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Antifungal Activity Evaluation of Co(II), Ni(II), Cu(II), Zn(II) and Fe(III) Mixed Ligand Complexes with Different Schiff Bases

M. M El-ajaily[1*], M. M. Miloud[2], T. H. Al-noor[3], R. K. Mohapatra[4] and N. S. Al-barki[5]

[1]*Department of Chemistry, Benghazi University, Benghazi, Libya*

[2]*Department of Botany, Benghazi University, Al-abiar branch, Libya*

[3]*Department of Chemistry, Baghdad University, Baghdad, Iraq*

[4]*Department of Chemistry, Government College of Engineering, Keonjhar, Odisha, India*

[5]*Department of Chemistry, Ajdabyia University, Ajdabyia, Libya*

Abstract

A 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 with an amino acid (L-Tyrosine) for one hour. 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 for one hour. The first Schiff base (HL1) used ad primary ligand and the second one is used as secondary ligand to form five mixed ligand complexes with Co(II), Ni(II), Cu(II), Zn(II) and Fe(III) ions. The synthesized mixed ligand complexes were subjected to several physiochemical techniques, in terms; CHN elemental analyses, molar conductivity, magnetic moments and spectroscopic tools (FT-IR, 1HNMR, electronic, E.P.R and mass spectra). The analytical and spectroscopic data showed the presence of an octahedral geometry for all the mixed ligand complexes. The free Schiff bases, metal salts and mixed ligand complexes were tested for their antifungal activities on some pathogenic fungi species [*A. niger, A. flavus, Alternaria alternata, Rhizopus stolonifer*].

Keywords: Schiff bases • 2-hydroxyacetophenone. L-Tyrosine • 4-dimethylbenzaldehyde • 2, 4-dinitrophenylhydrazine • Mixed ligand complexes • Antifungal activity

Introduction

The Schiff base compounds have played as good ligands in the synthesis of coordination compounds. The extensive characterization of these compounds have an important role due to their ((physiological and pharmaceutical)) activities. 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 have most active against [A. niger, A. flavus, Alternaria alternata, Rhizopus stolonifer]. Nair et al. have been reported four complexes with a Schiff base formed from the refluxing of 3-aminobenzoic acid (C7H7NO2) and fromindole-3-carboxaldehyde. The antimicrobial activities of the Schiff base and its complexes were examined by diffusion method and the obtained results showed that the free Schiff base to be less active than its 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 prepared and investigated by several analytical and spectroscopic tools. The results confirmed the existence of square planar geometry for both Ni(II) and Cu(II) complexes, whereas, a tetrahedral geometry was confirmed for Co(II) complex. The biological activity of all compounds were examined against some pathogenic organisms [1]. Andiappan et. al.[6] Synthesized and characterized a series of lanthanide complexes with a Schiff base ligand; N2, N3-bis (anthracen-9-ylmethylene) pyridine-2, 3-diamine in ratio 1:2 by condensation step of 2,6-diaminopyridine and anthracene-9-carbaldehyde. The Schiff base and its metal complexes were tested for their cytotoxicity activity against cervical (HeLa) anticancer cell lines and human breast cancer (MCF7). This study aims to show the effect of the Schiff base, 3-aminobenzoic acid and [Co(II), Ni(II), Cu(II), Zn(II) and Fe(III)] mixed ligand complexes on

[*]***Address to correspondence:*** *M. M El-ajaily, Department of Chemistry, Benghazi University, Benghazi, Libya; E-mail: melajaily1@g.mail.com*

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four fungi [*A. niger, A. flavus, Alternaria alternata, Rhizopus stolonifer*].

