



## **SYNTHESIS, CHARACTERISATION AND ANTIDIABETIC SCREENING OF Co(II),Cu(II),Zn(II) AND La(II) COMPLEXES OF GLIMEPERIDEA STANDARD SYNTHETIC ALLOPATHIC DRUG.**

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### **Abstract:**

Metal complexes 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  $(GLM)_2Co_2H_2O$ ,  $(GLM)_2Cu$ ,  $(GLM)_2Zn$ , and  $(GLM)_2La_2H_2O$ . 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 octahedral Co(II), La(II). The thermal behavior of these complexes studied 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..

### **Keywords:**

FTIR Spectra, TGA, DTG, , Glimeperide, HPMC-5CPS

### **Introduction:**

Glimeperide, is a bi-substituted urea derivatives can exist in keto and enolic 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.al1., (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.al2., (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-workers3-4 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 ( $E_a$ ), order of reaction ( $n$ ), frequency factor ( $Z$ ), entropy change ( $S$ ), Free energy ( $\Delta F$ ) 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)





## Material and Method:

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 and Lanthanum(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. 2.2 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  $\text{cm}^{-1}$ . The spectra were recorded as KBr pellets. The thermogravimetric (TG and DTG) analysis was carried out in dynamic nitrogen atmosphere ( $20 \text{ ml}\cdot\text{min}^{-1}$ ) with a heating rate of  $10^\circ\text{C}/\text{min}$ . using shimatzu

TGA-50H Thermal Analyzer at IIT Bombay (Mumbai) Electronic spectra recorded at Qualichem Laboratory, Nagpur. 2.3 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<sup>5</sup> as modified by Turner and Anderson<sup>6</sup>. 2.4 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  $\text{H}_2\text{O}_2$  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.

## Result and Discussion:

**3.1 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 in table (1) suggest the formulae  $[\text{Co}(\text{GLM})_2] \cdot 2\text{H}_2\text{O}$ ,  $[\text{Cu}(\text{GLM})_2]$ ,  $[\text{Zn}(\text{GLM})_2]$ , and  $[\text{La}(\text{GLM})_2] \cdot 2\text{H}_2\text{O}$  for respective complexes.

**3.2 MOLAR CONDUCTANCE** The complexes were dissolved in DMF and the molar conductivities of  $10^{-3}\text{M}$  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  $30.15\Omega^{-1}\text{mole}^{-1}\text{cm}^{-2}$  indicating that all the metal complexes are non-electrolytes.

**3.4 ELECTRONIC SPECTRAL STUDIES** Electronic spectra of the ligand shows two high intensity bands at 47431 and 32233  $\text{cm}^{-1}$ , indicating  $n \rightarrow n^*$  and  $\pi \rightarrow \pi$  transitions respectively of the ligand moiety. The electronic spectra of La(II) complex displays band at 32130 and 27393  $\text{cm}^{-1}$ . The two bands corresponds to  $4\text{T}_{1g}(\text{F}) \rightarrow 4\text{A}_{2g}(\text{F})$ ,  $4\text{T}_{1g}(\text{F}) \rightarrow 4\text{A}_{1g}(\text{P})$  suggesting octahedral geometry of these complexes. The Cu(II) complex displays a band at 26130  $\text{cm}^{-1}$   $4\text{E}_{1g}(\text{F}) \rightarrow 4\text{T}_{2g}(\text{F})$ , Zn(II) complex displays single absorption band at 31225  $\text{cm}^{-1}$ . This is due to Ligand  $\rightarrow$  Metal charge transfer spectra..

**3.3 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 free GLM ligands in order to determine the coordination sites that may be involved in complexation. The tautomeric equilibrium depends on the extent of conjugation, nature and position of the substituent, polarity of the solvent etc.

**3.5 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<sup>16</sup>, (2000) Cotton et al<sup>17</sup>, (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 4.72 B.M. respectively which indicates the presence of Cu(II) and Zn(II) complexes have tetrahedral structure.

### 3.6 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<sup>18-26</sup>, 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 analytical method proposed by Freeman-Carroll<sup>27-28</sup> and Sharp-Wentworth<sup>29-30</sup>. Freeman-Carroll Method<sup>26-27</sup> The straight line equation derived by Freeman and Carroll, which is in the form of  $(\Delta \log dw/dt)/(\Delta \log W_r) = n - E_a/2.303R \cdot (\Delta 1/T)/(\Delta \log W_r)$  Where,  $dw/dt$  = rate of change of weight with time  $W_r = W_c - W$   $W_c = W_t$ . 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  $(\Delta \log dw/dt)/(\Delta \log W_r)$  Vs  $(\Delta 1/T)/(\Delta \log W_r)$

