

**Essential and Trace Ions**

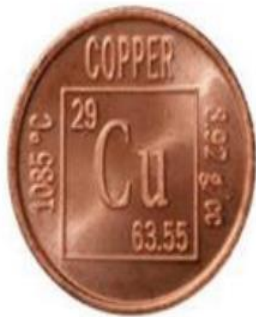
**Inorganic pharmaceutical**

**Chemistry**

**Dr. widad abd al jabbar**

**Lecture four**

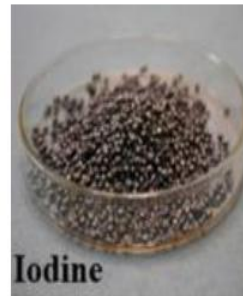
**Essential ions (Iron, copper, sulphur, iodine, and zinc) have specialized biochemical functions.**



**Copper**



**Zinc**



**Iodine**



**Sulfur**



**Iron**

# Essential and Trace Ions: Iron (Fe)

Iron is essential to the primary metabolic processes in the cell

- In the respiratory chain, iron serves as an electron carrier
- In higher organisms, iron is responsible for transport of molecular oxygen
- These functions are due to the ability of iron to exist in coordination compounds in different states of oxidation and bonding
- Fe (+2) and Fe(+3)

# Essential and Trace Ions: Iron (Fe)

Most of iron found in body is associated with two types of proteins:

1. Hemoproteins which are those iron containing proteins responsible for respiration and for carrying oxygen e.g., Hemoglobin(Hb), Myoglobin, Cytochrome c
2. 2. Iron storage and/or transport proteins e.g., Ferritin, Transferrin, Hemosiderin

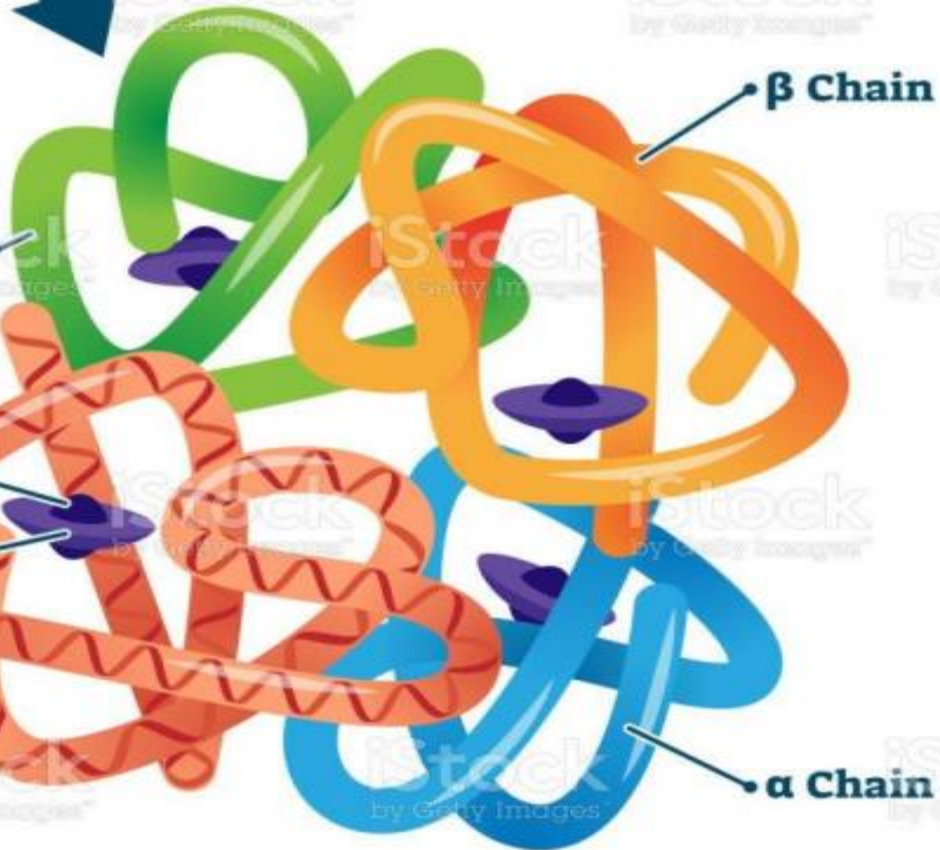
# Essential and Trace Ions: Iron (Fe)

