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Characterization of novel complex Ciprofloxacin Ag(I)

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ABSTRACT

The fluroquinolone family member ciprofloxacin is well known for its drug design and coordinating ability towards metal ions. The coordination chemistry of this drug with metal ions of biological and pharmaceutical importance is of considerable interest. Novel Ag (I) complex of Ciprofloxacin (CIP) was synthesized and characterized on the basis of their physical properties, (FT-IR and electronic) spectral studies. The TG/DTA analysis of the complexes was carried out. The morphology and size distribution of the complex polymer was obtained by transmission electron microscopy (TEM).

Keywords: Ag(I) complex, ciprofloxacin, spectral studies, TG-DTA, TEM.

INTRODUCTION

Quinolones are amongst the most widely prescribed families of antibiotics, both in human and veterinary medicine, due to their broad spectrum of activity and safety profile. However, their overuse/misuse seems to be basis of emergence and dissemination of microbial resistance that results from the bacterial adaptations and compromises antimicrobial efficiency.[1-5]

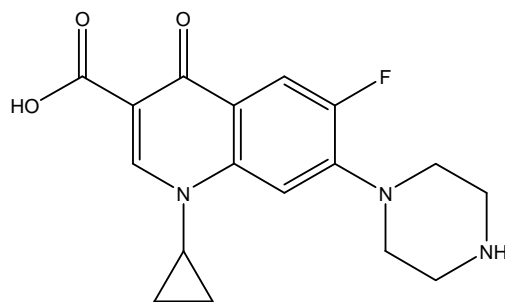
The interactions between metal ions and various quinolones have been reported in the literature. These studies have been primarily directed towards the identification of functional groups directly linked to the metal and establish the structure formed by these coordination complexes. Other investigations aim to show the effect of metal ions upon antibacterial activity. The crystal structures of quinolone complexes indicate that quinolone antibiotic can participate in the formation of complexes in a number of ways.

Fluroquinolones (FQ) were developed to increase quinolone antibacterial activity by changes in the basic quinolone structure.

In the last decades, coordination polymers of silver(I) have attracted much attention since they are potentially emissive or medicinally active materials. [6-9]. The silver(I) ions are regarded as extremely soft acids favoring coordination to soft bases, and have given rise to an interesting array of stereo chemistries and geometric configurations with the coordination numbers of two to six. Previous related work on silver (I) coordination polymers has concentrated on the use of nitrogen-donor ligands or oxygen donor ligands or combination with both donor, but the use of both nitrogen- and oxygen-donor ligands such as analogous quinolone to construct robust polymers and networks are rare. Ciprofloxacin [H-cip = 1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid], is a member of second generation quinolone antibiotics family [9-12].

It is a broad- spectrum antibiotic that is active against both gram positive and gram negative bacteria. It functions by inhibiting DNA gyrase, a bacterial type II topoisomerase and topoisomerase IV, which is an enzyme necessary to separate replicated DNA by inhibiting cell division.

Although a series of its mononuclear complexes have appeared in the literature, such as Zn, Cd, Fe, Co, Cu, V, ciprofloxacin acting as a bridging polydentate ligand to synthesize coordination polymer still remains largely unexplored and its silver complex has never been reported. In order to investigate the coordination diversity and comparison with silver mononuclear complex of norfloxacin $[\text{Ag}(\text{H-Norf})_2\text{NO}_3]$, we herein describe preparation and structural characterization of an unprecedented 1D ladder- like $\text{Ag}(\text{I})$ coordination polymer $\{[\text{Ag}_4(\text{H-Cip})_2(\text{Cip})_2(\text{NO}_3)_2] \cdot 4\text{-H}_2\text{O}\}_n$ (H-Cip = ciprofloxacin, Cip = deprotonated ciprofloxacin). The crystal structure was studied previously by Zhen-Feng Chen *et.al.*, we have extended this work by carrying out IR, TG/DTA and UV spectroscopic study.



