M.Sc. Semester-III, Paper: CC-11 (Bio-Inorganic Chemistry)
Unit-1 Metal ions in Biological Systems (Contd.-1)
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⟹ Heavy metals?

Heavy metal refers to any metallic element that has a relatively high density and is toxic or poisonous at low concentration. Heavy metals are mercury (Hg), cadmium (Cd), arsenic (As), Chromium (Cr), thalium (Tl) and Lead (Pb). The most pollutants heavy metals are Cd, Hg & Pb. They are natural components of Earth's crust. They cannot be destroyed or degraded. To a small extent they enter our bodies via food, drinking water and air. As trace elements some heavy metals, e.g. Cu, Zn, Se are essential to maintain the metabolism of the human body. However, at higher concentration they can lead to poisoning. Heavy metals can enter a water supply by industrial and consumer waste, even from acidic rain, breaking down soils and releasing heavy metals into streams, lakes, rivers and ground water.

⟹ Toxicity of Heavy metals:

Heavy metal poisoning/toxicity could result, for instance from drinking water contamination (e.g. lead pipes), high ambient air concentration near emission sources or intake via the food chain. Heavy metals are dangerous because they tend to bioaccumulate (i.e., an increase in the concentration of a chemical in a biological organism over time compared to the chemical concentration in the environment) compounds accumulate in living things any time they are taken up and stored faster than they are broken down (metabolized) or excreted.

⟹ Toxicity of Cadmium/Cadmium poisoning: Cadmium (Cd) is used in electroplating, storage batteries, vapour lamps and in some solders. It has no use in living organisms. Over-exposure may cause fit fatigue, headaches, nausea, vomiting, abdominal cramps, diarrhea, and fever. In addition, progressive loss of lung function (emphysema), abnormal build up of fluid within the lungs (pulmonary edema), and breathlessness (dyspnea). In some cases, affected individuals may exhibit increased salivation; yellowing of the teeth, an unusually rapid heart beat (tachycardia), low levels of iron within the red blood cell (anemia), bluish discolouration (Cyanosis) of the skin and mucous membranes due to insufficient supply to these tissues. Individuals with Cd-poisoning may also experience improper functioning of the canals with the kidney characterized by excretion of abnormally high levels of proteins in the urine (proteinuria), minor changes in liver function, &/or softening of certain bones (Osteomalacia). It is a cummulative poison for mammals and very dangerous for pregnant women.

⟹ Toxicity of Lead/Lead poisoning: Lead has no biological function. It is a very poisonous metal. Lead production workers, battery plant workers, welders and solders may overexposed to lead. It is stored in the bone but may affect any organ system. The effects of lead poisoning varies depending on the age of the individual and the amount of exposure. Lead overexposure may cause children to be less playful, clumsier, irritable and sluggish (lethargic). In some cases, symptoms include headaches, vomitting, abdominal pain, lack of apetite (anorexia), constipation, slurred speech (dysarthria), changes in Kidney function, unusually high amounts of protein in the blood (hyperproteinemia), and unusually pale skin (pallor) resulting from a low level of iron in the red blood cells (anemia). Some affected children experience learning or behavioral problems such as mental retardation and selective deficits in language, cognitive function, balance, behaviour and school performance. In some cases, symptoms may be life-threatening.

* In adults, over-exposure to lead may cause high blood pressure and damage to the reproductive Organs. Additional symptoms include fever, headaches, fatigue, sluggishness, vomiting, loss of appetite (anorexia), abdominal pain, constipation, joint pain, loss of recently acquired skills, irritability, listlessness, difficulty sleeping, altered consciousness etc. Some affected individuals experience decreased muscle strength and endurance, kidney disease, wrist drop, and behavioral changes such as hostility, depression, and/or anxiety. It is excreted in urine and feces.
* It developes abnormalities in fertility and pregnancy.
* It inhibits the synthesis of haemoglobin in mammals.
* The lead polluted air has its adverse effects on vegetables, e.g. the road vegetables are dried up by the exposure of lead polluted air.