Experimental

Chemicals and physical measurements

All chemicals and reagents used in this study were of Analar grade (BDH/Aldrich). They include; 2-hydroxyacetophenone, L-tyrosine, 4-dimethylaminobenzaldehyde, 2,4-dinitrophenylhydrazine, $CoCl_2.6H_2O$, NiCl2.6H2O, $CuCl_2.2H_2O$, ZnCl2, $FeCl_3.6H_2O$, absolute ethanol and Dimethylformamide (DMF). The (CHN) analyses were done by using 2400 elemental analyzer. The molar conductance measurements were performed on a BC 3020 Professional Benchtop Conductivity Meter, Benghazi University. Magnetic susceptibility was determined using a Johnson Matthey instrument at room temperature
(25°C) with $Hg[Co(SCN)_4]$ as blank. The infrared spectra were recorded as KBr disc on a Perkin-Elmer 1430 IR Spectrophotometer. The nuclear magnetic resonance spectra of the Schiff bases (HL1 and HL2) and their Zn(II) mixed ligand complex were recorded on Varian Gemini 200-200MHz spectrometer using TMS as internal standard and d6-DMSO as a solvent The electronic spectra were recorded on a Unicam Model UV-2 spectrophotometer. The mass spectra were carried out by using Shimadzu QP-2010 Plus. The EPR spectra were recorded by using EMX ESR spectrometer (Bruker) 1998 Y. All the mentioned analyses except molar conductivity were done at Micro analytical center, Cairo University, Giza, Egypt [2].

Synthesis of Schiff bases and their mixed ligand complexes

The Schiff bases of (HL1) Scheme 1, and (L2) Scheme 2 and their mi

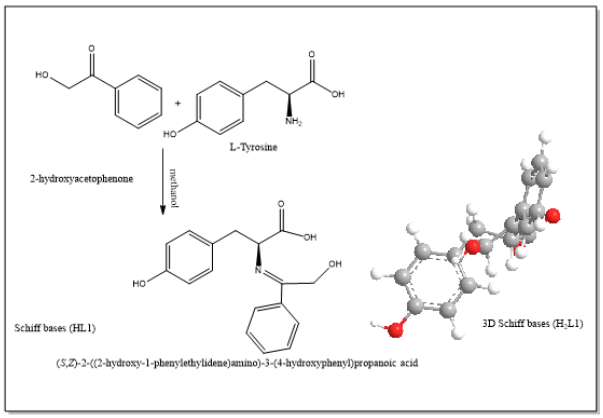

Figure1: Structural of schiff base (HL1).

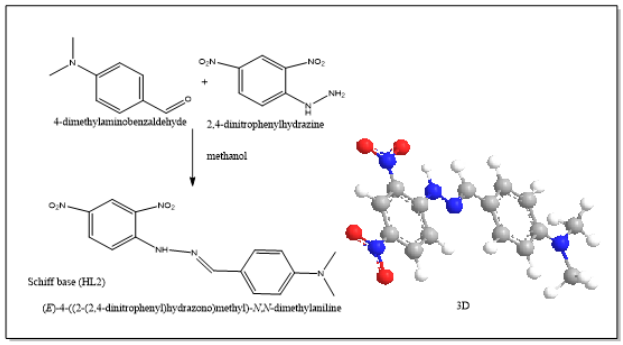

Figure2: Schiff base (HL2).

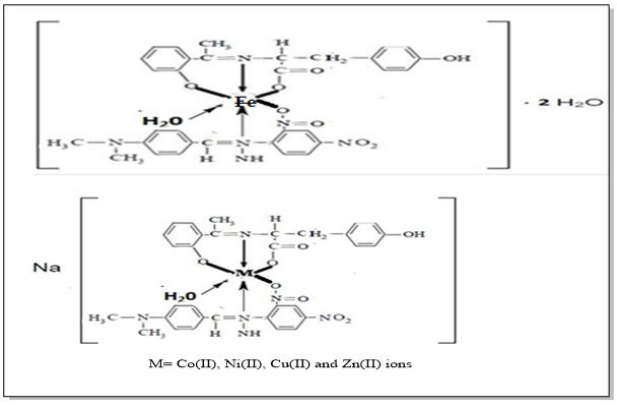

Figure3: Structure of mixed ligand complexes.

Fungal species: Four test organisms, *Aspergillus niger, Aspergillus flavus, Alternaria alternate* and *Rhizopus 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.

