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Copper (Cu)-Complexes of Schiff Base and their Antibacterial Activity

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ABSTRACT

Coordination chemistry is a chemical science term associated with ligand-shaped coordination compounds, i.e. the association of metal and molecules. As functional materials, charge-separated organic molecules have a wide range of applications. Zwitterionicity is demonstrated as a general design paradigm for the activation of strong bonds in coordination chemistry. Due to their ability to develop inert complexes with metal ions of transition series, Schiff bases are the most recognized compound in coordination chemistry with broad application in the field of pharmaceutics. This study paper summarizes the synthesis via traditional method and magnetic stirrer of the Schiff base and its metal complex. The antibacterial function of the Schiff base's metal complex has also been discussed. Using ^1H NMR and elemental analysis, the compound's structure was reported. The obtained Schiff bases have been evaluated against bacteria such as E. coli and S. aureus. It is interpreted in this paper that the magnetic stirrer method has been shown to be a better method for Schiff base preparation and to improve its yield.

Keywords: Antimicrobial activity, Coordination compound, Magnetic stirrer, Metal complex, Schiff base

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INTRODUCTION

In the field of pharmaceuticals, several studies have been performed in recent decades on polydentate ligands that constitute metal-coordinate complexes. Metal ions interact strongly with different biomolecular forms, including protein, antibiotics, and nucleic acid. These biomolecules, which are bound specifically to transition metal ions, may be used to shape antimicrobial drugs in the pharmaceutical sector. Schiff base have application as antidyslipidemic [1], anthelmintic [2], antitubercular [3], antidepressant [4] and many more. Copper ions have the ability to bind to DNA and cleave it in the presence of ascorbate or hydroquinone. As a result, copper ions can destroy the ability of the cancer cell to replicate [5].

A research article has discussed interaction between copper complex based Schiff bases with bovine serum albumin for increasing the potential to target cancer cells [6]. The general method for synthesis of Schiff base reaction is given in Figure 1.

In present paper synthesis and application of simple copper complexes with salicylaldehyde based Schiff base are reported. Furthermore, the antimicrobial activities of the copper complex of these Schiff bases were tested on selected kinds of bacteria.

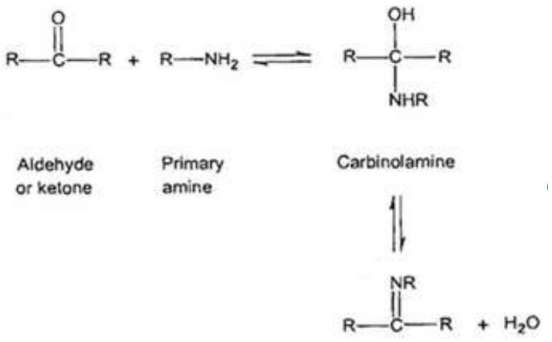


Figure 1. Pictorial representation of general reaction for preparation of Schiff base from aldehyde or ketone and primary amine forming an intermediate.

LITERATURE SURVEY

A research paper revealed comparative study between antimicrobial activity of metal complex of ligand and simple ligand by testing it against gram positive bacteria *Staphylococcus Aureus*. Metal complex of Schiff base obtained from salicyl-aldehyde and 1, 2-phenylenediamine with the bivalent transition metals Zn and Cu was characterized and tested. It was concluded from the experiment that the metal complex of salicylaldehyde ligand shows more activity than salicylaldehyde ligand [8]. A Schiff base formed by 2-Hydroxy-6penta-decylbenzaldehyde and 6-bromo-3-chloro1-benzo-thiophene-2-carboxy-licacidhydrazide was synthesized and tested anti-fungal and anti-bacterial activity against *B. subtilis* and *S. aureus* [9].

Another research paper by Xueqiong Yin and colleagues' synthesized Schiff base from O-Carboxy-Methyl Chitosan (CMC) and parasubstituted benzaldehydes. Synthesized Schiff base were evaluated from FTIR and 13C-NMR. Antimicrobial performance of the synthesized compound was examined against *S. aureus* and *E. coli* [10]. Literature survey shows that many observations have been seen on the synthesis and characterization of copper complexes of benzaldehyde.

Several methods have been developed for preparing metal complex of the Schiff base. However, the method for preparation of salicylaldehyde based Schiff base using magnetic stirrers is lesser known which has been proved advantageous to the startups and small-scale industries as the cost required for instrumentation is low. Thus, the research study mainly focuses on the preparation of the metal complex using the conventional method of magnetic stirrer.

