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Synthesis and characterization of Ag (I) complex with Candesartan

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ABSTRACT

New complex of Ag (I) Candesartan (CAN) of the composition Ag [(CAN) H_2O] NO_3 has been synthesized by the interaction of $AgNO_3$ with said ligand in ethanol medium. The complex so obtained has been characterized on the basis of IR, UV and thermogravimetric analyses.

Keywords: Ag complex, Candesartan, IR, UV, TG/DTA.

INTRODUCTION

Candesartan cilexetil is an esterified prodrug of candesartan, a non- peptide angiotensin II type 1 (AT_1) receptor antagonist used in the treatment of hypertension. It is in a class of drugs called angiotensin receptor blockers (ARBs). Angiotensin, formed in the blood by the action of angiotensin converting enzyme (ACE), is a powerful chemical that attaches to angiotensin receptors found in many tissues but primarily on smooth muscle cells surrounding blood vessels. Angiotensin's attachment to the receptors causes the muscle cells to contract and the blood vessels to narrow (vasoconstriction) which leads to an increase in the blood pressure. Candesartan cilexetil blocks the angiotensin receptor and thereby prevents the action of angiotensin. As a result blood vessels expand and blood pressure is reduced. [1-5] .Candesartan cilexetil is rapidly and completely bioactivated by ester hydrolysis during absorption from gastro intestinal tract to candesartan. As with other angiotensin II receptor antagonists, candesartan is indicated for the treatment of hypertension. Results of the CHARM study (early 2000s) demonstrated the morbidity and mortality reduction benefits of candesartan therapy in congestive heart failure. Thus, while (ACE) angiotensin converting enzyme, inhibitors are still considered first line therapy in the heart failure, candesartan can be used in combination with an ACE to achieve improved mortality and morbidity vs. an ACE alone and additionally is an alternative in patients intolerance of ACE inhibitor therapy.

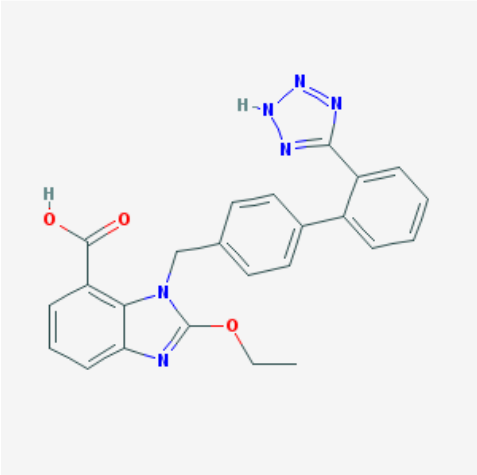

Fig I: 2D Structure of candesartan
2- ethoxy – 1-({ 4-[2-(2H- 1,2,3,4- tetrazole -5 –yl) phenyl] phenyl}methyl) – 1H – 1,3 – benzodiazole -7 –carboxylic acids

MATERIALS AND METHODS

Materials:
All chemicals used in this study were of analytical grade. This included candesartan of the formula $C_{24}H_{20}O_3$ and 440.40 g/mol and metal salt $AgNO_3.H_2O$. Candesartan was obtained from a pharmaceutical company. The organic solvent ethanol was purchased from BDH and used without further purification.

Synthesis of Ag (I) candesartan complex:
Complex was prepared by dissolving pure Candesartan (10mM, 4.4 gm.) in ethanol and adding solution to ethanolic silver nitrate solution (10mM, 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
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 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.

RESULTS AND DISCUSSION

TABLE 1: UV ANALYSIS OF COMPLEX:
UV Spectra analysis:
The electronic spectra of candesartan display absorption bands at 254nm and 271nm which are assigned to n-∏ *and ∏-∏ *transition, respectively. The electronic spectra of the complex show a shift in frequency i.e. at 433, 319 and 260 nm. This shift was attributed to the effects of the crystal field upon the interelectronic repulsion between the 4d electrons. [6,7]

Sr. No.	Compound	Wavelength in nm	Wavelength in cm^{-1}
1.	candesartan	254 271	39370 36900
2.	Ag candesartan	433 319 260	23094 31347 38461

IR Spectra Analysis:

The FT-IR spectrum gives the detailed information about the functional groups in the interaction in complex formation. The IR spectra of candesartan cilexetil shows characteristic peak in between 2800-2850 cm^{-1} (-O-H functional group), 2957 cm^{-1}(C-H group stretching), 1710cm^{-1} (carboxyl carbonyl).

