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ORIGINAL ARTICLE **OPEN ACCESS**

Synthesis of Fe (II), Co(II), Ni(II) and Cu(II) complexes using Schiff base ligands exhibiting multifarious biological activities

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ABSTRACT
In the present study, a series of mononuclear Fe(II), Co(II), Ni(II) and Cu(II) complexes with Schiffbase ligands have been prepared. All the synthesized compounds were visualized for their physical appearance. All synthesized compounds were stable at room temperature with colouration ranging from cream to red. The antibacterial activities of the synthesized complexes were elaborated by screening them against two strains of Gram positive (Staphylococcus aureus and Bacillus cereus) and two strains of Gram negative (Escherichia coli and Pseudomonas aeruginosa) bacteria, from the zones of inhibition, it can be depicted that metal complexes are moderately more potent inhibitors of gram positive rather than gram negative bacterial strains. Furthermore, The order of antioxidant activity exhibited by the complexes was found to be in order of Cu(II) > Ni(II) > Fe(II) > Co(II) due to infringement the free radical sequence by donation of a hydrogen atom.
Keywords: *Schiff base ligands, Condensation, Antibacterial, Antioxidant*

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INTRODUCTION

Schiff bases are common ligands in coordination chemistry. Schiff bases are generally bidentate, tridentate, tetradentate or polydentate ligands. This classification is basically depends upon the number of donor atoms present, such as Nitrogen(N), Oxygen(O) and Sulphur(S). These Schiff base ligands are expanded enormously to combine with metal ion and produce very stable complexes. Schiff bases have a wide variety of applications in different areas, such as biological chemistry, organic and inorganic chemistry [1].

Schiff bases are important class of compounds due to their flexibility, structural similarities with natural bilogical substances and also due to the presence of imine moiety (-N=CH-) which is potential in elucidating the mechanism of transformation and resamination reaction in biological system [2]. Coordination of metal ions by different ligands changes the reduction-oxidation potentials of a reaction, making it easier or sometimes more difficult to occur. The mechanism of reaction can involve binding to a metal in vivo or the metal complex may act as a vechile for the activation of ligands [3].

Sometimes, preparation of Schiff base ligands is difficult to take place. It leads to adopt an alternative way, such as template condensation. The template condensation methods lie at the heart of macrocylclic chemistry. Template reaction participated in preparation of macrocyclic ligands in absence of metal ion and also in isolating the macrocyclic complexes. Transition metals played a role as templating agent [4].

Metal complexes play an essential role in agriculture, pharmaceutical and industrial chemistry [5]. Schiff bases and their metal complexes are used as catalysts in various biological systems, polymers and dyes. Their use in birth control and food packages are also in consideration [5]. Schiff base metal complexes serve as model for biologically important species. The metal complexes showed more potential to react against bacterial species and microbes as compared to parent ligands [6]. The existences of metal ions which are bonded to biologically active compounds enhance their activities. In recent years, transition metal complexes are reported for their vast contribution in the area of medicine and pharmaceutical. These complexes showed activity such as antiviral, antibacterial, antifungal, antiphrastic, antitumor, anticancer and anti-HIV [7].

A series of metal complexes using Schiff base ligands showed activity against Gram positive and Gram negative bacteria and determined MIC value [8]. This bioactivity was substained with SEM study [Pd

(L)(Cl)] possess bactericidal as well as bacteriostatic activity [9]. Semi-synthetic pencillin type antibiotic also affect growth of Gram positive and Gram negative bacteria by preventing cell wall formation [10]. Two azo group containing Schiff base ligands and their complexes are synthesized which also showed antimicrobial activity [11]. The compound [CuLphen] showed antimicrobial activity [12] and Cu (II) complexes with semicarbazones and thiosemicarbazones are also reported [3].

The Schiff bases and their metal complexes were reported for their antioxidant and radical scavenging [3]. Antioxidant activity of the compounds was evaluated and the ligand indicated the radical scavenging relative to complexes and L-ascorbic acid as a water soluble standard [13].