METHODLOGY

Schiff base metal complex are naturally organized using a reflux process. This approach, however, consumes energy and time. Magnetic stirrers are used in manufacturing in order to save time and fuel.

Reagents and materials

Salicylaldehyde, phenyl hydrazine, glycine, aniline and hydrazine hydrate of reagent grade were bought from Sigma–Aldrich Company and used as supplied. Organic solvent such as ethanol of A.R. grade was used. Magnetic stirring was carried out by the SSU magnetic stirrer.

Synthesis of ligand

Conventional refluxing method: 1.22 ml of salicylaldehyde (0.01 mol) and 0.92 aniline (0.01 mol) were dissolved into 10 ml of ethanol in a round bottom flask. With continuous stirring, a few drops of sodium hydroxide (0.1N) were added and the mixture was connected to a condenser in a water bath and refluxed for 7 hours-8 hours at 85°C. For cooling, the solution obtained was held in ice water. An orange-red ppt, *i.e.* L1, was obtained and recrystallized from ethanol. In the similar way, L2 was obtained from salicylaldehyde and 0.31 ml hydrazine hydrate (0.01 mol), L3 was obtained from salicylaldehyde and 0.41 ml glycine (0.01 mol), L4 was obtained from salicylaldehyde and 0.98 ml phenyl hydrazine (0.01 mol). (Where L1- Salicylaldimine, L2-Hydrazine hydrate Salicylaldimine, L3- Glycine Salicylaldimine, L4- Phenylhydrazine Salicylaldimine).

Magnetic stirrer method: An ethanol solution of benzaldehyde (0.01 mol) (1.22 ml in 10 ml of ethyl alcohol) and aniline (0.01 mol) (0.92 ml in 10 ml of ethyl alcohol) was added at room temperature in a clean beaker. Additionally, thermometers and magnetic agitators were applied to the beaker and dropwise NaOH (0.1N) solution was added to the salicyaldimine solution. The beaker shook magnetically at room temperature for 3 hrs. The resulting orangish red precipitate was purified and washed with ethanol and diethyl ether. After washing it was drained in a desiccator with calcium chloride. In the similar way, L2 was obtained from salicylaldehyde and 0.31 ml hydrazine hydrate (0.01 mol), L3 was obtained from salicylaldehyde and 0.41 ml glycine (0.01 mol), L4 was obtained from salicylaldehyde and 0.98 ml phenyl hydrazine (0.01 mol).

Preparation of metal complex of ligand

Conventional refluxing method: In a round bottom flask, an ethanolic solution of (1.59 g in 10 ml ethanol) copper sulphate (0.01 mol) and L1 was mixed along with sodium hydroxide with continuous stirring and was refluxed for 6 hour at 90°C-95°C. The solid filter was precipitated and recrystallized from ethanol. After recrystallization Cu- L1 complex was obtained. In the similar way, Cu-L2 complex, Cu-L3 complex and Cu-L4 complex were synthesized.

Magnetic stirrer method: In a clean beaker, an ethanolic solution of (1.59 g in 10 ml ethanol) copper sulphate (0.01 mol) and ligand L1, L2, L3, L4 was prepared at room temperature. Both the solution of CuSO4 and L1 were mixed along with sodium hydroxide and stirred on a magnetic stirrer for 5 h at room temperature. The solid filter was precipitated and washed with diethyl ether. After washing Cu- L1 complex was vacuum dried. In the similar way, Cu-L2 complex, Cu-L3 complex and Cu-L4 complex were synthesized. Yield of synthesized ligands

and their complexes were recorded and are given in the Table 1, Table 2.

Antibacterial activity: The antibacterial performance of the prepared compound was examined by a well diffusion assay method. For quality purpose, Std. strains *S. aureus* ATCC 25923 and *E. coli* ATCC 25922 were used. Nutrient agar medium was prepared and autoclaved for the well diffusion assay. The inoculum of 150 µl of each bacterium was spread with a swab on the plate of culture media/ nutrient agar.

