Synthesis, Characterization and Antimicrobial Studies of Thorium and Cerium Complexes with Lorazepam

Praveen Kumar Verma, K. Chaturvedi, R. Chaturvedi

***Abstract*— Lorazepam [LZM] and other 1, 4 benzodiazepine drugs are the Schiff bases tend to react with the metals to form the complexes. In the present paper, ligand LZM reacts with thorium and cerium metals to form the drug-metal derivatives. Synthesized complexes were characterized by Elemental analysis, Potentiometric and Spectroscopic methods. The general formula of the synthesized complexes have been given by $[L_1M(NO_3)_4]$ and the geometry of the complexes were found to be octahedral. Where L_1= lorazepam, and M = thorium or cerium metal. Antimicrobial study shows that all the synthesized complexes are bioactive. Biological studies have been carried out on some selected bacteria *(E. coli, S. aureus, S. typhi)* and fungi *(A. niger, A. flavous, P. triticena)* at different concentrations.**

***Index Terms*— Lorazepam (LZM), LZM-Ce and LZM-Th Derivatives.**

I. Introduction

Lorazepam (LZM) is the 1, 4 benzodiazepine drug act as hypnotic, tranquilizing[1-4] and anticonvulsant[5-8] agents. Tendency of these drugs to form the complexes with transition and rare earth metal ions and the enhancement of biocidal activities[9-11] after complexation led to considerable interest in their coordination chemistry. In the present work the thorium and cerium complexes of lorazepam was prepared and characterized on the basis of elemental analysis and spectral studies. They were also screened for their antimicrobial activities

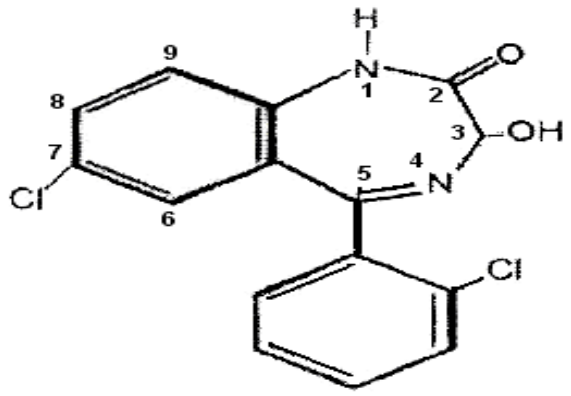


Fig.1:- LORAZEPAM

II. Experimental

All the chemicals used were of analytical grade. Potentiometric analysis had been carried out with the help of Elico-120 pH meter and IR spectra were recorded on Perkin-Elmer 842 spectrometer using KBr matrix. Antifungal and antibacterial studies were done by Broth Serial Dilution Method.

The stock solutions of metal nitrates were prepared in double distilled water while LZM in alcohol. The complexes were prepared by mixing the equimolar solutions of metal nitrates and ligand in 1:1 ratio. The Potentiometric titrations had been carried out which confirms the 1:1 stoichiometry of all the complexes.

III. Result and Discussion

All the synthesized complexes were found to be stable at room temperature. The analytical data of the ligands and their metal complexes are given in table-I.

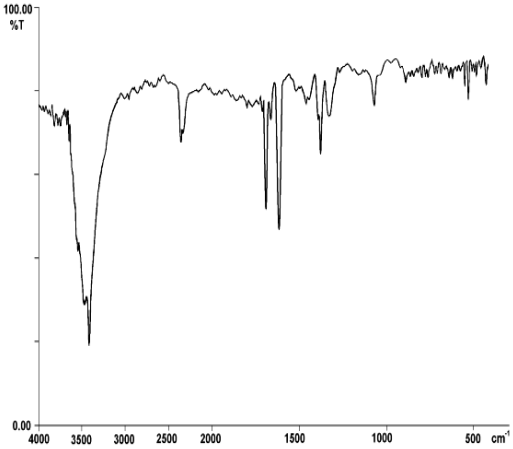
S. No.	Compound	Color	Melting Point	% Analysis				
				C	H	N	Cl	Metal
1	Lorazepam	White	160^0 C	56.04	3.11	8.72	22.10	-
2	LZM-Th complex	Yellow	>360 ^{0}C	22.47	1.25	10.48	8.86	28.96
3	LZM-Ce complex	Brown	>360 ^{0}C	25.38	1.41	11.84	10.01	19.75

IR spectra of LZM shows the bands at 1704 cm^{-1}, 1628 cm^{-1} and 750 cm^{-1}confirms the presence of C=O, C=N and –Cl group respectively. The C=N band in thorium and cerium complexes of LZM shows the lowering of band i.e. at 1618 cm^{-1}

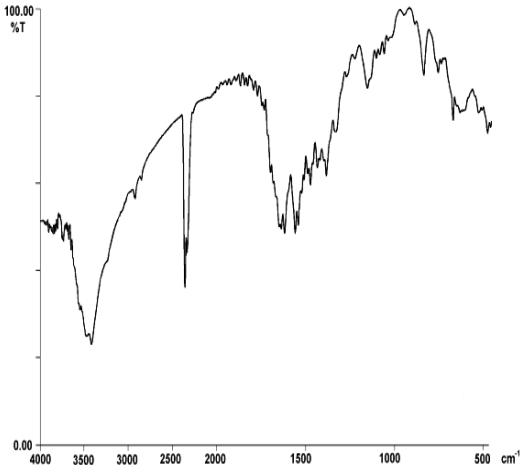
and 1620 cm^{-1}. Above facts indicate the involvement of azomethine nitrogen (N_4) in complexation. The IR spectral bands of metal complexes in the region 410-550 cm^{-1} are tentatively assigned to M-N linkage.

