals octahedral geometry for all the mixed ligand complexes. In addition, these compounds were also tested for their antifungal activities against *Aspergillus niger, Aspergillus flavus, Altarnaria alternata, Rhizopus stolonifer*.

Keywords: Schiff Bases; Mixed Ligand Complexes; Antifungal Activity

Introduction

The Schiff base compounds are commonly used as ligands in the synthesis of coordination compounds [1,2]. These compounds have an important role due to their physiological and pharmaceutical activities [3,4]. Miloud et al [5] have studied the antifungal activities of five mixed ligand complexes with a Schiff base as main ligand and 2-aminobenzoic acid as co-ligand by using agar well diffusion method. It was found that some of the complexes are most active against *Aspergillus niger, Aspergillus flavus, Altarnaria alternata, Rhizopus stolonifer*.

Nair et al [6] have also reported four complexes with a Schiff base formed from 3-aminobenzoic acid and indole-3-carboxaldehyde. The antimicrobial activities of these compounds were examined by diffusion method and the results confirmed that the free Schiff base is less active than its metal complexes. Three complexes of divalent metal ions with a Schiff base formed from the reaction of 4-diethylaminosalicylaldehyde and 1-(4-aminophenyl) ethanone oxime have been investigated. The results are in good agreement with square planar geometry for Ni(II) and Cu(II) complexes, while, a tetrahedral geometry for Co(II) complex [7]. The biological activity of all the compounds was examined against some selected pathogenic organisms. Andiappan et al [8] have reported a series of lanthanide complexes with a Schiff base obtained by the condensation of 2,6-diaminopyridine and anthracene-9-carbaldehyde. The Schiff base and its metal complexes were tested for their cytotoxic activity against cervical (HeLa) and human breast cancer (MCF7) cell line.

In this study, we have reported the antifungal activities of some Schiff base mixed ligand complexes of Co(II), Ni(II), Cu(II), Zn(II) and Fe(III) chelates against some fungal strains such as *A. niger, A. flavus, A. alternata, R. stolonifer*.

Experimental

Chemicals and physical measurements

All the chemicals and reagents used in this study were of AR grade. The characterizations such as CHN analyses, molar conductivity, magnetic moment measurements and spectral analyses of these synthesized Schiff base ligands and their mixed ligand complexes has already been reported [9]. But here we are reporting the antifungal activities of these compounds.

Synthesis of Schiff bases and their mixed ligand complexes

The Schiff base (HL1), namely; [(S,Z)-2-((2-hydroxy-1-phenylethylidene)amino)-3-(4-hydroxyphenyl)propanoic acid] was synthesized by the condensation of 2-hydroxyacetophenone and L-Tyrosine (Figure 1). Whereas, the other Schiff base (HL2), namely; (E)-4-((2-(2,4-dinitrophenyl)hydrazono) methyl)-N,N-dimethylaniline] was synthesized by refluxing 4-dimethylaminobenzaldehyde and 2,4-dinitrophenylhydrazine (Figure 2,3). The Schiff bases and their mixed ligand complexes have

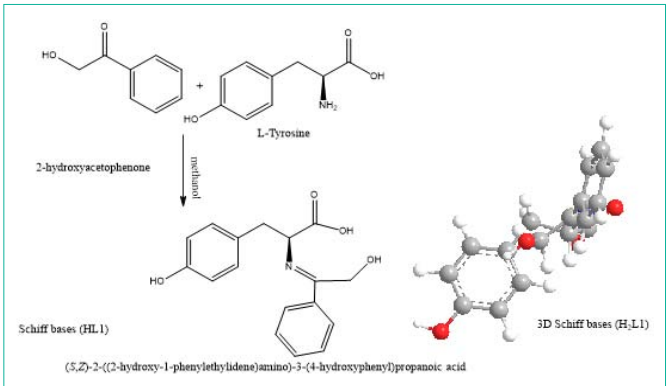

Figure 1: Structural of Schiff base (HL1).

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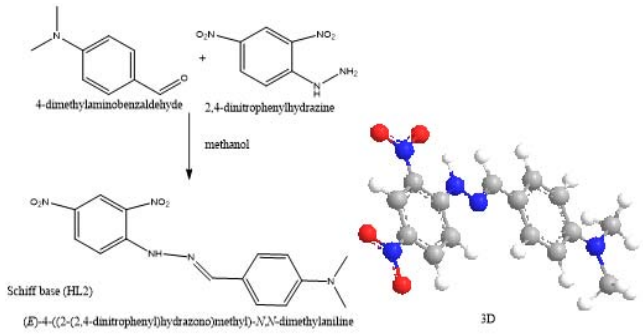

Figure 2: Schiff base (HL2).