Eventually, on the agar plate, 7 mm wells were punched. The plate was held for 24 h at 37°C in an incubator. In the DMSO solution, the synthesized compounds and amoxicillin trihydrate were dissolved (in 10%). Two wells were filled with DMSO (10%) and distilled water as negative standards, one well was filled with positive standard amoxicillin trihydrate, and four wells were filled with ligand synthesized copper complexes. The growth incubation diameter was noted. Two plates were prepared for compounds synthesized by both the method for testing against *S. aureus* and *E. coli.*

Table 1. Structure of Schiff bases by condensation of salicylaldehyde and aliphatic/ aromatic aniline.

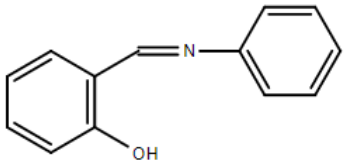
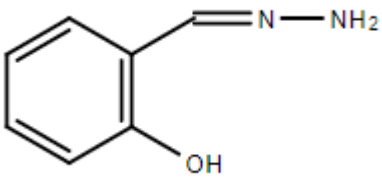
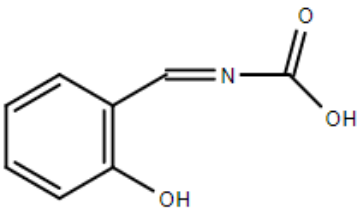
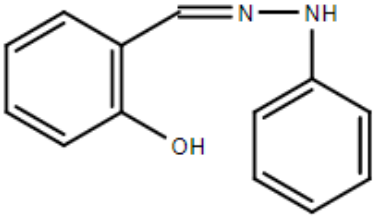
Sr no.	Name of the compound	Aldehyde	Amine	Structure
L1	Salicylaldimine	Salicylaldehyde	Aniline	 Salicylaldimine
L2	Hydrazine hydrate salicylaldimine	Salicylaldehyde	Hydrazine hydr	 Hydrazine hydrate salicylaldimine complex
L3	Glycine salicylaldimine	Salicylaldehyde	Glycine	 Glycine salicylaldimine complex
L4	Phenylhydrazine salicylaldimine	Salicylaldehyde	Phenyl hydrazin	 Phenylhydrazine salicylaldimine complex

Table 2: Schiff base obtained by condensation of salicylaldehyde and amines.

Sr. No.	Compound Name	Color	Yield (%)	
			Conventional method	Magnetic stirrer method
1	L1 Schiff base	Orangish red ppt.	78.12	85.67
2	L2 Schiff base	White ppt.	72.18	88.43
3	L3 Schiff base	Brown ppt.	72.25	89.01
4	L4 Schiff base	Yellow ppt.	81.62	92.64

RESULT AND DISCUSSION

Two different methods were used for the preparation of the Schiff base one of which was conventional while the other was using magnetic stirrer. Table 3 discusses the Schiff base yield obtained from both methods. Thin layer chromatography was used to determine the purity of the compound. The chemicals used were of analytical grade.

Table 3: Cu complex of synthesized ligand. It can be observed from the table that the yield of copper complex of salicylaldimine and phenylhydrazine salicylaldimine has increased significantly using magnetic stirrer method.

Sr. No.	Compound name	Color	Yield (%)	
			Conventional method	Magnetic stirrer method
1	Cu- L1 salicylaldimine complex	White ppt.	65.32	71.11
2	Cu-L2 hydrazine hydrate salicylaldimine complex	White ppt.	61.78	65.89
3	Cu-L3 glycine salicylaldimine complex	White ppt.	59.87	68.04
4	Cu-L4 phenylhydrazine salicylaldimine complex	White ppt.	68	70.21

^{1}H-NMR

The pattern of bondings of the complex are supplementary carried out in (400 MHz) DMSO-d6. The spectrum in Figure 2, 3, 4 and 5 revealed the bonding pattern of the compound.

The ^{1}H-NMR study revealed the structure of the ligand. The product yield obtained from both methods was compared and it was concluded that the compound yield of magnetic stirrer technique was greater than that of the standard approach.

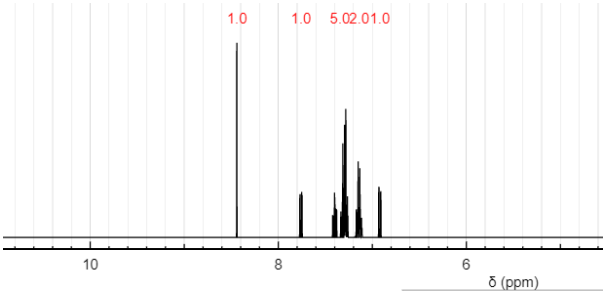


Figure 2. ^{1}H-NMR spectrum of salicylaldimine. The spectrum shows different peaks indicating different environments for the hydrogens.

