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Synthesis and Characterisation of Co(II) Cu(II) Zn(III) and La(II) Complexes of Standard Antidiabetic Drugs

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ABSTRACT

Metal complxes of Glimeperide drugs were prepared and characterized based on elemental analysis, FT-IR, Molar conductance and thermal analysis (TGA and DTG) technique. From elemental analysis data, the complexes were proposed to have general formulae $(GLM)_2Co2H_2O$, $(GLM)_2Cu$, $(GLM)_2Zn$,and $(GLM)_2La2H_2O$. The molar conductance data reveal that all the metal complexes are non-electrolytic, IR spectra shows that GLM are coordinated to metal ions in a neutral bidentate manner from the ESR spectra and XRD-spectra. It is found that the geometrical structures of these complexes are tetrahedral Cu(II) ,Zn(II) and octrahedral Co(II), La(II). The thermal behavior of these complexesstudied using thermogravimetric analysis (TGA and DTG) techniques. The results obtained shows that the hydrated complexes lose water molecules of hydration followed immediately by decomposition of the anions and ligand molecules in the successive unseparate steps. Thermogravimetric analysis was carried out to study the decomposition and various kinetic parameters. Freeman Carroll and Sharp Wentworth method have been applied for calculation of kinetic parameters. While data from freeman Carroll method have been used to determine various thermodynamic parameters such as order of reactions, energy of activation, frequency factor, entropy change, free energy change and apparent entropy change and order of reaction.

Key words: FTIR Spectra, TGA, DTG, , Glimeperide.

INTRODUCTION

Glimeperide, is abi-substituted urea derivatives can exist in keto andenolic form when dissolved in an organic solvent and react with various metal ions to form intensely coloured metal complexes that provide the basis for their use as a sensitive reagent.

The thermal degradation study of complexes has become a subject of recent interest. It is important property of complexes, which decides the thermal stability and processability of the complexes. The study of thermal behaviour of complexes in air at different temperature provides important information about its practical applicability.

Iqbal S.A.*et.a1[1].,* (2005) synthesized the metal complexes of glimeperide characterized by FTIR, elemental analysis and TGA-DTG parameters. The thermal analysis (TGA) was performed at the heating rate of 10°C/min. in nitrogen atmosphere.

Wilma Cyril*et.al[2].,* (2011)studied kinetics and Thermal decomposition of Cu(II) complex of of hydroxyl quinoline-5-sulphonic acid

Thermal data have been analyzed by Freeman Carroll and Sharp-Wentworth method Thermal analysis (TGA and DTG) is a typical analytical technique to describe the relationship between physico-chemical changes and temperature.[1-2] In order to synthesize complexes having practical applications. There is a need to investigate the effect of heat on complexes in order to establish thermal stability.

Iqbal and co-workers[3-4] have synthesized and characterized complexes of tolbutamide and glimeperide by FTIR, elemental analysis and TGA-DTA technique.

Thermal studies of complexes were carried out to determine their mode of decomposition, the activation energy (Ea), order of reaction (n), frequency factor(Z), entropy change (S), Free energy (ΔF) and apparent entropy change (*S). Thermal decomposition curves were discussed with careful attention of minute details. The freeman Carroll and Sharp-Wentworth methods have been used to calculate thermal activation energy and thermal stability.

However, very little work has been carried out on the synthesis and characterization and thermal degradation studies of the metal complexes of glimeperide.

Hence in this work we prepare complexes of Cu(II), Co(II), Zn(II) and La(II) transition and inner transition metals with glimeperide drug molecule. The solid complexes were characterized using different physico-chemical methods, like elemental analysis (C,H,N,S and metal content), IR and thermal analysis (TGA and DTG)

EXPERIMENTAL

Materials and reagents

All chemicals used were of analytical reagent grade (A.R.) and of highest purity. They included glimeperide (Zim laboratories, Nagpur), Copper(II) Chloride ,Zinc(II) chloride,Cobalt(II) chloride andLanthanum(II) Chloride heptahydrate (Hi media Lab, Mumbai) organic solvents used absolute ethyl alcohol, DMF. These solvents were spectroscopic pure from BDH, hydrogen peroxide, hydrochloric and nitric acid (E.Merck) were used. De-ionized water was used in all preparations.

