TOXIC EFFECTS OF HEAVY METAL IONS ON HUMAN BODY

Dr. Saugata Sain
Associate Professor
Department of Chemistry
Bankura Christian College
Bankura-722101,West Bengal, India.

What is Chemical Toxicology?

It is a branch of science for studying the toxic chemicals and their modes of action.

- Toxic chemicals are discharged mainly by industries into the air, water and soil.

- They enter into the human food chain from the environment.

Sources of some common Toxic Metals

- Arsenic: Coal burning, As-containing insecticides and herbicides, chemical waste, As-contaminated ground water.
- Cadmium: Zn-extraction and industrial use of Zn(Cd always present in commercial Zn), several industrial operations.
- Lead: Pd based paints, antiknock agents in petrol, mining, industry.
- Mercury: Industrial effluents, organomercurials(fungicides), electrochemical industries using Hg-bed as electrodes.
- Copper: Generally from various Cu salts.
- Chromium: Metal plating, stainless steel, Cr(VI) solution.
- Zinc: Industrial waste, plumbing, metal plating.
- Plutonium and other radio elements: Nuclear explosion and reactors.

VARIOUS DAMAGES BY NON-BIODEGRADABLE METALLIC POLLUTANTS

- Electrolytic imbalance arises due to excess intake of these toxic metals. These inhibit proper distribution of Na^{+}, K^{+}, Ca^{2+} and Mg^{2+} ions across the biological membrane which control nerve, kidney, cardiac, muscle activity.
- By altering the membrane permeability produces deleterious effects on the life processes.
- Deposition of excess metals in different vital organs cause severe irritations.
- Replacing certain active moieties like the replacement of biochemically active PO_4^{3-} group by comparable AsO_4^{3-} group.

- The toxic and carcinogenic activity of Cr(VI) arises due to oxidising activity generating poisonous free radicals.
- Cell damage by the radiation from the radioactive elements.
- Interference through competitive inhibition, e.g., replacement of Ca^{2+} by Cd^{2+} in bone metabolism (itai-itai disease in Japan).
- The heavy metals (Hg^{2+}, Cd^{2+}, As^{3+}, Pb^{2+} etc) interfere with the proteins and enzymatic processes due to their extreme affinity to –SH groups.

COPPER TOXICITY

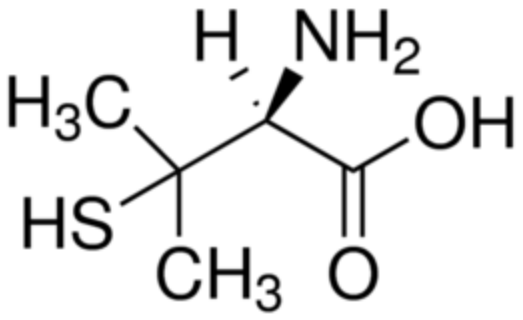
Trace amount of copper is essential for life. Its role is very important in metalloenzymes and metalloproteins (ascorbic acid oxidase, superoxide dismutase, blue copper proteins, hemocyanin, ceruloplasmin, cytochrome c oxidase etc)

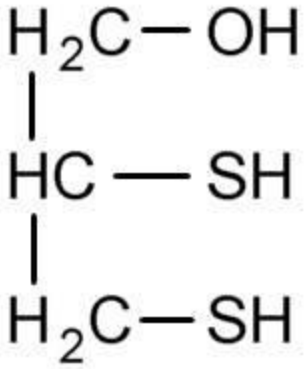
Lethal Dose:LD_{50}(mouse) = 0.05 g/Kg

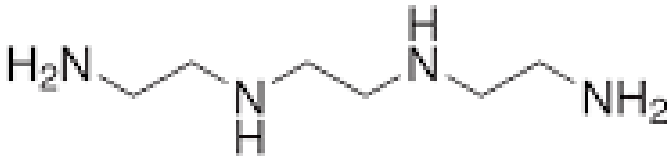
- Moderately low concentration of copper may cause vomiting and considerable gastrointestinal irritation.
- The toxic action due to its affinity for -SH groups of enzyme proteins.
- Wilson's disease arises due to genetic disorder in Cu metabolism.
- Patients are found to have the low levels of apoceruloplasmin (responsible for Cu Transport) due to genetic failure to synthesise the protein.
- Clinical symtoms:Cu accumulates in various organs (liver, kidney, brain etc), high internal absorption of Cu, renal damage, low level of Cu in plasma, increased excretion of Cu in urine.

Antidotes for detoxification of Cu

D-penicillamine, British Anti Lewisite(BAL), Triethylene tetramine







IRON TOXICITY

- Iron is an extremely important essential element for human body due to its presence in oxygen transport proteins(hemoglobin,myoglobin,hemerythrin),iron storage protein(ferritin, phosvitin),electron transport proteins(ferredoxins,cytochromes)and enzymes(nitrogenase, catalase).

- Excessive iron accumulation may occur due to the genetic disorder in the disease like hemosiderosis, hemochromatosis, thalassaemia, sickle cell anaemia, leukemia, etc.

