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Complex of silver (I) 1-(furan-2-ylmethylene) urea and its Anti-microbial studies

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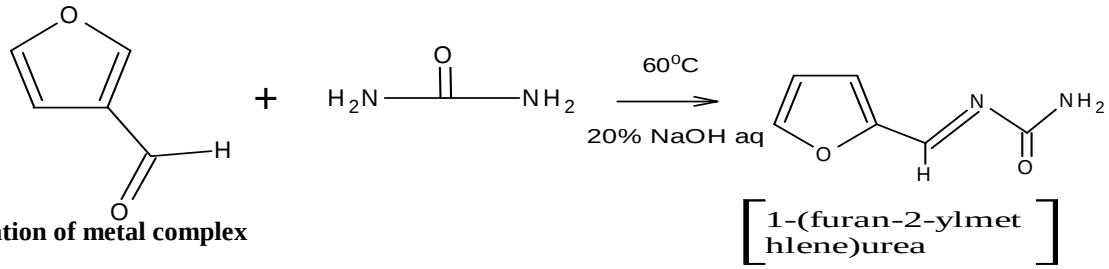
Abstract
Complex of silver (I) with 1-(furan-2-ylmethlene) urea (FUR) has been synthesized. The complex was characterized by infrared spectroscopy, melting point, elemental analysis solubility test, conductivity and antimicrobial study. The infrared spectra showed that the ligand acted as a tridentate donor coordinating through the carbonyl oxygen, the amine nitrogen and the azomethine nitrogen. The UV study showed a shift in the band due to n-π* and π-π* in the complex as compared to the ligand. The compound is insoluble in most organic solvent. Its anti-microbial study showed that the complex has improved activity against the selected organism as compared to the free ligand and the uncomplexed of metal.
Keywords: Silver, 1-(furan-2-ylmethlene) urea, antimicrobial and complex.

Introduction
Silver has been known for its healing and antibacterial properties since the Hippocrates. Its ions and compounds have been known to be toxic to bacteria, viruses, algae and fungi [1,2]. Unlike other heavy metals, silver is considered to be harmless to humans except an excessive intake which do cause a condition known as argyria [2]. Interest in the use of silver as anti-microbial agent has been renewed in recent years after a decline in its usage in the past [2]. Many manufactures have introduced silver into their products to reduce microbial activities. For example Kohler introduced a line of toilet seats that include anti-microbial agent formed into the plastic which inhibits the growth of odour causing bacteria, mold and mildew. In the field of medicine silver or silver compounds are used in a wide range of applications [2]. The biological activities of many silver(I) complexes have also been reported [3,4,6]. The biomedical applications and uses of silver (I) complexes are related to their anti-microbial action which appears to involve interactions with DNA [5]. Silver sulphadiazine is a topical anti-infective cream, used worldwide for dermal injuries. It has a broad antibacterial spectrum including all microbial species likely to infect wounds [6]. The ability of silver(I) complexes to adopt geometries with variable structural nuclearity and structural diversity make the study of silver(I) chemistry very attractive [5,6,7,8,9]. The reaction between the metal ions and ligand is known to depend on steric and interactive information stored in the ligand and is governed by the metal ions through the demands of their coordination geometries [10,11]. In this we paper present the results of the synthesis, characterization, and anti-microbial studies of the complex of silver (I) nitrate with 1-(furan-2-ylmethylene with the aim of studying the effect of complexation on the activity of the silver metal ion.

Materials and methods
Reagents
All the reagents used for this study and were obtained from Sigma Aldrich and BDH and were used without further purification.
Preparation of ligand
The ligand was prepared as described in the literature [10]. About $40cm^{-3}$ of analar grade furfuraldehyde was measured and poured into a $250cm^{-3}$ flat bottom flask, 40g of urea added, followed by $9cm^{-3}$ of distilled water. The mixture was heated on a water bath until a temperature of $60^{o}C$ was reached, and then $1cm^{-3}$ of 20% NaOH solution was then added and heating continued for another 20 minutes. The mixture was cooled on an ice bath and the

precipitate filtered and washed with cold water (10^{o}C) and then it was dried at a temperature at 50^{o}C. The dried powder obtained was washed with n-Hexane and recrystallized twice from methanol- water solution (30/70%) and dried. Equation below shows the reaction of furfuraldehyde with urea.