Instruments

Molar conductance of solid complexes in DMF was measured using Systronics conductivity meter, elemental microanalyses of the isolated solid complexes for C,H,N were performed at CDRI, Lucknow, using (HMS-932CLECO) Vario elemental analyzers. Infrared spectra were recorded on Perkin-Elmer, FTIR type 1650 spectrophotometer in wave number 400-4000 cm^{-1}. The spectra were recorded as KBr pellets.

The thermogravimetric (TG and DTG) analysis was carried out in dynamic nitrogen atmosphere (20 $ml.min^{-1}$) with a heating rate of 10°C/min. using shimatzu TGA-50H Thermal Analyzer at IIT Bombay (Mumbai) Electronic spectra recorded at Qualichem Laboratory, Nagpur.

Synthesis of metal complexes

Metal complexes are synthesized by adding metal salt solution in appropriate solvent to the solution of the ligand. The mixture was refluxed for 3-4 hours. Then the precipitate of metal complexes was obtained. It was filtered, washed and dried in vacuum desiccators.

All selected metals forms 1:2 complexes with glimeperide, were confirmed by Jobs method of continuous variation[5]as modified by Turner and Anderson[6].

Estimation of metals in complexes

An accurately weighed portion of the different complexes ranged from 10 to 30 mg was placed in Kjeldhal flask. A measured volume of concentrated nitric acid ranged from 5 to 10 ml was added initially to the powdered complexes to start the fast wet oxidation digestion. This mixture had been digested with some drops of H_2O_2 solution using a gradual heating. This treatment was conducted until most of the powdered complexes were dissolved and the remaining solution had the colour of the corresponding metal salt. This solution was then diluted upto a 50 ml. with distilled water and the metal content was determined by titration against standard EDTA solution at a suitable pH value using the suitable indicator.

RESULTS AND DISCUSSION

Composition and structures of metal complexes

The isolated solid complexes of Cu(II), Co(II), Zn(II) and La(II) with GLM ligands were subjected to elemental analysis (C, H, N, S. and metal content), I.R., Molar conductance, thermal analysis (TG and DTG) to support the tentative structure. The results of elemental analysis listed

Table 1: Thermogravimetric data of Glimeperide-Cu complex by Sharp-Wentworth[28-29] method

Temp. (°C)	°K Temp (T)	1000/T	% Mass Loss	Change in Wt. 'c' grams	1-c	Dc/dt	log(dc/dt)	log(1-c)	log(dc/dt)/1-c	Weight % (%)
30	303	3.30033	0.638	0.00006	0.99994	0.00009	-4.05164	-0.00003	-4.05187	99.362
50	323	3.09598	1.106	0.00010	0.99990	0.00012	-3.92395	-0.00004	-3.92435	98.894
70	343	2.91545	1.534	0.00014	0.99986	0.00017	-3.77705	-0.00006	-3.77758	98.466
90	363	2.75482	2.148	0.00019	0.99981	0.00020	-3.69867	-0.00008	-3.69939	97.852
110	383	2.61097	2.635	0.00024	0.99976	0.00022	-3.65637	-0.00010	-3.65724	97.365
130	403	2.48139	2.958	0.00027	0.99973	0.00024	-3.61347	-0.00012	-3.61444	97.042
150	423	2.36407	3.275	0.00030	0.99970	0.00027	-3.56881	-0.00013	-3.56987	96.725
170	443	2.25734	3.629	0.00033	0.99967	0.00030	-3.52480	-0.00014	-3.52596	96.371
190	463	2.15983	4.017	0.00036	0.99964	0.00033	-3.48241	-0.00016	-3.48368	95.983
210	483	2.07039	4.432	0.00040	0.99960	0.00038	-3.42467	-0.00017	-3.42605	95.568
230	503	1.98807	5.031	0.00046	0.99954	0.00042	-3.38055	-0.00020	-3.38209	94.969
250	523	1.91205	5.594	0.00051	0.99949	0.00050	-3.30383	-0.00022	-3.30551	94.406
270	543	1.84162	6.593	0.00060	0.99940	0.00057	-3.24715	-0.00026	-3.24909	93.407
290	563	1.77620	7.556	0.00069	0.99931	0.00059	-3.23207	-0.00030	-3.23429	92.444
310	583	1.71527	7.969	0.00072	0.99928	0.00061	-3.21413	-0.00031	-3.21645	92.031
330	603	1.65837	8.324	0.00076	0.99924	0.00063	-3.19810	-0.00033	-3.20052	91.676
350	623	1.60514	8.648	0.00078	0.99922	0.00065	-3.18558	-0.00034	-3.18808	91.352
370	643	1.55521	8.917	0.00081	0.99919	0.00067	-3.17559	-0.00035	-3.17817	91.083
390	663	1.50830	9.138	0.00083	0.99917	0.00068	-3.16753	-0.00036	-3.17016	90.862
410	683	1.46413	9.32	0.00085	0.99915	0.00069	-3.16117	-0.00037	-3.16384	90.680
430	703	1.42248	9.467	0.00086	0.99914	0.00070	-3.15540	-0.00037	-3.15812	90.533
450	723	1.38313	9.598	0.00087	0.99913	0.00071	-3.14976	-0.00038	-3.15250	90.402
470	743	1.34590	9.725	0.00088	0.99912	0.00072	-3.14431	-0.00038	-3.14708	90.275
490	763	1.31062	9.849	0.00089	0.99911	0.00073	-3.13884	-0.00039	-3.14164	90.151
510	783	1.27714	9.974	0.00091	0.99909	0.00889	-2.05090	-0.00039	-2.05276	90.026

