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PREPARATION, CHARACTERIZATION AND ANTI-INFLAMMATORY STUDIES SOME LIFE ESSENTIAL METALS WITH DICLOFENAC POTASSIUM

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ABSTRACT

This paper deals with the study of life essential metals with diclofenac postassium. The conductivity, molecular weight, infrared, magnetic susceptibility and electronic spectra has been studied and the explanation of results has been shown as was found by the study.

KEYWORDS: Diclofenac Potassium, Methanol, Gastric Lesion, Anti-Inflammatory Drug, Carrogecnan Newbeuld, Analgesic Antipyretic

Diclofenac has analgesic, anti-inflammatory and antipyretic properties, all related to it supervision of the cycloonygenase (Cox01 and Cox-2) activities. Its profile of adverse effects is similar to other NSAD's with gastro-intestinal and renal complications being the most common and some times making it necessary to interrupt treatment. Quantity of the drug for children and other diseased persions in various cases of disease has little role with used drug. methatrereat and cyclosporine. Diclofenac main indications are for the treatment of osteoarthritis symptomate treatment of rheumatic disease, cancer pain as an adjustment of opioid therapy, musculosreletal condition, headache and postoperative pain Na et al. 2004.

Complexes of Diclofenac potassium an anti-inflammatory drug with Cu(II), Fe(II), Ni(II) and Zn(II) has been synthesised and properties has been studied by molecular conductance, magnetic moment and spectral measurement and I.R. measurement , bidentate anionic ligand. Anti-inflammatory effect has been evaluated by carrageen an induced rat paw edema test Anuradha et al. 2000.

The Fe (II) complexes were found less active than the parent drug while the complexes of Ni, Cu, and Zn were found more potent than their basic drugs Dr. Williams Chem. 1972.

Diclofenac potassium is a analgesis as well as anti-inflammatory drug.

EXPERIMENTAL

Chemical were used A.R. Grade. The Complex of potassisum has been contributed by A.P.C.P. Pharma Limited Haridwar and used as such GW Watt et al.1974.

PREPARATION OF COMPLEXES

The stoichlometric ratio of the complexes were determined by spectrophotometrics conductometric method. Divalent forms of complexes were isolated from methand. To a hot soln of the ligand in the same solvent in ratio M:L::1:2 were added and boiled for 5-10 hours. A regular pH of the Solution i.e. 5-10 was established throughout the experiment, using either NH_3or Hcl during the process. The complexes were purified and dehydrated by the ususal process taking methanol as a solvent and anhydrous desicator. The purity of complexes were correctrised by T.L.C. C. Preeti et al 1976.

To characterised the complexes the physical properties for example melting point was determine by the usual process.

Raste campher method was used by us for the molecular weight determinations. Elemental analysis were carried out on a Heraeus Carlo Erba 1108 analyzer. The impurity like sulphate and metals were determined by usual method. The I.R. Spectra were determine by Varian 3100F.T. infrared spectrophotometer in KBr between range 200-4000cm-1. Electronic spectra were recorded on Shimadzu 210Å UV/Lis spectrophotometer. Elico CM 82T was used for the determination of molar conductance. Magnetic suscetability of the complexes were determined by using $CuSO_4$. SH_2O as calibrant Clark's et al.1986.

RESULTS AND DISCUSSION

The observe data were shown in the table No-1. All complexes are non-electrolyte in nature.

The complexes were bi-Polar in nature and Zn Comlex was found dia-magnetic while others paramagnetic. The molar conductance in DMF of Cu(II), Fe(II), Ni(II) and Zn(II) complexes is 97, 93, 98, 99,

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respectively indicate 1:2 electrolyte in nature. The [Cu (C_{14}, H_{10}, Cl_2 $NO_2)_2$ $2H_2O$] is aquamarine, [Fe (C_{14} H_{10} Cl_2 $NO_2)_2$ $2H_2O$] is dark brown, [Ni (C_{14} H_{10} Cl_2 $NO_2)_2$ $2H_2O$] is light green, [Zn (C_{14} H_{10} Cl_2 $NO_2)_2$ $2H_2O$] is white R. Menasse et al.1978..

A comparison of the infrared spectral data of the ligand and their complexes indicate the following changes. The ligand shows characteristic frequency due to ν_{N-H} at 3400-3200 cm^{-1} and ν_{C-O} at 1660-1640 cm^{-1}. The spectra of Cu(II), Fe(II), Ni(II) and Zn(II) show shifting of N-H and CO stretching bonds indicating the coordination through these group. The ν_{M-OH} bending band at 940-935cm^{-1} in aqua complexes of Cu(II), Fe(II), Ni(II) and Zn(II) indicating the presence of coordinated aqua molecule in the complex JRJ Seronson et al 1987.

All the complexes show broad bands 3600-3400cm^{-1} by medium peaks at 940-935cm^{-1} assignable. The presence of H_2O molecules co-ordination was observed as usual

The UV and visible spectra of Cu(II) Fe(II) and Ni(II) exhibit two bands at 289, 280nm 371, 364nm and 335-324nm respectively. These bonds may be assigned as charge transfer bond may be M→L or L→M. However no absorption occur in the Zn(II) complexes having d^{10} configuration. This on the bases of aforesaid discussion the following tentative octahedral structure may be assigned DH Brown et al. 1980.

