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SYNTHESIS, CHARACTERIZATION AND ANTIFUNGAL ACTIVITY OF SCHIFF BASE AND ITS METAL COMPLEXES

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ABSTRACT

The synthesis of a series of some novel Schiff base complexes of Cu (II), Ni (II), Co (II), Cd (II) and Zn (II) with a tetradentate Schiff base has been achieved by the reaction of 5-phenyl-1,3,4-thiadiazol-2-amine with 4-ethoxy-3-hydroxybenzaldehyde in ethanol under refluxing condition. The melting points were determined in open glass capillaries tubes. Purity of the compounds was checked by thin layer chromatography (TLC) on silica gel G plates and spots were located by using iodine chamber. All the newly synthesized metal complexes and ligand were characterized on the basis of elemental analysis, IR and ^{1}HNMR spectral studies. All compounds were screened for their antifungal activity against A. niger C. albicans and C. krusei using fluconazole as a standard drug. It has been found that metal complexes show enhanced antifungal activity as compared to ligand.

KEYWORDS: Co, Cu Ni, Cd and Zn complexes, Schiff base, antifungal activity, Fluconazole.

INTRODUCTION

The biological activity is related to their interaction with several metal ions. Schiff bases ligand and their metal complexes play an important application in the area of polymer sciences, food and dyes industry, agriculture, biological sciences as antibacterial[1,2], antifungal[3], antimicrobial[4,5,6] and anti-inflammatory[7,8] etc. Co-ordination compounds exhibit different characteristic properties which depend on the metal ion to which they are bound, the nature of the metal as well as the type of ligand etc. These metal complexes have found extensive applications in various field of human interest. Thiadiazole and its derivatives play an important role in the drug discovery realm. In particular the structure analogue of thidiazole derivatives presents various pharmacological activities such as antifungal[9,10], antimicrobial[11,12] and anti-inflammatory[13], anticonvulsant[14,15] and anticancer[16] activity etc. In view of this report and in conjunction with our interest in the synthesis of Schiff bases, our research focuses on the synthesis, characterization and antifungal evaluation of novel Schiff base. In this paper, we have synthesized and characterized a new Schiff base ligand 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol and its complexes with different metals.

MATERIALS AND METHODS

Chemistry

All reagents and solvents used in this work were analytical grade and used directly. The melting points were determined in open glass capillaries tubes. Purity of the compounds was checked by thin layer chromatography (TLC) on silica gel G plates and spots were located by using iodine chamber. Elemental analysis (C, H, N) of all the synthesized compounds were determined by perkin-Elmer 2400 elemental analyzer. The IR spectra were recorded on a Beckman Acculab-10 spectrometer (ν max in cm^{-1}) and the ^{1}H NMR spectra were recorded by Brucker DPX-300 MHz using $CDCl_3$ as solvent.

Pharmacological studies

All the newly synthesized metal complexes were tested for their antifungal activity. The effects of unknown metal complexes were compared with the standard drug fluconazole. Antifungal activity was performed against Aspergillus niger, Candida albicans and Candida krusei. Antifungal activity was assayed by standard agar disc diffusion method.[17]

RESULTS AND DISCUSSION

The synthesized Schiff base ligands and their complexes were evaluated for their antifungal activities against fungal strains named A. niger, C. albicans and C. krusei. The ligands and their complexes showed variable antifungal activities against the fungal strains. In table 1 we can see that ligands showed an inhitory week effect against the tested organism with diameter of inhibition zones. The ligands antifungal activity becomes more pronounced on coordination with the metal ions under the some experimental condition.

Table-1: Antifungal activity of ligand and its complexes.

