derivatives has been demonstrated through formation of intermediate metal complexes of Schiff bases [1–5].

In our laboratory the role of dioxouranium(VI) ions in biochemical processes is under investigation and several complexes between UO_2^{2+} and biomolecules have been hitherto prepared and studied. Recently, the interaction of dioxouranium(VI) acetate with the ligand pyridoxal has been studied and the bonding of dioxouranium(VI) to phenolic and aldehydic oxygen atoms of pyridoxal has been proved [6, 7]. The influence of uranyl ions on amino-acid–pyridoxal complexes has been investigated as well.

The pyridoxal–glycine–uranyl acetate system has been studied both in solution and in solid state by electronic spectra and i.r. measurements respectively. The electronic spectra of an equimolar mixture of methanolic pyridoxal and glycine show peaks near 360 nm and 320 nm. The peaks markedly increase, when uranyl is added in equimolar amount, as a function of time with a red shift to 390 nm and 343 nm respectively. The band at 278 nm, due to the phenolic group of pyridoxal, appears also slightly shifted to 275 nm and two isosbestic points are present at 290 nm and 275 nm. The resulting spectrum of methanolic pyridoxal–glycine–uranyl complex is identical to that of a pyridoxylidene–glycine–dioxouranium(VI) mixture.

The results obtained in the solid state indicate that ternary complexes 1:1:1 are formed and the elemental analysis is in agreement with the formulation: $UO_2(C_8H_8NO_2)(C_2H_3NO_3)(CH_3COO)2H_2O$.

The i.r. spectrum of the uranyl solid complex was compared with the spectra of the free components. Changes in the i.r. absorptions are observed in particular in the regions where the azomethine C=N stretching, the phenolic carbon–oxygen stretching and the asymmetric carboxyl stretching respectively occur. In fact, the azomethine stretch, ν_{CN}, is assignable to the strong band near 1610 cm^{-1} and the ν_{COO} and ν_{CO} to the absorption peaks near 1570 cm^{-1} and 1510 cm^{-1} respectively.

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Behavior of Copper Complexes in Very Restricted Fields Provided by Reversed Micelles

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Copper ion, in its various forms, plays an important role in many biological reactions. This versatility of copper stems from its feasible redox property and possibility of coordination to a number of common ligands to form complexes of different structure, *e.g.*, octahedral, tetrahedral or square-planar, and mononuclear or polynuclear structures. To date, numerous studies have been performed on the preparation and characterization of model copper complexes in conjunction with the structure and function of the copper metallo–enzymes. However, metal ions in reversed micelles, one of enzyme pocket models, have not attracted much attention. As part of our investigations on the metal ion behavior in reversed micelles [1] correlating with the activity of water and the restricted field effect provided in the micelles, we recently explored redox properties of copper ion and chelation of common ligands of biochemical interest such as imidazole to Cu(I) or Cu(II) ion.

When aqueous Cu(II) chloride is solubilized in chloroform containing 0.20 *M* hexadecyltrimethylammonium chloride (CTACl) and 0.20 *M* or less of water, the predominant species formed is the chloride-bridged polymeric complex. This complex shows absorption bands at 294 and 408 nm. Upon the addition of imidazole to this system, the intensity of both bands decreases and a new band appears at about 280 nm. From an analogous experiment in aqueous media, this was assigned to a charge-transfer band of the copper–imidazole complex. The change of the band intensity as a function of imidazole concentration showed a clear break at the point where $[Im]/[Cu(II)] \doteqdot 2$. In contrast, the presence of 1.0 *M* water abolished the break, just like in the bulk aqueous solution.

In chloroform containing CTACl, Cu(I) chloride is also readily solubilized and the Cu(I) ion is subject to a very slow oxidation by oxygen present in the medium. The oxidation is drastically facilitated by the addition of aqueous hydrogen peroxide. Interestingly, the resulting absorption spectrum was exactly the same as that of Cu(II) chloride itself dissolved in the reversed micelles except the apparent extinction coefficients at λ_{max}'s. On the other hand, Cu(II) chloride complex is reduced instantaneously by the addition of 2-mercaptoethanol as evidenced by a disappearance of 294 and 408 nm bands. Chelation

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