Spectral and thermal studies of homodinuclear and heterodinuclear glutathione complexes

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The complexes of the types \([M_2LSO_4 \cdot 2H_2O]\) where \(L = \text{GSH}\), \(M = \text{Co(II)}, \text{Cu(II)}, \text{Zn(II)}, \text{Cd(II)}\) and \([MM'LSO_4 \cdot 2H_2O]\) where \(L = \text{GSH}\), \(M = \text{Cu(II)}, M' = \text{Zn(II)}\) and \(M = \text{Co(II)}, M' = \text{Cd(II)}\) have been prepared and characterized by elemental analysis, magnetic susceptibility measurements, IR, EPR, electronic spectral studies and thermal analysis. Deprotonation and coordination of thiol group occurs and glycine residue binds with the metal ions in all the complexes. Copper(II) and cobalt(II) complexes show low magnetic moment. EPR spectral data show that complexes have planar geometry. Ligand to metal charge transfer are observed in all the complexes and d-d transition are also observed in copper(II) and cobalt(II) complexes. Thermal decomposition of all the complexes proceeds via first order kinetics.

Metal complexes of glutathione (GSH) serve important functions in our biological system and play a dominant role in protein metabolism. They are important constituents of enzymes, proteins and are present in many parts of the biological system.\(^1\)

\[
\begin{align*}
\text{HOOC-CH}_2-\text{NH-CO-} & \text{CH-NH-CO-CH}_2-\text{CH}_2-\text{CH-COOH} \\
\text{CH}_3\text{SH} & \text{NH}_2
\end{align*}
\]

Glutathione (GSH)

Glutathione, a naturally occurring tripeptide with the sequence γ-glutamylcysteinyl glycine, is frequently the most prevalent intracellular thiol with concentrations up to 8 mmol\(^{2}\). GSH is a biological reducing agent in thiol dependent enzyme reactions. It was recently reported in anticancer activity and were chosen as target molecules for the design of parasiticidal drugs to combat infectious diseases.\(^3,4\) Its metal complexes are involved in the toxicology of several metals.\(^5\)

Because of the presence of potential binding sites, glutathione exhibits a wide range of stereochemistries on complexation with metal ions.\(^6,7\)

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Experimental

All the reagents used were of analytical grade and used without further purification. Glutathione (reduced) was procured from Aldrich.

Synthesis of complexes

\([M_2LSO_4 \cdot 2H_2O]\) Complexes: To glutathione (1.6×10\(^{-4}\) mol) dissolved in water (20 ml), \(\text{ZnSO}_4\) or \(\text{CuSO}_4\) or \(\text{CoSO}_4\) or \(\text{CdSO}_4\) (3.2×10\(^{-4}\) mol) in water (20 ml) was added dropwise and stirred for 0.5 h. \(\text{Zn(II)}\) and \(\text{Cu(II)}\) complexes were precipitated at pH 5.5, whereas \(\text{Co(II)}\) and \(\text{Cd(II)}\) complexes were precipitated at pH 6.5.

\([MM'LSO_4 \cdot 2H_2O]\) Complexes: To glutathione (1.6×10\(^{-4}\) mol) dissolved in water (20 ml), \(\text{ZnSO}_4\) and \(\text{CuSO}_4\) (1.6×10\(^{-4}\) mol) each in water (20 ml) was added dropwise at a time. Similar procedure happens with \(\text{CoSO}_4\) and \(\text{CdSO}_4\) (1.6×10\(^{-4}\) mol) each in water (20 ml). In the first case \([M = \text{Cu(II)}, M' = \text{Zn(II)}]\) complexes were precipitated at pH (5.5) and the precipitates of \(M = \text{Co(II)}\) and \(M' = \text{Cd(II)}\) appears around pH 6.5. All the precipitates were filtered and washed with water and ethanol and finally dried in vacuo over fused \(\text{CaCl}_2\).

The complexes were analysed for C, H, N in RSIC Chandigarh, India. Metals were estimated on a AA-640-13, Shimadzu (Japan) atomic absorption spectrophotometer in solutions prepared by decomposing the complexes in conc. \(\text{HNO}_3\). Magnetic susceptibility measurement at room temperature were carried out in the powdered state on a vibrating sample magnetometer PAR 155 with 5000 G field strength, using high purity nickel metal (saturation moment 55 emu g\(^{-1}\)) as calibrant. The electronic spectra (900-300 nm) of the complexes in solid state were recorded on a Jasco Unidec-430B double beam spectrophotometer, IR spectra were reported in the range of 4000-400 cm\(^{-1}\) and 400-100 cm\(^{-1}\) in KBr and polyethylene disc respectively. EPR spectra of powdered state at room temperature were recorded on a Varian model E-4 spectrometer (x-band) using DPPH (g = 2.0023) as the standard. TG and DTA were recorded on Rigaku Rotaflux PTC-10A using 3-8 mg samples and the heating rate was 5/10 deg. min\(^{-1}\).
Table 1—Characterization data of the complexes