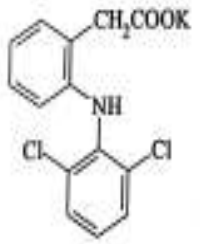

Figure 1: Structure of Diclofenac potassium

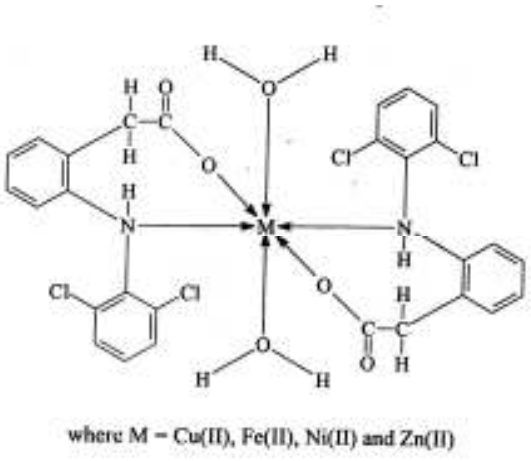

Figure 2: Structure of Diclofenac potassium complexes

Table 1: Characterization Data of the complexes

Complex/ colour/ m.pt.^{0}c	Molecular weight found (calculated)	Found/ (Calculated) %					left B.M.	Am II^{-1} cm^{-2} met^{-2}
		M	C	H	N	G		
[Cu($C_{14}H_{10}Cl_2NO_2)_2.2H_2O$]	689.55	9.21	48.72	2.90	4.06	20.60	1.97	97
Aqua marins, 128		(9.19)	(48.70)	(2.88)	(4.04)	(20.58)		
-[Fe($C_{14}H_{10}Cl_2.O_2)_2.2H_2O$]	664.90	8.41	50.53	3.01	4.21	21.36	5.81	93
Dark Brown, 180		(8.40)	(50.50)	(3.00)	(4.23)	(20.36)		
-[Ni($C_{14}H_{10}NCl_2O_2)_2.2H_2O$]	684.70	8.57	49.07	3.51	4.09	20.74	5.86	98
Light green, 230		(8.54)	(40.04)	(3.48)	(4.07)	(20.70)		
-[Zn($C_{14}H_{10}NCl_2O_2)_2.2H_2O$]	691.39	9.46	48.60	3.47	4.05	20.54	Diamagnetic	99
White, 120		9.42	48.58	3.45	4.01	20.5		

ANTI-INFLAMMATORY ACTIVITY

Anti-inflammatory activity of the complexes were performed using a plethysmometer to measure carrageenan induced rat paw volume following the method of Winter et. Al. Adult male wister albino rats (90-125gm.) were fasted for 18 hrs but with free access to water. Each treatment i.e. plain drug and complexes was administrated at a dose of 100mg/kg, body weight orally in 0.5% CMC suspension. Half an hour following the treatment, 0.1ml of 1% solution of carrogeenan was

injected in the right hind paw planter aponeurosis,the paw volume was measured immediately before giving carrageenan and again 3 hr later by means of plethysmometer Figgis et al.1976.

Edemo was measured in a precalibrated plethysmometer as a dirrerence between the volume of the paw measured before and 3 hours after giving carrageenan. The percentage inhibition of inflammation after 3 hours was calculated by the method of Newbeuld.The volume reveal that at equal doses, the Fe(II) and Zn(II) complexes are more active than the durg itself. Fe(II) and Zn(II) complexes possible depressed the synthes of the proinflammatory (vasodilator), prostaglandine PGE2 in the carrageenan pouch modal of inflammation. This is in constituent with the work of Lee and Lands and recently confirmed by Moddox, who found a depression in PGE2 synthesis and concomitant increase in a anti-inflammatory (vasoconstrictor) Prostaglandin PGE2, following the addition of copper sulphate or chloride to seminal vesicle homogenates Winter et al.1969.

These results suggest that the mechanism action Fe(II) and Zn(II) complexes may be in a part at the level of prostaglandin mediation of inflammation. This is to say, these complexes may play a role in decreasing the synthesis of proinflammation PGE2, and concomitantly increases the synthesis of the anti-inflammatory PGE2. The result presented in table-2 show that diclofenac complexes of Ni(II), Cu(II) and Zn(II) are more active than the parent drug, while the Fe(II) complex becomes much less active F.A.Cotton1984.

Table 2: Anti-Inflammatory Activity of Diclofenac Potassium and its complexes

Compound	No. of Animals used in each group	Dose (mg/Kg) body wt.	Initial volume (0.0 hrs)	Final volume after 3.0 hrs	Volume of edeing (final-initial)	% inhibition
Control	10	100	0.610	1.140	0.530	
Plain drug	10	100	0.682	0.995	0.313	40.84
Fe-drug complex	10	100	0.810	1.640	0.354	33.20
Ni-drug complex	10	100	0.830	1.400	0.310	41.50
Cu-drug complex	10	100	1.006	1.176	0.170	67.92
Zn-drug complex	10	100	0.729	0.909	0.180	66.03

* *- Average of 5 reading

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