of mercapto and imidazole groups to Cu(II) ion in reversed micelles is also studied by ESR and NMR. Results obtained will be discussed with particular attention to the properties of copper metalloenzymes.

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Interaction of the Transition Metal Ions with Natural Peptides

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NMR, CD, EPR and absorption spectra studies as well as polarographic and potentiometric studies on metal ion interaction with two natural peptide *i.e.* glutathione (GSH) and thyrotropin releasing factor (TRF, L-pyroglutamyl-L-histydyl-L-prolinamide) have revealed quite unusual features of both tripeptides as the chelating agents [1–4].

In the case of Cu(II), Co(II) and Ni(II)–TRF systems, the tripeptide acts as the tridentate ligand with formation of the metal ion bonds with N3 imidazol, N^- of the peptide linkage between Pyr and His and the amide nitrogen of pyroglutamic acid. CD spectra studies have shown that the conformation of the chelate rings is very sensitive on the deprotonation process of N1 imidazole nitrogen (see also [4]).

GSH and its oxidized form GSSG with Cu(II) and Co(II) forms very interesting redox system [2]. Both forms of the glutathione are extremely sensitive on the presence of cupric ions in the solution, especially at higher pH region. All studies have shown that the cysteine residue is the most specific coordination site for all studied metal ions *i.e.* Cu(II), Co(II) and Ni(II).

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The Structure and Action of Eseroline: a New Antinociceptive Drug

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The synthesis of eseroline and its salts has been performed in an attempt to clarify the relationship between structure and activity of physostigmine and eseroline.

Eseroline as a free base is quite unstable and is easily oxidized [1], whereas its salts with acids like salicylic, fumaric, tartaric *etc.* are stable even in solution in presence of antioxidant agents. The structure, conformation and electronic properties of eseroline have been investigated through ^1H and ^{13}C NMR, mass spectrometry, UV and IR spectroscopies. All of these measurements show that the structure is similar to that of physostigmine. The ^{13}C NMR spectrum is closely related to that of physostigmine, thus allowing to safely establish the same spatial arrangement of the dipirrolic moiety in both molecules.

Eseroline has antinociceptive activity comparable in potency to that of morphine. At variance with physostigmine, eseroline shows high affinity for the opioid receptor sites as demonstrated by its ability in inhibiting stereospecific [^3H]-naloxone binding in homogenates of rat brain [2]. The groups interacting with the opioid receptor sites are the phenolic ring and the pyrrolidine nitrogen which show the same distance between the phenolic ring and the piperidine nitrogen of the morphine molecule. Eseroline, although derived from physostigmine by hydrolysis