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Synthesis and antimicrobial evaluation of some novel Schiff base metal complexes of 124-triazole derivative

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Abstract
This research work involves the preparation of some biologically active metal complexes of Co(II), Ni(II) and Cu(II) Chlorides with the Schiff base ligand derived from salicyladehyde and 4-amino-124-triazole. The prepared ligand and its metal complexes were evaluated for antibacterial and antifungal activity. The antimicrobial studies were carried out using disc diffusion method. The inhibitory zone values (in mm) of the compounds against the growth of microorganisms are observed for both the ligand and its metal complexes. The activity results show that the metal complexes are more potent than the parent ligand.

Keywords: Schiff bases, Metal complexes, antimicrobial activity.

1. Introduction
Schiff base ligands readily coordinate with a range of metal ions yielding stable complexes which exhibit interesting physical, chemical, biological and catalytical properties [1]. Recently there has been considerable interest in chemistry of the metal complexes of Schiff bases containing O, N and S donor [2]. Research has shown significant progress in utilization of metal complexes as drugs to treat several human diseases like carcinomas, lymphomas, infection control, anti-inflammatory, diabetes and neurological disorders [3]. Moreover, Schiff bases derived from various heterocycles have been reported to possess cytotoxic [4], anticonvulsant [5], antiproliferative [6], antimicrobial [7], anticancer [8], and antifungal activities [9]. Antimicrobial resistance is fast becoming a global concern with rapid increase in multidrug resistant bacteria. To overcome the alarming problem of microbial resistance to antibiotics, the discovery novel active compounds against new targets is a matter of urgency. Many of the crude drugs, which are sources of medicinal preparations, still originate from wild growing material. This revival interest was generated by discovery of the antibacterial and antifungal activity of several metal complexes (saha *et al.*, 2009) [10]. In the medicinal chemistry, azole are widely used and studied class of antimicrobial and anti- inflammatory agents due to their safety profile and high therapeutic index. The synthesis of high nitrogen containing heterocyclic systems has been attracted to many pharmaceutical and agrochemical industries. The triazole nucleus is one of the most important heterocycles which is a feature of natural products and medicinal agents. Triazole has a basic, five membered, heterocyclic ring containing two carbon and three nitrogen atoms having molecular formula $C_2H_3N_3$. Triazole and its derivatives possess a great significance in medicinal chemistry and numerous heterocyclic compounds containing triazole with different biological activities can be synthesized from them. Schiff base transition metal complexes possess excellent characteristics, structural similarities with natural biological substances, prepared by relatively simple preparatory procedures and the synthetic flexibility that enables design of suitable structural properties [14]. Compounds containing an azomethine group (-CH=N-), known as Schiff bases are formed by the condensation of primary amine with a carbonyl compound. Schiff base ligands and their metal complexes have a variety of applications in biological, clinical, analytical and industrial fields (Gupta and sutar, 2008; Kumar *et al*., 2009) [15]. Among these heterocyclic Schiff base ligands and their metal complexes do have significant interest because of their pharmacological properties (Sinha *et al*., 2008; Budhani

et al., 2010 [16]. The present investigation deals with the synthesis and antimicrobial investigation the Schiff base ligand 2-[(1,2,4)-triazol-4-yliminomethyl]-phenol derived from salicylaldehyde and 4-amino-124- triazole and its Co(II), Ni(II) and Cu(II) complexes.

2 Experimental Techniques

2.1 Materials and Methods

All the chemicals used were of Analar grade. Salicyladehyde and 4-amino 124- triazole were respectively obtained from Avra Synthesis. Co(II), Ni(II) and Cu(II) chlorides were purchased from Merck. Solvents were purified and distilled before use.

2.2 Preparation of the ligand 2-[(1,2,4)-triazol-4-yliminomethyl]-phenol

In a clean and dry round bottom flask, 4 amino-124- triazole [0.05 mol] in ethanol and 0.05 mol of salicyladehyde was taken. The above mixture was refluxed for about 2 - 4 h. Then the reaction mixture was evaporated slowly and then cooled. Crystalline product was collected by filtration was washed with ethanol, purified and then dried.

2.3 Preparation of metal complexes

The ligand 2-[(1,2,4)-triazol-4-yliminomethyl]-phenol in methanol (2mmol), Co(II)/Ni(II)/Cu(II) chloride (1mmol) dissolved in ethanol was added drop wise. The above mixture was refluxed for 6 h. The reaction mixture was cooled and then filtered. It was washed with methanol and then dried. (yield : 65-70%).

