Synthesis, Characterization and Hypoglycemic Activity of Zn(II), Cd(II) and Hg(II) Complexes with Glibenclamide

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A series of group 12 elements for Zn(II), Cd(II), Hg(II) complexes of glibenclamide were synthesized and characterized using various spectroscopic techniques and magnetic moments. The complexes exhibited significant activity against gram-negative and gram-positive bacteria species. Zn(II) complex showed remarkable hypoglycemic activity whereas Cd(II) and Hg(II) complexes exhibited antibacterial activity.

Key words sulfonylurea; glibenclamide; antibacterial activity; diabetes; hypoglycemic activity

Inorganic elements play crucial roles in biological and biomedical processes, and it is evident that many organic compounds used in medicine do not have a purely organic mode of action; some are activated or biotransformed by metal ions including metalloenzymes, others have a direct or indirect effect on metal ion metabolism.[1,2] Metals like chromium, zinc, vanadium, copper, selenium, *etc*., have been reported in lowering the blood sugar level (Hypoglycemia). At the molecular and cellular level, zinc is intimately involved in insulin synthesis, secretion and signalling, and thus, the consequent actions of insulin on metabolism.[3,4] In addition to antiviral, antibacterial, antifungal and anticancer properties,[5] various clinical and epidemiological studies suggest that reduced Zn status is associated with diabetes.[3,4,6,7] Moreover, zinc is known to be essential for the function and/or structure of several enzymes *e.g.*; dehydrogenases, aldolases, peptidases, phosphatases, an isomerase, a transphosphorylase, aspartate transcarbamylase, pancreatic carboxpeptidase, and tryptophan desmolase.[8] Zinc-dependent metalloenzymes are also found among oxidoreductases, transferases, hydrolases, lyases, isomerases and ligases.[9]

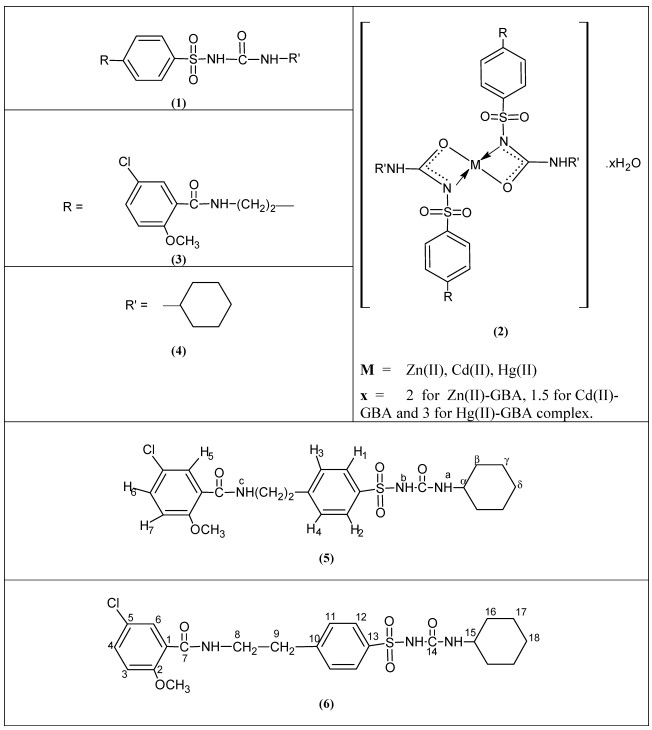
Sulfonylureas have received much attention because of their pharmacological activities in the treatment of non-insuline dependent diabetes mellitus (NIDDM) to enhance the sensitivity of tissues to insulin and to stimulate the pancreas to secrete more insulin and comprise the largest group of oral hypoglycemic agents. These are structurally dissimilar, differing primarily with respect to the substituent R at *para* position of the benzene ring and the group attached to the terminal urea nitrogen R′ (**1**). Inspite of side effects like hypoglycemia, central nervous system problems and skin reactions,[10—12] glibenclamide, a second generation sulfonylurea drug, is being used widely due to its safe administration with other drugs, low production of diuresis, no significant antidiuretic effect, no or low disulfiran like reaction as well as dual route of excretion without effecting glucose tolerance.[13—16]