1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-quinoline-3-carboxylic acid

Fig.1: Structure of Ciprofloxacin

MATERIALS AND METHODS

Synthesis of silver complex of ciprofloxacin:

Complex was prepared by dissolving (10 milimole, 3.3gm) ciprofloxacin in ethanol and adding this solution to ethanolic silver nitrate solution, (10 milimole, 1.69gm.). The pH was adjusted 6-7 by adding NaOH in water. The reaction mixture was refluxed for 4hrs. The reaction mixture was kept overnight at room temperature. A fine powdered product was obtained. The solution was filtered. The complex was dried in the oven.

INSTRUMENTATION

Melting points were taken in open capillaries on a melting point apparatus. Ultraviolet (UV) spectra were recorded in the range 200-800 nm on Perkin Elmer UV spectrometer by making solutions in DMSO. The Infra-red (IR) spectra were recorded as KBr pellets in range $4000\text{-}400\text{cm}^{-1}$ on Shimadzu FTIR balance. In order to throw more insight into the structure of the reported complexes, thermal studies on the solid complexes using Thermogravimetric (TG) and derivative thermal analysis (DTA) were performed.

UV SPECTRA ANALYSIS:

The electronic spectra of free ciprofloxacin reflected at 243 and 298 which attributed to $\pi\text{-}\pi^*$ and $n\text{-}\pi^*$ intraligand transitions (these transitions occur in case of unsaturated hydrocarbons which contain ketone groups). With respect to the free ciprofloxacin, the emission peak of polymer undergoes a slight red shift. The emission of polymer may be mainly originated from intraligand $\pi\text{-}\pi^*$ excited state of ciprofloxacin. However it is severely quenched upon silver coordination due to weak metal-metal interactions of Ag-Ag, leading to decreased luminescence intensity. [13, 14]

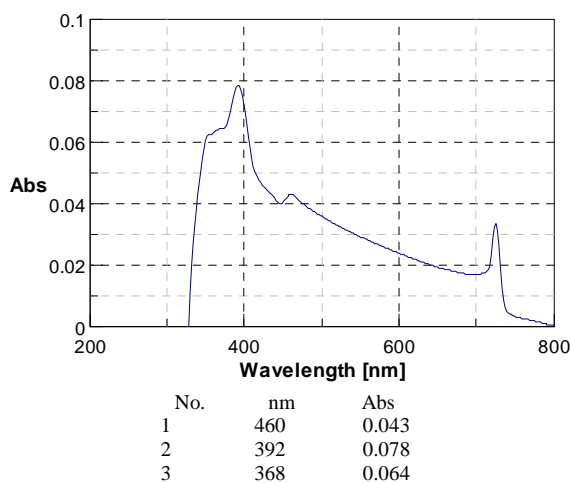


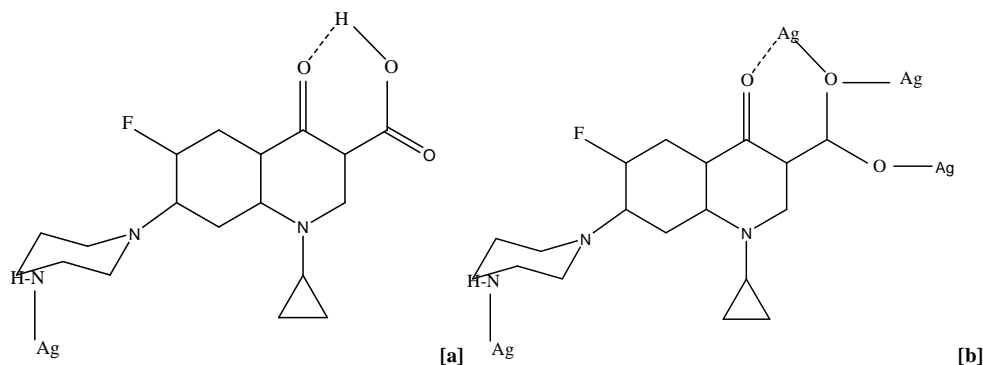
Fig II: UV spectra of Ciprofloxacin Ag Complex

IR SPECTRA ANALYSIS:

The infrared spectra of the two complexes are compared with those of free ligand, in order to determine the site of coordination that may be involved in chelation. There are some guide peaks in the spectra of the ligand, which are of good help for achieving this goal. These peaks are expected to be involved in chelation. The position or intensities of these peaks are expected to be changed upon chelation. The infrared spectra of fluoroquinolones are quite complex due to the presence of the numerous functional groups in the molecules, therefore their interpretation is based on the most typical vibrations being the most important region in the IR spectra of fluoroquinolones between $\sim 1800\text{ cm}^{-1}$ and 1300 cm^{-1} .