- Acute iron toxicity results from accidental intake of $FeSO_4$ tablets causing erosion of gastrointestinal tract.
- Chronic iron poisoning arises from regular excess intake of iron from cooking vessels.

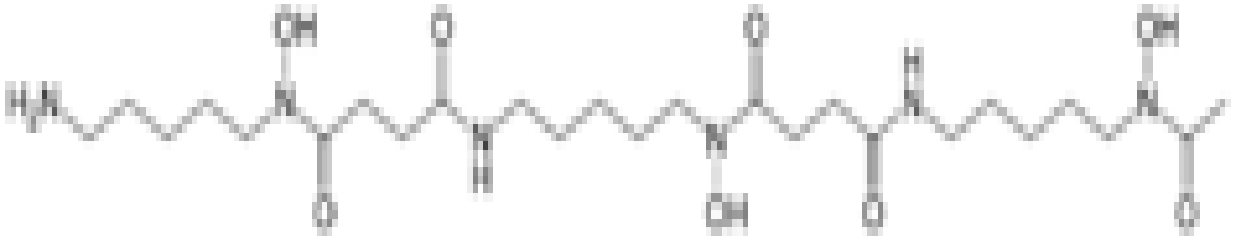
Symptoms of dreaded diseases

- In hemosiderosis, iron deposit occurs in different parts of the body among the patients receiving repeated blood transfusions.
- In homochromatosis, deposition of iron occurs in organs like liver, spleen, pancreas, skin etc due to the breakdown of blood cells.

- The disease African siderosis found in the members of Bantu tribe in South Africa, who consume beer brewed in iron pots, resulting excess iron deposition in liver, heart and kidney.

An Important Antidote:

The chelating antidote used for detoxification of iron is the desferrioxamine B, having a very high thermodynamic affinity specially for Fe(III).



ARSENIC TOXICITY

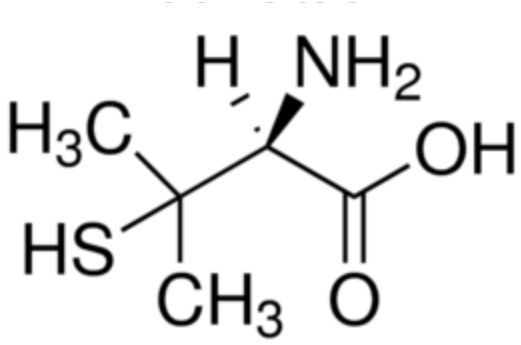
It is not an essential element for human. Although it is found in tissues in very small quantities as ultramicro trace element

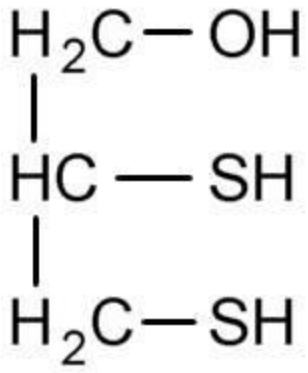
Lethal Dose: LD_{50}(rat) = 0.07 g/Kg

- Arsenic causes serious air and water pollution problems in environment.
- It is accumulative, potent and protoplasmic poison.
- Its salts (not elemental form) are readily absorbed through the gastrointestinal tract.
- Toxicity originates due to its interaction with the –SH groups of different enzymes causing denaturation.
- Causes uncoupling of phosphorylation as in glucose metabolism.
- Extremely high carcinogenic activity resulting skin, mouth, esophagus, larynx and bladder cancer.
- Loss of appetite and weight, diarrhoea, gastrointestinal problems, peripheral neuritis and dermatitis resuting from chronic poisoning.

Antidotes for detoxification of As

D-penicillamine and British Anti Lewisite(BAL)





CADMIUM TOXICITY

It is not an essential element for human.

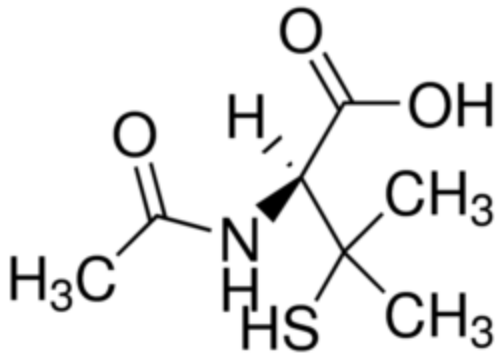
But Cd exists as ultramicro trace element in living systems. Although its biological role is not well established, nevertheless it is expected to be beneficial.

Lethal Dose: LD_{50}(mouse) = 0.027 g/Kg

- Cd^{2+} leads to decalcification in bones probably through competitive inhibition with Ca^{2+}.
- Bones become so weakened that they break even on turning in bed.
- The disease with above mentioned symptoms broke out in some areas of Japan is known as itai-itai.
- The metal produces severe kidney problem.
- Inactivate several S-containing enzymes and proteins by blocking –SH groups also(enzyme bound cadmium accumulates in liver, kidney and reproductive organs).
- Cd^{2+} substitutes Zn^{2+} from several enzymes resulting toxicity.
- Exposure to metallic cadmium dust from industrial operations causes hypertension, cardiovascular problems and acute damage of worker's lungs.