Screening for antifungal assay

Antifungal activity test: The antifungal activity of the all compounds (ligands, metal salts and their complexes (were evaluated by the agar well diffusion method. All fungi were sub-cultured and prepared for the assessment of ligands and their complexes activity. The compounds were dissolved in DMF solution. The (PDA)medium was poured in to 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 [3]. The plates have been kept to dry and a sterile cork borer (7 mm in diameter) were then used to punch wells in the agar medium. Subsequently, wells were filled with 20 µl 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. 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 whole (mm) as below:

Results and Discussion

Figures 1-3 show the synthesis of the Schiff bases and their mixed ligand complexes and their characterization is given in literature review.

Antifungal activity

Schiff bases are generally tridentate ligands (HL1) or bi-dentate ligand (HL2) forming very stable complexes with metals, Figure 3. On complexation, the ligand with the O donor system might have inhibited enzyme 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. Table 1 and Figures (4-17) show results of antifungal activity in three concentrations for the (metal salts, Schiff bases and mixed ligand complexes against the fungi [Aspergillus niger, Aspergillus flavus, Alternaria alternata and Rhizopus stolonifer]. DMF is used as solvent and negative control.

The complexes studied, [Fe(L1)(L2)H2O].2H2O showed significant antifungal activities compared to other complexes [4]. The CoCl2.6H2O) showed high antifungal activity against Alternaria alternate, moderate activity towards A. niger and R. stolonifer species and A. flavus show less activity. The NiCl2.6H2O exhibited a high antifungal activity against A. niger and R. stolonifer, it was moderately effective against A. flavus and Alternaria alternate. The CuCl2.2H2O exhibited moderate activity against R. stolonifer, less activity against A. niger. But no activity against A. flavus and Alternaria alternate. The ZnCl2 exhibited high activity against A. niger, moderate activity against R. stolonifer, but no activity against A. flavus and Alternaria alternate. The FeCl3.6H2O showed moderate activity against A. flavus, R. stolonifer and Alternaria alternate, but no activity against A. niger. The results on antifungal activity of the (HL1)] reveal a higher activity in Alternaria alternata, moderate activity against other fungi tested due to chelation process. The (HL2)] did not show any activity against test fungi. From the above results it clearly observed that the fungal activity depends upon the nature of metal ion. 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 is knows that lipo solubility is an important factor controlling antifungal activity [5].

S.No.	Fungal sp./ Compounds	Diameter of inhibition zone of fungi (mm)											
		Concentration in mg/ml											
		A. niger			A. flavus			Alternaria 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)	-	-	-	-	-	-	-	-	-	-	-	-

Table1: Antifungal activity for the metal salts, Schiff bases and mixed ligand complexesagainst some pathogenic fungi.

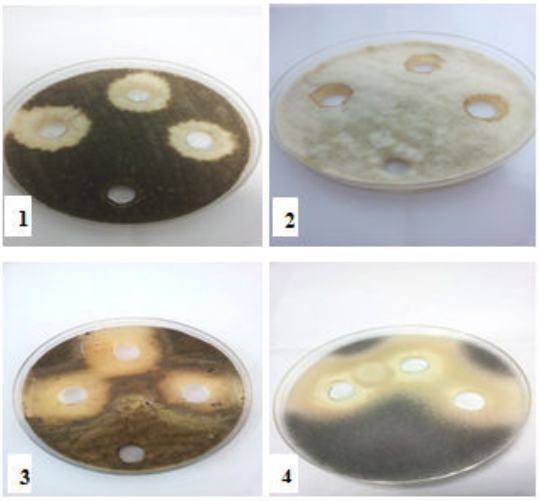

Figure4: Effect of $CoCl_2.6H_2O$ on 1- *Aspergillus niger* , 2- *Aspergillus flavus*, 3- *Alternaria alternata* and 4- *Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

