M.Sc Semester-III, Paper: CC-11 (Bio-Inorganic Chemistry)

Unit-1 Metal ions in Biological Systems

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Bio-inorganic Chemistry is a branch of Chemistry in which we make study of significant role of metal ions in biological systems (animals & plants). The metal ions are responsible for initiating or inhibiting reactions in biological systems.

⟹ Essential and trace elements

The mineral elements can be classified as essential/principal elements (Macronutrients) and trace elements (Micronutrients).

* Essential/Principal elements (Macronutrients)?

Elements which are required for the maintainance of life, and essential for life processes in biological systems (animals & plants) are called essential/principal elements (Macronutrients). They may be metallic or non-metallic. There are seven essential elements/macronutrients of biological systems: Sodium(Na), Magnesium(Mg), Potassium(K), Calcium(Ca), Phosphorus(P), Sulphur(S) & Chlorine(Cl). Na, K & Cl are involved mainly in the maintainance of acid-base balance and osmotic pressure/control of water metabolism. Ca, Mg & P as constituents of bones and teeth. Phosphorus also as constituent of body cells of soft tissues such as muscles, liver etc. Sulphur(S) in cysteine, methionine, thiomine, biotine, lipoic acid and CoA. All essential elements are not required by every animal or plants.

* Trace elements (Micronutrients)?

Elements which are present in trace/small amounts in the biological systems are called trace elements/micronutrients. They are divided into three groups:

(i) Essential trace elements: Trace elements which are essential for life processes in biological systems. These are Iron(Fe), Iodine(I), Copper(Cu), Zinc(Zn), Manganese(Mn), Cobalt(Co), Molybdenum(Mo), Selenium(Se), Chromium(Cr) and Fluorine(F).

(ii) Possibly essential trace elements: Trace elements which are less essential for biological systems. These are Nickel(Ni), Tin(Sn), Vanadium(V) & Silicon(Si).

(iii) Non-essential trace elements: Trace elements which are not essential for biological systems. These are Aluminium(Al), Boron(B), Germanium(Ga), Cadmium(Cd), Arsenic(As), Lead(Pb) and Mercury(Hg).

⟹ Role of Metal ions in biological Systems/Processes:

1. Sodium(Na^+): Sodium(Na^+) is a common and essential cation present in extracellular fluids of human and other animals. It present to a good extent in bones as phosphate (Na_3PO_4) and mainly exists as chloride(NaCl) and bicarbonate($NaHCO_3$). In human, it present 90gm/70kg of its weight. The main functions/role in biological systems are:

(i) It activates certain enzymes in animal body.

(ii) It regulates acid-base equilibrium in biological systems.

(iii) The intake of Na^+ ion in excess amounts may cause hypertension. Excessive Na^+ ion is harmful to plants and aquatic life.

(iv) It is essential for the formation of HCl in stomach and conduction of nerve impulse and muscle contraction.

(v) It is responsible for the transport of glucose and amino acids into cell.
(vi) It play major role in preservation of normal irritability of muscle and permeability of the cell.
(vii) It is important in nerve action and in the function of heart.
(viii) It maintains the osmotic pressure of the body fluid and thus protects the body against excessive fluid loss.

2. Potassium(K^+): It is also common and essential cation, mostly present in intracellular fluid as well as extracellular fluid of biological systems. In human, it present 170gm/70kg of its weight. The main functions/role in the biological systems are:
(i) It activates a variety of enzymes, such as glycolytic enzyme pyruvate kinase.
(ii) It promotes oxidation of glucose into ATP, which is source of energy.
(iii) It is also responsible for the transmission of nerve signals.
(iv) Certain enzymatic reactions controlled by Na^+/K^+ ratio. The Na^+ & K^+ ions differ in concentration on the opposite sides of the cell membranes. The ratio of Na^+ & K^+ ions concentration is called concentration or ionic gradient.
(v) It plays important role in metabolic functions like protein biosynthesis by ribosomes.
(vi) It controls osmotic pressure and water retention.
(vii) It influences acid-base equilibrium like Na^+ ion in extracellular fluid.
(viii) It is essential for nerve impulse and muscle contraction.
(ix) It is essential in plants for their healthy growth and development.

