Synthesis, Characterization and Antibacterial Activity of Mixed Ligands of Schiff Base and It’s Metal(II) Complexes Derived from Ampicilin, 3-Aminophenol and Benzaldehyde

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Abstract: Schiff base ligands were synthesis via a condensation of the ligands in methanol in 1:1:1 molar ratio reactions. The transition metal(II) complexes were formed by the reaction of Co, Cu, Mn, Fe with the Schiff base and ampicillin and they were characterized via FTIR, electronic spectra, melting points, solubility and molar conductance. The invitro antibacterial activities of the complexes were tested using four bacterial stra ins; gramnegative; (Escherichia coli, salmonella typhi) and grampositive; (staphylococcus pyogenes and staphylococcus aureus). The complexes were formed in good yield and they have various shades of colors and sharp melting points. The IR spectrum of the HL (Table4) displays a new at (1651) cm\(^{-1}\) which is due to \(\upsilon(HC=N)\) group of the azomethine stretching vibrations of th e ligand, on complexation these band has been shift ed to lower frequencies (1651), (1621), (1651), and (1627)cm\(^{-1}\) for complexes [Co(Ampi)(3AMPB)Cl], [Cu(Ampi)(3AMPB)], [Mn(Ampi)(3AMP)Cl] and [Fe(Ampi)(3AMPB)] respectively. The overlap band at (1688)cm\(^{-1}\) stretching vibration is due to \(\upsilon(C=O)\) for β-Lactam group, these band has been shifted to lower frequency at (1370-1425)cm\(^{-1}\) for complexes showing that the coordination is thro ugh the Oxygen atom of β-Lactam group. The band sat (525), (526), (524) and (526)cm\(^{-1}\) were assigned to \(\upsilon(M-O)\) for compounds of Co, Cu, Mn, Fe, indicating that to the carbocyclic oxygen, and oxygen of β-Lactam group of the ligand are involved in coordination with metalions. The bands at (659), (669), (660), and (698)cm\(^{-1}\) were assigned to \(\upsilon(M-N)\) for compounds Co, Cu, Mn, Fe respectively, indicating that the nitrogen is involved in coordination with metal ions. The electronic spectral data of the complexes suggest an Octahedral and tetrahedral geometry for all the complexes. The molarconductivity indicates that the synthesized complexes are all non-electrolytes and soluble in protic solvent such as methanol and ethanol. The invitro antibacterial screening of Schiff base and its metal complexes showed that they are potential antibacterial agents against the tested microorganisms.

Keywords: SchiffBase, 3-aminophenol, Benzaldehyde, Ampicilin, Metal Complexes, Antibacterial Activity

1. Introduction

Schiff bases and their complexes are versatile compounds synthesized from the condensation of an amino compound with carbonyl compounds and widely used for industrial purposes and also exhibit a broad range of biological activities including antifungal, antibacterial, antimalarial, antiploriferative, anti-inflammatory, antiviral, and antipyretic properties [1] Schiff base are the compound containing azomethine group (-HC=N-). The acid/base catalysis or heating is employed for the synthesis of Schiff bases as their reactions are mostly reversible [2].

The aim of the research is to synthesize, characterize and evaluate the antibacterial activity of the synthesized Schiff base and its metal (II) complexes of Fe(II), Co(II), Cu(II) and Mn(II) ions.

While the specific objectives of the study will be to:

i. Prepare Schiff base using a mixed ligands of 3-aminophenol and Benzaldehyde.

ii. Synthesize Schiff base metal complexes of Fe(II), Co(II), Cu(II) and Mn(II) ions.

iii. Synthesize Schiff base and ampicillin with its metal
complexes of Fe(II), Zn (II), Co(II), Cu(II) Ni(II) and Mn(II) ions.

iv. Determine the physico–chemical properties of Schiff base and its metal complexes using different analytical technique like melting point, FTIR, conductivity, solubility test and UV/Visible spectrophotometer.

v. Study the antibacterial activity of the Schiff base and its metal(II) complexes.

2. Materials and Method

All chemicals, reagents and drug that were used in this research are of Analar grade. The metals used are; NiCl₂.6H₂O, ZnCl₂, FeSO₄.7H₂O, 3-aminophenol and Benzaldehyde. The ligands that were used in the research which were obtained from Department of Chemistry, Gombe State University, Nigeria. For the conduct of this research routine laboratory apparatus were used such as; Fourier Transform Spectroscopy (FT-IR), UV/Visible Spectrophotometer, stop watch, conductivity meter, melting point apparatus, Hot plate and magnetic stirrer, Oven, Weighing Balance, Auto clave, pH Meter, Petri Dishes, Pestle and Mortar, Water Bath

2.1. Synthesis of Schiff Base 3-aminophenol Benzaldehyde

The Schiff base was synthesized by a slight modification of literature [3]. This is done by the condensation of recrystallized from ethanol and dried, and preserved in a desiccator for 24hr over CaCl₂. The precipitate was separated by suction filtration. It was recrystallized from ethanol and dried at room temperature for 24hr in a desiccator. The precipitate was washed with excess of ethanol and dried at room temperature for 24hr in a desiccator over CaCl₂ [4].