The two bands observed at 1706 cm^{-1} and 1620 cm^{-1} in the spectrum of free CIP have been assigned to the stretching vibration of carboxylic $\nu(\text{COOH})$ and the carbonyl $\nu(\text{C=O})$, respectively.

The band at around 1710 cm^{-1} due to the $\nu(\text{C=O})$ vibration of the carboxylic group is not detected, indicating deprotonation and probably interaction of this moiety with the metal ion, and the very strong slightly split band at around 1384 cm^{-1} can be assigned to $\nu_3(\text{NO}_3)^- + \nu_s(\text{OCO})$ and confirms the presence of the nitrate group.



Scheme I .Two coordination modes of ciprofloxacin in polymer complex

Here H-Cip ligand acts as neutral monodentate ligand coordinates with N of piperazinyl ring, whereas 4-oxo and 3-carboxylate oxygen do not take part in coordination. Differing from $\text{Ag}(\text{H-Norf})_2(\text{NO}_3)_3$ where the local coordination environment around Ag (I) ion is approximately linear and composed of two strong interactions of Ag-N by piperazinyl N atoms from two different H-Norf and two weak interactions of Ag...O by O atoms from one NO_3^- anion.

Here in [b] Ag(I) is five coordinated tetragonal pyramid Ag(I) is surrounded by five O atoms: two from bidentate NO_3^- , one from 4-oxo and the other two from 3-carboxylate of deprotonatedCip .[16]

THERMOGRAVIMETRIC ANALYSIS:

The content of a particular component in a complex changes with its composition and structure. Thus the content of such components can be determined based on the mass losses of these components in the thermogravimetric plots of the complex. Therefore in order to throw more insight into the structure of the reported complexes, thermal studies on the solid complexes using the Thermogravimetric and derivative thermogravimetric analysis techniques were performed.

The data obtained indicate that the ciprofloxacin is thermally stable in the temperature range 25- 50 °C. Decomposition of the CIP starts at 50 °C and finished at 750 °C with two stages. The first stage of decomposition occurs at maximum temperature of 132 °C and is accompanied by weight loss of 7.81% corresponding exactly to the loss of acetylene molecule (C_2H_2). The second stage of decomposition occurs at two maxima 315 and 382 °C and is accompanied by weight loss of 74.04% corresponding to the loss of $4\text{C}_2\text{H}_2 + \text{C}_2\text{H}_4 + 3\text{NO} + \text{HF} + 1.5 \text{H}_2$. The actual weight loss from these stages is equal to 81.85%, very closer to calculated value 81.88 %.[17]

The firstdecomposition peakoccurred at 250°C – 350°C with a weight loss of16.37% from TG graph. This loss if calculated is due to acetylene, water molecules and nitrate ions, closer to16.35%. The TG plot of the complex then shows fast decomposition in between 300 °C to 850 °C which depicts rapid decomposition of rest of the ligand, leaving behind metallic residue. The TG plot shows total massloss of 76%. DTA plot shows all exotherms attributed to ligand decomposition.