Preparation of metal complex

1-(fura-2-ylmethlene)urea (6.20g) was dissolved in 100cm^{-3} of boiling distilled water in a 250cm^{-3} beaker. Silver nitrate salt (3.79g) was weighed and dissolved in 50cm^{-3} of distilled water and then added to the ligand solution and heating continued for 10 minutes. It was then removed from heat and filtered immediately. The filtrate was concentrated and allowed to cool the resulting precipitate was filtered and dried. The equation below shows the stichiometry of reaction of the metal salt and ligand.

$MX.nH2O + 2(C_6H_6O_2N_2) \longrightarrow [M(C_6H_6O_2N_2)_2]X.nH_2O$
(Where M is Ag^+, X is NO_3, n is 0, 1, 2, 3)

Physical measurements

The metal ion was determined gravimetrically after removing the organic residue by digesting with a few drops of concentrated nitric acid. The infra red spectra data of ligand and complex were recorded on Genesis II FTIR spectrometer as KBr discs over a range of 4000-500cm^{-1}. The conductivity was determined on Jenway 4330 conductivity and pH meter in DMSO. Melting point analysis was done on Electrothermal melting point apparatus and UV analysis was carried out on Cecil 9000 series UV/Visible spectrophotometer. The HNMR of the ligand was carried out on ^{1}H and ^{13}C Mercury- 200BB.

Antimicrobial sensitivity test

The test organisms used were isolates of *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Bacillus subtilis*. Pure cultures of the test isolates were obtained from the Microbiology bank of the Department of Biotechnology Advanced Laboratory of Sheda Science and Technology Complex, Abuja. Nutrient Agar was used for the repeated sub culturing and preservation of the isolates before being used for the anti-bacterial assay. It was prepared according to the manufacturer's specification and sterilized inside the autoclave at 121^{o}C for 15 minutes. The medium was then poured into sterile petri plates. All flasks and equipments used were sterilized accordingly inside the hot air oven. The hood was sterilized by swabbing with 70% ethanol using cotton wool. The test bacteria were seeded onto the Mueller-Hilton agar surface by streaking using a sterile cotton bud for each organism. The agar well diffusion method was used for the antimicrobial assay. This was done using a cork borer of 10mm diameter, which was sterilized after each use by dipping in 70% ethanol and flaming with the Bunsen flame. To each test organism, 100µl of 20mg/cm^{3} of the complex (equivalent to 1mg/well) were then applied to each of the holes using sterile tips attached to a micropipette. Chloramphenicol anti-biotic drug was used as the standard. The set up was then incubated for 24 hours at 37^{o}C in the incubator. The zone of inhibition were then taken after the incubation period using a graduated ruler and recorded in millimetre (mm). All tests were carried out in duplicates.

Result and discussion

The ligand precipitated as a brown powdered compound insoluble in most organic solvent and has a melting point > 200^{O}C. The reaction of Ag(I) metal salt with the ligand gave a 12% yield of a black powdered metal complex. From the elemental analysis the metal composition of the complex was found to be 48.3%. Calculated metal composition is 49.6%; C 18.14%; H 8.05% and N 7.05%. A formula was proposed as $[Ag(C_6H_6N_2O_2)]NO_3$. This indicates that the compound precipitated as 1:1 molar ratio metal-ligand complex. The compound is insoluble in most organic solvent and decomposed between 237.7- 238^{o}C. The conductivity indicates a non-electrolyte as shown by its conductance values (0.488µS) in DMSO solution at room temperature. The infrared spectra of the ligand and the metal complex showed vibration bands due to carbonyl O, azomethine N and the primary amine N. These bands were observed in the ligand at 1672.03cm-^{1}, 1532.87cm-^{1} and 3323.01cm-^{1} respectively. On complexation the carbonyl band shifted by approximately 12.29cm^{-1}. This indicates that the carbonyl oxygen was involved in