2.2. 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 [5]. The Schiff base and its metal complexes was characterized by using different physico-chemical techniques like Melting point, UV/Visible spectrophotometer, FTIR, Conductivity, Solubility test.

2.3. Antibacterial Activity

The four bacterial species were used two gram-negative (Escherichia coli, Salmonella typhi) and two gram-positive (Staphylococcus aureus, Streptococcus pyrpgens), were obtained from pharmaceutical microbiology Department of the Gombe state University. The antibacterial activity of the ligand and the complexes was determined by the disc diffusion technique. The compounds were screened in vitro. A 1mg/ml solution in DMSO was used. Ceftriaxone and subactam were used as standard reference drug. The bacterium was maintained on nutrient agar and the agar media was incubated for different microorganism culture tests. After 24hrs of incubation at 37°C the bacteria, the diameters of zone of inhibition (mm) thus formed around each disc containing the test compound was measured [3].

3. Results and Discussion

3.1. Physical Characteristics and Analytical Data of Ligands/Complexes

In general, the complexes of [Co(Ampi)(3AMPB)Cl], [Cu(Ampi)(3AMPB)], [Mn(Ampi)(3AMP)Cl] and [Fe(Ampi)(3AMPB)] were obtained by heating under reflux of respective metal salts with HL and ampicillin in 1:1 molar ratio. The Schiff base and its metal(II) complexes shows various shades of colors ranging from Milk, Milk, Yellow-green, Milk, Grey for The HL and the complexes of Co, Cu, Mn Fe respectively. The HL and the complexes of Co, Cu, Mn, Fe obtained gave a sharp melting point indicating the isolation of fairly pure complexes (<300, 286-288), (283-284), (279-283), (285-287) °C of HL, Co, Cu, Mn, Fe respectively [6]. The Schiff base and its metal (II) complexes were prepared in good yield, ranging from 50-80% (7). The molar conductance of the complexes was determined in DMSO. It was found to be 4.1, 6.1, 3.1, 13.2 and 5.7Ω⁻¹cm²·mol⁻¹ for the Co, Cu, Mn, Fe complexes respectively. These low values suggested their non-electrolytic nature [7, 8].
has been shifted to lower frequency at (1370-1425) cm$^{-1}$ for the β-Lactam group, the se band complexed [Co(Ampi)(3AMPB)Cl], [Cu(Ampi)(3AMPB)], respectively. The overlap band at (1688) cm$^{-1}$ for [Mn(Ampi)(3AMP)Cl] and [Fe(Ampi)(3AMPB)] complexes (Co(Ampi)(3AMPB)Cl), [Cu(Ampi)(3AMPB)], assigned to (π-π transition. The UV-Vis spectrum of the Schiff base ligand HL, measured in DMSO solution between 200-1100 nm at room temperature. In the spectrum of the Schiff base ligand HL, the absorption band observed at (212 nm) (47169 cm$^{-1}$) which is due to υ (HC=N-) group of the Schiff base of 3Aminophenolbenzaldehyde, Ampi=Ampiciline MeOH=Methanol, EtOH=Ethanol, Dist.H=Distilled water, P. Ether=Petroleum ether, D. Ether =Diethyl Ether, DMSO=Dimethylsulphoxide, 3AMPB=Schiff base of 3Aminophenolbenzaldehyde and ampicillin ligands, Where C=Cool, H=hot, S=Soluble, SS=Sparingly Soluble, NS=Not Soluble, HL=Schiff base of 3Aminophenol benzaldehyde and ampicillin ligands, MOL. WGT=Molecular weight, M. P=melting points.

