

Synthesis, Characterization and Antibacterial Screening of Schiff Base and It's Metal (II) Complexes Derived from 3-Aminophenol and Salicylaldehyde

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Authors' contributions

This work was carried out in collaboration among all authors. Authors NYP and BM designed, supervised and reviewed all the drafts of the manuscript. Authors MSM, JON and MMS carried out the research and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

New Schiff base ligand was synthesis *via* a condensation of the ligands in methanol. The Schiff base were synthesized in 1:2 molar ratio reactions. The complexes $[\text{Mn}(\text{HL}_1)_2\text{Cl}]$, $[\text{Cu}(\text{HL}^1)_2]$ and $[\text{Ni}(\text{HL}^1)_2\text{Cl}]$ have been characterized on the basis of FTIR, electronic spectra, melting points/decomposition temperature, solubility and molar conductance. The *in-vitro* antibacterial activity of the complexes was tested using two gram-negative (*Escherichia coli* and *Salmonella typhimurium*) and two gram-positive (*Staphylococcus pyogenes* and *Staphylococcus aureus*) bacterial strains. The IR bands of Schiff bases showed a broad-band at 3317 cm^{-1} . The strong bands at 1590 cm^{-1} range was assigned to $\nu(\text{C}=\text{N})$ vibration which reveals coordination of the carbonyl group of the aldehyde and the amine group of the 3-aminophenol and salicylaldehyde

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which ascertain the formation of the azomethine bond. The $\nu(\text{C}=\text{N})$ observed at 1603, 1591 and 1591 cm^{-1} range in the spectra of the complexes showed a shift to higher frequencies in all the complexes. These show the participation of the azomethine nitrogen in the coordination. The bands at 690, 512 and 512 cm^{-1} were assigned to (M–N) and the bands at 538, 461 and 461 cm^{-1} were assigned to (M–O). The electronic spectral data of the complexes suggest an octahedral and tetrahedral geometry for all the complexes. The molar conductivity indicates that the synthesized complexes are all non-electrolytes and soluble in protic solvent such as methanol and ethanol. The synthesized metal complexes showed improved broad-spectrum antimicrobial activity against gram-positive and gram-negative bacteria better than the Schiff base. Thus, the complexes should be considered as possible lead compounds to be developed into antibiotics against the tested bacterial strains *E. coli*, *S. typhimurium*, *S. aureus* and *S. pyrogens*.

Keywords: Antibacterial activity; FTIR; In-vitro; non-electrolytes; Protic solvent; Schiff base ligands.

1. INTRODUCTION

Most of metals ions are essential components to maintain homeostasis and play crucial role in many biological processes by involving as cofactors in the biological functions of proteins and operating a many regulations, stabilization, completion courses of cellular function [1]. Schiff base (HL) are the compound containing azomethine group (-HC=N-) [2]. The acid/base catalysis or heating is employed for the synthesis of Schiff bases as their reactions are mostly reversible [3]. The chemistry of metal complexes including ordinary complexes, chelates and mixed ligand complexes has been extensively studied till date for their bioinorganic relevance as well as a wide range of physicochemical properties [4]. Infectious diseases still remain a crucial and challenging problem because of a combination of factors including rising infectious diseases and the increasing number of multi-drug resistant pathogens. Thus, there is still need to discover new compounds with enhanced antimicrobial activities to combat drug resistance menace [5]. In light of this, the aim of this research was to synthesis, characterize and test the antibacterial activity of Schiff base and their metal complexes derived from 3-aminophenol and salicylaldehyde against some selected gram-positive and gram-negative bacterial strains. To the best of our knowledge the results report herein indicates the novel potency of our complexes as a potential lead for the

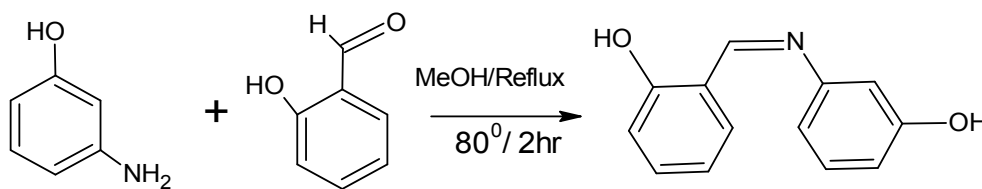
development of a cheaper, more effective and potent antibiotic.