coordination. The azomethine N and primary amine N were not visible. This may be a result of strong coordination of this coordination sites to the metal ion [6]. The UV/Vis spectra analysis of the ligand showed absorptions at 321.7, 348.7 and 352.0nm. The band at 321.7nm is assigned to π-π*, while the ones at 348.7 and 352.0nm are assigned n-π*. These bands shifted on complexation to the metal ion indicating an interaction between the ligand and metal ion. The observation made is similar to the previous report [5,11].The ^{1}HNMR analysis of the ligand 1-(furan-2-ylmethylene)urea in DMSO showed multiplet peaks in the range 6.65-6.99 (6.00-7.50) corresponds to the furan ring: the peak at 7.55 (7.50) is due to the H around the carbonyl group while peaks in the range 5.4-5.75 (6.50) is assigned to the amine (NH_2). These when compared with the NMR data of the ligand generated by chemdraw Ultra 10.0 confirmed the structure of the ligand.

Microbial study

Antimicrobial activities of the ligand, Ag(I)-FUR and free metal salt was determined. The inhibitory concentration at 1mg/L (IC) of the ligand, silver complex and free metal salt against gram positive and gram negative bacteria are summarized in Table 1. It was observed that the ligand showed higher activity against *S. aureus* and *B. substilis* than the metal complex. However, in *E.coli* and *K.pneumonia* the activity of the complex is equal and higher respectively than the ligand. The standard drug showed a higher activity in *S. aureus*, *K. pneumonia* and *B. substilis*. While the ligand and complex showed a higher activity in *E. Coli*. The activity index of the ligand is in the range 44.8-105.3%. The uncomplexed metal however showed a higher activity than the ligand and the metal complex. This increase in activity may be explained on the basis of chelation theory [6]. Lipids and polysaccharides are some important constituent of cell wall and membranes, which are preferred for metal ion interaction. In addition to this, cell wall also contains many aminophosphates, carbonyl and cysteinyl ligands, which maintain the integrity of the membrane by acting as a diffusion barrier and also provides suitable sites for binding. Chelation can considerably reduce the polarity of the metal ion, which in turn increases the lipophilic character of the chelate. Thus, the interaction between metal ion and the lipid is favoured. However in the metal complex the nature of the ligand appears to have reduced the activity of metal ion. The ligand on reaction with the metal ion formed a stable complex with reduced activity when compared to the un-complexed counterpart. Some important factors that influence the activity of complexes are nature of the metal ion, nature of the ligand, coordinating sites, and geometry of the complex, concentration, hydrophilicity, lipophilicity and presence of co-ligands. Steric and pharmokinetic factors also play a decisive role in deciding the potency of an antimicrobial agent [6].

Table 1: Result showing the zone of inhibition of microorganism growth in mm

Organisms	FUR	Ag (FUR)	Ag^{+} solution	Chloramphenicol	Activity index of ligand (%)
Staphylococcus aureus	17	15	40	34.5	49.3
Bacillus subtilis	17	16	40	29.5	57.6
Escherichia coli	20	20	42	19	105.3
Klebsiella pneumoniae,	13	18	42	29	44.8

Conclusion

The complex of silver(I) with 1-(fura-2-ylmethlene)urea has been synthesized and the result showed that the compound is a stable compound. It is insoluble in most organic solvents. The microbial study indicates that the activity of the metal ion against microorganisms is reduced upon complexation. Further study is ongoing to confirm the observed trend.

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