3.2. Solubility Test of the Complexes

The solubility of the complexes of [Co(Ampi)(3AMPB)Cl], [Cu(Ampi)(3AMPB)], [Mn(Ampi)(3AMP)Cl] and [Fe(Ampi)(3AMPB)] was studied in various solvent in both hot and cool process. The complexes are not soluble in water, pet. ether and diethyl ether (cool and hot), it is sparingly soluble in chloroform. But all the complexes are soluble in MeOH(cool and hot), EtOH (hot) and DMSO(cool and hot). Their solubility is as 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 (4) and [9].

| Compound | DIST.H.O | MeOH | EtOH | Acetone | Chloroform | P. Ether | D. Ether | DMSO |
|----------|----------|------|------|---------|------------|----------|----------|------|
| Co(Ampi)(3AMPB) | NS | NS | S | S | SS | S | S | S | NS | NS | NS | NS | NS | S | S |
| Cu(Ampi)(3AMPB) | NS | NS | S | SS | S | SS | SS | SS | SS | SS | SS | SS | SS | S | S |
| Mn(Ampi)(3AMPB) | NS | NS | SS | SS | SS | S | NS | NS | NS | NS | NS | SS | SS | S | S |
| Fe(Ampi)(3AMPB) | NS | NS | SS | SS | SS | S | NS | NS | NS | NS | NS | NS | SS | S | S |

3.3. Electronic Spectral Data of Ligands and Complexes

The electronic spectrum of the ligand HL was measured in DMSO solution between 200-1100 nm at room temperature. In the spectrum of the Schiff base ligand HL, the absorption band observed at (212 nm) (47169 cm$^{-1}$), which assigned to (π-π transition. The UV-Vis spectrum for the complexes ([Co(Ampi)(3AMPB)Cl], [Cu(Ampi)(3AMPB)], [Mn(Ampi)(3AMP)Cl] and [Fe(Ampi)(3AMPB)]) shows a band at (335nm) (29850 cm$^{-1}$), (267nm) (37453 cm$^{-1}$), (280nm) (35714 cm$^{-1}$) and (323nm) (30959 cm$^{-1}$) for the complexes of [Co(Ampi)(3AMP)Cl], [Cu(Ampi)(3AMPB)], [Mn(Ampi)(3AMP)Cl] and [Fe(Ampi)(3AMPB)] which show (T$g$-A$g$), (T$g$-Eg), (A$g$-T$g$) and (T$g$-Eg) transition. The Transitions, similar to those found for distorted octahedral complexes [4, 10, 11].

| Compound | Absorptioninnm | Absorptionin cm$^{-1}$ | Bandassignment | Geometry |
|----------|-----------------|-------------------------|----------------|----------|
| HL | 212 | 47169 | n-n$^*$ | Octahedral |
| Co(Ampi)(3AMPB)Cl | 335 | 29850 | T$g$-A$g$ | Octahedral |
| Cu(Ampi)(3AMPB) | 267 | 37453 | T$g$-Eg | Tetrahedral |
| Mn(Ampi)(3AMPB) | 280 | 35714 | A$g$-T$g$ | Octahedral |
| Fe(Ampi)(3AMPB) | 323 | 30959 | T$g$-Eg | Tetrahedral |

* = Transition state

3.4. Major FTIR Spectral Data of Ligands and Complexes

The IR spectrum of the HL (Table 4) displays a new at (1651) cm$^{-1}$ which is due to υ (HC=N-) group of the Schiff base of 3Aminophenolbenzaldehyde, Ampi=Ampiciline, MeOH=Methanol, EtOH=Ethanol, Dist.H=Distilled water, P. Ether=Petroleum ether, D. Ether =Diethyl Ether, DMSO=Dimethylsulphoxide, 3AMPB=Schiff base of 3Aminophenolbenzaldehyde and ampicillin ligands, Where C=Cool, H=hot, S=Soluble, SS=Sparingly Soluble, NS=Not Soluble, HL=Schiff base of 3Aminophenol benzaldehyde and ampicillin ligands, MOL. WGT=Molecular weight, M. P=melting points. The IR spectrum of the HL (Table 4) displays a new at (1651) cm$^{-1}$ which is due to υ (HC=N-) group of the Schiff base of 3Aminophenolbenzaldehyde, Ampi=Ampiciline, MeOH=Methanol, EtOH=Ethanol, Dist.H=Distilled water, P. Ether=Petroleum ether, D. Ether =Diethyl Ether, DMSO=Dimethylsulphoxide, 3AMPB=Schiff base of 3Aminophenolbenzaldehyde and ampicillin ligands, Where C=Cool, H=hot, S=Soluble, SS=Sparingly Soluble, NS=Not Soluble, HL=Schiff base of 3Aminophenol benzaldehyde and ampicillin ligands, MOL. WGT=Molecular weight, M. P=melting points.