⟹ Toxicity of Mercury/Mercury poisoning: Mercury is used by dental assistants and hygienists, and chemical workers. It has no biological function.
* It is highly toxic to fungi, plants and animals.
* It is a contaminated poison for mammals and fishes.
* Symptoms of mercury poisoning include fatigue, depression, sluggishness (letheragy), irritability and headaches.
* If mercury vapours are inhaled, they are absorbed in lungs, dissolve in the blood and ultimately they are carried to the brain. This causes irreversible damage to central nervous system
* Contact with Hg produces nervousness, fear, inability to make decision, heaviness, irritability, headache, pessimism, fatigue, sleeplessness, trembling of limbs, filling teeth and diarrhoea.
* There may be behavioral and neurological changes associated with over exposure to mercury poisoning, such as excitability and quick tempered behaviour, lack of concentration and loss of memory.
* CH_3Hg & $(CH_3)_2Hg$ produce nervous disorders in marine animals. It brings about genetic changes.

⟹ Arsenic poisoning/Toxic effect of Arsenic: Arsenic (As) is an essential ultra trace element present in red algae, chicks and some mammals including humans.
* It is moderately toxic to plants and highly toxic to mammals when present in considerable amount.
* Lewisite, a gaseous arsenic compound having formula $Cl_2AsCH=CHCl$, present in living systems combine with -HS-containing enzyme forming lewisite-enzyme product, and thus enzyme activity weakened. British Anti Lewisite (BAL) forms a complex with Lewisite, and thus destroys the poisonous effect of Lewisite.
* Arsenic containing drinking water causes severe damage to skin, liver and kidneys.
* Arsenic compounds are very toxic against insects, so best farmers used them as insecticides/pesticides
* Over exposure of arsenic vapours may cause headache, drowsiness, confusion, seizures, and life-threatening complications
* Inorganic arsenic accumulates in the liver, spleen, kidney, lungs and gastro intestinal tract. It then passes through those sites but leaves a residue in tissues such as skin, hair & nails. Symptoms of acute exorg. arsenic poisoning include severe burning of the mouth, throat, abdominal pain, nausea, vomiting, diarrhea, low blood pressure, and muscle spasms. Individuals with severe As-poisoning may experience heart problems (Cardiomyopathy), renal tubular acidosis, breakdown of the haemoglobin of red blood cells, irregular heart rhythms (Ventricular arrhythmias), yellowing of the skin, mucous membranes and whites of the eyes (jaundice).
* In cases of chronic poisoning, weakness, muscle aches, chills, and fever may develop.

⟹ Detoxification of Heavy metals:

Removal of metallic toxic substances from the body/biological systems is referred as detoxification. In conventional medicine, detoxification can also be achieved artificially by techniques such as dialysis and chelation therapy. There is a firm scientific base in evidence-based medicine for this type of detoxification.

For mild cases of heavy metal poisoning just eliminating your exposure to heavy metals can be enough to treat the condition depending on the underlying cause, this might mean taking sometime away from work or changing your diet. For more severe cases, the standard treatment is chelation therapy. This involves giving medication, either through a pill or injection, that binds to the heavy metal in your body. These medications are known as chelators. As they bind to the metal chelators help to usher them out of your body as waste.

Heavy metal poisoning is the accumulation of various heavy metals in your body. Environmental and industrial factors expose you to high levels of heavy metals everyday, including the foods you eat and air you breathe. An effective heavy metal detox includes more than incorporating healthy fruits and vegetables. To minimise the effect of heavy metal poisoning or prevent it altogether, you need to eliminate some foods from your diet. This is especially true for processed foods and excess fats. These foods have minimal nutritional value and slow down the detox process. This is because fats tend to soak up the harmful substances you want to remove. Some foods to limit or avoid in your heavy metal detox diet include: brown rice, because it often contains arsenic. Some fishes (long & larger-lived) as they tend to contain more mercury, alcohol, non-organic foods.