2.4 Antimicrobial activity

The ligand and its complexes were tested against the bacterial species: *Shigella sonnei, Klebsiella pneumoniae, Proteus vulgaris, Salmonella typhi, Proteus mirabilis* and the fungal species *Curvularia lunata, Aspergillus fumigates, Aspergillus niger, Atternaria solani and Bipolaris sps*. These studies were carried out using Kirby Bayer Disc diffusion method (Bayer *et al*., 1966) [17]. *Streptomycin* and *Nystatin* were used as the standard for antibacterial and fungal activities respectively. The test organisms were grown on Nutrient Agar medium in petri plates for bacterial species and PDA broth medium for fungal species. The compound was dissolved in DMSO solution and soaked in filter paper disc of 5mm diameter and 1mm thickness. The discs were placed on the previously seeded plates and incubated at 37ºC and the diameter of inhibition zone around each disc was measured after 24h for bacterial and 48 h for fungal species.

3 Results and Discussion

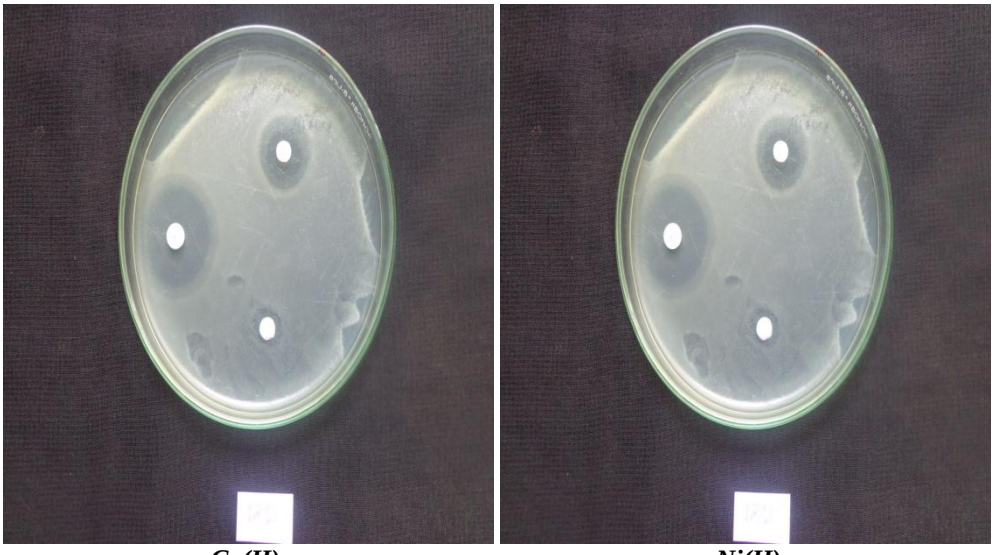
The *in vitro* antibacterial and antifungal investigation results are given in (Table-1 & 2) respectively. DMSO is used as negative control and *streptomycin* is used as positive control for bacterial and *Nystatin* for antifungal activities. It has been observed that all compounds exhibited very significant and better antibacterial and antifungal activity. The free ligand shows potent activity against *shigella sonnei, klebsiella pneumoniae* and *salmonella typhi and lesser activity against Proteous mirabilis* bacterial species and it has no antifungal activity against on *Curvularia lunata, Aspergillus fumigates* and *Bipolaris sps*. Among the metal complexes Cu(II) complexes show higher antibacterial activity and good antifungal activity than the other metal complexes (figure-1). It shows potent antifungal activity on *Bipolaris sps* (figure-2). All the metal show better activity against the bacteria *Proteous mirabilis* than the reference positive control used. The Co(II) complexes show moderate activity. These observations show that the majority of the metal complexes are more active than the free ligand. The results are tabulated.

Table 1: Antibacterial activity of the ligand and its metal complexes on *Proteous mirabilis*

Compound (M)		Zone of inhibition (in mm)		
		M	**B**	**C**
A	Ligand	11	24	10
M1	CoL_2Cl_2	25	14	10
M2	NiL_2Cl_2	27	14	-
M3	CuL_2Cl_2	26	12	11