It is found that complexes of some active drugs are more effective than the ligand themselves.[17—21] It is the reason that transition metal complexes of established drugs are gaining much biological significance.[22—24] The chemistry of sulphonylureas and their metal complexes have created great interest and enthusiasm among the chemists because of their pharmacological importance. Some studies on the coordination chemistry of sulphonylurea drug with Zn^{2+}, Cd^{2+} and Hg^{2+} metals ions have been carried out which is an attempt to examine the mode of action and drug delivery.[25,26]

Keeping in view the concept of coordination of suitable metals as central atom, the biologically active compounds often become more effective than desirable drugs.[27] Hence, the objective of this study was to synthesize a metal based drug after long term clinical studies establishing safety (lack of toxicity) and efficacy which would be recommended for the people with diabetes.

Results and Discussion

Zinc(II), Cadmium(II), Mercury(II)–Glibenclamide Complexes The elemental analyses of these complexes fit into the general formula $[M(GBA)_2]\cdot xH_2O$, where M=Zn(II), Cd(II) and Hg(II) and x=2 for Zn(II), 1.5 for



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Cd(II) and 3 for Hg(II) complex. This indicated a four coordinated environment around these metals if ligand coordinated in a bidentate mode.

Comparison of IR spectra of these complexes shows that N–H stretching band in the ligand (3325 cm^{-1}) have disappeared in these complexes. The protons in $–SO_2NHCO–$ group have been replaced by metals on coordination with nitrogen atom. Carbonyl stretching band of the ligand (1709 cm^{-1}) has shifted in Zn(II), Cd(II) and Hg(II) complexes to 1650 cm^{-1}, 1657 cm^{-1} and 1646 cm^{-1} respectively, whereas $\nu_{asym}(SO_2)$ and $\nu_{sym}(SO_2)$ remained almost at the same position (between 1317—1320 cm^{-1} and 1156—1159 cm^{-1}) compared to ligand (1330 cm^{-1}, 1157 cm^{-1}). The bands due to M–O and M–N frequencies are observed at 774 cm^{-1} and 530 cm^{-1} for Zn(II), 774 cm^{-1} and 446 cm^{-1} for Cd(II) and at 747 cm^{-1} and 557 cm^{-1} for Hg(II) complexes. These observations show that coordination of ligand with all these metals occurs through nitrogen and carbonyl oxygen atom of $–SO_2NHCO–$ moiety. It coordinates in a bidentate mode.

Absorption spectra of all these complexes are transparent in visible part of the spectrum because all these metal ions have completely filled *d*-orbital and as such have no bands due to *d–d* transitions. However, presence of high intensity bands between 33000 cm^{-1} and 45000 cm^{-1} in the spectra of these complexes are indicative of presence of ligand and thus formation of the complexes. Moreover, these complexes are diamagnetic. On the basis of these observations, the structure for all these complexes is believed to be tetrahedral which is evidently supported by ^{1}H- and ^{13}C-NMR studies of these complexes.

The ^{1}H-NMR data suggest that in all these complexes, various signals of the ligand reappeared with slight variation. The most downfield signal in the ligand (10.3 ppm) due to N^b–H proton has disappeared in the spectra of all these complexes, revealing the removal of proton (N^b–H) during complexation. This observation further supports the deduction made on the basis of IR spectral studies that $–SO_2NHCO–$ proton is replaced by metal upon coordination. The N^a–H signal at 6.30 ppm has broadened as its proton coupled with the cyclohexyl ring proton (H^{α}). Other signals of cyclohexyl ring protons become broad on complexation. The N^c–H proton signal at 8.30 ppm, remains unaffected during complexation. The signals due to aromatic ring protons remain unchanged. The ^{1}H-NMR spectrum suggests that in all these metal complexes [(Zn(II), Cd(II) and Hg(II)–GBA] $–SO_2N^bHCO–$ proton is replaced by these ions upon coordination with the ligand. The broadening of N^a–H and cyclohexyl ring signals point out that C=O is also involved in metal binding. This observation is further supported by ^{13}C-NMR studies.