Buoyant by these facts, the current research study describes the synthesis, antimicrobial activity of transition metal complexes of different Schiff base obtained by condensation reactions. The compounds were also screened for antioxidant activities using DPPH as a radical scavenger.

MATERIAL AND METHODS

Chemical used

All chemicals will be used of analytical reagent garde [AR] and highest purity. All metal (II) compounds can be used as chloride, sulphate or acetate salts. The solvent such as ethanol, methanol will be used.

Synthesis of Shiff Base

The Schiff base ligand (L) (Scheme 1) was prepared according to literature methods with a few modifications [14].The Schiff base ligands were preapared by the condensation of salicylaldehyde with semicarbazide and thiosemicarbazide in 2:1 ratio.

Synthesis of Shiff Base Metal (II) Complexes

A solution of metal(II) chloride in ethanol (2 mM) was refluxed with an ethanolic solution of the Schiff base (2 mM) for ~5 h. The solution was then reduced to one-third on a water bath. The solid complex precipitated was filtered, washed thoroughly with ethanol and dried in vacuo. The oxovanadium(IV) complex was synthesized from the sulphate salt by the same procedure but in the presence of 5 mL of 5% aqueous sodium acetate solution [15].

Antimicrobial activity

The in vitro biological screening effects of the investigated compounds were tested against the bacteria: *Bacillus cereus, Staphylococcus aureus, Escherichia coli*, and *Pseudomonas aeruginosa* by the well diffusion method [16] using agar nutrient as the medium. The stock solution (10^{-2} M) was prepared by dissolving the compounds in DMSO. In a typical procedure [17] a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using a micropipette and the plate was incubated 24-48 h at 35°C. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected. The inhibition zone was developed, at which the concentration was noted.

Antioxidant activity

For in vitro radical scavenging evaluation, DPPH (1,1-diphenyl-2-picryl-hydrazyl) is originated to be a set assay since it exhibits immediate and consistent activity for the tested compounds [18]. DPPH radical scavenging activity was determined for Schiff bases and their transition metal(II) complexes by measuring the change in molar absorbance value of DPPH at 517 nm at various concentrations in DMSO, using ascorbic acid (Vitamin C) as a standard drug [19]. Add 1 mL of above-prepared solutions to the 1 mL DPPH solution prepared in DMSO (5 mg in 100 mL) and made the resultant solution up to 3 mL by adding further DMSO. Shake the prepared mixture vigorously and allowed to stand in darkness for nearly 30 min at room temperature. By taking DPPH with DMSO as a reference or blank, the molar absorbance of the compounds was noted at 517 nm. The decrease in DPPH values of molar absorbance at 517 nm and change in color of the solution helps in deciding the radical scavenging power of an antioxidant and confirms the DPPH radical scavenging by the antioxidant by donation of hydrogen radical or electron to form a stable DPPH-H molecule. The percentage inhibition radical scavenging activity of free radical production from DPPH was calculated using standard formula.

Result and discussion

Syntheses

The Schiff base ligands were prepared by the condensation of salicylaldehyde with semicarbazide and thiosemicarbazide in 2:1 ratio (Fig 1) whereas Another Schiff base ligands were preapared by the condensation of salicylaldehyde with 2-Methyl-3-semicarbazide and 2-Methyl-3-thiosemicarbazide in 2:1 ratio.

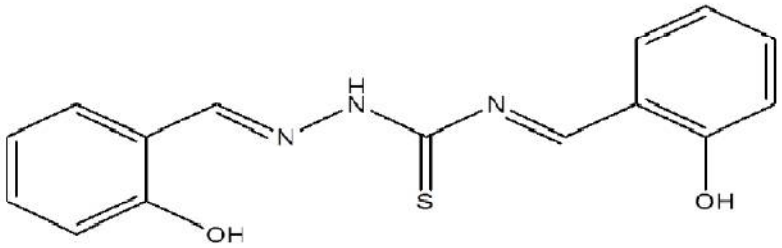

Figure-2: 1,4-bis(2-hydroxybenzylidene)thiosemicarbazide

All the complexes synthesized were solids, non-hygroscopic, bright colours and stable in air at room temperature, insoluble in most of the organic solvents except DMF and DMSO. A brief summary of some physical and analytical data is presented in Table 1.

