Role of metal ion Copper in biological System:

Copper is necessary for the activity of Cytochromes, Catalase, tyrosinase, monomine Oxidase and Ascorbic Oxidase.

Traces of Copper are needed for normal synthesis of hemoglobin; the erythrocytes are having a colourless Copper containing protein called erythrocuprein in small amounts.

Cerebrocuprein is a Copper containing protein present in Brain. Erythrocuprein, Cerebrocuprein is a Copper containing protein, hepatocuprein present in the liver are all now identified to be an enzyme - cytosolic Superoxide dismutase: It is a protein having 32,000 molecular weight and contains two Copper ion per molecule.

Ceruloplasmin is a Copper containing protein (Bluish coloured) Present in Plasma. It is regarded to be identical with enzyme polyphenol Oxidase. It also helps in the conversion of ferrous iron of plasma to ferric iron and its incorporation into ferritin.

Serum is having Copper bound to ceruloplasmin associated with alfaglobulin fraction and also Copper loosely bound to albumin function.

In the intestinal mucosal cell, Copper is associated with a low molecular weight metal binding protein called metallothionein.

Ceruloplasmin is a Copper containing glycoprotein which is synthesized in the liver. It is not a transport form of copper.

Sources:-

(a) Richest: liver, Kidney, Other meats, nuts, etc.

(b) Poor: milk

Effect of Copper deficiency:-

1) In Copper-deficient lambs, low cytochrome Oxidase activity causes neonatal ataxia.

2) The experimental animals on a Copper deficient diet lose weight, and ultimately die.

3. Copper deficiency produces marked skeletal changes, osteoporosis, and spontaneous fractures.

Metal ion's Toxic Effect in Biological system.

(i) Iron Toxicity:- To treat iron overload in biological system the chelation therapy plays important role.

Acute iron poisoning, such as that resulting from accidental ingestion of $FeSO_4$ tablets, results in corrosion of the gastro intestinal tract.

Chronic iron poisoning, or hemochromatosis, arises from digestion of excess iron usually supplied by vessels used for cooking.

A classic case of the latter is Siderosis induced in members of the Bantu tribe in South Africa, they consume large quantities of beer brewed in Iron pots and Suffer from deposite of iron in liver, Kidney and heart, Causing failure of these organs.

The Chelating agent of choice for iron toxicity is the siderophore desferrioxamine, a polypeptide having a very high affinity for Fe^{3+} ion but not for other metals. ~~Ferr~~ Ferroxamine chelates occurs naturally in bacteria as iron-transport agents.

The active are of bioinorganic research is requrided to provide better ligands for chelation therapy.

(ii) Plutonium Toxicity or Plutonium Poisoning.

The chelating agents which are developed to treat iron toxicity is also useful in therapeutics for Plutonium Poisoning. Diethylenetriamine penta acitic acid (DTPA) salts and siderophores are especially effective.

Some improvement over the naturally occuring chelates has been made by tailoring the ligand to encapsulate completely the eight-coordinate Pu (IV) center.

Although few individuals have been affected, ingestion of ^{239}Pu, for example, as small particles of PuO_2, at nuclear-reactor sites can have dire consequences.

^{239}Pu emits high energy α particle, leading to maligenancies of liver, lung, and lymph nodes, to which tissues it is transported by transferrin, with a maximum tolerated dose of only 1.5 μg. Plutonium is most toxic metal.

(iii) **Cadmium and Lead Toxicity:-** Cadmium and Lead Toxicity in our biological system shows the following symptoms and explained as follows.

Now Gastrointestinal, neurological and kidney toxicity are among the symptoms experienced by acute of chronic exposure to these heavy metals.

The use of unleaded gasoline and removal of lead-containing pigments from paint have substantially diminished the quantity of this element released to the environment each year., Cadmium sources, include alkaline-batteries, Pigment, and plantong

Lead poisoning can be treated by chelating therapy using $CaNa_2$ (EDTA) (acute) or Penicillamine (chronic) Although both Cd (II) and Pb(II) bind to sulfhydryl groups in thioneiy.

yet we have little information at the molecular level on the mechanism by which these elements induce toxicity.

(iv) **Copper Toxicity:-** Wilson's disease is an example of Cu Toxicity.

The Patients suffering from Wilson's disease have low levels of the copper-storage protein Ceruloplasmin, No method have been found for the alteration Metabolism of such gene and gene products responsible.

Chelation therapy, using K_2Ca (EDAT), the Ca^{2+} ion being added to replenish body Calcium Stores depleted by EDTA Coordination, 2,3-dimercapto propan-1-ol (BAL, British Anti Lewisite) or d-penicillamine to remove excess copper, Causes the symptoms to disappear

The sulfhydryl groups of the latter two compounds presumably effect removal of copper as Cu(I) thiolate Complexes,

Wilsons disease offers an excellent opportunity for modern methodologies to isolate and clone the gene responsible for the altered Cu metabolism, which ultimately provide a rational basis for treatment

Note:- Due to copper Toxicity the clinical manifestations are liver disease neurological damage, and brown or green rings in the Cornea of eyes (i.e Kayser-Fleischer disease)