INTRODUCTION
Thiosemicarbazones are special class of Schiff base with two N and two S donors which are of great interest owing to their significant antibacterial, antiviral, antimalarial, anti-inflammatory activity, anti-leprotic, and anti-cancer activities (Shawish et al., 2014). Thiosemicarbazones usually are chelating ligands capable of coordinating with transition metal ions. They coordinate to the metal ion through sulfur and nitrogen of the hydrazine (Chandra et al., 2007 and Salman et al., 2014). This class of compounds has received great interest from chemist and other scientist due to their bonding modes, biological activities, structural diversity, and ion-sensing ability (Mishra et al., 2013). Moreover, due to the presence of various manageable sets of sulfur and nitrogen atoms capable of donating electrons pair, which makes them useful as chelating ligands in the preparation of metal complexes (Singh et al., 2001).

Thiosemicarbazone compounds are synthesized by condensation reaction of thiosemicarbazide or its derivative and an aldehyde or a ketone. In this paper, we report the synthesis of thiosemicarbazone from isatin (1H-indole-2,3-dione) and thiosemicarbazide (hydrazinecarbothioamide). The Ni(II) and Cu(II) complexes were also synthesized using hydrated Ni (II) and Cu (II) chlorides. The investigation of their biological activity was also carried out using some pathogenic bacteria and fungi.

MATERIALS AND METHODS
Materials
All reagents used in this study were of analytical grade and were used without further purifications. The infrared spectra of the ligand and the complexes were recorded as KBr discs on Shimadzu FTIR-8400S Fourier Transform Spectrophotometer in the range of 400 – 4000 cm⁻¹. The magnetic susceptibilities of these complexes were measured using Magnetic Susceptibility balance MK1. Molar conductance of the complexes were measured using Janway 4010 conductivity meter. The metal content in the complexes was determined using AAS Buck Scientific 210 VGP. All glassware were washed thoroughly with detergent and rinsed several times with distilled water and kept at 110°C in an oven for 3 hours.

Methodology
Preparation of Isatin-thiosemicarbazone
The ligand was obtained by addition of an ethanolic solution containing 0.105 g (10 mmol) of thiosemicarbazide in 10 ml of ethanol to a solution 10 mmol of 1H-indole-2,3-dione in 10 cm³ of ethanol followed by the addition of 0.5 cm³ of acetic acid. This mixture was refluxed for 2 hours to obtain a yellow precipitate which was filtered off, washed with ice-cold ethanol and dried in a desiccator over P₂O₅. (Nur Nadia et al., 2015).
Preparation of M (II) thiosemicarbazone complexes (M= Ni or Cu)
The complexes were obtained by addition of 5 cm³ of 0.8 M ethanolic NaOH to an ethanolic solution (30 cm³) of the ligand (0.8810 g, 4 mmol) followed by the addition of a solution of 2 mmol hydrated M (II) chloride in 20 cm³ of ethanol. The resulting mixture was refluxed for 3 hrs and the precipitate formed was filtered off, rinsed with hot ethanol and dried in a desiccators over P₂O₅ (Nur Nadia et al., 2015). The synthesis of these complexes is represented schematic in the following equation:

![Figure 1: schematic representation of Thiosemicarbazone synthesis](image1)

Estimation of the metal content in the complexes
To determine the metal content in the complexes, 0.0100 g of each metal complex was digested with 15 cm³ of 33% aqueous HCl solution. Using distilled water, the volume was made to 100 cm³ and the working solutions were prepared by serial dilution of this stock solution with distilled water. The amount of metals in the complexes were measured against bank solution using AAS machine (Hassan et al., 2013).

Determination of water of crystallization
0.2g of each complex was placed in a cleaned crucible of known weight and kept in an oven at 110°C until constant weight was obtained (Vogel, 1972). The percentage of water in the complexes was calculated using the following equation:

% of water = \( \frac{\text{Mass complex taken} - \text{Mass in air}}{\text{Mass in air}} \times 100\% \)

Magnetic Susceptibility Measurement
This was achieved by placing each of the complexes into a capillary tube of known mass (m₁) up to 1.5 to 2.5 cm length. The capillary tube and its content were weighed and the mass (m₂) was recorded. The gram magnetic susceptibility was calculated from the equation:

\( \chi_g = \frac{LC(R_1 - R_o)}{m \times 10^9} \)

Where

\( R_o = \) readings from the balance for empty capillary
\( R_1 = \) readings from the balance for loaded capillary tube
\( L = \) the length (in cm) of the complex in the capillary tube,
\( C = \) the balance calibration constant (C = 1) and
\( m = \) is the mass of the complex taken.