gives a straight line from which slope can be calculated, also we obtained energy of activation ( $E_a$ ) and intercept on Y-axis as order of reaction ( $n$ ). The change in entropy ( $\Delta S$ ), frequency factor ( $Z$ ), apparent entropy ( $S^*$ ) can also be calculated by further calculation. Sharp-Wentworth Method<sup>28-29</sup> Using the





equation derived by Sharp and Wentworth  $(\Delta \log dc/dT)/((1-c)) = \log A/B - E_a/(2.303 R) \cdot 1/T$  Where,  $dc/dT$  = Rate of change of fraction of weight with change in temperature.  $\beta$  = Linear heating rate  $dT/dt$  by plotting the graph between  $(\Delta \log dc/dT)/((1-c))$  Vs  $1/T$ , We obtained the straight line which gives energy of activation ( $E_a$ ) from its slope. The thermodynamic activation parameters of decomposition process of dehydrate complexes namely activation energy ( $E_a$ ), enthalpy ( $\Delta H$ ), Entropy ( $\Delta S$ ) and Gibb's free energy change of decomposition ( $\Delta G^\circ$ ) 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<sup>-1</sup>. 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 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
33	306	3.30958	1.106	0.00010	0.99990	0.00012	-3.92395	-0.00004	-3.92435	98.894	70	343
35	308	3.291545	1.534	0.00014	0.99986	0.00017	-3.77705	-0.00006	-3.77758	98.466	90	363
38	311	2.75482	2.148	0.00019	0.99981	0.00020	-3.69867	-0.00008	-3.69939	97.852	110	383
40	313	2.61097	2.635	0.00024	0.99976	0.00022	-3.65637	-0.00010	-3.65724	97.365	130	403
43	316	2.48139	2.958	0.00027	0.99973	0.00024	-3.61347	-0.00012	-3.61444	97.042	150	423
45	318	2.36407	3.275	0.00030	0.99970	0.00027	-3.56881	-0.00013	-3.56987	96.725	170	443
48	321	2.25734	3.629	0.00033	0.99967	0.00030	-3.52480	-0.00014	-3.52596	96.371	190	463
50	323	2.15983	4.017	0.00036	0.99964	0.00033	-3.48241	-0.00016	-3.48368	95.983	210	483
53	326	2.07039	4.432	0.00040	0.99960	0.00038	-3.42467	-0.00017	-3.42605	95.568	230	503
55	328	1.98807	5.031	0.00046	0.99954	0.00042	-3.38055	-0.00020	-3.38209	94.969	250	523
58	331	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-Cu complex by Freeman and Carroll<sup>26-27</sup> method Temp (°C) %  
Mass Loss Change in Wt. (gm.) Time in Sec.  $\frac{dw}{dt}$   $\log \frac{dw}{dt}$   $w_r = w_c - w$   $\log w_r$   
T (K)  $\frac{1}{T(K-1)}$   $(\log \frac{dt}{dt}) / (\log w_r)$   $\frac{1}{T} / \log w_r$   $\alpha = \frac{w_t}{w_c}$   $g_a = \frac{1-(1-\alpha)^{1-n}}{1-n}$   
T<sup>3</sup> x 10<sup>-7</sup>  $g_a/T^3$  x 10<sup>7</sup>  $\frac{1}{T}$  x 10<sup>-3</sup>  $\log \frac{g_a}{T^3}$  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! 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-(3-ANALYTICAL DATA OF GLIMEPERIDE COMPLEXES

Sl. No. Molecular formula of complexes Molecular weight (gm/mol) % Analysis  
 found (calculated) C H N O S Metal H2O 1. (C<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>Co•2H<sub>2</sub>O

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<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>Cu 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<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>Zn  
 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<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>La•2H<sub>2</sub>O 1156.144 48.88 (49.82) 2.82 (5.70) 9.66

TABLE (4): I.R. SPECTRA (4000-400cm<sup>-1</sup>) OF THE GLM AND THEIR METAL COMPLEXES

Compounds γ (OH) Enolic γ (NH) γ (SO<sub>2</sub>) Asym γ (SO<sub>2</sub>) Sym γ (C=O) Amide γ  
 (m-O) (C<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>Co•2H<sub>2</sub>O 3100-3320 Br. - 1375 sh. 1100 sh. 1460 sh.  
 530 m. (C<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>Cu 3220-3320 br. 3100 br. 1365 sh. 1120 sh. 1481  
 sh. (C<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>Zn 3220-3363 br. 3024 br. 1340.8 m. 1160.6 sh. 1481  
 sh. (C<sub>24</sub>H<sub>34</sub>N<sub>4</sub>O<sub>5</sub>S)<sub>2</sub>La•2H<sub>2</sub>O 3280-3310 - 1305 sh. 1160 w. 1480 sh. 577 m.-

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) ΔS\* (Kj/mole) ΔF (Kj/mole) Z S\* n F.C. W.W. [CC  
 (C<sub>15</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub>S)<sub>2</sub>Cu 30-150 150-350 350-510 9.926 58.408 65.68 32.87