2. MATERIALS AND METHODS

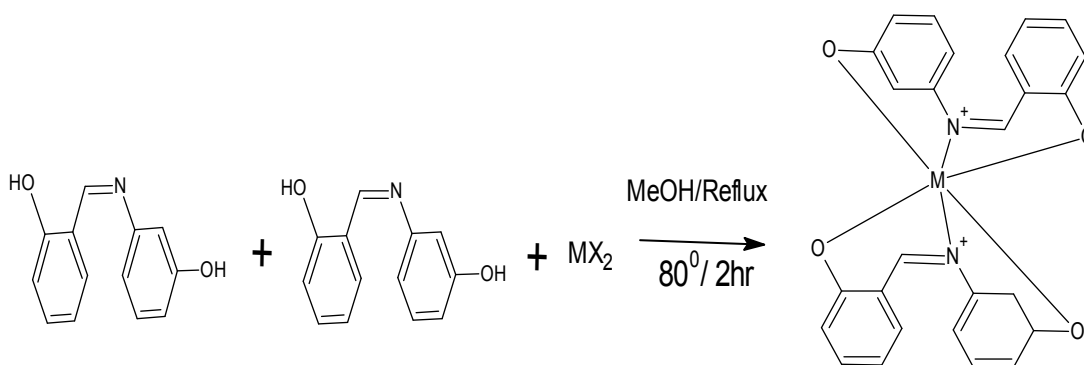
All chemicals, reagents and drug that were used in this research are of Analytical grade. The metals used are; $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, MnCl_2 , $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, 3-aminophenol and salicylaldehyde. The molar conductivity of the Schiff base and the metal (II) complexes were examined by digital conductivity meter AVI-848. Perkin Elmer version 10.03.09 and standard KBr techniques were used for identification of the functional groups present in the ligands and the complexes. The decomposition temperatures of the ligand and the complexes were obtained using Electro Thermal Melting Point (SMP10).

2.1 Synthesis of 3-aminophenol and Salicylaldehyde (HL¹)

The ligand was obtained by condensation of equimolar (1:1) mixture of salicylaldehyde (2 mmol, 0.24 g) with 3-aminophenol (2 mmol, 0.22 g) in 20 ml methanol and then refluxed on a hot plate with stirring for 1 hr. The orange crystalline solid obtained was filtered, washed with ethanol and then recrystallized from methanol and dried in a desiccator over calcium chloride (CaCl_2) for 24 hr [4,6].



Scheme 1. Synthetic route to get the target ligand



Scheme 2. Metal (II) complex synthetic route (M= FeSO₄, NiCl₂.6H₂O, ZnCl₂)

2.2 Synthesis of Schiff Base and Metal (II) Complexes

The complex is synthesized by adopting a literature procedure as reported by [4] where hot methanolic solution (2 mmol, 0.27 g of MnCl₂.4H₂O, (2 mmol, 0.48 g of NiCl₂.6H₂O, 2 mmol, 0.33 g of CuSO₄.5H₂O) were added to methanolic solution of the HL¹ (2 mmol, 0.46 g) in drops with constant stirring (1:2 molar ratio). The mixture was refluxed on a hot plate for 3 hrs. The product obtained was concentrated to half its volume, filtered, washed with distilled water, diethyl ether and dried in desiccator over (CaCl₂) [4,7,8].

2.3 Characterization of Schiff Base and Its Metal (II) Complexes

Characterization involve simple fingerprint of compounds already known, or more extensive investigation designed to establish the formula and structure of a new compound [9]. The Schiff base and its metal complexes were characterized by using different physico-chemical techniques like melting point, UV-visible spectrophotometer, FTIR, conductivity and solubility test [10,11].

3. RESULTS AND DISCUSSION

The physical characteristics of the Schiff base and the metal complexes (HL¹, Cu(HL¹)₂, Ni(HL¹)₂Cl and Mn(HL¹)₂Cl) are presented in Table 1. The HL¹, Cu and Mn complexes have shown an orange colour while, Ni complex have shown a tert-green colour which is agreement with the work reported by [11]. They are non-hygroscopic solids, stable in air, infusible at higher temperature ranges from

(200), (190-197), (195-200) and (185-192) for the Schiff base and the complexes of Cu, Ni, Mn respectively. They have a good yield at the range of 64-80%. The molar conductivity values of the Schiff base and the complexes are measured in DMSO and were found to be in the range of 1.5-20.2 Ω⁻¹cm²mol⁻¹. These high values indicate that, they are non-electrolytic in nature as reported by [12-14].

The solubility of the complexes shows that the complexes are soluble in methanol (cool and hot), ethanol (cool and hot), diethyl ether (cool and hot) and DMSO (hot) and sparingly soluble in acetone (cool and hot), chloroform (cool and hot) and it is not soluble in H₂O (cool and hot) and petroleum ether (cool and hot) as presented in Table 2. Their solubility is as a results of the interaction between the hydrogen ion in the complexes and the oxygen atom in the solvent which results in the formation of hydrogen bond [15,16].