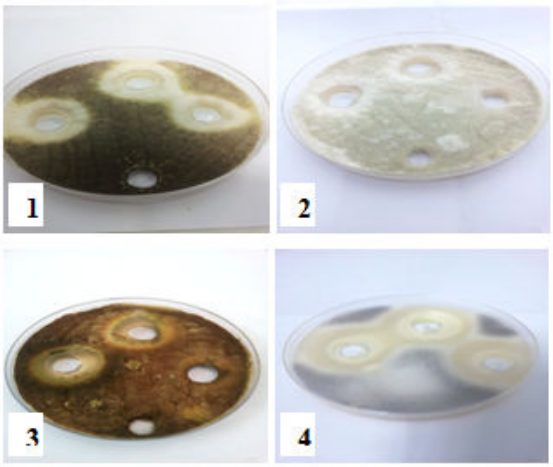

Figure5: Effect of $NiCl_2.6H_2O$ on 1- *Aspergillus niger*, 2- *Aspergillus flavus*, 3- *Alternaria alternate* and 4- *Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

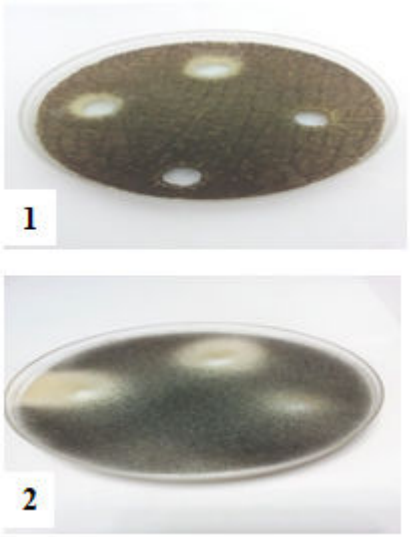

Figure6: Effect of $CuCl_2.2H_2O$ on 1- *Aspergillus niger* and 2- *Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

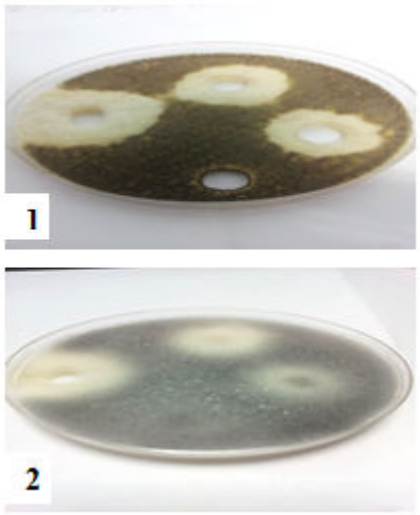

Figure7: Effect of $ZnCl_2$ on 1- *Aspergillus niger* and 2- *Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

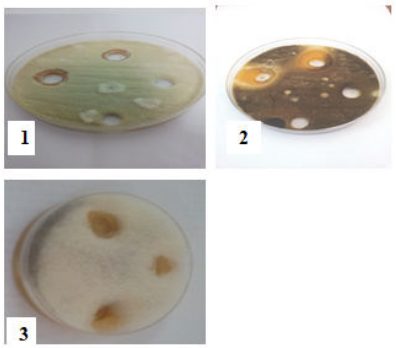

Figure8: Effect of $FeCl_3.6H_2O$ on 1- *Aspergillus flavus*, 2- *Alternaria alternate* and 3-*Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

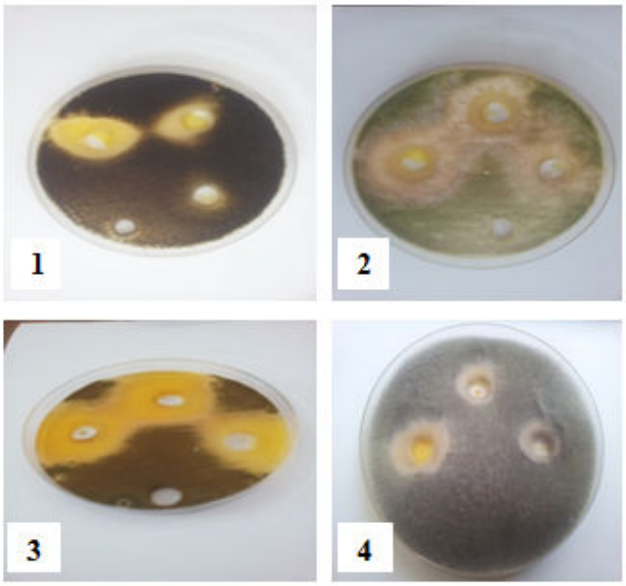

Figure9: Effect of $C_{18}H_{21}NO_5$ (HL1) on 1- *Aspergillus niger*, 2- *Aspergillus flavus*, 3- *Alternaria alternata* and 4- *Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentrations, respectively (from right to left) compared with control.