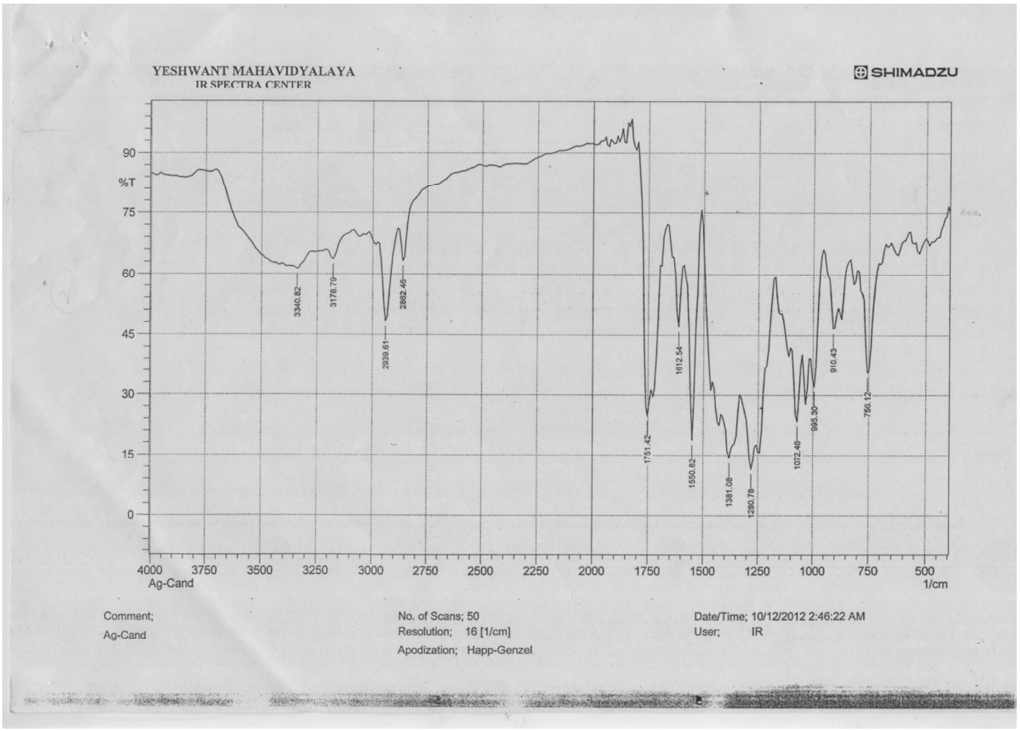

Fig. II I.R Spectra of Complex

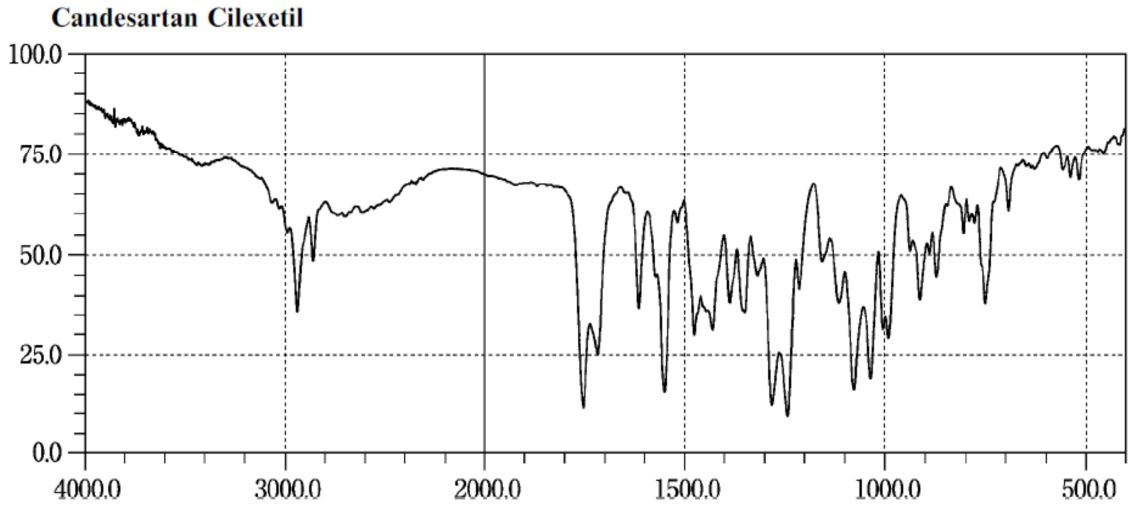

Fig.III I.R Spectra of Candesartan

A very strong band corresponding to NO_3 stretching of free nitrate anions is observed at 1381 cm^{-1}. The other bands in the spectrum of each complex are similar to those in the corresponding ligand spectrum except for slight shifts in their positions and changes in their intensities due to coordination. The HC=N stretching frequency in the IR spectrum of the drug was observed at 1666 cm^{-1}. This band was shifted towards lower frequency 1612 cm^{-1} in the

spectra of metal complex indicating the participation of CH-N nitrogen in coordination (M-N) with the metal. Broad bands in the range 3220- 3400 cm^{-1} are due to presence of coordinated water molecule present in the metal complex. [8]