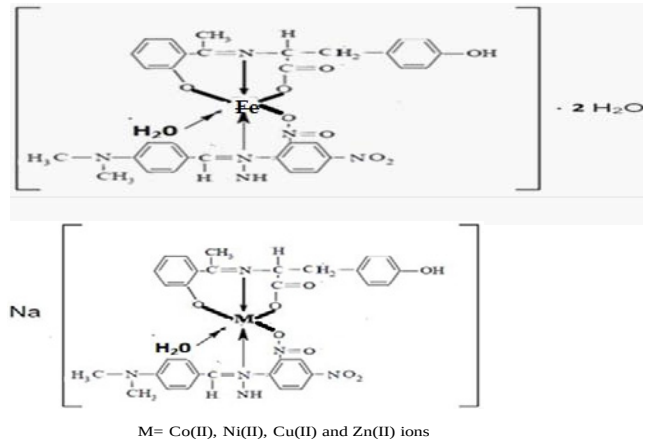

Figure 3: Structure of mixed ligand complexes.

been reported earlier [9].

Fungal species: Four test organisms such as *A. niger, A. flavus, A. alternata and R. stolonifer* were collected from the Laboratory of Applied Microbiology, University of Omar AL-Mukhtar, Libya. They were cultured in Petri plates containing Potato Dextrose Agar (PDA) media and incubated at 27°C for three days with periodic sub-culturing at 4°C.

Antifungal activity test: The antifungal activity of all these compounds was evaluated by agar well diffusion method [10]. All fungi were sub-cultured and prepared for the assessment of ligands and their complexes. The test compounds were dissolved in DMF solution. The PDA medium was poured into the sterile petri plates and allowed to solidify. The inoculum used was prepared using the fungal species from a 72-hour culture on PDA. The fungal suspension of each test fungi was evenly spread over the media by sterile cotton swabs. The plates have been kept to dry and a sterile cork borer (7mm in diameter) were then used to punch wells in the agar medium. Subsequently, wells were filled with 20µl of each compounds at various concentration of 25, 50 and 100 mg/mL and allowed to diffuse at room temperature for 15 min. The plates were incubated at 27°C for 48-72 hrs. The experiments were conducted in three duplicates. After the incubation, the plates were observed for formation of clear inhibition zone around the well indicated the presence of antifungal activity evaluated by measuring the diameter of the inhibition zone around the hole (mm).

Results and Discussion

In vitro antifungal activity

Our Schiff bases are tridentate (HL1) and bi-dentate (HL2) ligands forming very stable complexes with the metal ions. On complexation, the ligand with the O donor system might have inhibited enzyme

Table 1: Antifungal activity for the metal salts, Schiff bases and mixed ligand complexes

Sl. No.	Compounds	Diameter of inhibition zone of fungi (mm)											
		Concentration in mg/ml											
		A.niger			*A.flavus*			*A. alternata*			*R.stolonifer*		
		25	50	100	25	50	100	25	50	100	25	50	100
1	$CoCl_2.6H_2O$	12	15	17	9	9	11	24	27	28	11	14	15
2	$NiCl_2.6H_2O$	20	25	26	-	10	12	-	17	18	13	20	22
3	$CuCl_2.2H_2O$	-	9	9	-	-	-	-	-	-	10	16	18
4	$ZnCl_2$	17	20	24	-	-	-	-	-	-	11	11	13
5	$FeCl_3.6H_2O$	-	-	-	-	10	12	-	15	15	11	12	14
6	$C_{18}H_{21}NO_5$(HL1)	-	13	16	7	10	12	23	28	30	8	11	13
7	$C_{15}H_{15}N_5O_4$.(HL2)	-	-	-	-	-	-	-	-	-	-	-	-
8	$Na[Co(L1)(L2)H_2O]$	-	-	-	-	-	-	-	-	-	-	-	-
9	$Na[Ni(L1)(L2)H_2O]$	-	-	-	-	-	-	-	-	-	-	-	-
10	$Na[Cu(L1)(L2)H_2O]$	-	-	-	-	-	-	-	-	-	-	-	-
11	$Na[Zn(L1)(L2)H_2O]$	-	-	-	-	-	-	-	-	-	-	-	-
12	$[Fe(L1)(L2)H_2O].2H_2O$	8	10	11	8	10	13	9	16	22	7	8	10
13	DMF(Control)	-	-	-	-	-	-	-	-	-	-	-	-

Control (DMF): No activity (there was no zone of inhibition)

Observation	Report
Inhibition zone > 15mm	Highly active
Inhibition zone >10mm	Moderately active
Inhibition zone > 5mm	Slightly active
Inhibition zone ≤5-0 mm	Inactive