The ^{13}C-NMR spectra of these complexes show almost all the signals corresponding to the ligand except some signals of aryl carbon and one signal due to C=O (^{14}C). The carbonyl signal in the free ligand at δ 163.7 ppm is shifted in the spectra of Zn(II), Cd(II) and Hg(II)–GBA complexes to at δ 161.6 ppm, 158.6 ppm and 160.6 ppm respectively. This upfield shift is justified by the fact that on complexation four membered chelates are formed in which π bond is delocalized between N–C=O bond. These observations confirm that in all these complexes coordination occurs *via* nitrogen and

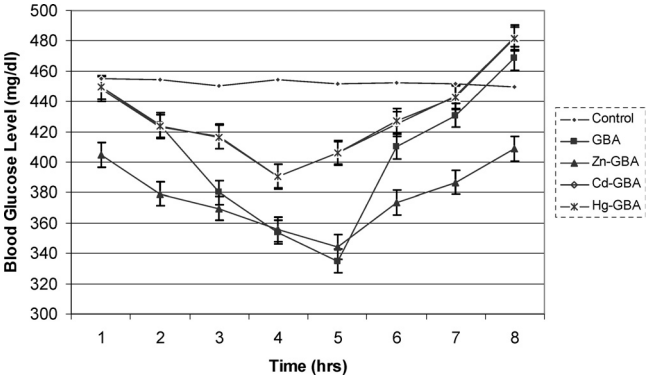

Fig. 1. Change in Mean Blood Glucose Level of Alloxan Diabetic Rabbits Treated with Glibenclamide and Its Zn(II), Cd(II) and Hg(II) Complexes

(C=O) carbonyl oxygen of $–SO_2NHCO–$ moiety resulting a four membered chelate. The proposed tetrahedral structure for Zn(II), Cd(II) and Hg(II)–GBA complexes is given in **2** whereas substituents of **1** for glibenclamide are given as **3** and **4**.

Hypoglycemic Activity Hypoglycemic activity of newly synthesized metal complexes of the drug as well as drug glibenclamide (GBA) has shown in Fig. 1. In order to determine their hypoglycemic activity, calculated amounts of these drugs and their metal complexes were orally administrated to different groups of alloxan diabetic rabbits. The change in mean blood glucose level (BGL) was monitored at the time of administration (0 h) and after each hour upto 8 h.

Among the complexes tested for their hypoglycemic activity, Zn(II)–GBA complexes have shown significant hypoglycemic activity compared to drug treated and control groups of alloxan diabetic rabbits. In all these cases the results were evaluated statistically. The profiles of various curves obtained by plotting variation in BGL as a function of time are shown in Fig. 1. The results indicate that zinc(II) complexes of glibenclamide have shown a significant hypoglycemic activity as compared to standard drug (glibenclamide) as well as Cd(II)–GBA and Hg(II)–GBA complexes.