<table>
<thead>
<tr>
<th>Compound colour</th>
<th>Found (Calcd) %</th>
<th>$\mu_{\text{eff}}$ (BM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L (GSH) (C$<em>{10}$H$</em>{17}$N$<em>{3}$O$</em>{5}$S)</td>
<td>39.0</td>
<td>5.55</td>
</tr>
<tr>
<td>Deep Brown</td>
<td>(39.1)</td>
<td>(5.54)</td>
</tr>
<tr>
<td>[Co$<em>2$LSO$<em>4$.2H$<em>2$O] (C$</em>{10}$H$</em>{19}$N$</em>{2}$O$_{2}$S$_2$Co)</td>
<td>21.59</td>
<td>3.37</td>
</tr>
<tr>
<td>Light Blue</td>
<td>(21.63)</td>
<td>(3.42)</td>
</tr>
<tr>
<td>[Cu$<em>2$LSO$<em>4$.2H$<em>2$O] (C$</em>{10}$H$</em>{19}$N$</em>{2}$O$_{2}$S$_2$Cu)</td>
<td>21.23</td>
<td>3.30</td>
</tr>
<tr>
<td>White</td>
<td>(21.27)</td>
<td>(3.36)</td>
</tr>
<tr>
<td>[Zn$<em>2$LSO$<em>4$.2H$<em>2$O] (C$</em>{10}$H$</em>{19}$N$</em>{2}$O$_{2}$S$_2$Zn)</td>
<td>21.12</td>
<td>3.38</td>
</tr>
<tr>
<td>White</td>
<td>(21.13)</td>
<td>(3.34)</td>
</tr>
<tr>
<td>[Cd$<em>2$LSO$<em>4$.2H$<em>2$O] (C$</em>{10}$H$</em>{19}$N$</em>{2}$O$_{2}$S$_2$Cd)</td>
<td>18.07</td>
<td>2.82</td>
</tr>
<tr>
<td>White</td>
<td>(18.13)</td>
<td>(2.87)</td>
</tr>
<tr>
<td>[CuZnLSO$<em>4$.2H$<em>2$O] (C$</em>{10}$H$</em>{19}$N$<em>{2}$O$</em>{2}$S$_2$ZnCu)</td>
<td>21.22</td>
<td>3.30</td>
</tr>
<tr>
<td>Light Blue</td>
<td>(21.20)</td>
<td>(3.35)</td>
</tr>
<tr>
<td>[CoCdLSO$<em>4$.2H$<em>2$O] (C$</em>{10}$H$</em>{19}$N$<em>{2}$O$</em>{2}$S$_2$CoCd)</td>
<td>19.66</td>
<td>3.09</td>
</tr>
<tr>
<td>Off White</td>
<td>(19.72)</td>
<td>(3.12)</td>
</tr>
</tbody>
</table>

Results and discussion

The elemental analysis (Table 1) reveals the presence of two metal atoms, one molecule of ligand (GSH), one sulphate group and two water molecules. These complexes are insoluble in water and common organic solvents like MeOH, EtOH, ether, acetone, benzene, DMF, DMSO.

The IR spectra of glutathione (GSH) shows a strong band at 2525 cm$^{-1}$ due to $\nu_{\text{SH}}$, which is absent in the spectra of the complexes indicating the deprotonation and coordination of the thiol group. This has been confirmed by the stretching band of $\nu_{\text{M-S}}$ appearing at 390-370 cm$^{-1}$ in all the complexes which supports the binding of metal ion with sulphur.

In glutathione, band at 1713 cm$^{-1}$ assigned to $-\text{COOH}$ group of the glycine residue is absent in all the complexes indicating that glycine $-\text{COOH}$ binds with metal ion in all the complexes. The complexes show broad band $-3500-3400$ cm$^{-1}$ due to $\nu_{\text{OH}}$ suggesting the presence of water molecule which is absent in GSH$^8$. The doublet peaks, appearing at 3350(s) and 3251(s) cm$^{-1}$ of GSH, are due to symmetric stretching vibrations of $-\text{NHCO}$ of the peptide group$^9$.

In the complexes, both the bands shifted to the higher frequency region 3600-3200 cm$^{-1}$. The bands appearing at 1655 (w) cm$^{-1}$ and 1540 (m) cm$^{-1}$ in free ligand are due to amide groups. In the complexes, these two bands shifted to higher frequency region 1680-1560 cm$^{-1}$. The band at 1715 cm$^{-1}$ in the ligand is assigned to the $\nu_{\text{CO}}$ stretching of the peptide bonds$^7$. This has been shifted to lower frequency at 1640 cm$^{-1}$ which indicates the coordination of the C=O groups with metal atom. The peak appearing at 3125-3000 cm$^{-1}$ in the free ligand is due to the $\nu_{\text{NH}}$ stretching frequency which comes from the zwitterion $\text{OOC-C-NH}^+$ of the amino acid moiety and there was no band due to free NH$_2$ group in the ligands. But in the complexes, the bands corresponding to NH$_2^+$ disappeared and bands around 3400 (b, s) cm$^{-1}$, 1630 (b, s) cm$^{-1}$ corresponding to the stretching and bending mode of vibrations of the coordinated NH$_2$ group were observed$^{10}$. Thus the zwitterion moiety in the free ligand changed to NH$_2$ in the complex. The bands at 970-950 cm$^{-1}$ ($\nu_1$), 1050 cm$^{-1}$ ($\nu_2$), 1185-1000 cm$^{-1}$ ($\nu_3$) and 660 cm$^{-1}$ ($\nu_4$) in the complexes, shows the presence of sulphate group. Here $\nu_1$ band is weak, while $\nu_4$ is of medium intensity$^{11}$.