Antidotes for detoxification of Cd

N-acetyl D-penicillamine



LEAD TOXICITY

Clinical signs of toxicity are most often seen at blood lead levels above 4µmol/lit. It is an extremely toxic element.

Lethal Dose: LD_{50}(rat) = 0.15 g/Kg

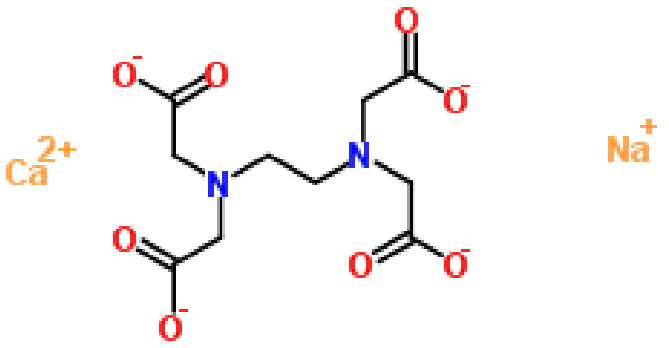
- Its hazardous effects due to industrial exposure.
- Accumulated in bones and soft tissues.
- Pb^{2+} can interfere with Ca^{2+} and consequently bones are affected.
- It interferes with the biosynthesis of porphyrin in hemoglobin synthesis , causing anemia.
- Damages the mitochondria of kidney cells resulting loss of glucose, amino acids and phosphate through urine.
- Severely affects the liver and gastrointestinal tract.
- Lead poisoning (plumbism) is more common to the children because of their propensity of chewing objects containing lead based paints.

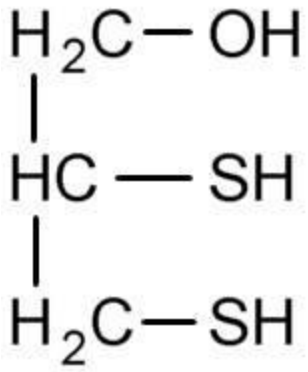
Clinical symtoms

- muscle pain, joint pain, anaemia, run down feeling, depression, chronic nephritis etc.
- It also causes abnormalities in fertility and pregnancy.

Antidotes for detoxification of Pb

$Na_2CaEDTA$ and British Anti Lewisite(BAL)





MERCURY TOXICITY

Mercury is a protoplasmic poison, toxic in all its forms, i.e., Hg, Hg_2^{2+} and Hg^{2+}.

[Lethal Dose:LD_{50}(mouse) = 0.027 g/Kg]

Two major disasters due to mercury:

1. The Minamata disaster occurred among the people eating see-fish from Minamata bay in Japan in 1953.

2. A massive disaster in Iraq in 1972 where several hundred people died after eating wheat which had been dusted with a mercury containing pesticide.

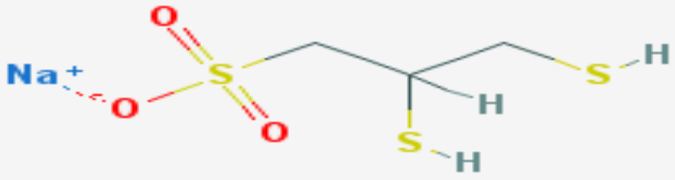
(These two tragic incidents created an awareness of Hg-toxicity)

- Once in the environment, Hg compounds undergo variety of transformations.
- Microorganism and vitamin B_{12} coenzyme transform inorganic mercury into methylmercury and dimethylmercury.
- Methylmercury compounds are much more toxic than all the other forms of mercury.
- Both Hg^{2+} and RHg^{+} preferably bind with the –SH groups of proteins and enzymes.
- Mercury interacts with hemoglobin and serum albumin having –SH groups.

- Creating enzyme inhibition by blocking –SH groups.
- Cellular dysfunction by binding with the cellular proteins.
- CH_3Hg^+ damages the nerve cells of brain and causing neurological disorders.
- Mercury diffuses through skin and is retained by liver, kidney, brain, heart, lung and muscle tissues.

Antidotes for detoxification of Hg

D-penicillamine, N-acetyl D-penicillamine and sodium-2,3-dimercaptopropane-1-sulfonate(Unithiol).



References

i. The Heavy Elements: Chemistry, Environmental Impact and Health Effects, J.E. Fergusson.

ii. Fundamental concepts of Environmental Chemistry, G.S. Sodhi.

iii. Bioinorganic Chemistry, I. Bertini, H. B. Gray, S. J. Lippard and J. S. Valentine.

iv. Elements of Bioinorganic Chemistry, G. N. Mukherjee and A. Das.

v. Bioinorganic Chemistry, A. K. Das.

vi. A Textbook on medicinal aspects of Bioinorganic Chemistry, A. K. Das.

THANK YOU