ABSTRACT

Blue copper proteins promote a number of critical biological processes including electron transfer, controlled radical reactions, excretion of toxic substances, degradation processes, enzyme activation, toxic radical scavenging and formation of metabolic intermediates. The most important function of blue copper proteins is to transfer electrons through a highly co-ordinate covalent bond between Cu (II) and sulfur atom. The structure, properties and function of copper blue proteins can be obtained by building small molecular analogues. However, the synthesis of copper thiolate is challenging because of relative instability of thiolate group toward both electrophillic attack and oxidative damage. Copper thiolates shows a reaction of dimerization and auto-redox reactions and form disulfides. Making of copper thiolates, need a steric bulk, non-coordinating solvents and strictly avoiding of potentially coordinating counter ions. In this study we have prepared six copper (II) thiol complexes by using mechano-chemical reaction between copper (II) ion and thiol (-SH) functional group containing molecules l-cysteine (LCS), n-acetyl-l-cysteine (NAC), glutathione reduced (GSH), d-penicillamine (PEN), mercaptosuccinic acid (MSH) and dl-dithiothreitol (DTT). Color change of thiol molecules after reaction with copper (II) ion indicates the complex formation. All thiol molecules changed into blue color except dl-dithiothreitol which is in parrot green color. Further, complex formation was verified through FT-IR, PXRD, thermal analysis, magnetic properties and DNA cleavage studies. FT-IR spectra shows thiol (-SH) stretch at 2545 cm^{-1} while it is missing in all copper (II) thiol complexes, indicating that thiol (-SH) group is deprotonated and coordinate as thiolate with copper (II) ion. Powder x-ray diffraction of thiol molecules show very sharp peaks that indicates thiol molecules are very crystalline in nature. After complex formation many peaks were disappeared and their intensity was decreased. The comparison of spectra indicates that crystalline form of thiol molecules changed into amorphous form. Thermal stability was determined by TGA, DTA and DSC. All complexes show thermal decomposition after 200^0C, and pattern of thermal decomposition is different from thiol molecules. The effective magnetic moment of copper (II) thiol complexes was determined at 315K and was found in the range of 1.14 to 1.78 BM. These indicate that copper (II) ion has one unpaired

electron in the 3d shell; therefore, complexes have magnetic moments which are very close to the value of 1.73 BM, which is only copper (II). DNA cleavage studies were carried out with human and pUC18 DNA with all synthesized copper (II) thiol complexes. Lysis was observed by subjecting the samples to gel electrophoresis against the standards. The results indicate that $[Cu(DTT)_2]$, $[Cu(LCS)_2]$, $[Cu(MSH)_2]$ and $[Cu(PEN)_2]$ cleaved both pUC18 and human DNA, it shows that these complexes has an ability to bind with DNA molecule. $[Cu(MSH)_2]$ and CUAC (Copper acetate monohydrate) did not show any effect on both pUC18 and human DNA. $[Cu(NAC)_2]$ has no effect on pUC18 DNA but it has an ability to cleave human DNA. On the basis of these results in-vivo studies are recommended for targeted delivery of complexes against cancerous cells.