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A mononuclear complex of silver (I) with nitazoxanide

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ABSTRACT

Reaction of Nitazoxanide (NTZ) with $AgNO_3$ yields an unusual mononuclear complex [Ag $(NTZ)_2$] NO_3 in which local coordination environment around Ag^+ ion is linear in which NTZ acts as monodentate ligand to bind Ag ion by N atom of amide group.

Keywords: Ag (I), NTZ, UV analysis, IR analysis.

INTRODUCTION

Nitazoxanide [2-(acetyloxy)-N-(5-nitro-2-thiazolyl) benzamide, NTZ] is a potent anti-parasitic and antiviral agent recently approved. The antiprotozoal activity of NTZ is believed to be due to interference with pyruvate: ferredoxin oxidoreductase (PFOR) enzyme dependent electron transfer reaction. The thiazole derivative Nitazoxanide first described by Rossignol, is a broad spectrum antibacterial and anti-parasitic agent, particularly efficacious against anaerobic bacteria and as an anthelminthic and antiprotozoal agent. It is used for the treatment of cryptosporidiosis and giardiasis in immune-competent patients. It is absorbed from gastrointestinal tract following oral administration and is rapidly hydrolyzed to an active desacetyl metabolite (tizoxanide). [1-6]

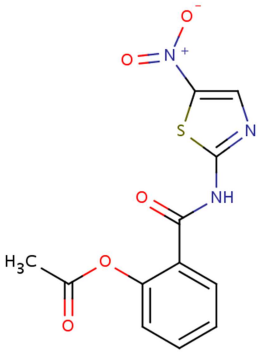

Fig. I. Structure of Nitazoxanide

MATERIALS AND METHODS

Synthesis of complex:
All chemicals used were of analytical grade. Pure sample of Nitazoxanide (NTZ) having molecular formula, $C_{12}H_9N_3O_5S$ and molecular weight 307 g/mol was obtained from pharmaceutical company. Metal salt was of Merck Chemicals.

Complex was prepared by dissolving Nitazoxanide (0.1mol) in ethanol and adding solution to ethanolic solution of silver nitrate (0.5mol.) .The reaction mixture was refluxed for 2hrs. The complex was dried in oven. Yellow coloured fine powdered complex is obtained.

INSTRUMENTATION:
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 4000-400cm^{-1} on Shimadzu FTIR. 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.

RESULTS AND DISCUSSION

UV VISIBLE SPECTRA OF $[Ag\ (NTZ)_2]NO_3$ COMPLEX:
The UV – VIS spectrum of Nitazoxanide solution exhibited four absorption bands at 210, 250, 346 and 436 nm. The NTZ spectrum is dominated by π -> π* transitions and exhibits an absorption band in the visible region at 436nm. There are at least two less intense transitions in the UV region at 210 and 250. The first and second absorption bands at 210 and 250nm were due to the π -> π* excitation of π – electron of the aromatic system. The third band at 346nm was due to the n-> π* transition involving lone pair of electrons on the carbonyl group while fourth band at 436nm could be assigned to intarmolecular charge transfer(ICT) from the 2- amino to 5- nitro group via thiazol ring. Coordination to Ag (I) does not change the spectrum profile but the bands become stronger, especially the one in the visible region 346- 436nm, which is responsible for Ag- NTZ yellow colour. [7-8]