Hemoglobin consists of four protein chains (tetramer), each of which contains a heme unit therefore it transports four oxygen molecules. The release (and binding) of oxygen is a cooperative process, i.e., loss (uptake) of the first oxygen molecule triggers the release of the remaining three

# HEMOGLOBIN



Red Blood Cell



$\alpha$  Chain

$\beta$  Chain

Iron

Heme Group

$\beta$  Chain

$\alpha$  Chain

# Essential and Trace Ions: **Iron (Fe)**

A heme unit is composed of a porphyrin ring and ferrous iron

Porphyrin is covalently bound to the protein portion. The porphyrin system of cytochrome c differs from the porphyrin of hemoglobin in the side chains of the molecule. The heme portion of cytochrome c molecule is shielded by the protein chain to prevent oxygen from interacting with iron

# Essential and Trace Ions: Iron (Fe)

In cytochrome c, present in the mitochondria iron functions as an electron carrier and can be present as ferrous ( $\text{Fe}^{+2}$ ) or ferric ( $\text{Fe}^{+3}$ ). In hemoglobin and myoglobin, iron complexes molecular oxygen.

The release and uptake of molecular oxygen by hemoglobin are influenced by:

- ✓ Oxygen tension
- ✓ PH
- ✓ Carbon dioxide concentration
- ✓ Presence of 2,3-diphosphoglycerate
- ✓ A decreased capability for transporting oxygen leads to iron-deficiency anemia



# Essential and Trace Ions: **Iron (Fe)**

**Ferritin** and hemosiderin are iron storage proteins found in the liver, spleen, and bone marrow, Ferritin is a water soluble, crystallizable iron protein built up from apoferritin

**Hemosiderin** is water insoluble and is considered by some to be a dehydrated ferritin.

-The major iron transport protein of blood plasma is a glycoprotein known as **transferrin**.

# Essential and Trace Ions: Iron (Fe)

Anemia is a general term for a condition in which:

1. circulating red blood cells are deficient in number.
2. Deficient in total hemoglobin content per unit of blood volume, *the net result is lower oxygen carrying capacity by the blood.*

Anemia due to decreased blood formation can be caused by deficiencies of (cobalamine, folic acid, pyridoxine and iron ), infections, renal insufficiency, malignancy, and marrow failure.

# Essential and Trace Ions: Iron (Fe)

-Anemia can be caused by excessive loss of blood which in turn caused by bleeding ulcer, haemorrhaging and menstrual flow.

-Anemia can be caused by blood destruction which is caused by haemolytic agents (drug therapy, infections, toxins )or defective haemoglobins(sickle cell anaemia, thalassemia)

# Essential and Trace Ions: Iron (Fe)

**Iron formulation utilized in iron deficiency must be:**

1-Biologically available, water soluble, ferrous sulphate is the standard to which other iron salts are compared.

2-must be not irritant, therefore sustained released iron formulation used.

**Parenteral iron preparations are indicated in:**

1.defect in iron absorption as in partial gastrectomy, steatorrhea .

2.iron salt may irritate GIT in ulcerative colitis, peptic ulcer

# Essential and Trace Ions: **Iron (Fe)**

The human lethal dose is 150 to 200 mg iron / kg body weight  
Ingestion of 10-15 (300mg ferrous sulfate tablet) may be lethal to a child, with a mortality rate near 50%

## **Poisoning treatment includes:**

- 1- Gastric lavage
- 2- Administration of salts (sodium bicarbonate and sodium dihydrogen phosphate) to form insoluble iron salts.
- 3- Oral administration of deferoxamine will prevent iron absorption.
- 4- Peritoneal dialysis has also been tried with poor results