3. Magnesium(Mg^{2+}): Magnesium (Mg^{2+}) is the most important metal ion in biological metabolism. Its daily requirement for infants: 100-150mg, Children: 150-200mg, Adults: 200-300mg. The normal level of Mg^{2+} in blood is 1-3mg/100ml.
The main functions/role are: (i) Mg^{2+} ion is present in Chlorophyll, a green pigment of plants, as Mg-complex. It absorb light from sun and brings about the process of photosynthesis in plants to convert CO_2 & H_2O into glucose.
(ii) 70% of the total Mg^{2+} content (about 21gm) of the body is combined with Ca and P in the complex salts of bone. The remainder is in the soft tissues and body fluids. It is the principal cation of the soft tissue.
(iii) It acts as activator for many of the phosphate group transfer enzymes.
(iv) It serves as remadies for constipation, obesity, liver and gall bladder disorders.
(v) It forms a complex with ATP, which required for most enzymatic reactions with in the cell.
(vi) It plays important role in many metallo-enzymes.
(vii) It is present in enzyme phosphatase which acts upon organic phosphates to hydrolyse them into free phosphates.
(viii) Intracellular fluid has high concentration of Mg^{2+} ion. It combines with ATP^{4-} & ADP^{3-} ions to form $[Mg(ATP)]^{2-}$ & $[Mg(ADP)]^-$. Thus, ATP & ADP exist as these forms in intracellular fluid at biological pH (7.0 to 7.5)

(ix) It present in the enzyme amino peptidase which hydrolyses polypeptides the free aminoacid end of the chain to form lower peptides and sometimes free amino acids.
(x) It functions as a co-factor for oxidative phosphorylation.

4. Calcium (Ca^{2+}): Calcium (Ca^{2+}) is most essential metal ion for biological system. Its daily requirement for infants (upto 1 year): 360-540mg, Children: 0·8-1·2gm, Adult: 800mg, Women during pregnancy & lactation: 1·2gm. It is major constituent of bones and teeth. It is present as phosphate in the bones of human beings and animals. Large amounts of calcium ions present in the bone tissues as $Ca_{10}(PO_4)_6(OH)_2$. The enamel on teeth is a double salt of calcium, $3Ca_3(PO_4)_2 \cdot CaF_2$.

* Roles/functions of Ca^{2+}: (i) Ca^{2+} plays an important role in biological processes, enzymatic systems and in skeletal formation. With phosphorus in the mineral hydroxy apatite, $[Ca_5(PO_4)_3(OH)]$, it is major constituents of bone, teeth and shells.
(ii) Ionised calcium (Ca^{2+}) acts as an agent of blood coagulation.
(iii) It regulates the excitability of nerve fibres and nerve centres.
(iv) It is required for the activation of several enzymes such as succinate dehydrogenase, ATPase and certain proteolytic enzymes.
(v) It acts as a messenger for hormonal action, trigger for muscular contraction.
(vi) It also plays a role in the stabilization of Protein structure and helps in the maintainence of rhythm of heart.
(vii) Ca^{2+} ion in the normal ratio with K^+ ion maintains the normal activity of muscles.
(ix) Deficiency of Ca^{2+} causes tetany, while excess of it causes calcification.

5. Iron (fe): Iron (fe) is an essential trace metal in biological systems/all forms of life. Egg, nuts, whole grain, spinach have moderate amount of iron. The total iron content of the normal adult is about 4-5gms. About 60-70% of the total iron is present in storage as Ferritin, 3% as myoglobin and only about 0·1% is carried in the plasma in combination with β-globulin transport protein transferrin. The hemoprotein and flavoprotein enzymes together make up less than 1% of the total iron.