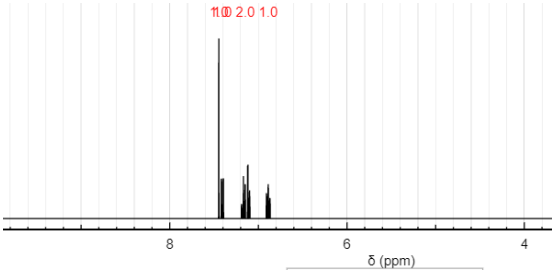


Figure 3. ^{1}H-NMR spectrum of hydrazine hydrate salicylaldimine. The spectrum shows different peaks indicating different environments for the hydrogens.

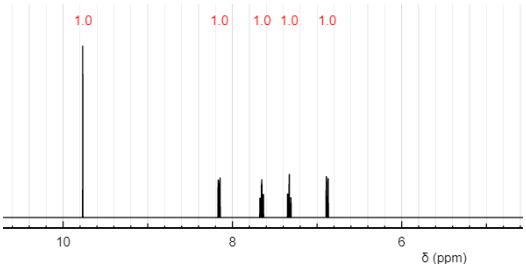


Figure 4. ^{1}H-NMR spectrum of glycine salicylaldimine. The spectrum shows different peaks indicating different environments for the hydrogens.

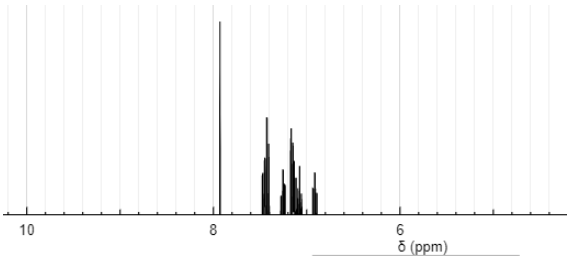


Figure 5. ^{1}H-NMR spectrum of phenylhydrazine salicylaldimine. The spectrum shows different peaks indicating different environments for the hydrogens.

ANTIMICROBIAL ACTIVITY

The data provided in Table 4 demonstrates inhibition activity of prepared copper complexes of Schiff base against Gram negative bacteria *E. coli.* and Gram positive bacteria S. aureus.

Table 4: The MIC (µg/ml) values of the synthesized ligand against S. aureus and E. coli. The Cu complex of prepared Schiff base have high activity towards S. aureus than E. coli.

S.No.	Compounds	Zones of inhibitions (in mm)	
		S. aureus	*E. Coli*
1	DMSO (Negative standards)	0.0	0.0
2	Distilled water (Negative Standards)	0.0	0.0
3	Cu- L1 salicylaldimine complex	18	17
4	Cu-L2 hydrazine hydrate salicylaldimine complex	22	15
5	Cu-L3 glycine salicylaldimine complex	19	17
6	Cu-L4 phenylhydrazine salicylaldimine complex	20	18
7	Amoxicillin (Positive Standards)	34	32

Cu- L2 hydrazine hydrate salicylaldimine complex shows highest activity against *S. aureus* and lowest activity against. The Cu-L2 hydrazine hydrate salicylaldimine complex demonstrated significant activity against *S. aureus* whereas Cu-L4 phenylhydrazine salicylaldimine complex demonstrated better activity against *E. coli*.

CONCLUSION

Schiff bases are highly versatile members of coordination compounds. They show various physiological and chemical properties along with active biological activity. The complex of Schiff base with metal ion has various applications such as antiviral, antitumor, antipyretic or anti-inflammatory agents. Many ongoing researches are focused on the chemotherapeutic activity of these complexes. In this research copper complex of Schiff base was prepared from salicylaldehyde and aliphatic/ aromatic amines using a magnetic stirrer. The proposed method of magnetic stirring proved to be a better method than the conventional method. There is a significant increase in the percentage of yield of Schiff base and their complex:% yield of magnetic stirrer >% yield of conventional method. The yield of salicylaldimine was increased by 5.79% using magnetic stirrer method. Thus, SME's or startup companies should adapt the preparation of Schiff base and their complex using magnetic stirrer method to increase the yield of product. The obtained complex showed very inquisitive activity against *E. coli.* and *S. aureus*. Further, many modified compounds can be formed using this method and lead to development of drugs for cancer.

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