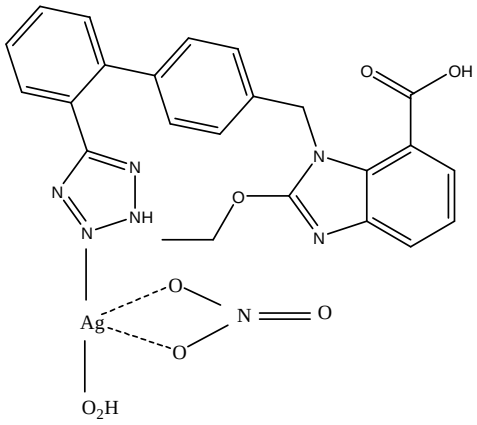

Fig. IV Proposed structure of complex

Thermal studies:

The complex is stable at room temperature and can be stored for several months without any change. Ag (I) complex of candesartan was studied by thermogravimetric analysis from ambient temperature from 30 ^{0}C to 1000 ^{0}C temperature inN_2 atmosphere.

The overall mass loss from the TG curve is 78.79%. The TG of the complex reveals mass loss in temperature range 25-315 ^{0}C corresponding to loss of NO_3 and H_2O. A horizontal plateau on the TG curve and exothermic peaks in DTA curve for the complex indicates the decomposition of the organic part of the chelate in the last step leaving of the metallic at the final temperature. The first mass loss corresponds to the formation of their respective anhydrous compounds. While the second mass loss is due to the decomposition of counter ions and candesartan molecule. [9]

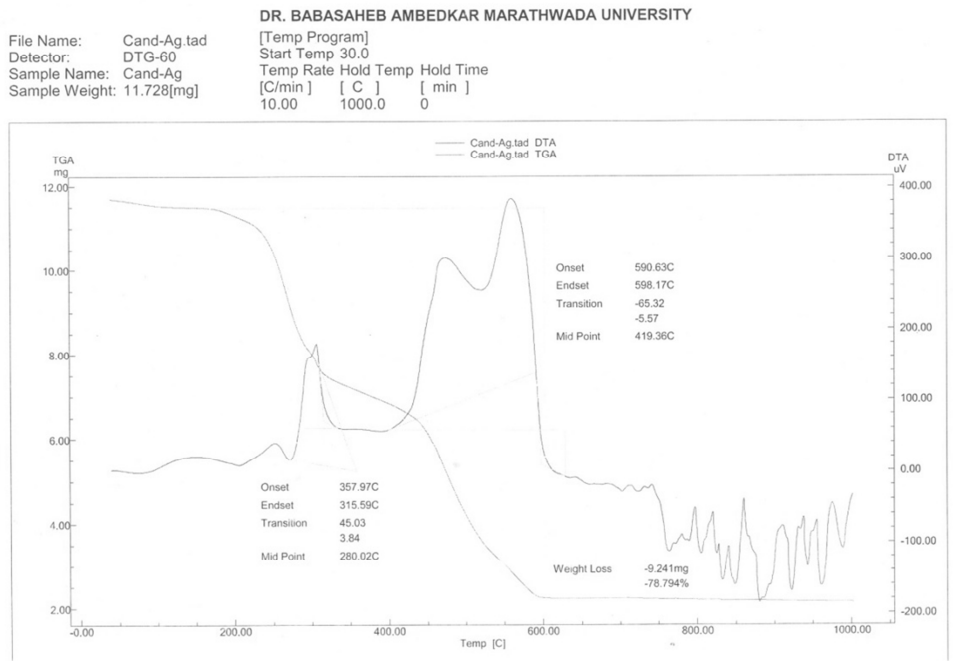

Fig. V Thermogram of complex (TG/ DTA)

CONCLUSION

Based on the electronic spectral results, a linear geometry has been suggested for the Ag (I) complex. The IR spectroscopic data supports the coordination via nitrogen atom of tetrazole ring of candesartan and H_2O with linear geometry around Ag (I).

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