# Essential and Trace Ions: **Iron (Fe)**

**Iron products**, there are three officially approved iron salts available for the oral administration of iron.

## **1. Ferrous sulphate (FeSo<sub>4</sub>.7H<sub>2</sub>O)**

- Ferrous sulfate U.S.P occurs as pale, bluish green crystals or granules which are odorless.
- it is oxidizes readily in moist air to form brownish yellow basic ferric sulphate [Fe<sub>4</sub>(OH)<sub>2</sub>(SO<sub>4</sub>)<sub>5</sub> ]
- Ferrous sulphate is the most widely used oral iron preparation and is considered as the drug of choice for treating uncomplicated iron deficiency

# Essential and Trace Ions: Iron (Fe)

Usual dose : 300mg,, two or three times a day  
Dosage forms: dried ferrous sulfate tablets, and syrup



# Essential and Trace Ions: Iron (Fe)

## 2. Ferrous fumarate

- Ferrous fumarate U.S.P occurs as a reddish orange to red-brown, odorless powder.
- It is resistant to oxidation on exposure to air so it may be superior to both ferrous sulphate and gluconate.
- Usual dose : 200mg, two or three times a day.
- Dosage forms: ferrous fumarate tablets



# Essential and Trace Ions: Iron (Fe)

## 3. Ferrous gluconate

- Ferrous gluconate occurs as a yellowish gray or pale greenish yellow, fine powder or as granules having a slight odor.
- It has a good bioavailability .
- Usual dose : 300mg, three times a day.
- Dosage forms: ferrous gluconate tablets

# Essential and Trace Ions: Iron (Fe)

## Parenteral administration of iron:

### 1–Iron dextran injection, U.S.P. (Imferon)

- Is a sterile , colloidal solution of ferric hydroxide  $[\text{Fe}(\text{OH})_3]$  complexed with partially hydrolyzed dextran(glucose polymer) of low M.wt., in Water for Injection.
- The PH will between 5.2 and 6.5. prior to mixing, it is a dark brown, slightly viscous liquid.
- It is for I.M. injection only.
- It is used only in confirmed cases of severe iron deficiency anemia where oral therapy is contraindicated.
- Usual dose: intramuscular, the equivalent of 100mg of iron once a day

# Essential and Trace Ions: Iron (Fe)

## 2- Iron sorbitex injection. U.S.P. (Jectofer)

- Is a sterile solution of a complex of iron , sorbitol, and citric acid
- The PH is between 7.2 and 7.9. by itself, iron sorbitex is a dark brown, clear liquid.
- Is to be administered by the I.M. route only.
- Usual dose: intramuscular, the equivalent of 100mg of iron once a day.
- The concurrent administration of oral iron is contraindicated
- The patient's urine can become dark due to the formation of iron sulfide

# Essential and Trace Ions: **Copper**

It is required for many enzymes, for synthesis of haemoglobin and for normal bone formation. Obtain the sufficient amount of copper from food, water, and cooking utensils so copper supplements are not necessary. The average daily intake is estimated at 2–5 mg per day. In liver where the copper become part of copper protein, ceruloplasmin, Copper is found in the brain in form of cerebrocuprein, in blood cells as erythrocuprein.

# Essential and Trace Ions: Copper

The importance of copper in :

## 1. haemoglobin formation.

- copper is required to prevent anemic conditions through:
  - a. facilitate iron absorption.
  - b. Stimulates enzymes involve heme and globin biosynthesis.
  - c. Involve in metabolism of stored iron.

## 2. It is important in oxidative phosphorylation (ATP production by cellular respiration )Copper is a constituent

3. It is associated with the formation of aortic elastin of cytochrome oxidase.

4. It is a component of tyrosinase, an enzyme responsible for conversion of tyrosine to the black pigment, melanin.

# Essential and Trace Ions: **Copper**

A copper deficiency in animals may cause loss of hair color which can be attributed to reduced tyrosinase activity.

- Albinism is associated with either an absence of or an inactive form of tyrosinase.