51.21 110.30 31.37 51.01 109.23 -28.85 -64.65 -112.5 -8.708 -27.29569 -  
69.9772 281.2 269.8 252.7 -44.2681 0.9 (C<sub>15</sub>H<sub>20</sub>N<sub>3</sub>O<sub>3</sub>S)<sub>2</sub>Co.2H<sub>2</sub>O 30-150  
150-350 350-510 5.815 51.027 69.718 33.67 55.14 109.37 32.66 54.38  
108.38 -33.98 -82.07 -116.8 -10.26227 -34.66047 -72.65703 322.8 268.3  
252.3 -48.5380 1.01 (C<sub>23</sub>H<sub>27</sub>O<sub>5</sub>ClN<sub>3</sub>S)<sub>2</sub>Zn 30-150 150-350 350-510 10.413  
58.409 65.042 29.77 67.76 114.2 28.68 66.14 113.92 -24.59 -67.76 -116.50 -  
7.421 -29.94992 -72.4653 284.3 263.0 252.0 -43.2123 0.98  
(C<sub>24</sub>H<sub>33</sub>N<sub>4</sub>O<sub>6</sub>S)<sub>2</sub>La 30-150 150-350 350-510 2.577 61.536 81.344 52.66  
85.94 138.23 52.16 85.13 138.14 -43.48 -82.05 -102.2 -13.12178 -39.54421 -  
43.09237 269.2 269.2 257.6 -44.2381 0.99

### Conclusion:

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, TGA method whose results are summarized in Tables-3,4,5. All the complexes prove to be formed in 2:1 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<sup>36</sup> 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.<sup>37</sup> . Analysis of data show that thisdrugs 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<sup>38</sup>. 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<sup>39</sup>. On comparing the hypoglycemic effect of these complxes 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<sup>40</sup>. 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.,<sup>41</sup> 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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**Table-1** Thermogravimetric data of Glimeperide-Cu complex by Sharp-Wentworth<sup>28-29</sup> method

Temp. (°C)	°K Temp (T)	$\frac{1000}{T}$	% Mass Loss	Change in Wt. 'c' grams	1-c	$\frac{dc}{dt}$	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-Cu complex by Freeman and Carroll<sup>26-27</sup> method

Tem p (° 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 <sup>-1</sup> )	(Log dt/dt) / (log wr)	(1/T) / (Log wr)	$\alpha = wt/wc$	$g\alpha = 1 - (1-\alpha)^{1/n}$	$T^3 \times 10^{-7}$	$g\alpha/T^3 \times 10^{-7}$	$1/T \times 10^{-5}$	$\log(g\alpha)/T$
30	4.0	0.00	90	0.00	-	0.00	-	3	0.00	1.3	-	0.0	0.0	2.7	0.00	3.30	-
	49	0205		0425	3.3	317	2.49	0	330	49	0.00	609	62	818	137	033	86.8
		7		0	71	1	886	3	0	3	132	3	8		6	0	8485
					7		6			1							6
50	8.5	0.00	15	0.00	-	0.00	-	3	0.00	1.3	-	0.1	0.1	3.3	0.00	3.09	-
	66	0435	0	0447	3.3	294	2.53	2	309	22	0.00	289	37	698	527	597	51.9
		2		9	48	1	150	3	6	9	122	1	8		2	5	4320
					8		0			3							2
70	9.2	0.00	21	0.00	-	0.00	-	3	0.00	1.3	-	0.1	0.1	4.0	0.00	2.91	-
	43	0469	0	0456	3.3	290	2.53	4	291	16	0.00	391	49	354	515	545	41.6
		6		7	40	7	660	3	5	9	114	0	6		5	2	7864
					3		9			9							7
90	9.4	0.00	27	0.00	-	0.00	-	3	0.00	1.3	-	0.1	0.1	4.7	0.00	2.75	-
	51	0480	0	0461	3.3	289	2.53	6	275	14	0.00	422	53	832	455	482	34.7
		2		6	35	6	819	3	5	2	108	3	2		5	1	4230
					7		1			5							2
110	9.5	0.00	33	0.00	-	0.00	-	3	0.00	1.3	-	0.1	0.1	5.6	0.00	2.61	-
	58	0485	0	0467	3.3	289	2.53	8	261	11	0.00	438	55	182	397	096	29.3
		6		9	29	1	900	3	1	5	102	4	1		0	6	9792
					9		7			8							7
130	9.6	0.00	39	0.00	-	0.00	-	4	0.00	1.3	-	0.1	0.1	6.5	0.00	2.48	-
	86	0492	0	0479	3.3	288	2.53	0	248	06	0.00	457	57	451	350	139	25.0
		1		7	19	4	998	3	1	7	097	7	3		3	0	5101
					0		5			7							3
150	9.9	0.00	45	0.00	-	0.00	-	4	0.00	1.2	-	0.1	0.1	7.5	0.00	2.36	-
	26	0504	0	0503	3.2	287	2.54	2	236	97	0.00	493	61	687	318	406	21.3
		3		9	97	2	182	3	4	4	093	8	5		8	6	7055
					7		6			0							8
170	10.	0.00	51	0.00	-	0.00	-	4	0.00	1.2	-	0.1	0.1	8.6	0.00	2.25	-
	41	0529	0	0548	3.2	284	2.54	4	225	81	0.00	567	70	938	306	733	18.1
		3		4	60	7	558	3	7	0	088	1	2		7	6	0571
					9		4			7							3
190	11.	0.00	57	0.00	-	0.00	-	4	0.00	1.2	-	0.1	0.1	9.9	0.00	2.15	-
	31	0574	0	0625	3.2	280	2.55	6	216	55	0.00	702	86	253	319	982	15.0
		4		9	03	1	262	3	0	0	084	7	3		6	7	9936
					5		3			6							1
210	12.	0.00	63	0.00	-	0.00	-	4	0.00	1.2	-	0.1	0.2	11.	0.00	2.07	-
	88	0654	0	0709	3.1	272	2.56	8	207	27	0.00	938	15	267	370	039	12.2
		6		2	49	2	517	3	0	7	080	9	1		1	3	4587
					2		0			7							5