Some foods can help you detoxify by getting rid of heavy metals from your body. These foods bind to the metals and remove them in the digestive process. Heavy metals detox foods to eat include: Cilantro, garlic, wild blue berries, lemon water, Spirulina, Chlorella, barley grass juice powder, Atlantic dulse etc.

Spl. Detoxification methods of heavy metals are mentioned below:

* For mercury, medicines used to counteract a mercury poisoning/toxicity are animal charcoal, pencillamine (2-amino-3-methyl-3-thiobutyric acid) etc.
* For lead, intravenous injection of $CaNa_2$ edta is given to the lead exposed person. This takes out the accumulated lead as Pb-edta complex which is excreted in urine.
* for copper, the accumulated excess Cu(II) is removed by injecting complexing ligand pencillamine. This ligand, which has NH_2 (amine), -SH (thio) & -COOH (carboxo) groups as donor sites, forms a soluble complex with excess Cu(II), excreted in urine as soluble Cu-pencillamine complex. Edta and trien (triethylene tetramine) are also capable of removing excess Copper (II).

⇒ **Role of Selenium in biological systems:**

Selenium (Se) is a trace inorganic element/mineral. It is well known that the element Se is considered as limited and not renewable source on earth. It is found in the environment in soil.

⇒ **Essentiality of Selenium:**

Selenium is a necessary element in humans, animals, micro-organisms and some other eukaryotes, but as yet its necessity to plants is in dispute. There are some documents that selenium has not been approved to be an essential microelement to artery plants Selenium may be essential for growth and development in algae (reported by Pilon-Smits, 2009)

* Selenium is involved in maintaining normal liver function, protein synthesis and protect the body from toxic minerals such as arsenic (As), cadmium (Cd), mercury (Hg) and lead (Pb).
* It plays an important role in the creation of male reproduction capacity and maintain the health of the eyes, hair and skin.
* Selenium helps your body (even in small amounts) make special proteins, called antioxidant enzymes. These play role in preventing cell damage.
* Selenium was the first element identified to occur in native vegetation at levels toxic to animals. On the other hands, Se deficiency in animal feeds can cause "white muscle disease", a degenerative disease of the cardiac and skeletal muscles.
* Additions of selenium prevented liver necrosis in rats deficient in vitamin-E.
* Its role in human health was established in 1973, when selenium, the last of 40 nutrients proven to be essential, was shown to be a component of glutathione peroxidase (GSH_x), an enzyme that protects against oxidative cell damage.
* The US recommended daily allowance of Se is 50-70 µg in human diets. Currently, all of the known functions of Se as an essential nutrient in humans and other animals have been associated with seleno proteins.
* The essentiality of Se for higher plants is still under debate, but Se is considered a beneficial nutrient for many plant species may be also for better oxidative stress resistance. Plants readily take up and assimilate Se, a capacity that may be used to diminish both Se-deficiency and toxicity in animals & humans.
* Plants can be used to clean up surplus Se from polluted areas (phytoremediation), and Se-enriched plant material may be considered fortified food (biofortification).
* Selenium supplementation caused significant weight and body fat reduction. However, small interventional studies in humans have reported contradictory results.

⇒ **Toxic effect/Toxicity of Selenium:**

Selenium was well known for its harmful effects. It was the first element identified to occur in native vegetation at levels toxic to animals.

* Poisoning of animals can occur through consumption of plants containing toxic level of selenium. Live stock consuming excessive amounts of selenized forages are afflicted with alkali disease and blind staggers.
* Typical symptoms of these diseases include loss of hair, deformed hooves, blindness, colic, diarrhoea, lethargy, increased heart and respiration rates, and eventually death.
* Selenium deficiency in animal feeds can cause "white muscle disease", a degenerative disease of the cardiac and sketelal muscles.