Table 2: Thermogravimetric data of Glimeperide-Cucomplex by Freeman and Carroll[26-27] method

Temp (°C)	% Mass Loss	Change in Wt. (gm.)	Time in Sec.	dw/dt	log dw/dt	wr = wc-w	log wr	T (K)	1/T(K-1)	(Log dt/dt) /(log wr	(1/T)/Log wr	α = wt/wc	gα = 1-(1-α)$^{1-n}$/1-n	T^3 x 10^{-7}	gα/T3 x10^7	1/T x 10^{-3}	log g(α)/T^3
30	4.049	0.0002057	90	0.0004250	-3.3717	0.003171	-2.498866	303	0.003300	1.3493	-0.001321	0.06093	0.0628	2.7818	0.001376	3.300330	-86.884856
50	8.566	0.0004352	150	0.0004479	-3.3488	0.002941	-2.531500	323	0.003096	1.3229	-0.001223	0.12891	0.1378	3.3698	0.005272	3.095975	-51.943202
70	9.243	0.0004696	210	0.0004567	-3.3403	0.002907	-2.536609	343	0.002915	1.3169	-0.001149	0.13910	0.1496	4.0354	0.005155	2.915452	-41.678647
90	9.451	0.0004802	270	0.0004616	-3.3357	0.002896	-2.538191	363	0.002755	1.3142	-0.001085	0.14223	0.1532	4.7832	0.004555	2.754821	-34.742302
110	9.558	0.0004856	330	0.0004679	-3.3299	0.002891	-2.539007	383	0.002611	1.3115	-0.001028	0.14384	0.1551	5.6182	0.003970	2.610966	-29.397927
130	9.686	0.0004921	390	0.0004797	-3.3190	0.002884	-2.539985	403	0.002481	1.3067	-0.000977	0.14577	0.1573	6.5451	0.003503	2.481390	-25.051013
150	9.926	0.0005043	450	0.0005039	-3.2977	0.002872	-2.541826	423	0.002364	1.2974	-0.000930	0.14938	0.1615	7.5687	0.003188	2.364066	-21.370558
170	10.413	0.0005291	510	0.0005484	-3.2609	0.002847	-2.545584	443	0.002257	1.2810	-0.000887	0.15671	0.1702	8.6938	0.003067	2.257336	-18.105713
190	11.314	0.0005749	570	0.0006259	-3.2035	0.002801	-2.552623	463	0.002160	1.2550	-0.000846	0.17027	0.1863	9.9253	0.003196	2.159827	-15.099361
210	12.884	0.0006546	630	0.0007092	-3.1492	0.002722	-2.565170	483	0.002070	1.2277	-0.000807	0.19389	0.2151	11.2679	0.003701	2.070393	-12.245875
230	14.603	0.0007420	690	0.0008170	-3.0878	0.002634	-2.579336	503	0.001988	1.1971	-0.000771	0.21976	0.2475	12.7264	0.004275	1.988072	-9.935268
250	16.81	0.0008541	750	0.0013404	-2.8728	0.002522	-2.598228	523	0.001912	1.1057	-0.000736	0.25298	0.2908	14.3056	0.005143	1.912046	-7.922182
270	27.221	0.0013831	810	0.0021815	-2.6612	0.001993	-2.700455	543	0.001842	0.9855	-0.000682	0.40965	0.5243	16.0103	0.013415	1.841621	-4.172467
290	44.295	0.0022506	870	0.0026006	-2.5849	0.001126	-2.948599	563	0.001776	0.8767	-0.000602	0.66660	1.0864	17.8454	0.040583	1.776199	-0.785237