Table-1: Physical data of all complexes.

Compound	Colour
Fe(II)+A	White
Co(II) +A	Cream
Ni(II) +A	Green
Cu(II) +A	Black

Antimicrobial activity

The antibacterial action of the synthesized compounds and standard drugs was checked by screening against four species of bacterial strains and the data is summarized in Table 2. A careful observation of the results indicated that tested compounds were active against the screened microbial species. The tested compounds bear comparable activities against parent standard drugs, Ampicillin. The decrease in the number of active bacterial cells on the treat- ment with these compounds may be attributed on the basis of cell permeability and lipophilicity. The ligands were found to be active probably due to the presence of hydroxyl function and azomethine chromophore which may lead to the formation of hydrogen bond- ing with active centers of the cells constituting the cell membrane and hence the permeability was increased [20]. Another concept is that these metal complexes can also affect the process of respiration of cells, leading to the blockage in the synthesis of proteins causing the death of organisms [21]. It is worth noting from the zones of inhibition, created by tested compounds, that ligands and their respective metal complexes are moderately more potent inhibitors of gram positive rather than gram negative bacterial strains. This is because gram positive bacteria have thick peptidoglycan layer without outer lipid membrane while gram negative bacteria have thin peptidoglycan layer and have an outer lipid membrane [22].

Table-2: Antibacterial activity of Schiff base ligands complexes.

Compound	*E. coli*	*P. aeruginosa*	*S. aureus*	*B. cereus*
Fe(II)+A	13	12	22	24
Co(II) +A	14	16	21	24
Ni(II) +A	14	13	24	22
Cu(II) +A	16	14	23	26
DMSO	-	-	-	-
Ampicillin	11	14	27	26

Antioxidant activity

Some immensely reactive and potentially destructive chemical reactive oxygen species (ROS) like superoxide anion, hydroxyl radical, and hydrogen peroxide were produced during biochemical processes occurring in our body which causes oxidative damage of proteins, lipids and nucleic acids resulting into various chronic diseases like atherosclerosis, Alzheimer, diseases, coronary heart disease, diabetes, cancer, eldering, Parkinson, etc.70. Hence, the antioxidant evaluation was carried for all synthesized compounds at different concentrations with DPPH radical, using ascorbic acid as a standard [23]. The most active Schiff base metal ligand was Cu(II) +A, exhibits 27% scavenging activity whereas minimum was shown by Co(II) +A (36%). The order of antioxidant activity exhibited by the complexes was found to be Cu(II) > Ni(II) > Fe(II) > Co(II) which can be explained by the potential of the samples to infringement the free radical sequence by donation of a hydrogen atom [24]. Hence, the concluded results of the

present study shows that all complexes showed good antioxidant activity but copper(II) complexes are the most potent.

Table-3: Antioxidant activity of Schiff base ligands complexes.

Compound	% DPPH Scavenging Activity
Fe(II)+A	42
Co(II) +A	36
Ni(II) +A	44
Cu(II) +A	47
Ascorbic Acid	56

CONCLUSION

The Schiff base ligands were successfully synthesized. All the metal (II) complexes exhibited better antibacterial properties. Also, the inhibition zones of the Schiff base ligands metal complexes showed that the all compounds were more toxic towards gram positive strains than gram negative strains. Additionally, the compounds also exhibited excellent antioxidant properties in scavenging free radicals. The results obtained from DPPH methods revealed that complexes are good antioxidants and stronger free radical scavengers.

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