* Functions/Roles of fe: (i) Iron functions mainly in the transport of O_2 to the tissues. (Hemoglobin).
(ii) It is also involved in the processes of Cellular respiration.
(iii) It is an essential component of hemoglobin, myoglobin, cytochromes and the respiratory enzyme systems (Cytochrome oxidase, Catalase and peroxidase)
(iv) The non-heme iron is completely protein bound which exists in the form of storage and transport. It is also utilized in the structure of xanthine dehydrogenase and succinate dehydrogenase, and also in the iron-sulphur proteins of the respiratory chain.
(v) In plants & bacteria, iron present as cytochromes & ferredoxin, which are responsible for electron transfer reactions in biological systems.
(vi) It is an important component of nitrogenase (a nitrogen fixing enzyme) which are required by some plants for fixation of atmospheric N_2.

(vii) The excessive intake of iron can cause siderosis and can damage organs. Excess iron is not excreted but remains deposited in livers, spleen and skin.

6. Cobalt (Co): Cobalt is an essential trace metal for many organisms. The main roles of Co are: (i) It is required for the synthesis of Vitamin B_{12}.
(ii) It activates a numbers of enzymes (iii) It is essential for healthy growth of animals
(iv) When infected intravenously, it is highly toxic to plants, moderately to mammals.
(v) Deficiency of Cobalt in soil adversely affects the health of grazing animals.

7. Copper (Cu): Copper is an essential trace metal for all organisms. The main roles of Cu are
(i) It is an essential constituent of metallo-proteins (metalloenzymes) like Ceruloplasma, hemoglobin, cytochrome etc. Hemocynin supplies O_2 to certain aquatic creatures & redox enzymes.
(ii) Enzymes containing Cu play an important role in the pigmentation of skin.
(iii) Excessive intake of Cu by human body is harmful, causes 'Wilson disease'. In this disease excess Cu^{2+} deposited in the liver, kidney and brain, which leads to disorders of nervous system. Copper comes from green vegetables, cereals, egg, meat etc.

8. Zinc (Zn): Zinc is an essential trace metal for almost all organisms. It comes from diet of egg, meat, milk, beans etc. The main roles (functions) of Zinc are:
(i) Zinc is a constituent of a large number of essential enzymes.
(ii) Its deficiency causes loss of appetite, slow healing of wounds, diminishes growth etc.
(iii) It is slightly toxic in macrodoses. Excessive intake of Zn may cause diarrhoea and vomiting; exposure of ZnO fumes often develop nausea, ulceration etc.

⟹ Sodium pump or Na^+-K^+ pump: Na^+ & K^+ ions are chemically similar but biologically different. Na^+ ions are pumped out of cytoplasm while K^+ ions are pumped in. This transport of ions is called Na^+-K^+ pump or simply Sodium pump. The difference in concentrations of two ions (Na^+ & K^+) inside & outside the cell membrane produces an electrical potential, which is crucial for the functioning of nerve and muscle cells. The ratio of Na^+ & K^+ ions concentrations is called ionic or Conc^n. gradient in cells. This pump operates across the cell membranes to maintain Conc^n gradient in cells.

*Mechanism: Sodium pump (Na^+-K^+) operation involves following two steps:

1. Phosphorylation of E (Asparate residue): Na^+-K^+ ATPase is phosphorylated by adenosine triphosphate molecule (ATP) in presence of Na^+ & Mg^{2+} ions into an intermediate (E-P). The site for phosphorylation is the side chain of a specific asparate residue (e.g. Phosphoprotein).

$$\underset{\text{(Asparate residue)}}{E} + ATP \xrightleftharpoons{Na^+/Mg^{2+}} \underset{\text{(Phosphorylated intermediate)}}{E\text{-}P} + ADP$$

2. Dephosphorylation of Intermediate (E-P): Phosphorylated intermediate (E-P) undergoes hydrolysis in presence of K^+ ions to form original (E) asparate residue.

$$E\text{-}P + H_2O \xrightleftharpoons{K^+} E + HPO_4^{2-}$$

During this reaction $3Na^+$ & $2K^+$ are transported per ATP hydrolysed. Therefore, the sodium pump generates an electric current across the plasma, i.e; the pump is electrogenic. Each operation of the cell pumps out larger number of Na^+ ion that it pumps into the cell. As a result, the interior of the cell acquires more negative charge while the exterior of the cell acquires more positive charge, producing electrical potential gradient across the cell membrane which is responsible for the transmission of nerve signals in the animals.

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