The magnetic moment of $[\text{M}_2\text{LSO}_4.2\text{H}_2\text{O}]$ where L = GSH, M = Cu(II) or Co(II) are in the range 0.80-1.05 BM (Table 1). The less magnetic moment values of these homodinuclear complexes are because of the presence of dimetallic complex formation$^{12-16}$. The other homodinuclear complexes $[\text{M}_2\text{LSO}_4.2\text{H}_2\text{O}]$, where L = GSH, M = Zn(II) or Cd(II) are diamagnetic.

The magnetic moment of heterodinuclear complexes $[\text{MM'}\text{LSO}_4.2\text{H}_2\text{O}]$ where L = GSH, M = Cu(II), M' = Zn(II) and M = Co(II), M' = Cd(II) are in the range 1.56-1.67 BM (Table 1). The less magnetic moment value of M = Co(II), M' = Cd(II) complexes than the expected may be because of low spin Co(II) which shows weak paramagnetic behaviour.

The ESR spectra of $[\text{Cu}_2\text{LSO}_4.2\text{H}_2\text{O}]$ in the solid state at room temperature are characteristic of a bini-
clear copper(II) complex of axial type $d_{x^2-y^2}$ (ref. 17). It is suggested that a $\delta$-type superexchange interaction between the $d_{x^2-y^2}$ orbitals of the two copper(II) ions takes place via $p\sigma$-orbitals of the bridging sulphate oxygen atom $[Cu(3d_{x^2-y^2})\ O \ 2 \ pr\ Cu(3d_{x^2-y^2})]^{18}$. The above complexes are four coordinates and $g$ value is 2.117 which suggest approximately planar geometry$^{12,15}$. EPR signal of $[CuZnL\ SO_4\ .2H_2O]$ complex at room temperature detects the unpaired electron as a single isotropic line, having $g = 2.113$ which suggests nearly a planar environment. For Co(II) complex there is extensive spin orbit coupling so EPR measurements are not possible.

The electronic spectral results showed that the amino group metal charge transfer and the carbonyl $\pi \rightarrow \pi^*$ transition are at about 40,000 cm$^{-1}$. The transition at around 30,000 cm$^{-1}$ has been assigned as a charge transfer due to carbonyl group to the metal$^{19}$. Bands at 25,000 cm$^{-1}$ region of the spectra of the complexes are most likely $S(\sigma) \rightarrow M(\pi)$ charge transfer bands and those in the 20,000-15,000 cm$^{-1}$ region to $S(\sigma) \rightarrow M$(II) charge transfer bands$^{16}$ along with $SO_4^{2-} \rightarrow M$(II) charge transfer bands in the complexes. The band at 9100 cm$^{-1}$ and 9500 cm$^{-1}$ in $[CoCd\ SO_4\ .2H_2O]$ and $[Co_2\ SO_4\ .2H_2O]$ respectively can be assigned as a transition from the lower filled orbitals to the $a_{1g}$ ($d_{z^2}$) orbital. This suggests that the transition involves non-bonding rather than antibonding orbitals$^{20}$. The ground state of Co(II) in a square planar environment is probably $2^2A_{1g}$ with the configuration $e_{g}^{1}b_{2g}^{2}a_{1g}$. The bands at 22721 cm$^{-1}$ and 22727 cm$^{-1}$ are probably due to transition from these orbitals to the empty $b_{1g}$ ($d_{x^2-y^2}$) antibonding orbitals. The bands at 15923 cm$^{-1}$ and 15700 cm$^{-1}$ of $[Cu_2L\ SO_4\ .2H_2O]$ and $[CuZnL\ SO_4\ .2H_2O]$ respectively are due to the transition of $2^2A_{1g} \leftarrow 2^2B_{1g}$ ($a_{1g} \ b_{1g} \ a_{1g} \ b_{1g}^2$).

Thermal studies have been carried out to evaluate kinetic parameters of solid state reactions involving weight loss or gain. TG studies of all the complexes showed loss of water upto 425 K.

From the TG curves, the order of reaction (n) and activation energy (E) of the reactions has been enumerated. The methods of Coats and Redfern$^{21}$ has been used for deriving kinetic parameters. It was found that the linearity appears after 5% of the initial decomposition since solids do not obey the first order kinetics in the initial stage$^{22}$. Decomposition of these glutathione complexes proceeds via the first order kinetics. The order of activation energy (E) is Cu < Co < Cd < Zn for homodinuclear complexes and Co-Cd > Cu-Zn for heterodinuclear complexes.

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**References**