310	53.398	0.0027132	930	0.0027506	-2.5606	0.000663	-3.178407	583	0.001715	0.8056	-0.000540	0.80359	1.6014	19.8155	0.064941	1.715266	0.552733
330	56.805	0.0028863	990	0.0028234	-2.5492	0.000490	-3.309794	603	0.001658	0.7702	-0.000501	0.85487	1.8933	21.9256	0.073819	1.658375	0.953780
350	58.409	0.0029678	1050	0.0028782	-2.5409	0.000409	-3.388795	623	0.001605	0.7498	-0.000474	0.87900	2.0680	24.1804	0.075177	1.605136	1.073373
370	59.567	0.0030266	1110	0.0029243	-2.5340	0.000350	-3.456336	643	0.001555	0.7331	-0.000450	0.89643	2.2169	26.5848	0.074753	1.555210	1.121916
390	60.531	0.0030756	1170	0.0029769	-2.5262	0.000301	-3.521876	663	0.001508	0.7173	-0.000428	0.91094	2.3609	29.1434	0.073794	1.508296	1.141126
410	61.616	0.0031307	1230	0.0030311	-2.5184	0.000246	-3.609834	683	0.001464	0.6976	-0.000406	0.92727	2.5535	31.8612	0.074314	1.464129	1.174889
430	62.737	0.0031877	1290	0.0030755	-2.5121	0.000189	-3.724443	703	0.001422	0.6745	-0.000382	0.94414	4.2660	34.7429	0.115930	1.422475	1.741538
450	63.667	0.0032349	1350	0.0031104	-2.5072	0.000141	-3.849694	723	0.001383	0.6513	-0.000359	0.95813	50.0000	37.7933	1.267597	1.383126	4.446279
470	64.399	0.0032721	1410	0.0031412	-2.5029	0.000104	-3.982297	743	0.001346	0.6285	-0.000338	0.96915	3.3603	41.0172	0.079398	1.345895	1.250144
490	65.042	0.0033048	1470	0.0031720	-2.4987	0.000071	-4.145757	763	0.001311	0.6027	-0.000316	0.97883	3.7101	44.4195	0.081756	1.310616	1.260916
510	65.68	0.0033372	1530	0.0032094	-2.4936	0.000039	-4.408124	783	0.001277	0.5657	-0.000290	0.98843	#REF!	48.0049	#REF!	1.277139	#REF!

Table 3: Analytical data of glimeperide complexes

S. No.	Molecular formula of complexes	Molecular weight (gm/mol)	% Analysis found (calculated)						
			C	H	N	O	S	Metal	H_2O
1	$(C_{24}H_{34}N_4O_5S)_2Co{\cdot}2H_2O$	1076.164	53.18 (53.52)	6.18 (6.13)	10.38 (10.40)	17.82 (17.84)	5.84 (5.94)	5.37 (5.47)	3.54 (3.34)
2	$(C_{24}H_{34}N_4O_5S)_2Cu$	1044.774	55.14 (55.13)	6.18 (6.31)	10.78 (10.72)	18.30 (18.37)	6.52 (6.12)	6.00 (6.08)	-
3.	$(C_{24}H_{34}N_4O_5S)_2Zn$	1044.604	55.10 (55.14)	6.18 (6.31)	10.82 (10.72)	18.48 (18.38)	6.28 (6.12)	6.82 (6.06)	-
4.	$(C_{24}H_{34}N_4O_5S)_2La{\cdot}2H_2O$	1156.144	48.88 (49.82)	2.82 (5.70)	9.66 (9.68)	16.80 (16.60)	5.62 (5.53)	11.98 (12.01)	3.28 (3.11)