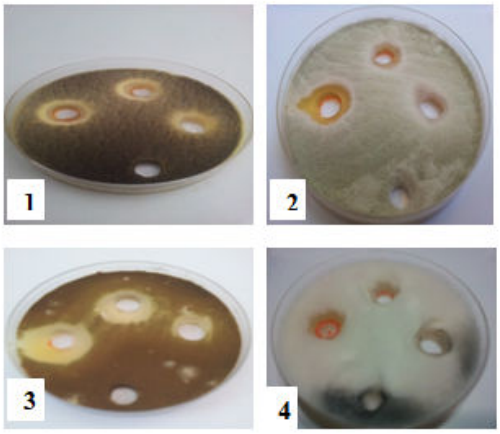

Figure10: Effect of $(Fe(L1)(L4)H_2O).2H_2O$ on 1- *Aspergillus niger*, 2- *Aspergillus flavus* , 3- *Alternaria alternata* and 4- *Rhizopus stolonifer* at 25, 50 and 100 mg/ml concentration, respectively (from right to left) compared with control.

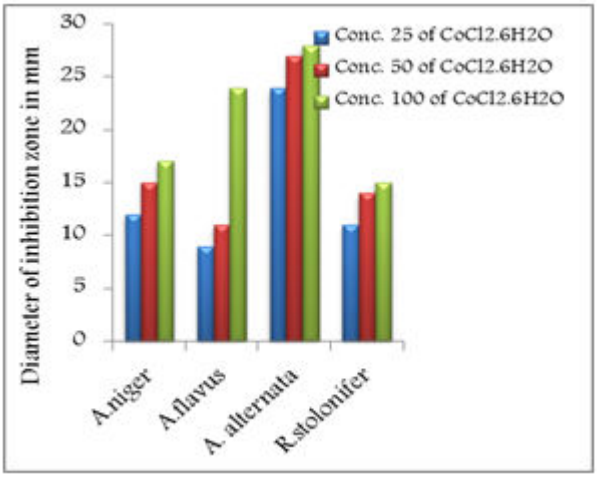

Figure11: Effect of $CoCl_2.6H_2O$ on different types of fungi.

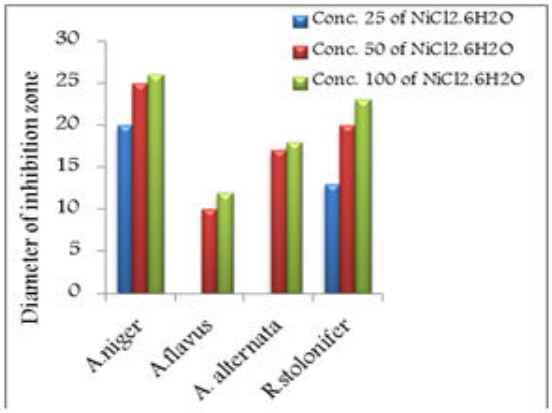

Figure12: Effect of $NiCl_2.6H_2O$ on different types of fungi.

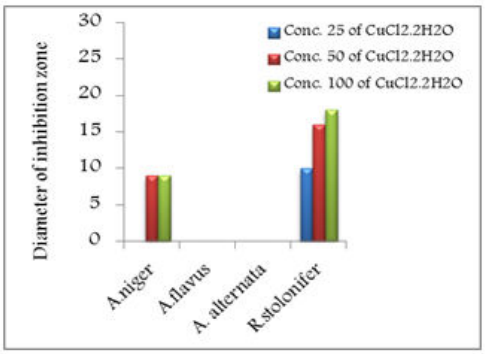

Figure 13: Effect of $CuCl_2.6H_2O$ on two types of fungi.