After the administration (orally) of these complexes and standard drug to alloxan diabetic rabbits a significant decrease in blood glucose level was observed. After 2 h of administration the blood glucose level (BGL) of the group treated with standard drug (glibenclamide) was 424.46±8.47 while groups treated with Cd(II)–GBA was 423.40±7.92 and Hg(II)–GBA was 423.60±8.11 where as the group treated with Zn(II)–GBA complexes was 379.20±18.90. After 4 h time duration the blood glucose level of the GBA and Zn(II)–GBA was comparable to standard drug (drug loaded group 354.80±10.27 and Zn(II)–GBA 355.80±9.80 respectively) but markedly less than the control group 454.20±5.97. The BGL of Zn(II)–GBA complex loaded group further decreased to 344.20±11.73 compared to drug loaded group 375.00±10.27. After 8 h standard drug as well as Cd(II)–GBA and Hg(II)–GBA lost their hypoglycemic activity (blood glucose level for glibenclamide 454.20±8.11, Cd(II)–GBA 443.20±10.47 and Hg(II)–GBA 442.60±9.29) but the complexes of Zn(II)–GBA remained active and showed hypoglycemic activity.

These observations show that in the three groups of exper-

Table 1. Minimum Inhibitory Concentration Data of Metal Complexes against Different Bacteria (MIC $\mu g/cm^3$)

Compound	Gram-negative bacteria										Gram-positive bacteria		
	1	2	3	4	5	6	7	8	9	10	11	12	13
Zn–GBA	1280	—	1280	1280	1280	1280	1280	1280	1280	1280	1280	1280	1280
Cd–GBA	640	640	1280	1280	320	640	1280	1280	640	640	160	640	1280
Hg–GBA	640	320	640	160	640	1280	1280	320	640	1280	160	640	640

1. *Pseudomonas* (*C*)*, 2. *E. coli* (*C*):, 3. *Salmonella typhi* (*R*)¶, 4. *Pseudomonas*, 5. *E. coli*, 6. *Ent. cloacae*, 7. *Ent. faecalis*, 8. *Proteus mirabilis*, 9. *Klebsiella pneumoniae*, 10. *Salmonella* sensitive, 11. *Staph. aureus*, 12. *Staph.* coagulase, 13. *Streptococcus*. *=mutant gene of the bacteria. ¶=resistant gene of the bacteria.

Table 2. Antibacterial Activity of Metal Complexes against Gram Positive and Gram Negative Bacteria

Compound	Zone of inhibition of organisms						
	Gram-negative bacteria			Gram-positive bacteria			
	E. coli	*B. bronchiseptica*	*S. cerevisiae*	*Staph. aureus*	*B. subtilis*	*M. luteus*	*M. flavus*
Zn–GBA	−ive	−ive	−ive	−ive	−ive	−ive	−ive
Cd–GBA	17.0 mm	Slightly+ive	Slightly+ive	18.0 mm	Slightly+ive	Slightly+ive	Slightly+ive
Hg–GBA	20.0 mm	16 mm	20 mm	19.0 mm	17.0 mm	16.0 mm	15.0 mm
Streptomycin sulphate standard	22.0 mm	20.0 mm	18.0 mm	25.0 mm	27.0 mm	20.0 mm	18.0 mm

Standard organism=streptomycin in sulphate, concentration=100 $\mu g/cm^3$, solvent=DMSO. −ive=no activity. Slightly+ive=less than 15 mm.

imental animals (drug and Cd(II)–GBA, Hg(II)–GBA complex loaded) the decrease in BGL was almost comparable upto 2 h (25—26%) while the decrease in GBL of the treated animals for Cd(II)–GBA, Hg(II)–GBA complex was suppressed as compared to the standard drug and lost their activity before the end of experiment (after 7 h). In the case of Zn(II)–GBA complex loaded group, although this decrease was more from start of experiment but after 4 h it was less than the other groups. In Zn(II)–GBA complex, this decrease continues upto the end of 5th hour (19% in standard drug and 22% in Zn(II)–GBA complex loaded group) (Fig. 1). At the end of the experiment (after 8 h), standard drug lost its action whereas the complexes of Zn(II) were still active and lowering the BGL. It is therefore concluded that the Zn(II)–GBA complex is not only more active but also has more hypoglycemic activity and faster on set of action with prolonged duration compared to the standard drug (glibenclamide).