Table 4: I.R. Spectra (4000-400cm^{-1}) of the glm and their metal complexes

Compounds	γ(OH) Enolic	γ(NH)	γ(SO_2) Asym	γ(SO_2) Sym	γ (C=O) Amide	γ (m-O)
$(C_{24}H_{34}N_4O_5S)_2Co{\cdot}2H_2O$	3100-3320 Br.	-	1375 sh.	1100 sh.	1460 sh.	530 m.
$(C_{24}H_{34}N_4O_5S)_2Cu$	3220-3320 br.	3100 br.	1365 sh.	1120 sh.	1481 sh.	
$(C_{24}H_{34}N_4O_5S)_2Zn$	3220-3363 br.	3024 br.	1340.8 m.	1160.6 sh.	1481 sh.	
$(C_{24}H_{34}N_4O_5S)_2La{\cdot}2H_2O$	3280-3310	-	1305 sh.	1160 w.	1480 sh.	577 m.-

in table (1) suggest the formulae $[Co(GLM)_2]2H_2O$, $[Cu(GLM)_2]$,$[Zn(GLM)_2]$, and $[La(GLM)_2]2H_2O$ for respective complexes.

Molar conductance

The complexes were dissolved in DMF and the molar conductivities of 10^{-3}M of their solutions at 298 K are measured. It is concluded from results listed in table (1) that the complexes are found to have molar conductance values of 13.18 to 30.15Ω^{-1} mole^{-1} am^{-2} indicating that all the metal complexes are non-electrolytes.

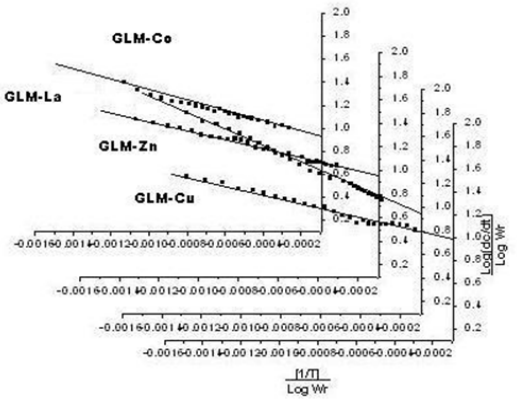


Fig. 1: FC,Kinetic plot of Glimeperide complexes using TGA data.(FC=Freeman and Carroll)

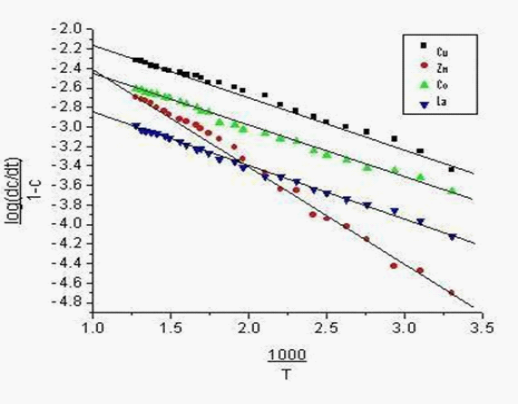


Fig. 2: Determination of activation energy by SW method

Table 5: Thermogravimetric data of Metal complexes of GLM drugs with corresponding to heating rate of 10°C/min

Complexes	Decomposition Temp. (°C)	%Wt. loss	Ea(Kj/mole) F.C.	Ea(Kj/mole) W.W.	ΔS* (Kj/mole)	ΔF (Kj/mole)	Z	S*	n
$[C_C(C_{15}H_{20}N_3O_3S)_2Cu$	30-150	9.926	32.87	31.37	-28.85	-8.708	281.2	-44.2681	0.9
	150-350	58.408	51.21	51.01	-64.65	-27.29569	269.8		
	350-510	65.68	110.30	109.23	-112.5	-69.9772	252.7		
$(C_{15}H_{20}N_3O_3S)_2Co.2H_2O$	30-150	5.815	33.67	32.66	-33.98	-10.26227	322.8	-48.5380	1.01
	150-350	51.027	55.14	54.38	-82.07	-34.66047	268.3		
	350-510	69.718	109.37	108.38	-116.8	-72.65703	252.3		
$(C_{23}H_{27}O_5ClN_3S)_2Zn$	30-150	10.413	29.77	28.68	-24.59	-7.421	284.3	-43.2123	0.98
	150-350	58.409	67.76	66.14	-67.76	-29.94992	263.0		
	350-510	65.042	114.2	113.92	-116.50	-72.4653	252.0		
$(C_{24}H_{33}N_4O_6S)_2La$	30-150	2.577	52.66	52.16	-43.48	-13.12178	269.2	-44.2381	0.99
	150-350	61.536	85.94	85.13	-82.05	-39.54421	269.2		
	350-510	81.344	138.23	138.14	-102.2	-43.09237	257.6		

