Lecture No:9
Inorganic pharmaceutical Chemistry 3rd stage / 1st semester

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Nonessential ions : Fluoride, bromide, lithium, gold, sliver and mercury

Introduction

- The ions discussed in this lecture are currently considered **nonessential**, even though **some of them have a beneficial pharmacological** action in appropriate dosage.
- Particularly with **fluoride**, it may be shown in the future that this anion is essential with minimum daily requirements.

Nonessential ions : Fluoride

1) Fluorides :

- Fluorides are widely used today for their anti-cariogenic action (inhibition of dental cavity development).

- Required for bones.

About 95% of orally taken fluoride is absorbed, and the remaining is excreted in the feces.

- ❑ About 50% of the ingested fluoride is excreted in the urine.
- ❑ Sodium fluoride has a wide range of therapeutic index.

Nonessential ions : Fluoride

- Fluoride reduces the prevalence of osteoporosis.
- Visible aortic calcification were actually higher in low fluoride area because fluoride facilitate calcium deposition in hard tissues (teeth and bones) rather than 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 by accumulated bromide ion.
- The use of bromide is stopped because of the possibility of bromism (bromide poisoning).

- Treatment of bromism by administration of sodium chloride (6 gm. daily in divided doses) or ammonium chloride used.

3- Lithium :

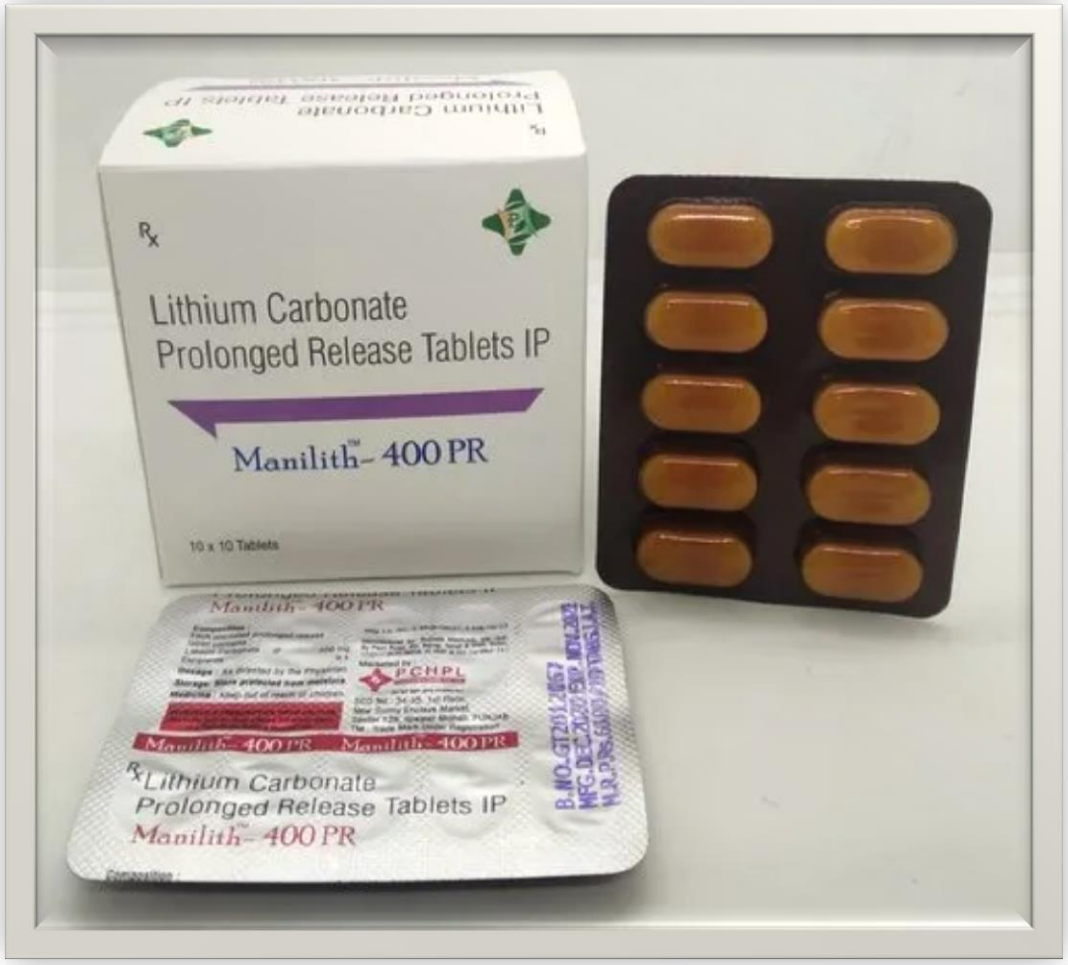
- **It is readily absorbed from intestine, accumulates in the body.**
- The extent of its accumulation **depends** on **sodium intake** (decrease sodium intake **accelerate** lithium accumulation) and potentiate toxicity.
- **Lithium intoxication is treated by withhold lithium and provide sodium intake.**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

- Lithium salts have been promoted at different times as central nervous system depressants.
- Lithium urate (very water soluble) is used to determine whether uric acid enhanced urea toxicity in guinea pigs.
- Lithium carbonate is administered orally in manic depressive disorder.

- The manic depressive reaction is characterized by extremes in emotion and behavior
- The patient becomes hyperactive , paranoid, then the danger of suicide increases.
- **The treatment with lithium carbonate included phenothiazine tranquilizers and electroshock therapy**
- **Lithium carbonate is administered** orally in doses of 300 to 600 mg three times a day to manic patients and should be discontinued if a satisfactory response is not obtained in 14 days.