The UV-vis was determined in DMF in the range 200-700 nm and the data are presented in Table 3. The assignments have been done by comparing the observed values with previous work done on similar research. In the Schiff base (HL¹), the band observed in the range 289 nm (34602 cm⁻¹) is due to π-π* electronic transition. The electronic spectra of the metal complexes ([Cu(3AMPSAL)₂], [Ni(3AMPSAL)₂Cl] and [Mn(3AMPSAL)₂Cl]) showed broad bands at 300 nm (33333 cm⁻¹), 312 nm (32051 cm⁻¹) and 298 nm (33557 cm⁻¹) respectively and are assigned to (d-d), (A₁g-T₂g), and A₂g-T₁g of an octahedral geometry [2,17].

The IR bands of Schiff base showed a broad band at 3319 cm⁻¹ (Table 4). The strong bands at 1590 cm⁻¹ range was assigned to the ν(C=N)

vibration which revealed coordination of the carbonyl group of the aldehyde and the amine group of the 3-aminophenol and salicylaldehyde which ascertain the formation of the azomethine bond. The bands observed at 3319 cm^{-1} were assigned to $m(\text{OH})$ vibrations and this bands were absent in the spectra of all the complexes. The disappearance of the band for the $\nu(\text{OH})$ vibration in the spectra of the complexes indicated the deprotonation of the phenolic proton. The $\nu(\text{C}=\text{N})$ observed at the range of $1603, 1591, 1591\text{ cm}^{-1}$ showed a shift to higher frequencies in all the complexes. These show the participation of the azomethine nitrogen in coordination. The bands at $690, 512, 512\text{ cm}^{-1}$ and $538, 461, 461\text{ cm}^{-1}$ were assigned to (M-N) and (M-O) respectively [4,18].

The antibacterial activities of the Schiff base and metal complexes are tested against two gram-negative (*E. coli* and *S. typhimurium*) and two gram-positive (*S. aureus* and *S. pyrogens*) and are presented in Table 5 and the results were found to be in agreement with previously published studies [19-22]. From the results it has reveal that the metal complexes are more active than the Schiff base due to chelation, which reduced the polarity of the metal atom mainly because of partial sharing of its positive charge with donor groups of the ligand and possible π -electron delocalization on the aromatic rings. This increased the lipophilic character, favouring its permeation into the bacterial membrane, causing the death of the organisms [12,23].

Table 1. Physical characteristics and analytical data of ligands /complexes

Complexes	Mol. Weight (g/mol)	Colour	Melting point(°C)	Yield (%)	Molar conductivity $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$
HL ¹	231.323	Orange	200	64	3.7
[Mn(HL ¹) ₂ Cl]	553.146	Orange	185-192	80	20.2
[Cu(HL ¹) ₂]	526.646	Tert-green	190-197	70	14.3
[Ni(HL ¹) ₂ Cl]	557.146	Orange	195-200	65	1.5

Where HL¹= Schiff base of 3-aminophenol and salicylaldehyde, Mol. weight= Molecular weight

Table 2. Solubility test of the complexes

Compound	Dist. H ₂ O		MeOH		EtOH		Acetone		CHCl ₃		P. ether		D. ether		DMSO	
	C	H	C	H	C	H	C	H	C	H	C	H	C	H	C	H
Mn(HL ¹) ₂ Cl	NS	NS	S	S	S	S	S	S	SS	SS	NS	SS	SS	S	S	S
Cu(HL ¹) ₂	NS	NS	S	S	S	S	SS	SS	SS	SS	NS	NS	N	S	SS	S
Ni(HL ¹) ₂ Cl	NS	NS	S	S	S	S	S	S	S	S	NS	NS	S	S	S	S

Where C = Cool, H = hot, S = Soluble, SS = Sparingly Soluble, NS = Not Soluble, MeOH = Methanol, EtOH = Ethanol, Dist. H₂O = Distilled water, CHCl₃ = Chloroform, P. ether = Petroleum ether, D. ether = Diethyl ether, DMSO = Dimethyl sulfoxide, HL¹ = Schiff base of 3-aminophenol and salicylaldehyde

Table 3. Electronic spectral data of the ligands and its complexes

Compound	Absorption (nm)	Absorption (cm ⁻¹)	Band assignment	Geometry
HL ¹	289	34602	$\pi-\pi^*$	
[Mn(HL ¹) ₂ Cl]	298	33557	A ₂ g-T ₁ g	Octahedral
[Cu(HL ¹) ₂]	300	33333	d-d	Tetrahedral
[Ni(HL ¹) ₂ Cl]	312	32051	A ₁ g-T ₂ g	Octahedral