Electronic spectral studies

Electronic spectra of the ligand shows two high intensity bands at 47431 and 32233 cm^{-1}, indicating n→n* and π→π transitions respectively of the ligand moity.The electronic spectra of La(II) complex displays band at 32130 and 27393cm^{-1} The two bands corresponds to $^4T_{1g}(F)\rightarrow{}^4A_{2g}(F)$, $^4T_{1g}(F)\rightarrow{}^4A_{1g}(P)$ suggesting octahedral geometry of these complexes. The Cu(II) complex displays a band at 26130cm^{-1} $^4E_{1g}(F)\rightarrow{}^4T_{2g}(F)$,Zn(II) complex displays single absorption band at 31225cm^{-1}.This is due to Ligand Metal charge transfer spectra..

IR Spectral studies

The IR data of the spectra of GLM ligand and there complexes are listed in table (4). The IR spectra of the complexes are compared with those of the freeGLM ligands in order to determine the coordination sites that may be involved in complexation[7-15] The tautomeric equilibrium depends

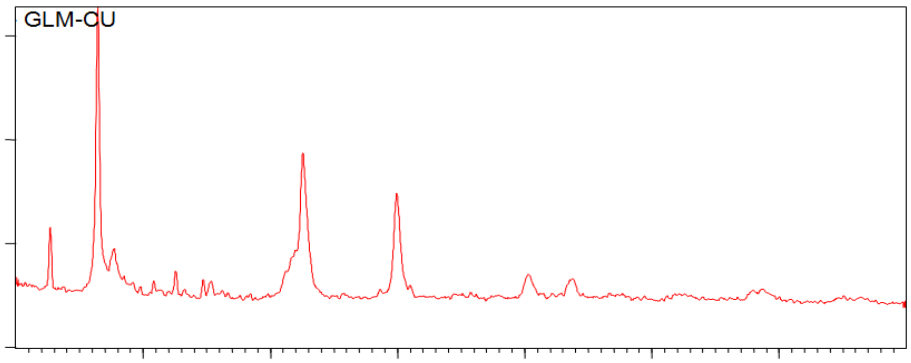


Fig. 1(1): X-ray difractogram of GLM-Cu Complex

Table 1(1): Cell data and crystal parameter of GLM-Cu Complex

a(Å) = 21.5867	Volume(abc)Å = 14060.360
b(Å) = 23.5386	Dcal. = 5.38736 g/cm^3
c(Å) = 27.6713	Dobs. = 5.38524 g/cm^3
Standard deviation = 0.027%	Crystal system = Orthorhombic
α=90°, β=90°, λ=90°	Porosity(%) = 0.03935
Density = 0.074306g/cm^3	Particle size = 15.5602microns
Space group = Pm	

2θ	I/I_0	$D_{(Obs)}$	$D_{(Cal)}$	*h*	*k*	*l*
12.7240	21.84	6.95731	6.96397	25	3	0
16.4612	100.00	5.38524	5.38736	0	1	5
17.7016	16.05	5.01057	5.00820	0	2	5
19.8348	2.59	4.47624	4.48231	0	4	4
20.8349	5.00	4.26360	4.26359	2	5	1
22.5976	9.06	3.93484	3.93691	4	4	1
25.3489	5.04	3.51367	3.51709	3	4	5
32.5464	46.93	2.75121	2.74909	-3	2	9
39.8827	35.12	2.26043	2.26123	0	6	10
50.4146	7.61	1.81016	1.81016	6	2	13
53.8220	5.99	1.70192	1.70195	3	13	4

on the extent of conjugation, nature and position of the substituent, polarity of the solvent etc