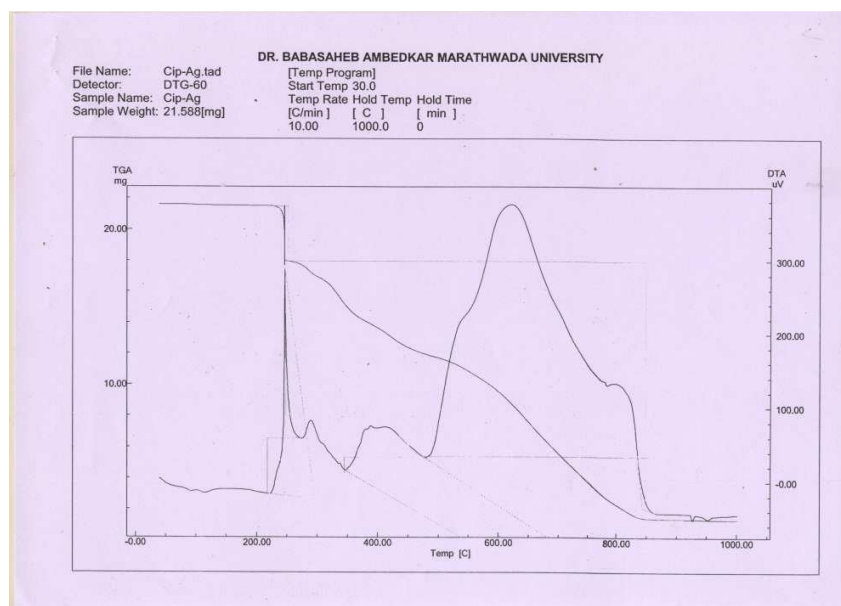


Fig.V TG/DTA Spectra of Ag Ciprofloxacin complex

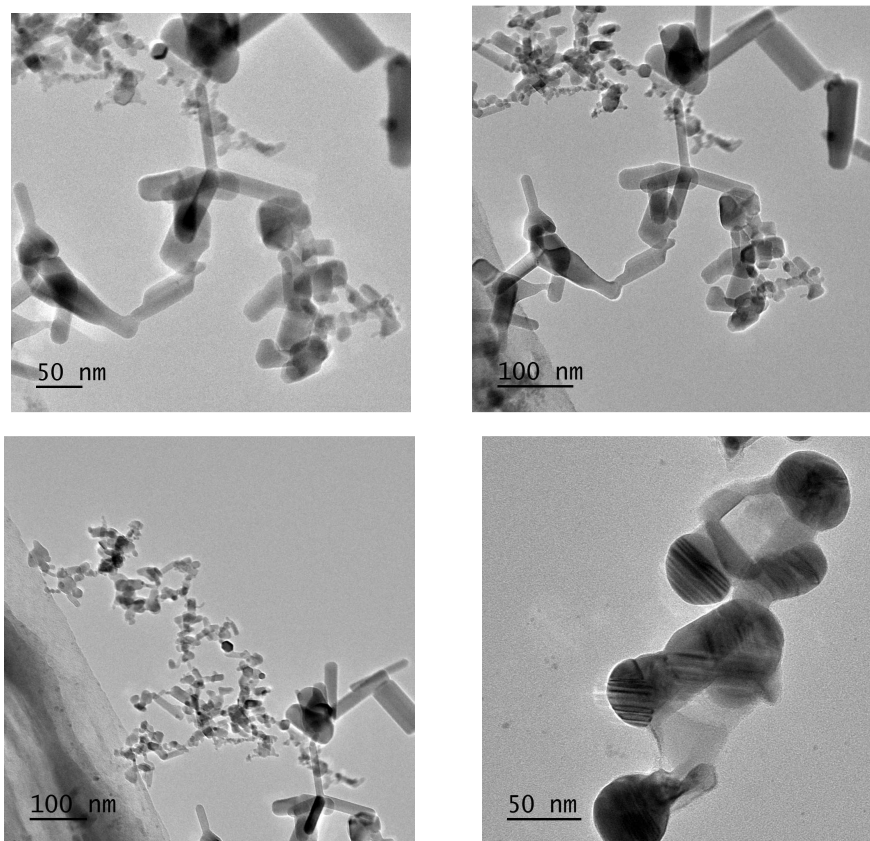


Fig.VI TEM Micrographs of the complex

CONCLUSION

We can conclude that the mode of action of these drugs and their metal complexes were extensively studied in the past, but there are still several questions to be answered hence effective research in the field is still the need of the hour.

This bonding mode was unexpected and, to the best of our knowledge, unprecedented in quinolone drug interactions toward metal ions. Therefore remarkable feature is that ciprofloxacin in exhibits unprecedented mixed coordination modes to the metal ion upto date, which is never reported in previous quinolone complexes, and much differs from $\text{Ag}(\text{H-NOrf})_2(\text{NO}_3)$.

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