Inorganic pharmaceutical chemistry

Non-Essential Ions
Fluoride, Bromide, Lithium, Gold, Silver, Lead, Mercury

Lecture four

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1) Fluoride

- **Fluorides are widely used today:**

1. For their anti cariogenic action (inhibition of dental cavity development).
2. Required for bones.

- About 95% of orally taken fluoride is absorbed.
- Sodium fluoride has a wide range of therapeutic index.

- Many reports indicated that fluoride reduces the prevalence of osteoporosis (loss of bone Calcium).
- Visible calcification (in men) were actually higher in low fluoride area because fluoride facilitate calcium deposition in hard tissues (teeth & bones) and not in the soft tissues.

2) Bromide

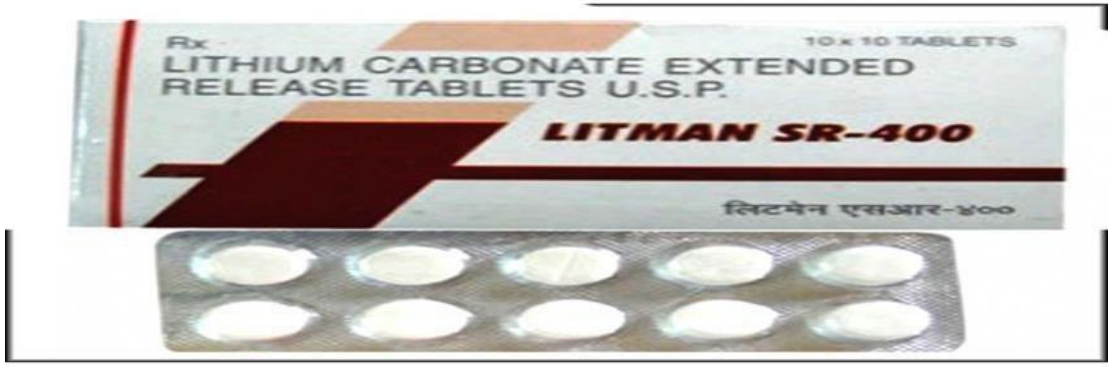
- Bromides were introduced into medicine in 1853 for their antiepileptic effect.
- Administration of small doses (0.5-2 gm) of bromide serve to cause depression to CNS, while large doses (4-8 gm) may depress all reflexes and cause narcotic type effect.
- Bromides usefulness in epilepsy depend on their ability to depress the motor areas of the brain, an effect brought about by large doses.

- Bromides are rapidly absorbed and are excreted mainly in urine, and repeated doses tend to cause accumulation with a consequent replacement of chloride ion.
- The use of bromide is stopped because of the possibility of bromism (bromide poisoning).

- The early sign of bromide intoxication include insomnia, restlessness, dizziness, weakness and headache.
- Treatment of bromism by administration of sodium chloride (6 gm. daily in divided doses) or ammonium chloride used (if sodium intake is restricted).

3) Lithium

- It is readily absorbed from intestine and accumulates in the body.
- The extent of its accumulation dependent upon sodium intake (decrease sodium intake accelerate lithium accumulation and potentiate its toxicity).
- Lithium intoxication is treated by withholding lithium salts and provide sodium intake.
- Lithium is a depressant to the CNS and has a diuretic action.



- Lithium carbonate is administered orally in manic depressive disorder.
- Lithium carbonate can affect thyroid function causing myxedema (deficient thyroid function) decreased protein-bound iodine levels and increased iodine uptake.
- Lithium can cause diabetes insipidus (increase urination without glucosuria).

4) Gold

- It is used in the rheumatoid arthritis, and therapeutic gold compounds are administered I.M.
- Orally is poorly absorbed and irritant.
- The gold is rapidly enters the plasma where it remains bound to albumin for several days so it is usually administered weekly.

- Gold toxicity involves the skin, mucous membrane, joints, blood, kidney, liver and nervous tissue.
- Treatment of toxicity involve:

1. Cessation of gold administration.
2. Giving supportive treatment.
3. Dimercaprol, can be used if toxicity sever, it is used to remove accumulated gold.

5) Silver

- In common with heavy metal is a protein precipitant.
- Action range from antiseptic, astringent, and irritant to corrosive, as the concentration of silver increases.
- Whenever silver preparation are used for long periods of time they can cause discoloration of skin, called argyria.

- The color range from gray to one suggesting marked cyanosis.
- Part of the pigment may be silver sulfide (Ag_2S), but it is also partly metallic sulfur resulting from the reduction of silver in the tissues.

- Reduction is facilitated by light.
- It is irreversible.
- Chelating agents are not effective since argyria involves free rather than ionized silver.

6) Lead

- Its salts were used topically as astringent.
- Oral lead generally absorbed slowly and excreted reasonably well.
- Inorganic lead can not pass through intact skin but it will absorbed through abraded skin, thus lead solution used as astringent could be absorbed systemically while organic lead such as tetraethyl lead can penetrate skin rapidly.

- Once absorbed , lead can be found initially in the erythrocyte and soft tissue, in the latter the kidneys contain the most lead with the liver, then over time redistribution occur to be found in bone, teeth and hair.

Lead poisoning

- While lead may be considered a protein precipitant by combining with the cysteine sulfhydryl groups of protein, chronic lead poisoning manifests itself by inhibition of heme synthesis.
- The most serious lead poisoning symptoms is:

1. Encephalopathy which is more common in children.
2. Renal damage.

Treatment of chronic lead poisoning

- Treatment is based on the use of chelating agents to remove the accumulated lead from erythrocyte and soft tissue.
- Dimercaprol and calcium disodium edetate are used initially followed by Pencillamine for follow up treatment.

Treatment of acute lead poisoning

Which result from oral ingestion and can be treated by:

1. Administering sodium or magnesium sulfate to precipitate the lead.
2. Followed by gastric lavage.

7) Mercury

- Metallic mercury is relatively non toxic as such since it is the mercurous Hg^{+} and the mercuric Hg^{+2} cations that are toxic, in addition to that mercury vapour is also toxic.

- Poisoning by soluble inorganic mercury salts can be avoided while organic mercurials (alkylated mercurials) compounds are very toxic and are the cause of most modern reports of mercury poisoning.

- Toxic effects of mercury similar to those of lead and arsenic, are due to its combining with protein sulfhydryl groups.

- Once absorbed, the mercuric cation concentrates mostly in kidney, with less concentration in liver, blood, bone marrow, and other tissues.
- It is excreted by kidney and colon.
- Acute poisoning usually occurs by ingestion of soluble mercuric salts, vomiting and diarrhea may result with diuresis (suppression of tubular reabsorption) followed by renal damage, this combination lead to fluid and electrolyte imbalance.

Treatment of acute poisoning

1. Gastric lavage.
2. Using of reducing agent such as sodium formaldehyde sulfoxylate to reduce the mercuric cation forming less soluble mercurous salts.
3. Using of chelating agents such as dimercaprol or pencillamine.

Mercurial salts are used as:

1. Diuretics.
2. Antiseptics.
3. Parasiticides.
4. Fungicides.

Disadvantages of organic mercurial diuretics:

1. Poor absorption from GIT, must be administered parentally.
2. Chronic mercury poisoning resulting from prolonged use.

Advantages of organic mercurial diuretics:

1. Little potassium loss and little alterationof the electrolyte balance of the body fluids.
2. No significant change in carbohydrate metabolism, eliminating the risk of onset of diabetes.
3. No interference with uric acid excretion, eliminating the risk of hyperuricemia.