Magnetic susceptibility studies

The room temperature magnetic moment of the complexes was found to be 4.66 B.M. which corresponds to the presence of Co(II), La(II) in octahedral geometry. Zayed *et al*[16]*.,* (2000)Cotton *et.a*[17]*.,* (1999)

In addition to that, the Cu(II), and Zn(II) complexes are found to have magnetic moment value of 4.62 B.M.and 4.72B.M.respectively which indicates the presence of Cu(II) and Zn(II) complexes have tetrahedral structure.

Thermal analysis (TGA and DTG)

In the present investigation, the weight losses for each complex were calculated within corresponding temperature ranges. The obtained data are listed in table (4). All complexes are thermally decomposed in three decomposition steps within the temperature range of 50-600°C .The TGA/ DTA data for the complexes are shown in Table-1,2 and 5

The thermoanalytical data are presented in table 1,2 and 5. In studying the decomposition kinetics[18-26], three methods mentioned in the literature were used in each case the least square plots were drawn. The first few points that did not fall on straight line were discarded. These types of deviations of points are reported in literature by several research workers. This is explained as due to the failure of obeying as first order kinetics always by the solids in their decomposition in the early stages fig-1 and 2..

Theoretical Consideration

To provide further evidence regarding the degradation system of analyzed compounds we derived the TG curves by applying an analyticalmethod proposed by *Freeman-Carroll*[27-28] and *Sharp-Wentworth*[29-30].

Freeman-Carroll Method[26-27]

The straight line equation derived by Freeman and Carroll, which is in the form of

$$\frac{\Delta \log \frac{dw}{dt}}{\Delta \log Wr} = n - \frac{E_a}{2.303R} \cdot \frac{\Delta \frac{1}{T}}{\Delta \log Wr}$$

Where, $\frac{dw}{dt}$ = rate of change of weight with time
Wr = Wc-W
W_c = Wt. loss at completion of reaction
W = Total wt. loss upto time 't'
E_a = Energy of activation
n = Order of reaction

The plot between the term $\frac{\frac{dw}{dt}}{Wr}$ Vs $\frac{\Delta \frac{1}{T}}{\Delta \log Wr}$ gives a straight line from which slope can be calculated, also we obtained energy of activation (Ea) and intercept on Y-axis as order of reaction (n). The change in entropy (ÄS), frequency factor (Z), apparent entropy (S*) can also be calculated by further calculation.

Sharp-Wentworth Method[28-29]

Using the equation derived by Sharp and Wentworth

$$\frac{\Delta \log \frac{dc}{dT}}{(1-c)} = \log \frac{A}{B} - \frac{Eq}{2.303\,R} \cdot \frac{1}{T}$$

Where, dc/dt = Rate of change of fraction of weight with change in temperature.
β = Linear heating rate
by plotting the graph between

$$\frac{\frac{c}{T}}{1} \text{Vs} = \frac{1}{T}$$

We obtained the straight line which gives energy of activation (Ea) from its slope.

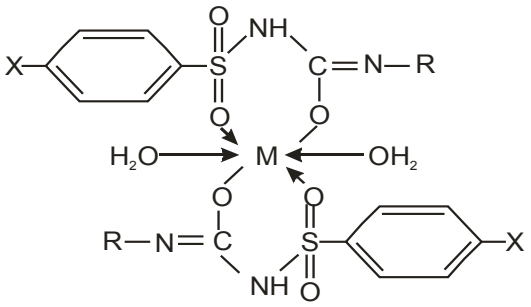
The thermodynamic activation parameters of decomposition process of dehydrate complexes namely activation energy (Ea), enthalpy (ΔH), Entropy (ΔS) and Gibb's free energy change of decomposition (ΔG°) are evaluated graphically by employing Free man-Carroll and Sharp-Wentworth relation. The data are summarized in Table 1,2,5.The activation energies of decomposition are found to be in the range 29.70 to 204.7 KJ.Mole^{-1}. The high value of activation energies reflect the thermal stability of complexes. The entropy of activation is found to have negative values in all the complexes which indicate that decomposition reactions process with lower rate than the normal ones[31-35]