- Lithium carbonate is contraindicated with patient with impaired renal function
- Lithium can cause diabetes insipidus (increase urination without glucosuria). Interfere with action of vasopressin.
- Also, since lithium toxicity increases with a decrease in sodium intake, patients on salt-restricted diets or those who are receiving diuretics should be monitored carefully.


20x10 Tablets
Lithium Carbonate Prolonged Release Tablets I.P. 400 mg
LITHSAG SR 400
SAG


Lithium Carbonate
Prolonged Release Tablets IP
Manilith™ 400 PR
10 x 10 Tablets
Manilith™ 400 PR
PCHPL
Manilith™ 400 PR
Manilith™ 400 PR
Lithium Carbonate
Prolonged Release Tablets IP
Manilith™ 400 PR

Non essential ions : Lithium

Mechanism of action in manic episode

- Its effect Na, K, Mg and Ca balance . Actions involve alteration in the metabolism of the neurotransmitters, norepinephrine and serotonin.
- Lithium carbonate can affect thyroid function causing myxoedema(deficient thyroid function), decreased protein bound iodine level and increased iodine uptake.
- Lithium reduces atherosclerotic heart disease.

4- Gold:

- It is used in the rheumatoid arthritis (R.A.) , and therapeutic gold compounds are administered by I.M.
- Orally is poorly absorb 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 system.

- **Treatment of toxicity involve cessation of administration, supportive treatment and dimercaprol can be used.**

R.A. Is the disease in which some factor triggers the continual release of enzymes , causing the breakdown of normal synovial membranes, cartilage, muscle, and bone

- In advanced cases the cartilage may completely destroyed and fibrous tissue may grow out of the exposed bone ends.
- Eventually the fibrous tissue may become calcified, resulting in the fusion of the joint.
- Gold is used primarily in the treatment of rheumatoid arthritis.
- It acts by stabilizing the lysosomal membranes, thereby reducing the enzymatic breakdown of the joint tissues

- Gold is used for non disseminated lupus erythematous but is contraindicated in disseminated lupus.
- **It should not be given in individuals with renal disease, a history of infectious hepatitis, skin or blood disorder, diabetes, pregnancy, hypertension, or congestive heart failure.**
- Official gold compounds
- Aurothioglucose injection. Usual dosage range: 10 to 50 mg weekly

Nonessential ions :

5- silver:

- Silver is protein precipitant.

- The action of silver ion on tissue ranges from antiseptic, astringent, and irritant to corrosive as the conc. of free silver ion increases. • Silver products are used topically

Nonessential ions :

- When silver preparations are used for long period of time, they can cause discoloration, called argyria.
- The color ranges from gray to cyanosis, part of the pigment may be silver sulfide(Ag2S) or Ag ion metallic resulting from the reduction of silver in the tissues.

Nonessential ions :

- Since this reduction is facilitated by light as in photographic emulsion, to the skin to become more discolored.
- The treatment is by 6% sodium thiosulfate and 1% potassium ferricyanide subcutaneously will remove the color.

Nonessential ions :

- **6- Mercury:**
- Metallic mercury is relatively non toxic as such since its the **mercurous Hg+** and the **mercuric Hg+2 cations** are toxic, in addition that mercury vapor is toxic.
- **Poisoning by soluble inorganic mercury salts can be avoided by adhering to a strict dosage schedule.**

Nonessential ions :

- while organic mercurial compounds (alkylated mercurials) are very toxic and are the cause of most reports of mercury poisoning.
- Toxic effects of mercury similar to that of Lead 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

Nonessential ions :

- Acute poisoning usually occurs by ingestion of soluble mercuric salts, vomiting and diarrhoea may result with diuresis (suppression of tubular reabsorption) and kidney damage.

Nonessential ions :

- **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 salt.

3. Using of chelating agents such as dimercaprol or pencillamine.

Nonessential ions :

- Chronic mercury poisoning can occur from industrial exposure, eating of foods contaminated with mercury, and long term exposure to topical mecurials.
- Affects the CNS causing behavioral and personality changes, tremors, insomnia and ataxia.

Nonessential ions :

- It is more difficult to treat than acute mercury poisoning and consists of removing the source of mercury, administrating chelating agents, and providing symptomatic treatment .
- N-acetyl- D,L- penicillamine has recently been recommended as a superior chelating as compared with dimercaprol in chronic mercury poisoning.

Nonessential ions :

Mercurial salts are used as :

- 1. Diuretics is to rid the body of excess fluid caused by cardiac edema.
- 2. Antiseptics
- 3. Parasiticides
- 4. Fungicides

Non essential ions :

Disadvantages of organic mercurial diuretics:

- Poor absorption from GIT so it is given parenterally.

Official mercury products

- Meralluride Injection
- U.S.P. occurs as a white to slightly yellow powder which is slowly affected by light. Meralluride is slightly soluble in water, and soluble in hot water and in glacial acetic acid.
- Usual Dose: Parenteral, 1 ml of the injection equivalent to 39 mg of mercury

Non essential ions :

and 43.6 mg of anhydrous theophylline (48 mg of hydrous theophylline) one or two times a week. Usual Dose Rang: 1 to 2 ml.

- **Sodium Mercaptomerin Injection**
- is a mercurial diuretic used for the treatment of congestive heart failure. It is an effective diuretic not only when given intramuscularly and intravenously but also when given subcutaneously.

- **Chlormerodrin Tablet:**

- is the one official mercurial diuretic administered orally.
- occurs as a white, odorless, bitter powder. It is sparingly soluble in water, slightly soluble in methanol and absolute alcohol, and practically insoluble in acetone and ether.
- ***Usual Dose Rang***: 55 to 110 mg daily.