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	$\alpha = wt/wc$	$g\alpha = 1-(1-\alpha)^{1-n}/1-n$	T <sub>3</sub> x 10 <sup>-7</sup>	$g\alpha/T$ x 10 <sup>7</sup>	1/T x 10 <sup>-3</sup>	log( $\alpha$ )/T <sup>3</sup>
230	14.603	0.0007420	690	0.008170	-3.0878	0.02634	-2.579336	5038	0.01988	1.1971	-0.00771	0.21976	0.2475	12.7264	0.04275	1.98807	-9.935268
250	16.81	0.0008541	750	0.013404	-2.8728	0.02522	-2.598228	5032	0.01991	1.1057	-0.00736	0.25298	0.2908	14.3056	0.05143	1.9046	-7.922182
270	27.221	0.0013831	810	0.021815	-2.6612	0.01993	-2.700455	5043	0.01984	0.9855	-0.00682	0.40965	0.5243	16.0103	0.04155	1.84162	-4.172467
290	44.295	0.0022506	870	0.026006	-2.5849	0.01296	-2.894839	5063	0.01991	0.8767	-0.00602	0.6660	1.0864	17.8454	0.04583	1.77619	-0.785237
310	53.398	0.0027132	930	0.027506	-2.5606	0.00663	-3.178407	5083	0.01984	0.8056	-0.00540	0.80359	1.6014	19.8155	0.04941	1.71526	-0.552733
330	56.805	0.0028863	990	0.028234	-2.5492	0.00490	-3.309794	6038	0.01667	0.7702	-0.00501	0.85487	1.8933	21.9256	0.04819	1.6375	-0.953780
350	58.409	0.0029678	1050	0.028782	-2.5409	0.00409	-3.388795	6035	0.01669	0.7498	-0.00474	0.87900	2.0680	24.1804	0.04757	1.60513	-1.073373
370	59.567	0.0030266	1110	0.029243	-2.5340	0.00350	-3.456336	6035	0.01669	0.7331	-0.00450	0.89643	2.2169	26.5848	0.04753	1.5210	-1.121916





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	$\alpha = wt/wc$	$ga = 1-(1-\alpha)^{1-n}/1-n$	T <sub>3</sub> x 10 <sup>-7</sup>	$ga/T$ x 10 <sup>7</sup>	1/T x 10 <sup>-3</sup>	log(g <sub>α</sub> )/T <sup>3</sup>
390	60.531	0.0030756	1170	0.0029769	-2.5262	0.00301	-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	0.00246	-3.609834	683	0.001464	0.6976	-0.000406	0.92727	2.5535	31.8612	0.074314	1.4649	1.174889
430	62.737	0.0031877	1290	0.0030755	-2.5121	0.00189	-3.72443	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	0.00141	-3.849694	723	0.001383	0.6513	-0.000359	0.95813	50.0000	37.7933	1.26757	1.383126	4.446279
470	64.399	0.0032721	1410	0.0031412	-2.5029	0.00104	-3.98297	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	0.00071	-4.1757	763	0.001311	0.6027	-0.000316	0.97883	3.7101	44.4195	0.081756	1.31066	1.260916
510	65.68	0.0033372	1530	0.0032094	-2.4936	0.00039	-4.408124	783	0.001277	0.5657	-0.000290	0.98843	#REF!	48.0049	#REF!	1.277139	#REF!