Minimum Inhibitory Concentration (MIC) of Metal Complexes The metal complexes of GBA were screened for their antibacterial activity against a number of gram-positive bacteria such as *Staphylococcus aureus*, *Staphylococcus* coagulase, and *Streptococcus* and gram-negative bacteria as *Pseudomonas* (*C*), *Escherichia coli*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Proteus mirabilis*, *Klebsiella pneumoniae* and *Salmonella* sensitive (Table 1). MIC was also conducted using blank solvent in order to ascertain and account for solvent inhibitory effect upon these bacteria.

Zn(II) metal complexes were found inactive or exhibiting very weak inhibitory effect against most of these bacteria with MIC value 1280 $\mu g/cm^3$ but did not show any activity against *E. coli*. However, the complexes of Cd(II) and Hg(II) of the drug showed considerable activity. Mercury complexes of the drug have shown considerable activity against these bacteria with MIC range 80 $\mu g/cm^3$ to mostly 640 $\mu g/cm^3$. Hg–GBA complexes are more active against *E. coli* (*C*) (MIC 80 $\mu g/cm^3$) than the other gram-positive bacteria. Likely, these are quite active against all the gram-negative bacteria but more active against *E. coli* (*C*), *Pseudomonas* and *Proteus mirabilis* (MIC 160—320 $\mu g/cm^3$). Similarly, cadmium complexes of the drug are also active against most of the gram-positive and gram-negative bacteria but more active against *E. coli*, *E. coli* (*C*), *Pseudomonas* (*C*), *Klebsiella pneumoniae*, *Salmonella* sensitive, *Staph.* coagulase, *Staph. aureus* and *Ent. cloacae* (MIC 160—640 $\mu g/cm^3$). Minimum inhibitory concentration data of these metal complexes against gram-positive and gram-negative bacteria have been shown in Table 1.

Antibacterial Activity of the Metal Complexes Antibacterial activity of these metal complexes was tested against different microorganisms using only one concentration of these complexes 100 $\mu g/cm^3$ and their activity compared with standard antibiotic streptomycin sulphate are reported in Table 2 which shows that all the complexes except Zn(II) have shown considerable activity against the organism. Complexes of Cd(II) and Hg(II) with GBA, showed good antibacterial activity (Table 2). Complexes of Cd(II) and Hg(II) with GBA, ligands have shown strong activity against *E. coli*, *Staph. aureus*, *Bordetella bronchiseptica*, *Micrococcus luteus*, *M. flavus* and *Sacchromyces cerevisiae*. The results are consistent with the previous studies[28—30] conducted on the metal complexes of the organic compounds which indicate that the natures of central atom and ligand exert action on the bacteriostatic and bactericidal activities of the complexes. These complexes can find their use as antibacterial agents. Further detailed investigation will determine whether these complexes are good candidates as antibacterial agent from therapeutic point of view.

Conclusion

It is found that the Zn(ii), Cd(II) and Hg(II) glibenclamide complexes are biologically active which are diamegnatic in nature but only Zn(II) complex of the drug has shown en-

hanced hypoglycemic activity and has become more effective and desirable drugs with lack of toxicity.

Experimental

Metal-salts and reagents/solvents of AnalR were procured from E. Merck Germany and Fluka Switzerland. Dimethyl sulphoxide was purchased from BDH Chemicals England. Oral hypoglycemic drugs (Glibenclamide) in their purest form were donated by E. Merck Germany whereas alloxan used for the induction of diabetes in experimental animals was purchased from Sigma-Aldrich Co., U.S.A. Elemental analyses (CHNS) of the synthesized complexes were carried out on Exeter Analytical CE-440 C, H, N, S analyzer where as metal analyses were performed on atomic absorption spectrophotometer model AA-680 equipped with GFA-4B Graphite Furnace Atomizer and ASA Arsenic analyzer. Mercury contents were determined on mercury analyzer Model SP-3D. Solutions for the determination of metal contents were prepared by digesting 0.055 g of each metal complex in 10 ml of concentrated nitric acid at 70—80 °C for 2 h followed by addition of 10 ml of concentrated perchloric acid and continued heating till white fumes ceased to evolve. All these solutions were diluted to 25 ml with doubly distilled water and amount of metals was measured against the blank solution using atomic absorption spectroscopy.