Ligand/ complexs	Fungal inhibition zone/mm		
	A. niger	C. albicans	C. krusei
HL	10	12	8
$Co(L)_2$	14	15	11
$Ni(L)_2$	19	26	15
$Cu(L)_2$	22	30	13
$Zn(L)_2$	20	28	20
$Cd(L)_2$	24	25	22
Fluconazole	22	29	19

Synthesis of 5-phenyl-1,3,4-thiadiazol-2-amine

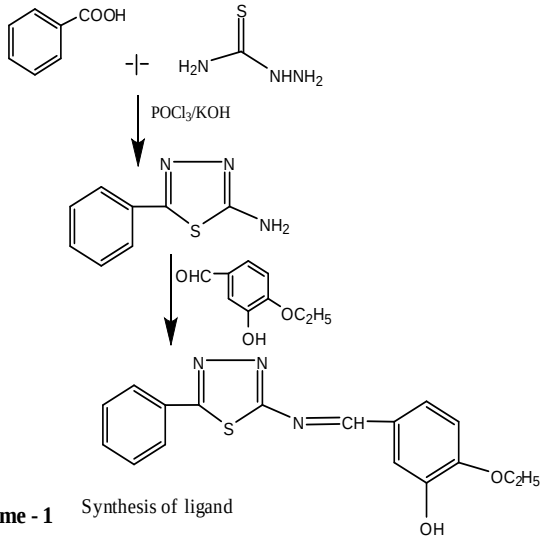
Benzoic acid (0.1 mol) and thiosemicarbazide (0.1 mol) in phosphorous oxychloride (30 ml) were refluxed gently for 30 min and cooled followed by careful addition of water (90 ml). The separated solid was filtered and suspended in water and basified with aqueous potassium hydroxide followed by filtration, drying and crystallization from mixture of DMF and ethanol to give 5-phenyl-1,3,4-thiadiazol-2-amine (as shown in **scheme I**). Yield 78%; m.p. 196^0 C; IR (KBr) ν_{max} in cm^{-1}; 3028 (C-H aromatic), 3015 (N-H), 1578 (C=N), 1327 (C-N), 1084 (N-N), 685 (C-S-C); ^{1}HNMr ($CDCl_3$) δ in ppm: 8.03-7.11 (m, 5H, Ar-H), 6.79 (s,2H, NH_2). Anal.Calcd. for $C_8H_7N_3S$: C, 54.22; H, 3.98; N, 23.71%. Found: C, 54.25; H, 3.96; N, 23.74%.

Synthesis of 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol

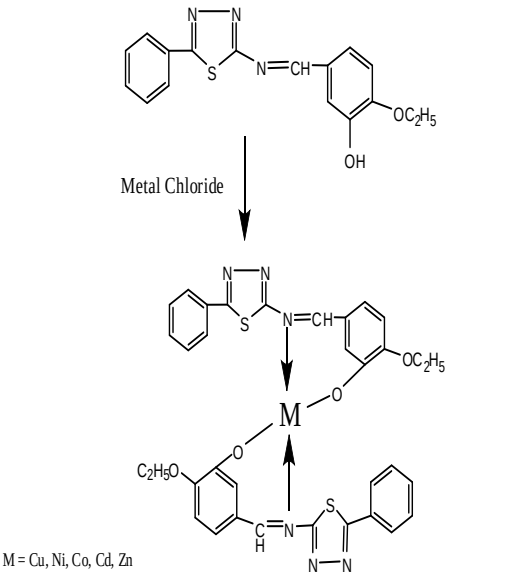
To a solution of 5-phenyl-1,3,4-thiadiazol-2-amine (1) (0.1 mol) in methanol (50 ml), substituted indolaldehyde (0.1 mol) was added in presence of glacial acetic acid (2 ml). The reaction mixture was refluxed for about 10 h. The excess of solvent was distilled off at reduced pressure and the solid thus obtained was recrystallized from acetone to give 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol. Yield 68%; m.p. 196^0 C; IR (KBr) ν_{max} in cm^{-1}; 3025 (C-H aromatic), 3423 (OH), 1580 (C=N), 1320 (C-N), 1087 (N-N), 678 (C-S-C); ^{1}HNMr ($CDCl_3$) δ in ppm: 12.19 (s,1H, OH), 8.07-7.13 (m, 8H, Ar-H), 3.25 (s, 3H, OC_2H_5). Anal.Calcd. for $C_{17}H_{15}N_3O_2S$: C, 62.75; H, 4.65; N, 12.91%. Found: C, 62.77; H, 4.68; N, 12.89%.