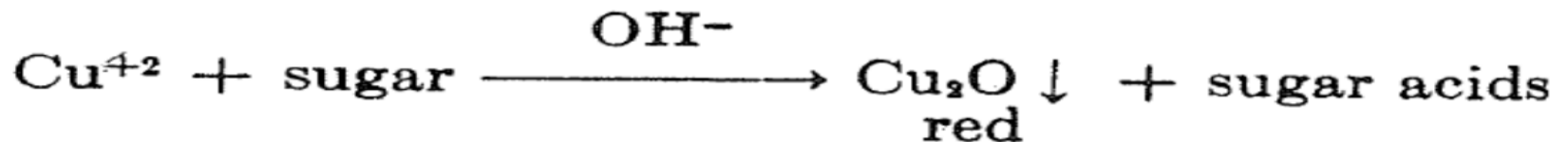
**Wilson disease a condition of excess copper storage** characterized by:  
increased copper levels in liver  
brain, kidney, and cornea.

Pencillamine is the drug of choice which is a chelating agent, in addition to diet restriction.

# Essential and Trace Ions: Copper

## •Uses of Copper

1. Topically as fungicide and astringents.
2. Antidote for phosphorous poisoning.
3. Essential component of Fehling and benedict solutions which are used for determination of glucose.  
**a positive test is the production of cuprous oxide.**



# Essential and Trace Ions : Zinc

Zinc essential for:

1. Several enzymes as alcohol dehydrogenase, alkaline phosphatase, carbonic anhydrase, glutamic dehydrogenase and others.
2. Zinc bound to RNA stabilizing secondary and tertiary structures.
3. For normal growth and reproduction.
4. It has a beneficial effect on tissue repair and wound healing.
5. Zinc complexes with insulin present in B cells of pancreas.
6. Necessary for vitamin A mobilization from liver and vit. A metabolism affected by zinc deficiency.



# Essential and Trace Ions : Zinc

- Low plasma zinc level is present in:
  1. Alcoholic cirrhosis (progressive liver disease).
  2. Uremia.
  3. Myocardial infarction.
  4. Cystic fibrosis with growth retardation.
- **Food sources of zinc includes : seafood, nuts, meat, eggs, and milk.**
- A person on vegetable diet may not receive a sufficient amount of zinc (**10–15 mg daily**) because phytic acid which found in vegetable proteins such as soya bean combine with zinc and decrease its absorption.
- Zinc sulfate is official as a topical astringent.

# Essential and Trace Ions : Sulfur

Sulfur is widely distributed throughout the body in:

## 1. Proteinase

- Sulfhydryl groups of cysteine

- Disulfide linkages in protein from cysteine

## 2. Mucopolysaccharides and sulfolipids as sulphate salts and esters.

- Dietary sulfur comes from these same groupings found in plant and animal foodstuffs.

- Sulfur has been used therapeutically as :

- Cathartic action.

- Parasiticide in scabies.

- Stimulant in alopecia

# Essential and Trace Ions :

## Iodine(Iodide)

- Most of the world's iodine is found in the ocean, where it is concentrated by seaweed. Iodine is reduced to iodide in the intestinal tract. Iodide is an essential ion necessary for the synthesis of two hormones produced by thyroid gland, triiodothyronine T<sub>3</sub> and thyroxine T<sub>4</sub>. If the thyroid doesn't have enough iodine, feedback systems in the body cause the thyroid to work harder, this can cause an enlarged thyroid gland (goiter). Iodine deficiency during pregnancy can lead to high blood pressure for the mother, and mental retardation for the baby.
- Iodine plays an important role in development of the central nervous system

# Essential and Trace Ions : Iodine(Iodide)

- Iodine uses:

- 1-to prevent iodine deficiency including goiter.
- 2-for treating a skin disease caused by a fungus
- 3-Iodine is also used to for radiation emergencies, to protect the thyroid gland against radioactive iodides, Potassium iodide tablets for use in a radiation emergency are available as FDA-approved products (ThyroShield).

**The usual daily iodine requirement for an average male is 140 micrograms and female about 100 micrograms**