Melting and decomposition temperatures of ligand and complexes were determined on melting point apparatus, Mel-Temp MP-D, Mitamura Rikon Kogyo Japan using sealed capillary method.

Absorption spectra of the ligands and their complexes in dimethyl sulfoxide (DMSO)/H_2O solution were recorded on Perkin-Elmer Lambda 20 spectrometer using a pair of 10 mm quartz cells. The concentration of solutions was in the range 10^{-4}—10^{-3} mol/l. The solid state infrared spectra of ligands and complexes in KBr disc were recorded on Fourier Transform Shimadzu FTIR 4200 infrared spectrophotometer.

^{1}H- and ^{13}C-NMR of the ligands and complexes in DMSO-d_6 recorded on Bruker 14.1T NMR spectrometer, operating at a frequency of 600 MHz. Magnetic moment measurements of various complexes were determined on Chyo Balance MSB-10 consisting an electromagnet, a direct current (DC) power source and a H-54 Mettler balance. Crystalline $Hg[Co(SCN)_4]$ was used as a standard. The susceptibility of $Hg[Co(SCN)_4]$ was taken as 16.44×10^6 centigrams units at 20 °C using standard procedure.[31]

Circular dichroism spectra of optically active complexes were recorded on Jasco 20A spectropolarimeter, equipped with xenon source and a recorder.

Hypoglycemic activity was determined by oral administration of drugs and their metal complexes to experimental animals by Automatic Drencher 30 ml capacity. The blood samples were withdrawn from the peripheral or mid-ear vein of the alloxan diabetic rabbits and glucose level was determined by One Touch Glucometer. It was used to monitor the blood glucose level of each animal at the time of administration of dose, 0 h and after that each hourly upto 8 h. The data obtained were statistically analyzed by using Microsoft Excel program.

The most of the complexes were insoluble in water, therefore, minimum inhibitory concentration (MIC) study was carried out in DMSO/water solution in the concentration range 10—1280 μg/cm^3. These compounds were first dissolved in DMSO and then diluted with water to such an extent where no precipitation of complexes occurs. Finally, MIC was determined against different bacteria which were grown on MacConkey agar.[32] MIC was also conducted using blank solvent in order to ascertain and account for solvent inhibitory effect upon these bacteria. On the basis of results obtained from MIC, antibacterial activity of these metal complexes was tested against different microorganisms using only one concentration of these complexes 100 μg/cm^3 and their activity was compared with standard antibiotic streptomycin sulphate.[33]

Glibenclamide IR: (KBr, cm^{-1}) 3370 (s, NH amide), 3325 (NH thionyl), 1709 (C=O), 1519 (C–N) 1330, 1157 (SO_2). UV (λ_{max} DMSO, nm), ($\varepsilon\times10^3$): 3.02 (33444), 1.94 (36630), 0.29 (40816), 2.32 (43859). δ_H (DMSO-d_6): 1—1.6 (m, 11H), 2.9 (t, J=2.3 Hz, –CH_2–Ar), 3.3 (b, αH), 3.5 (q, –^{c}N–CH_2–), 3.8 (s, CH_3), 7.1 (d, J=7.3 Hz, H^7), 7.5 (d, J=6.8 Hz, 3H), 7.6 (s, H^5), 7.8 (d, J=6.8 Hz, 2H), 8.3 (bs, ^{c}N–H), 10.3 (s, ^{b}N–H). δ_C (DMSO-d_6): 24.17 (C_{17}), 24.97 (C_{18}), 32.27 (C_{16}), 34.63 (C_9), 39.92 (C_8), 48.27 (C_{15}), 114.14 (C_3), 124.81 (C_1), 129.29 (C_4), 129.49 (C_6), 124.81 (C_{10}), 127.30 (C_{11}), 129.29 (C_{13}), 138.19 (C_5), 150.46 (C_2), 155.68 (C_7), 163.69 (C_{14}).