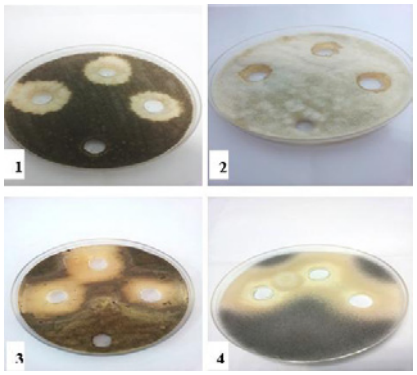

Figure 4: Effect of $CoCl_2.6H_2O$ on 1- *Aspergillus niger*, 2- *Aspergillus flavus*, 3- *Alternaria alternata* and 4- *Rhizopus stolonifer* at 25,50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

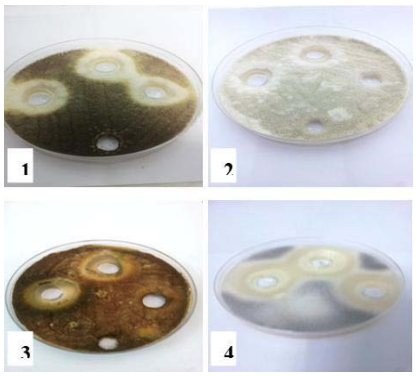

Figure 5: Effect of $NiCl_2.6H_2O$ on 1- *Aspergillus niger*, 2- *Aspergillus flavus*, 3- *Alternaria alternata* and 4- *Rhizopus stolonifer* at 25,50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

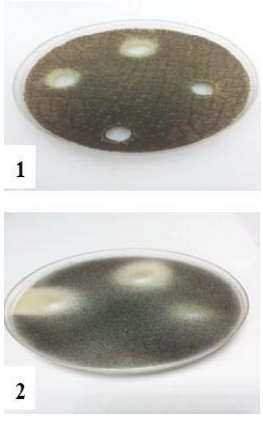

Figure 6: Effect of $CuCl_2.2H_2O$ on 1- *Aspergillus niger* and 2- *Rhizopus stolonifer* at 25,50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

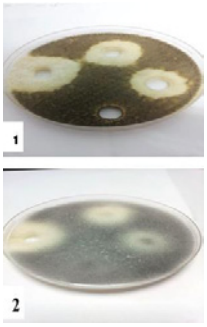

Figure 7: Effect of $ZnCl_2$ on 1- *Aspergillus niger* and 2- *Rhizopus stolonifer* at 25,50 and 100mg/ml concentrations, respectively (from right to left) compared with control.

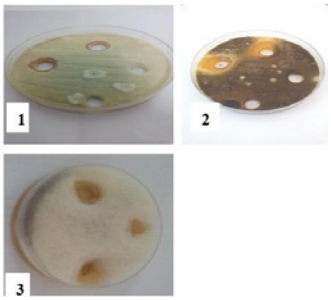

Figure 8: Effect of $FeCl_3.6H_2O$ on 1- *Aspergillus flavus*, 2- *Alternaria alternate* and 3- *Rhizopus stolonifer* at 25,50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

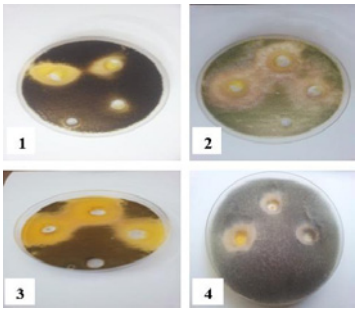

Figure 9: Effect of $C_{18}H_{21}NO_5$(HL1) on 1- *Aspergillus niger*, 2- *Aspergillus flavus*, 3- *Alternaria alternata* and 4- *Rhizopus stolonifer* at 25,50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

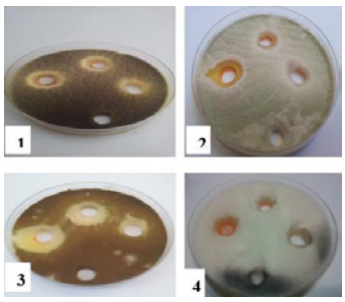

Figure 10: Effect of $(Fe(L1)(L4)H_2O).2H_2O$ on 1- *Aspergillus niger*, 2- *Aspergillus flavus*, 3- *Alternaria alternata* and 4- *Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentration, respectively (from right to left) compared with control.

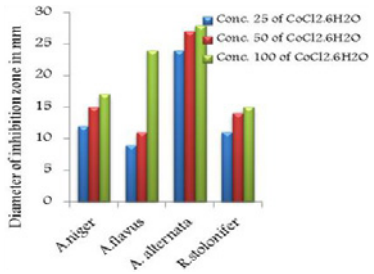

Figure 11: Effect of $CoCl_2.6H_2O$ on different types of fungi.

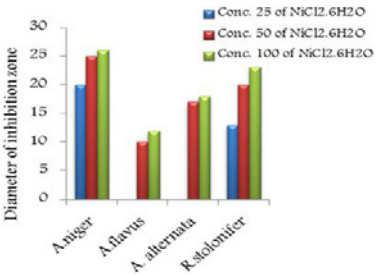

Figure 12: Effect of $NiCl_2.6H_2O$ on different types of fungi.