Synthesis of metal complexes

A mixture of the Schiff base under investigation (0.01 mol) in 20 ml ethanol and the same amount of the same solvent of metal salt (0.01 mol) were refluxed for 2 h at 70-80^0C on water bath. On cooling coloured solid product was collected by filtration and then washed several times with hot ethanol. The product was dried in air and stored in desiccators over anhydrous $CaCl_2$ under vacuum (as shown in **scheme II**).



Scheme - 1 Synthesis of ligand



Scheme - II General structure of metal complex

Ni complexe of 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol

Green powder; yield 64%; m.p. >340^0 C; IR (KBr) ν_{max} in cm^{-1}; 3025 (C-H aromatic), 1580 (C=N), 1320 (C-N), 1087 (N-N), 678 (C-S-C), 768 (C=O); Anal.Calcd. for $C_{36}H_{34}N_6NiO_4S_2$: C, 58.63; H, 4.65; N, 11.40%. Found: C, 58.63; H, 4.68; N, 11.43%.

Cu complex of 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol

Green powder; yield 60%; m.p. >340^0 C; IR (KBr) ν_{max} in cm^{-1}; 3028 (C-H aromatic), 1582 (C=N), 1322 (C-N), 1085 (N-N), 676 (C-S-C), 765 (C=O); Anal.Calcd. for $C_{36}H_{34}CuN_6O_4S_2$: C, 58.24; H, 4.62; N, 11.32%. Found: C, 58.23; H, 4.65; N, 11.33%.

Co complex of 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol

Green powder; yield 63%; m.p. >340^0 C; IR (KBr) ν_{max} in cm^{-1}; 3026 (C-H aromatic), 1583 (C=N), 1324 (C-N), 1089 (N-N), 675 (C-S-C), 766 (C=O); Anal.Calcd. for

$C_{36}H_{34}CoN_6O_4S_2$: C, 58.61; H, 4.65; N, 11.39%. Found: C, 58.63; H, 4.68; N, 11.42%.

Cd complex of 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol

Green powder; yield 57%; m.p. $>340^0$ C; IR (KBr) ν_{max} in cm^{-1}; 3024 (C-H aromatic), 1582 (C=N), 1320 (C-N), 1087 (N-N), 676 (C-S-C), 768 (C=O); Anal.Calcd. for $C_{36}H_{34}CdN_6O_4S_2$: C, 54.65; H, 4.33; N, 10.62%. Found: C, 54.63; H, 4.37; N, 10.65%.

Zn complex of 2-ethoxy-5-((5-phenyl-1,3,4-thiadizol-2-ylimino)methyl)phenol

Green powder; yield 59%; m.p. $>340^0$ C; IR (KBr) ν_{max} in cm^{-1}; 3025 (C-H aromatic), 1578 (C=N), 1324 (C-N), 1087 (N-N), 678 (C-S-C), 767 (C=O); Anal.Calcd. for $C_{36}H_{34}N_6O_4S_2Zn$: C, 54.65; H, 4.33; N, 10.62%. Found: C, 54.63; H, 4.37; N, 10.65%.

CONCLUSION

Schiff base complexes of Cu (II), Ni (II), Co (II), Cd (II) and Zn (II) were prepared and characterized by several techniques using elemental analysis (C, H, N), IR and ^{1}HNMR spectral studies. The Schiff base ligand and complexes were tested for their antifungal activity. The variation in the activity of different metal complexes against different micro-organism depends on their impermeability of the cell or the differences in ribosomes in microbial 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.

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