Zinc(II)–Glibenclamide Complex Glibenclamide 2.96 g (6.0 mmol) and KOH 0.336 g (6.0 mmol) were dissolved in 75 ml of ethanol by stirring for 15 min at room temperature. An ethanolic solution of 0.655 g (3 mmol) zinc(II) acetate was dropwise added to the well stirred ligand solution. Initially a clear solution was formed. Further, stirring for 1 h resulted in the formation of colorless precipitate. The volume of the mixture was reduced to 40 ml by slow evaporation on a water bath at 60 °C. After settled down at room temperature, a colorless amorphous powder obtained was washed with ethanol, acetone and dried at room temperature, mp 232—235 °C. Yield: 84 %.

It is colorless, amorphous, diamagnetic powder, mp 230—235 °C (dec.). As the complex melts and decomposes, hence at low electron volts a weak molecular ion peak is found at m/z 1053=(1089−2H_2O). IR: (KBr, cm^{-1}) 3380 (s, NH, str.), 1650 (C=O, str.), 1530 (C–N, str.) 1320, 1156 (SO_2, unsym, sym str.), 774 (M–O), 530 (M–N). UV (λ_{max} DMSO, nm), ($\varepsilon\times10^3$): 3.52 (37030), 2.21 (37310), 0.20 (43470), 0.08 (40980). δ_H (DMSO-d_6): 1—1.6 (m, 11H), 2.8 (t, J=2.3 Hz, –CH_2–Ar), 3.3 (b, αH), 3.5 (q, –^{c}N–CH_2–), 3.8 (s, CH_3), 7.1 (d, J=7.3 Hz, H^7), 7.5 (d, J=6.8 Hz, 3H), 7.6 (s, H^5), 7.8 (d, J=6.8 Hz, 2H), 8.3 (bs, ^{c}N–H). δ_C (DMSO-d_6): 24.53 (C_{17}), 25.34 (C_{18}), 32.87 (C_{16}), 34.73 (C_9), 40.56 (C_8), 48.29 (C_{15}), 114.24 (C_3), 124.68 (C_1), 124.67 (C_{10}), 127.15 (C_{11}), 128.36 (C_4), 128.37 (C_{13}), 129.72 (C_6), 142.46 (C_5), 155.88 (C_7), 161.648 (C_{14}) while C^2 has disappeared. *Anal.* Calcd for $[Zn(C_{23}H_{28}ClN_3O_5S)_2]\cdot2H_2O$: C, 51.06; H, 5.84; N, 7.63; S, 5.80; M, 5.92; Found: C, 50.96; H, 5.64 ; N, 7.61; S, 5.72; M, 5.73.

Cadmium(II)–Glibenclamide Complex Powdered cadmium(II) acetate 1.59 g (6.0 mmol) was added to a hot solution of 2.96 g (6.0 mmol) of glibenclamide (GBA) ligand and 0.336 g (6.0 mmol) KOH in 75 ml absolute ethanol. The reaction mixture was refluxed for 1 h and then its volume was reduced to 30 ml. By evaporating on water bath at 60 °C, a colourless product separated upon cooling the solution. It was filtered, washed with ethanol, acetone and dried at 80 °C. Yield: 77%.