Praveen Kumar Verma, Department of Chemistry, Sainath Group of Education, Agra.
K. Chaturvedi, Department of Chemistry, Agra College, Agra.
R. Chaturvedi, Forensic Science Laboratory, Agra

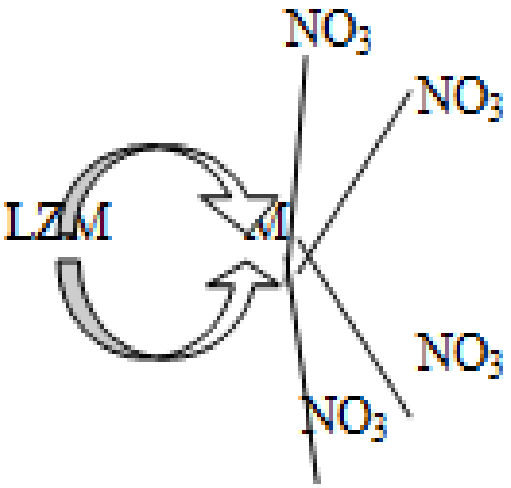
IR SPECTRUM OF Th - LZM COMPLEX



IR SPECTRUM OF Ce - LZM COMPLEX



On the basis of elemental and spectral studies the tentative structure of metal complexes of LZM are as follows:-



Where,
M= Th or Ce metal

IV. Antimicrobial Study

All the synthesized complexes were screened for their biocidal activity. For attempting the antibacterial and antifungal study the solution of the synthesized complexes were prepared at different concentrations (250ppm, 500ppm, 750ppm and 1000ppm) and tested against few selected bacteria *E. coli*, *S. typhi*, *S. aurius* and the fungi *A. niger*, *A. flavous* and *P. triticena*. The results obtained are given in table-II and table-III.

TABLE-II

Compound	Zone Of Inhibition Of Bacteria											
	E. coli				*S. typhi*				*S. aurius*			
	250 ppm	500 ppm	750 ppm	1000 ppm	250 ppm	500 ppm	750 ppm	1000 ppm	250 ppm	500 ppm	750 ppm	1000 ppm
Lorazepam	-	-	-	18.66	-	-	-	12.0	-	-	-	18.66
LZM-Th	40.0	78.86	72.86	75.71	41.43	67.14	70.0	74.29	38.57	57.14	57.14	68.57
LZM-Ce	35.57	68.57	72.86	74.29	41.43	67.14	68.57	71.43	38.57	62.86	62.86	68.57
Th Nitrate	-	-	-	-	-	-	-	-	-	-	-	-
Ce Nitrate	-	-	-	-	-	-	-	-	-	-	-	-

TABLE-III

Compound	Zone Of Inhibition Of Fungi											
	A. niger				*A. flavous*				*P. triticena*			
	250 ppm	500 ppm	750 ppm	1000 ppm	250 ppm	500 ppm	750 ppm	1000 ppm	250 ppm	500 ppm	750 ppm	1000 ppm
Lorazepam	-	-	-	20.0	-	-	-	17.33	-	-	-	20.0
LZM-Th	41.43	55.71	58.57	67.14	40.0	64.29	65.71	71.43	35.71	55.71	55.71	60.0
LZM-Ce	40.0	52.86	61.43	65.71	37.14	52.86	55.71	60.0	35.71	55.71	55.71	58.57
Th Nitrate	-	-	-	-	-	-	-	-	-	-	-	-
Ce Nitrate	-	-	-	-	-	-	-	-	-	-	-	-

Data clearly shows that thorium and cerium complexes of LZM are almost equally effective against the above bacteria while in the case of *S. aurius* LZM-Ce complex show little bit more effectiveness. Result also shows that the thorium and cerium complexes of LZM are almost equally effective against all the above fungi

Above data also suggests that the drug-metal complexes are more active as compared to drug ligands and metal nitrates.

ACKNOWLEDGEMENT

For conducting the elemental analysis CDRI, Lucknow and IR analysis from St. John`s College, Agra is gratefully acknowledged. Authors also being very thankful to Agra College, Agra for providing the useful lab facilities.

REFERENCES

[1] W. J. Geary, Coord. Chem. Rev., 7, 81(1971).
[2] C. Preti and G. Tosi, J. Coord. Chem., 8, 223(1979).
[3] C. Preti and G. Tosi, Transition Met. Chem., 3,246(1978).
[4] G. Minghetti, M. L. Ganadu, C. Foddai, M.A. Cinellu, F. Demartin and M. Manassero, Inorg. Chim. Acta, 86, 93(1984).
[5] W. Schollek, W.D Horst, W. Schlosser, Adv. Pharmacol. Chemother., 16, 45(1979).
[6] F. C. Colpaert, NIDA Res. Monogr., 116,245-266, Drug Discrim. Appl. Drug Abuse Res. (1991).
[7] S. D. Iversen, Br. Assoc. Psychopharmacol. Monogr., 6, 75-88(1985).
[8] M. Buehrer, P. O. Maitre, C. Crevoisier, D. R. Stanski, Clin. Pharmacol. Ther., (St. Louis), 48(5), 555(1990).
[9] Sanu Singh, Praveen Verma, Pawan Pathak, K. Chaturvedi, R. Chaturvedi, Indian J. Applied and Pure Bio. Vol. 23(1), 143-146(2008).
[10] Praveen Verma, K. Chaturvedi, R. Chaturvedi, J. Chemtracks, 11(1), 297-302(2009).
[11] N. Sharma, P. Gautam, K. Chaturvedi, R. Chaturvedi, J. Indian Council of Chemists, Vol. 21(2), (2004).