Table 1. Physical Characteristic sand Analytical Data of Ligands/Complexes.

| Compounds | MOL. WGT | COLOR | M. P°C | %YIELD | MolararconductivityΩ$^{-1}$ cm$^2$ mol$^{-1}$ |
|-----------|----------|-------|--------|---------|---------------------------------|
| HL | 458.393 | MILK | <300 | 75 | 4.2 |
| Co(Ampi)(3AMPB)Cl | 552.823 | MILK | 286-288 | 80 | 6.1 |
| Cu(Ampi)(3AMPB) | 522.393 | YELLOW-GREEN | 283-284 | 78 | 3.1 |
| Mn(Ampi)(3AMPB)Cl | 548.893 | MILK | 279-283 | 50 | 13.2 |
| Fe(Ampi)(3AMPB) | 514.393 | GREY | 285-287 | 65 | 5.7 |

Where HL=Schiffbase of 3Aminophenolbenzaldehyde and ampicillin ligands, MOL. WGT=Molecular weight, M. P=melting points.
Table 4. Major FTIR Spectral Data of Ligands and Complexes.

| Compound         | v(N-H)P | v(N-H)S | v(C-C) | v(C=C) | v(C=) | v(C-N) | v(C-S) | v(C-H) | v(M-N) | v(M-O) |
|------------------|---------|---------|--------|--------|-------|--------|--------|--------|--------|--------|
| HL               | 3541    | 3270    | 2384   | 1658   | 1651  | 1450   | -      | -      | -      | -      |
| Co(Ampi)(3AMPB)  | 3572    | 3491    | 1135   | 1370   | 1211  | 576    | 2384   | 659    | 525    |        |
| Cu(Ampi)(3AMPB)  | 3541    | 3401    | 1119   | 1370   | 1621  | 1493   | 576    | -      | 669    | 526    |
| Mn(Ampi)(3AMP)   | 3572    | 3492    | 1210   | 1370   | 1651  | 1210   | 576    | 2380   | 660    | 524    |
| Fe(Ampi)(3AMPB)  | 3485    | 3319    | 1134   | 1425   | 1627  | 1450   | 576    | -      | 698    | 526    |

Ampi=ampicillin, 3AMPB=3Aminophenolbenzaldehyde.

3.4. Antibacterial Activity of the Ligands/Complexes of (3AMPB)

The antibacterial activity of the Metal complexes of Schiff base derived from (HL) and Co, Cu, Mn Fe showed a good antibacterial activity against Gram-negative (*Escherichia coli* and *Salmonella typhi*). The Co, Cu, Mn Fe complexes caused strong inhibition for *E. coli* and *Salmonella typhi*. The importance of these lies in the fact that, these complexes could be applied fairly in the treatment of some common diseases caused by *E. coli* and *Salmollatyphi*. However, Co, Cu, Mn Fe complexes were specialized in inhibiting Gram-positive bacterial strains (*Staphylococcus aureus* and *Streptococcus pyrogens*). The importance of this unique property of the investigated Schiff base complexes lies in the fact that, it could be applied safely in the treatment of infections caused by any of these particular strain [1, 14, 15].

Table 5. Antibacterial Activity of the Ligands and Complexes.

| Compounds        | CONCENTRATION (mg/ml) | Gram-negative |  |  |  |  |  |
|------------------|-----------------------|--------------|---|---|---|---|---|
|                  |                       | E. Coli(50/100) | Salm(50/100) | Staph(50/100) | Strept(50/100) |  |
| HL               | 11/15                 | 8/10         | 15/16 | 14/20 |
| Co(Ampi)(3AMPB)  | 18/20                 | 6/5          | 17/18 | 11/12 |
| Cu(Ampi)(3AMPB)  | 22/25                 | 7/9          | 21/20 | 11/15 |
| Mn(Ampi)(3AMP)   | 19/20                 | 13/12        | 15/19 | 14/17 |
| Fe(Ampi)(3AMPB)  | 15/17                 | 12/14        | 11/17 | 8/10  |

Where; E.coli=*Escherichi coli*, SALM=*Salmonellatyphi*, STAPHY=*Staphylococcus aureus*, STREPT=*Streptococcus pyrogens*, HL=Schiff base, 3AMPB=3 aminophenolbenzaldehyde, Ampi=Ampicillin.

4. Conclusion

The complexes are multi-colored, colors, they have good % yields with sharp melting point. The electronic spectral data of the complexes suggest an Octahedral and tetrahedral geometry for the complexes. The Results of the molar conductivity indicate that the synthesized complexes are non-electrolytes and 1:2 electrolytes as compared with the electrolytic value of CaCl$_2$. The *invitro* antibacterial screening of schiff base and its metal complexes showed that they are potential antibacterial agents against the tested microorganisms. The formation of the schiff base and its respective metal(II) complexes are shown in Figures 1 and 2 and the proposed Structures based on the data of the synthesize schiff base and the metal (II) complexes are shown in figures 3 and 4 below respectively.

Figure 3. Proposed structure of Schiff base of (3AMPB).

![Figure 3](image1)

Figure 4. Proposed structure of metal (II) complexes.

![Figure 4](image2)
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