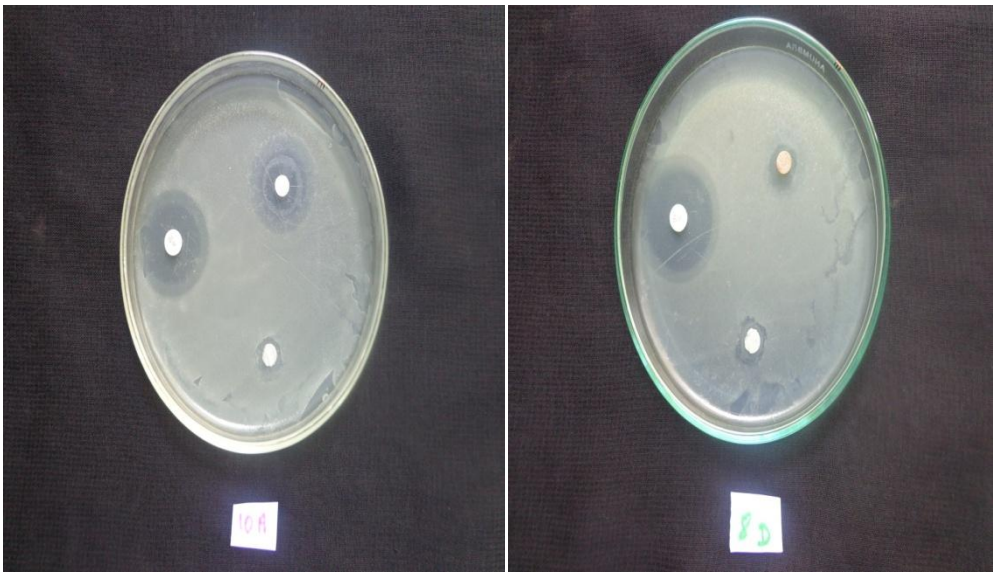
Table 2: Antifungal activity of the ligand and its metal complexes on *Bipolaris sps*

Compound (M)		Zone of inhibition (in mm)		
		M	**B (+)**	**C (-)**
A	Ligand	-	13	-
M1	CoL_2Cl_2	10	14	-
M2	NiL_2Cl_2	10	16	-
M3	CuL_2Cl_2	24	13	-



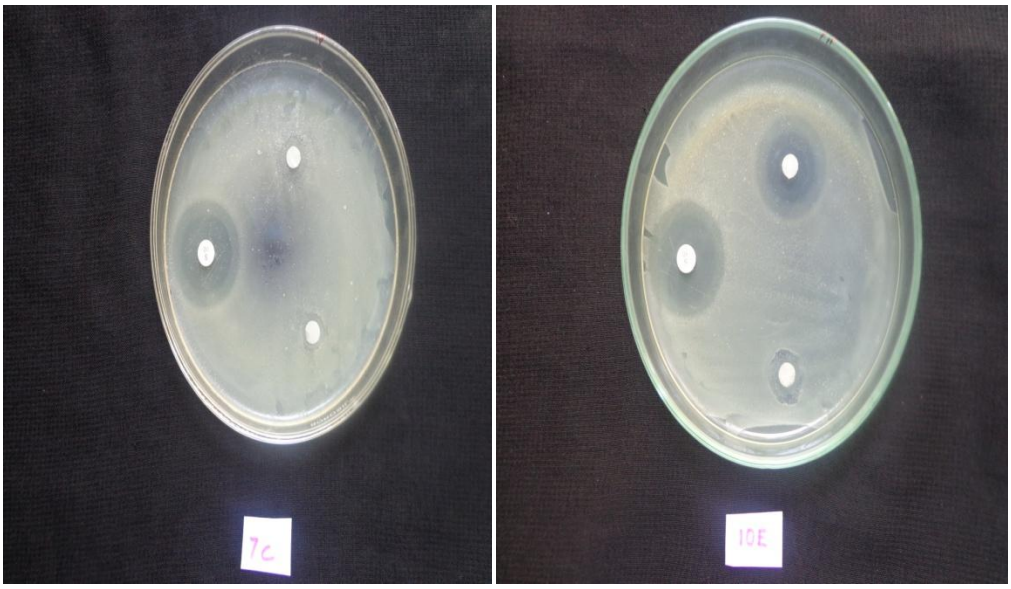
Co(II) ***Ni(II)***

Fig 1: Antibacterial activity of the metal (II) complex and its ligand on *Proteous mirabilis*



Cu(II) ***Ligand***

Fig 2: Antifungal activity of the ligand and its Cu(II) complex on *Bipolaris sps*



Ligand **Cu(II)**

Conclusion

Schiff base ligand 2-[(1,2,4)-triazol-4-yliminomethyl]-phenol and its complexes were prepared and its *in vitro* antimicrobial studies have been evaluated. The antimicrobial activities results indicate that the metal complexes show higher activity than the ligand. The activity with respect to the metal in the complexes follow the order: Cu(II) > Ni(II) > Co(II).

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