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NOTE

Synthesis and Characterisation of Mn(II) and Zn(II) Complexes with Cimetidine

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Inflammation is an essential component of all ulcers. Complexes of metals were found to enhance antiulcer activity of drugs. Cimetidine is the most useful drug in the management of peptic and duodenal ulcers. The complexes of cimetidine may be of higher biological interest. In the present work, the synthesis and characterisation of Mn(II) and Zn(II) with cimetidine is reported.

Aluminium and magnesium salts are used in therapy as antacids for neutralising hydrochloric acid present in stomach. Inflammation is an essential component of all ulcers. Copper complexes were found to enhance antiinflammatory actions of parent drugs[1]. A complex of bismuth salt with citric acid has been shown to promote healing of both gastric and duodenal ulcers as effectively as histamine H_2-receptor antagonist drugs.[2] Cimetidine is the most useful drug in the management of peptic and duodenal ulcers[3], having a substituted aromatic group and a polar 'urea equivalent' group connected by a flexible chain[4]. It accelerates the healing of benign gastric ulcers. The complexes of cimetidine with essential metal ions may be of higher biological interest. In the present work, we present the synthesis and characterisation of Mn(II) and Zn(II) with cimetidine.

M/s. Eskayef (SKF) Limited had supplied pure samples of the drug cimetidine. Purity was further tested by thin layer chromatography. All the chemicals and reagents used were of AnalaR grade.

A weighed quantity of drug (1 mole) was dissolved in ethanol. Metal salt solution (1 mole) was prepared separately. Both solutions were mixed slowly with stirring at room temperature and refluxed for 2 h. On cooling the complex separate out which was filtered off, washed well with distilled water and dried in a desiccator.

Metals were estimated by standard methods[5]. Formation of 1 : 1 complex between drug and metal salts were confirmed by Job's method of continuous variation as modified by Turner and Aderson using conductance as index property[6]. Thermal studies were carried out using Stanton Redcroft STA Model

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780 in a static air atmosphere. IR spectra were recorded in the solid state (KBr pellets) on spectrophotometer model no. IR 470 Shimadzu (Japan).

Various data of analysis of complexes are given in Table-1. All complexes are stable in dry air but absorb moisture when kept open for a long time. Both the complexes are insoluble in water but slightly soluble in the common solvents.

TABLE-1
PHYSICAL, CHARACTERISTICS OF CIMETIDINE (L_1) COMPLEXES OF Mn(II) AND Zn(II)

Complex yield (%) (colour)	Analysis found (calcd.) M	C	H	N	S	Stability constants 'K'	Log K L/mole	Free energy change ΔF kcal/mole	μ_{eff} (B.M.)
$MnL_1(H_2O)_2SO_4$ (60) (Brown)	12.66 (12.56)	27.00 (27.44)	4.67 (4.61)	19.78 (19.21)	14.91 (14.63)	0.245×10^6	5.389	–7.419	5.92
$ZnL_1(H_2O)_2SO_4$ (68) (white)	14.00 (14.60)	26.54 (26.80)	4.77 (4.50)	18.40 (18.76)	14.44 (14.28)	0.0849×10^6	4.928	–6.740	diamag

TABLE-2
THERMAL STABILITY DATA OF COMPLEXES OF Mn(II) AND Zn(II)

Complex	Temp. range I step (°C)	% Weight loss Exp.	Calcd.	Temp. range II step (°C)	% Weight residue Exp.	Calcd.	Order of reaction	Activation energy (kcal mol^{-1})
$MnL_1(H_2O)_2SO_4$	100–150	7.0	8.2	250–350	14.0	19.0	1	3.247
$ZnL_1(H_2O)_2SO_4$	150–175	12.0	8.05	300–380	19.0	18.1	1	5.217

The TGA studies indicate that metal complexes of cimetidine decompose in two steps: the first decomposition corresponds to the loss of water molecules while second step decomposition of the loss of ligand and formation of metal oxides. The weight of residue (metal oxide) corresponds to the formation of MnO_2 from Mn(II) and ZnO in case of Zn(II) complex of cimetidine. Activation energy and order of reaction were determined by TGA studies using Broido method (Table-2).

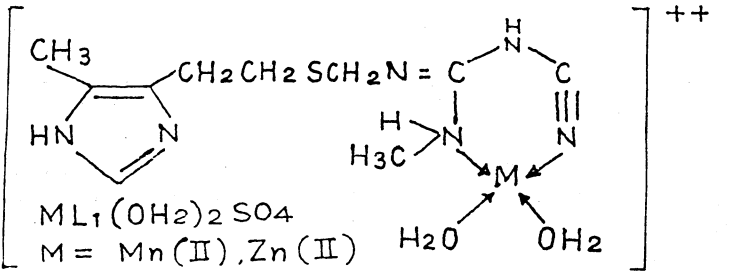
IR spectra: The bands around 3600–3200 cm^{-1} indicate presence of water of coordination in the complexes. The bands around 2900–2600 cm^{-1} show the presence of heterocyclic N-atom. Presence of different bands in the region of 1700–1400 cm^{-1} indicates formation of six-membered chelate rings of the type H—C=N— in both the complexes. The presence of absorption frequencies in the region 990–800 cm^{-1} may be due to (—C—N) and (M—O) linkages in the complexes. The band in the region 850–500 in complexes is attributed to the presence of (M—O) and (M—N) linkage in the complexes.

Magnetic moment value of Mn(II) complex indicates high spin tetrahedral stereochemistry while Zn(II) complex shows diamagnetic nature indicating tetrahedral geometry of the complex.

Molar conductivities of these complexes could not be measured as these are

slightly soluble in the common solvents including N-methyl-2-pyrrolidone and N-N-dimethyl formamide.

On the basis of elemental analysis the general formula of complexes comes out to be $MnL_1(H_2O)_2SO_4$ and $ZnL_1(H_2O)_2SO_4$. The following structure may be assigned to these complexes on the basis of above studies.



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