Antimicrobial Studies
The antibacterial activity of the synthesized ligand and its Ni(II) and Cu(II) complexes were carried out in vitro by disc diffusion method as described by Khan et al. (2014) using cultures of Salmonella typhimurium, Escherichia coli and Staphylococcus aureus, and amoxicillin was used as standard drugs, while a DMSO-wetted disk was used as negative control. Aspergillus flavus, Aspergillus niger and Muco species (induca) are the three pathogenic fungi used for the antifungal activity of the ligands and complexes. Various concentrations of these compounds were used. Ketoconazole and DMSO wetted disks were used as standard fungicide (Positive Controls) negative control respectively.

RESULTS AND DISCUSSION
The Schiff base was prepared as reported. It is a yellow flaky product with good yield of 83.23% and melting point of 240°C. The Ni(II) complex is brown whereas Cu(II) complex is green. The decomposition temperatures of these complexes were found to be 280°C and 255°C respectively, which is high, suggesting good stability (Table 1). The effective magnetic moments of at room temperature were determined to be 3.37 BM and 0.94 BM for Ni(II) and Cu(II) complexes respectively, which suggested that the complexes are paramagnetic in nature. The molar conductivity values obtained were found to be 9.1 and 17.3 ohm⁻¹cm⁻¹mol⁻¹ for the Ni(II) and Cu(II) complexes respectively, very low values, suggesting their non-electrolytic nature (Spina, et al., 2008). All these are presented in Table 1.
The infrared spectroscopy of the ligand and its Ni(II) and Cu(II) complexes were recorded on KBr discs using FTIR-8400S Fourier Transform Infrared spectrophotometer from 400 – 4000 cm⁻¹. The band at 1681 cm⁻¹ and 1134 cm⁻¹ in the spectrum of the ligand were assigned to the azomethine group i.e C=N and ν(C=S) stretching frequencies respectively. The band assigned to ν(C=O) of the free ligand and its complexes likely become COO⁻ upon deprotonation. The assigned ν(C=N) of the indole ring remained intact in the spectra of the complexes which is another supporting evidence for the coordination of this group with these metal ions after deprotonation. The assigned to ν(C=O) of the free ligand and its complexes (Hussain et al., 2014) shifted to 1319 cm⁻¹ in the spectra of the complexes which is another supporting evidence for the coordination of indolic oxygen to the metal ions (Khan et al., 2015).

The percentages of nickel and copper in the respective complexes were found to be 10.52 and 11.18% respectively (Table 3). The synthesized complexes were found to be hydrated and the water content in them was determined. The percentage of water was found to be 10.60% and 9.10% for the Ni(II) and Cu(II) complexes respectively. This is as shown in Table 4.

From the results of the above analyses and the information available from the literature, the empirical formulae of these complexes were determined. The results obtained suggested the general formula [ML₃]₃H₂O where M = Ni²⁺ or Cu²⁺ as presented in Table 5.
The ligand and the complexes were evaluated for antibacterial activities using three bacteria isolate namely, salmonella typhirium, Staphylococcus Aureus and Escherichia Coli. Amoxicillin as standard drug to serve as positive control. A comparative study on the antimicrobial activities of these compounds indicated that the metal complexes exhibited higher antibacterial activity than the ligand but lower antibacterial activity compared with the standard. These compounds were tested for antifungal activity against muco spp, aspergillus niger and aspergillus flavus using Ketoconazole as standard. The result revealed that all the synthesized compounds were active on the three organism. The result further indicated that complexes exhibited higher potential as antifungal growth inhibition compared to the ligand, but less so less active than ketoconazole. These results are similar to that of Nair and Josephyus, 2010, Ahmed et al., 2011and Kothari, 2015 and are recorded in Table 6.

From the results of the analyses on these compounds and the information available in the literature, we suggest the following general structure for these complexes as presented in figure 3:

![Figure 3: The proposed structure of the complexes M = Ni^{2+} and Cu^{2+}.](image)

**CONCLUSION**
We have successfully synthesized the thiosemicarbazone from the condensation of from 1H-indole-2,3-dione (Isatin) and thiosemicarbazide. Ni(II) and Cu(II) complexes of were synthesize from the ligand successfully. The ligand and complexes were characterized using various spectroscopic techniques; and their antibacterial and antifungal activities were studied using Amoxicillin and ketoconazole as standards respectively. The results of the antimicrobial studies revealed that the ligand and the complexes are more active on E. coli and S. typhirium than they are on S. aureus though they are not as active as Amoxicillin. As for the anti-fungal activity, the ligand shows no activities on A. flavus and mucor spp respectively, while Ni (II) complex show no effect on A. niger. The antimicrobial activities of these compounds are less than that of Ketoconazole that was used as standard drug.

**REFERENCES**

from Cuminaldehyde and 4 Aminoantipyrine, Chem Sci Trans, 3(3); 937-944.


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