It is colorless, amorphous, diamagnetic powder, mp 257—260 °C (dec.). As the complex melts and decomposes, hence at low electron volts a weak molecular ion peak is found at m/z 1100=(1127−1.5H_2O). IR (KBr, cm^{-1}) 3355 (s, NH), 1657 (C=O), 1550 (C–N), 1320, 1159 (SO_2), 774 (M–O), 446 (M–N). UV (λ_{max} DMSO, nm), ($\varepsilon\times10^3$): 2.13 (49019), 2.20 (44052), 2.80 (33444). δ_H (DMSO-d_6): 1—1.7 (m, 11H), 2.8 (t, J=2.3 Hz, –CH_2–Ar), 3.3 (b, αH), 3.5 (q, –^{c}N–CH_2–), 3.8 (s, CH_3), 7.1 (d, J=7.3 Hz, H^7), 7.5 (d, J=6.8 Hz, 3H), 7.6 (s, H^5), 7.8 (d, J=6.8 Hz, 2H), 8.3 (bs, ^{c}N–H). δ_C (DMSO-d_6): 24.55 (C_{17}), 25.29 (C_{18}), 32.91 (C_{16}), 34.70 (C_9), 40.53 (C_8), 48.51 (C_{15}), 114.20 (C_3), 124.67 (C_{10}), 126.997 (C_{11}), 128.23 (C_4), 128.24 (C_{13}), 129.67 (C_1), 129.68 (C_6), 155.82 (C_7), 158.555 (C_{14}). *Anal.* Calcd for $[Cd(C_{23}H_{28}ClN_3O_5S)_2]\cdot1.5H_2O$: C, 49.0; H, 5.27; N, 7.45; S, 5.69; M, 9.97; Found: C, 48.82; H, 5.04; N, 7.22; S, 5.60; M, 9.90.

Mercury(II)–Glibenclamide Complex To a 100 ml ethanolic solution of 4.94 g (10.0 mmol) ligand and 0.56 g (10.0 mmol) of KOH, 0.79 g (5.0 mmol) of mercury(II) acetate was added while stirring at room temperature. Initially quite a clear solution was formed. Further stirring for 1 h resulted the formation of colourless product. It was filtered, washed with ethanol, acetone, dimethyl ether and dried at 80 °C. Yield: 72%.

It is colorless, amorphous, diamagnetic powder, mp 230—232 C (dec.). As the complex melts and decomposes, hence at low electron volts a weak molecular ion peak is found at m/z 1188=(1124−3H_2O). IR: (KBr, cm^{-1}) 3375 (NH), 1646 (C=O), 1527 (C–N) 1319, 1158 (SO_2), 747 (M–O), 557 (M–N). UV (λ_{max} DMSO, nm), ($\varepsilon\times10^3$): 2.24 (48393), 2.04 (43057), 2.33 (34428). δ_H (DMSO-d_6): 1.0—1.6 (m, 11H), 2.9 (t, J=2.3 Hz, –CH_2–Ar), 3.4 (b, αH), 3.5 (q, –^{c}N–CH_2–), 3.8 (s, CH_3), 7.1 (d, J=7.3 Hz, H^7) 7.5 (d, J=6.8 Hz, 3H), 7.6 (s, H^5), 7.8 (d, J=6.8 Hz, 2H), 8.3 (bs, ^{c}N–H). δ_C (DMSO-d_6): 24.48 (C_{17}), 25.21 (C_{18}), 32.58 (C_{16}), 34.70 (C_9), 40.45 (C_8), 48.89 (C_{15}), 114.75 (C_3), 124.68 (C_1), 124.68 (C_{10}), 127.47 (C_{11}), 128.63 (C_4), 128.64 (C_{13}), 129.66 (C_6), 155.80 (C_7), 160.592 (C_{14}). *Anal.* Calcd for $[Hg(C_{23}H_{28}ClN_3O_5S)_2]\cdot3H_2O$: C, 44.46; H, 5.03; N, 6.76; S, 5.09; M, 16.14; Found: C, 44.43; H, 4.80; N, 6.49; S, 4.83; M, 16.70.

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