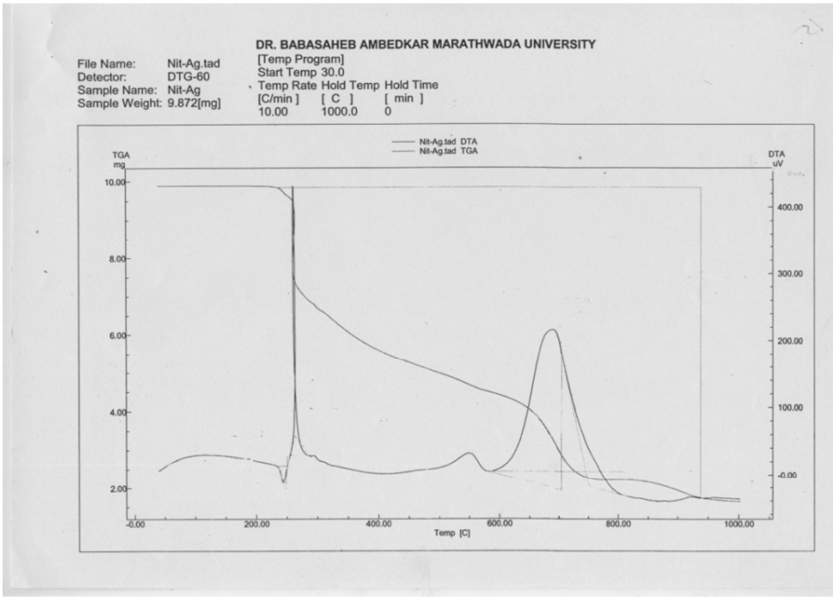

Fig. II TG/ DTA of Complex

IR SPECTRA OF $[Ag\ (NTZ)_2]NO_3$ COMPLEX
In order to clarify bonding and the effect of the metal ion on the ligand, the IR spectra of the free ligand and the metal complexes were studied and assigned based on careful comparison of their spectra with that of the free ligand. The *ν* (N-H) stretching was at 3357cm^{-1} in NTZ drug. This frequency shifted to lower range 3350-3240 cm^{-1} indicating coordination of ligand through amido N-H.

New band appeared at lower frequency in the spectra of the complexes were probably due to metal-nitrogen. A very strong band corresponding to NO_3 stretching of free nitrate anions is observed at 1378 cm^{-1}. [9]

THERMOGRAVIMETRIC ANALYSIS OF [Ag (NTZ)$_2$]NO$_3$ COMPLEX

The thermogram of [Ag (NTZ)$_2$] NO_3 chelate shows that the first step decomposition within the temperature range 200 ^{0}C- 300 ^{0}C corresponds to loss of hydrated and coordinated water molecules. The subsequent steps correspond to the removal of the NTZ ligand leaving metal oxide as the residue. The overall weight loss amounts to 70.34%. [10-11]

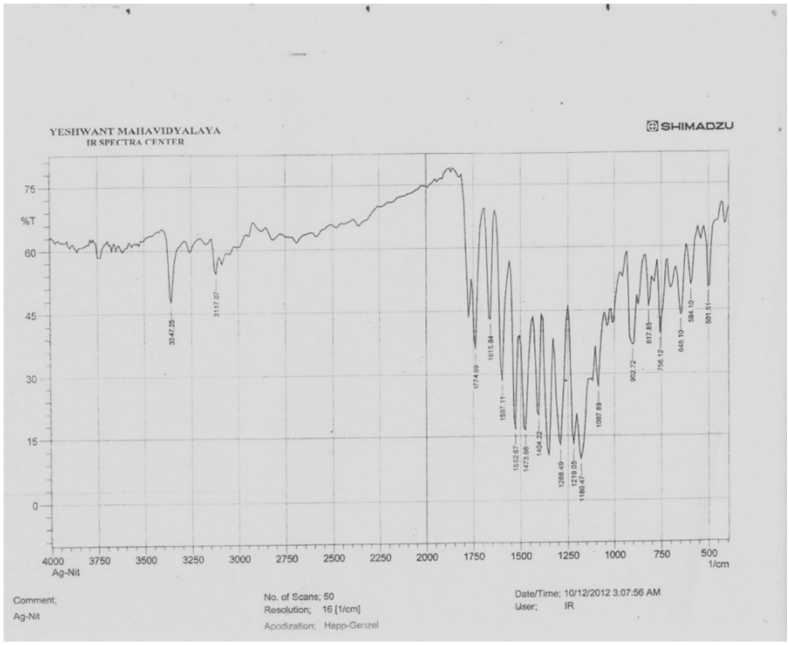

Fig. III I.R spectra of complex

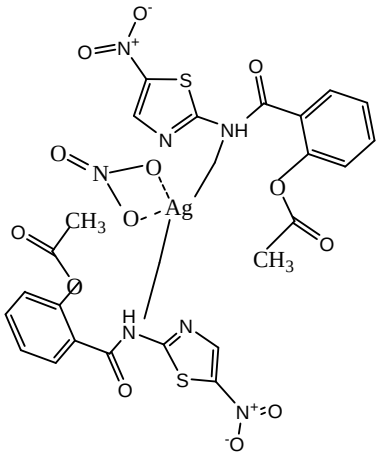

Fig. IV. Structure of complex

CONCLUSION

The results of this study indicated that the ligand, CAN coordinated to Ag (I) through amide nitrogen. This assignment is corroborated by spectral data. The thermal data confirm the suggested formula. Thus linear geometry is suggested for the complex. From the above data the proposed structure for complex is given in Fig. IV

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