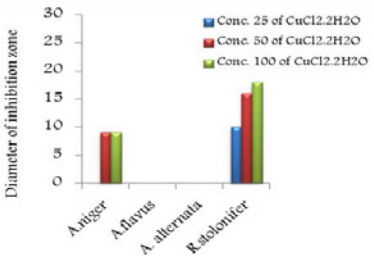

Figure 13: Effect of $CuCl_2.6H_2O$ on two types of fungi.

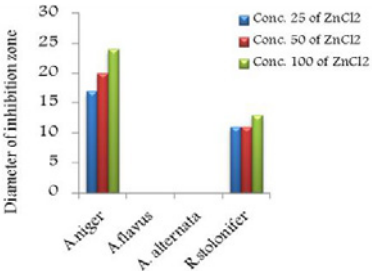

Figure 14: Effect of $ZnCl_2$ on two types of fungi.

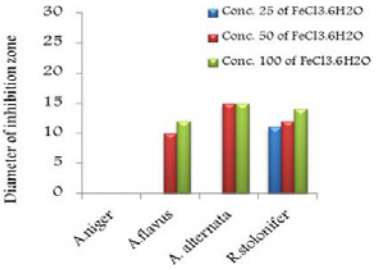

Figure 15: Effect of $FeCl_3.6H_2O$ on three types of fungi.

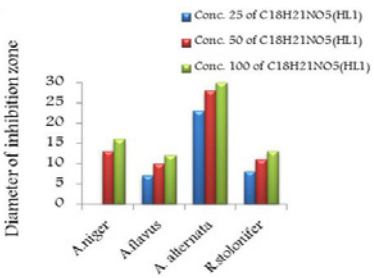

Figure 16: Effect of $C_{18}H_{21}NO_5$(HL1) on different types of fungi.

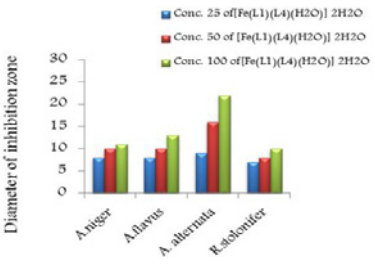

Figure 17: Effect of [Fe(L1)(L4)(H_2O)])$2H_2O$ on different types of fungi.

production, since enzyme, which requires a free –OH group for their activity appear to be especially susceptible to deactivation by the ions of the complexes.

The *in vitro* antifungal activities in three concentrations for these compounds are shown in (Table 1) and (Figure 4-17). DMF is used as negative control. The complex, [Fe(L1)(L2)H_2O].$2H_2O$ displayed significant antifungal activity compared to other complexes [11]. The salt, $CoCl_2.6H_2O$ showed significant activity against *A. alternata*, moderate activity towards *A.niger* and *R. stolonifer* and less activity against *A. flavus*. $NiCl_2.6H_2O$ exhibited high activity against *A.niger* and *R. stolonifer*, whereas, moderately effective against *A. flavus* and *A. alternata*. $CuCl_2.2H_2O$ exhibited moderate activity against *R. stolonifer* and less activity against *A.niger*. But no activity shown against *A. flavus* and A. alternate. $ZnCl_2$ exhibited high activity against *A.niger*, moderate activity against R.stolonifer, but no activity against *A. flavus* and A. alternate. $FeCl_3.6H_2O$ showed moderate activity against *A. flavus*, *R. stolonifer* and *A. alternata*, but no activity against *A.niger*. The Schiff base ligand (HL1) revealed higher activity against *A. alternata* and moderate activity against other tested fungal strains. The Schiff base ligand (HL2) did not show any activity. From the above results it is clearly observed that the fungal activity depends upon the nature of metal ion [12]. The variation in the activity of different metal complexes against different microorganism depends on their impermeability of the cell. The lipid membrane surrounding the cell favors the passage of any lipid soluble materials and it knows that lipo solubility is an important factor controlling antifungal activity [13,14].

Conclusion

The mixed ligand complexes with Schiff bases formed by the condensation of [2-hydroxyacetophenone and L-Tyrosine] (HL1) as primary ligand and [4-dimethylaminobenzaldehyde with 2,4-dinitrophenylhydrazine] as secondary ligand (HL2) are

electrolytic in nature except Fe(III) mixed ligand complex. The complex, $[Fe(L1)(L2)H_2O].2H_2O$ displayed significant antifungal activity compared to other tested metal complexes. The Schiff base ligand (HL1) revealed higher activity against *A. alternata* and moderate activity against other tested fungal strains. The Schiff base ligand (HL2) did not show any activity.

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