HL¹ = Schiff base of 3-aminophenol and salicylaldehyde

Table 4. Some selected FTIR spectral data of the Schiff base and the complexes

Compound	$\nu(\text{C}=\text{N})$	$\nu(\text{O}-\text{H})$	$\nu(\text{M}-\text{N})$	$\nu(\text{M}-\text{O})$
HL ¹	1590	3319	-	-
Mn(HL ¹) ₂ Cl	1591	-	512	461
Cu(HL ¹) ₂	1603	-	690	538
Ni(HL ¹) ₂ Cl	1591	-	512	461

Where HL¹ = Schiff base of 3aminophenol and and salicylaldehyde

Table 5. Antibacterial activity of the ligands and complexes

Compound	Concentration (mg/ml)			
	Gram-negative		Gram-positive	
	<i>E. coli</i>	<i>S. typhimurium</i>	<i>S. aureus</i>	<i>S. pyrogens</i>
HL ¹	11.97	6.20	9.29	11.81
[Mn(HL ¹) ₂ Cl]	17.10	7.12	14.45	9.90
[Cu(HL ¹) ₂]	13.20	8.25	8.76	15.24
[Ni(HL ¹) ₂ Cl]	22.49	6.91	11.10	13.12

Where *E. coli* = *Escherichia coli*, *S. typhi* = *Salmonella typhi*, *S. aureus* = *Staphylococcus aureus*,
S. pyrogens = *Streptococcus pyrogens*, HL¹ = Schiff base of 3Aminophenolbenzaldehyde

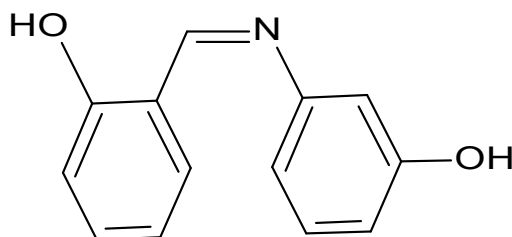


Fig. 1. Proposed structure of Schiff base of (3AMP)

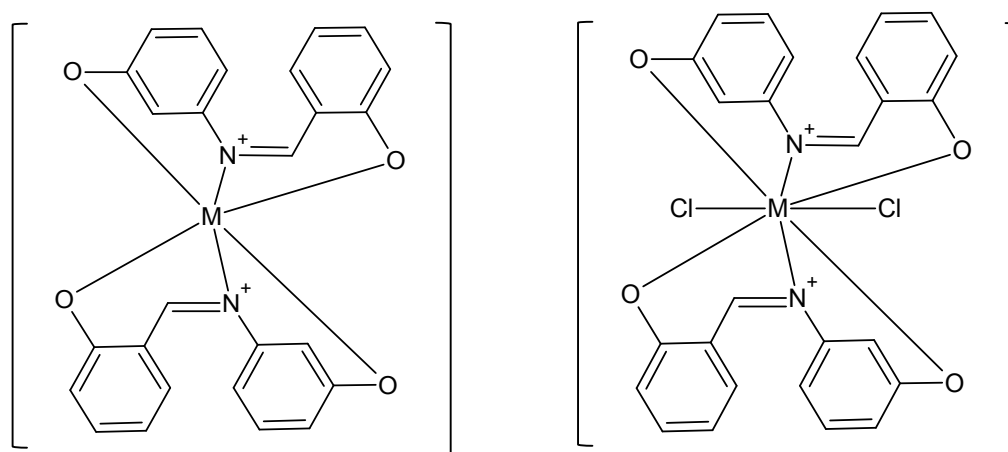


Fig. 2. Proposed structure of Schiff base of (3AMP) and its metal two complexes
 Where M = FeSO₄, NiCl₂, ZnCl₂

The proposed structure of the synthesized Schiff base and the metal (II) complexes are shown in Figs. 1 and 2 above respectively.

4. CONCLUSION

The Schiff base and its respective metal complexes have been synthesized in good yield and characterized with FTIR, electronic spectra, melting points, solubility and molar conductance. The electronic spectral data of the complexes suggest an octahedral and tetrahedral geometry for all the complexes. The molar conductivity indicates that the synthesized

complexes are non-electrolytes and 1:2 electrolytes as compared with the electrolytic value of CaCl₂. The synthesized metal complexes showed improved broad-spectrum antimicrobial activity against gram-positive and gram-negative bacteria better than the Schiff base. Thus, the present study revealed that the complexes [Mn(HL₁)₂Cl, Cu(HL₁)₂ and Ni(HL₁)₂Cl] can be further explored as potential leads compounds to be developed into antibiotics against the tested bacterial strains *E. coli*, *S. typhimurium*, *S. aureus* and *S. pyrogens*. To the best of our knowledge this study has not been presented in the literature, and hence, it will

contribute valuable knowledge to antimicrobial literature.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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