DISCUSSION

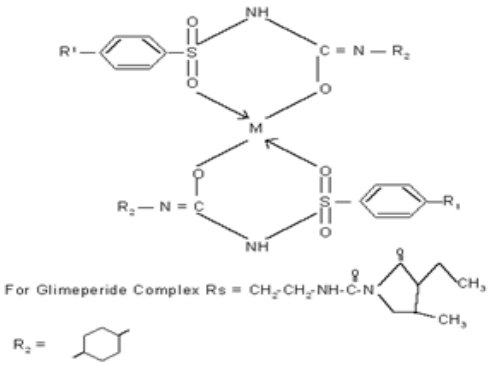
The complexes of Cu,Zn,La and Co were synthesized with oral hypoglycemic agents i.e. glimeperide the formulae suggested for the complexes are well supported by the Jobs method of continuous variation as modified by Turner and Anderson,moreover,the formulae of the complexes further gets supports from the analytical data.

The structure of the complexes are supported from variety of spectroscopic technique like I.R,Electronic spectra,TGAmethod whose results are summarized in Tables-3,4,5. All the complexes prove to be formed in2:1 ligand metal ratio The complexes are formed after enolisation of the drugs which is indicative by the presence of only metal oxygen bonds and not the metal nitrogen. The Cu and Zn complexes shows tetrahedral structures while La and Co complexes shows octahedral structures in which the six co-ordination is fulfilled by two water molecule in which the oxygen of the water is vertically joining to the metal atom, above and below the plane of the molecule.

Thus on the bases of analytical data and spectroscopic studies the following structure-1 and 2 may be assign for the Cu,Zn and La, Co complexes respectively.



M=Co,La Structure 1 and 2



M=Cu,Zn

CONCLUSION

As the reported metal complexes of Glimeperide drugs are able to dissociate at stomach pH, therefore its dosages, to be given to subject animals should be such that it should not be dissociate in stomach i.e. at pH 1.2 for this complexes prepared enteric coated to make at the drug bioavailable as it is, i.e. at duodenum and small intestinal pH (5.5 to 6.8 pH)

Drug is coated with a polymer *HPMC-5CPS* (Hydroxy propylmethyl cellulose) which does not permit drug to dissolve in stomach (i.e. pH 1.2) and such polymer dissolves rapidly at deodenal pH (5 - 5.5) thus drug releases at 5.5 pH and is available for absorption. At this pH complex is stable, non-dissociatable and absorbable. Therefore dosage forms for animals study is prepared as enteric coated, polymerized in this dosage forms are not soluble at pH 12. This drug delivery system is adopted for further study[36]

The hypoglycemic effects Glimeperide the well known sulphonyl ureas, were inverstigated on the blood sugar levels of male albino rats by using Folin Wu method.[37] . Analysis of data show that this drugs caused a marked decrease in blood sugar level to the extent while their complexes reduced the blood sugar level to than the parent drug.

This blood sugar lowering effect of sulphonyl ureas seems to be related to the stimulation of insulin secretion on the other hand, many studies have strongly indicated the presence of long term or extra pancreatic action of sulphonyl ureas[38]. The hypoglycemic activity of sulphonyl ureas may also be attributed to the stimulation of glycolysis and to the inhibition of glycogenesis in the liver by itself or by enhancing insulin action[39].

On comparing the hypoglycemic effect of these complexes with their parent drugs, it was revealed that in the three groups Glimeperide-Zn(II) treated albino rat had lowest blood sugar level being 49.72 mg/100 ml. respectively on an average. These facts clearly indicate a better hypoglycemic activity of complexes as compared to their parent drugs which is in agreement with the earlier findings of Iqbal and co-workers[40]. This improved hypoglycemic activity may be related to smaller particle size of metal complexes than drugs as on complexation particle size is reduced which may promote the ratio of absorption of complexes in gastro-intestinal tract. Results of the present work are also in conformity with the hypoglycemic effect of copper-phenformin complex over parent drug phenformin as mentioned by Piccini *et al.,*[41]

These interesting observations on metal-complexes of oral sulphonylureas used as anti-diabetic agents for lowering blood sugar concentration may likely substantiate the use of these complexes after extensive clinical studies.

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