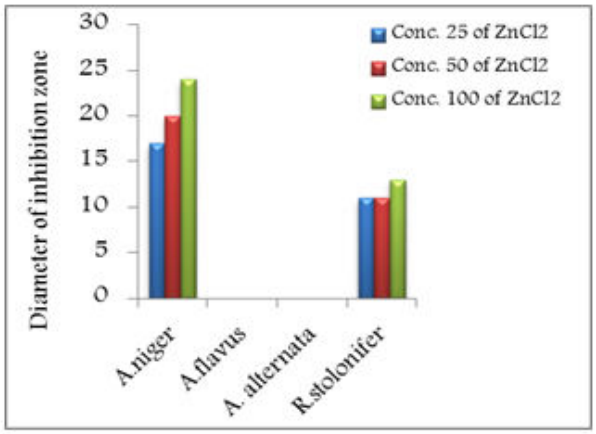

Figure 14: Effect of $ZnCl_2$ on two types of fungi.

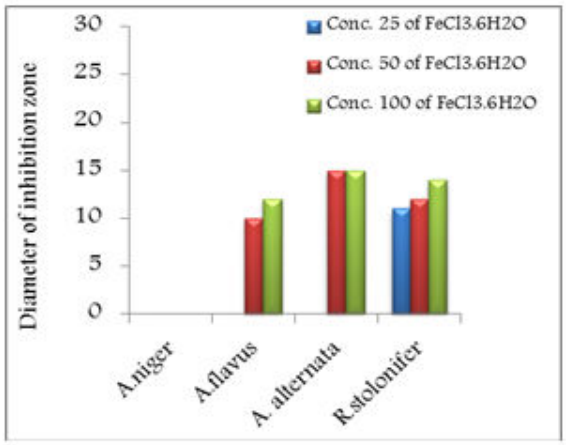

Figure 15: Effect of $FeCl_3.6H_2O$ on three types of fungi.

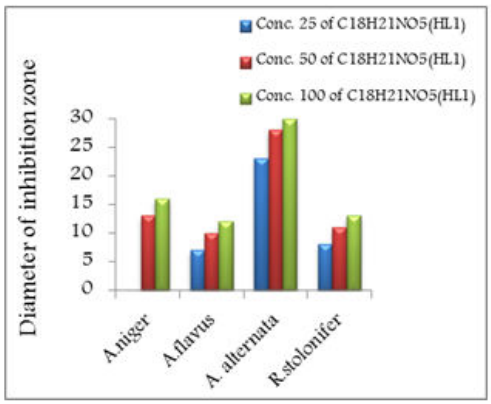

Figure 16: Effect of $C_{18}H_{21}NO_5$ (HL1) on different types of fungi.

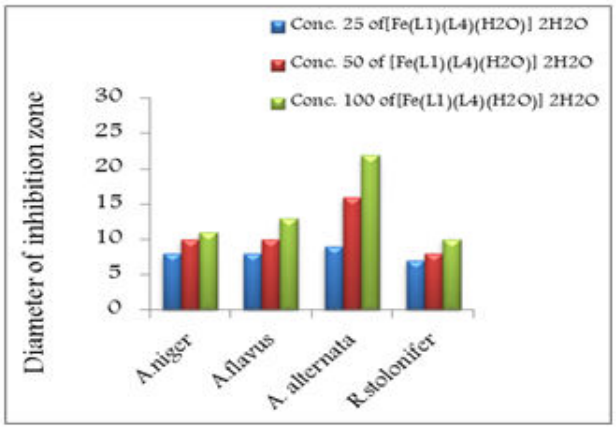

Figure 17: Effect of $[Fe(L1)(L4)(H_2O)])2H_2O$ on different types of fungi.

Conclusion

The mixed ligand complexes of Co(II), Ni(II), Cu(II) Zn(II) and Fe(III) ions with Schiff bases formed the condensation of [2-hydroxyacetophenone and L-Tyrosine] (HL1) as primary ligand and [4-dimethylaminobenzaldehyde with 2,4-dinitrophenylhydrazine] as secondary ligand (HL2) were electrolytes types in nature, whereas, Fe(III) mixed ligand complex with the same Schiff bases revealed to be nonelectrolyte in nature.

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