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Unit -I

INTRODUCTION TO BIOINORGANIC CHEMISTRY

PART - I

(a) Basic Concept

Bioinorganic chemistry is one of the most recently explored fields of inorganic chemistry. The field is concerned with the function of all metallic and non-metallic elements in biological system both in vitro as well as in vino. The interest in the field is mostly connected with -

(i) improved method of preparations

(ii) the synthesis of inorganic complexes and metal chelates as a mimic for various naturally occurring biomolecules.

(iii) the introduction of metal into biological systems as probes and drugs.

(iv) the investigation of inorganic elements in nutrition and toxicity

(v) the increased concern about the environmental hazard caused by some metal ions.

(vi) the recognition of the importance of an increasing number of trace elements in plant, animal and human nutrition.

(b) Classification

Essential and non-essential elements - The living system have two type of constituents as follows :

(a) Organic constituents: These are main constituent of living system. They are derived from inorganic elements like C, H, O, N. They comprises about 90% of solid materials e.g. proteins, carbohydrates, fats, etc.

(b) Inorganic constituents: Although these constitute a relatively small amount of total body weight yet. They are important for maintaining vital activities of a living system.

In general when analysis of ash of animal tissues is carried out, it is having at least 30 elements. Elements essential at low concentration may be toxic at higher concentration e.g. NaCl is toxic at high concentration because it upset the electrolytic balance. It is possible to divide the 30 elements into two main groups:

(1) Essential elements - These are the elements which are indispensable for maintaining normal living state of a tissue or whole of the body. Depending upon their absolute amounts in the body it is further possible to divide these elements into two sub-groups:

(a) Macro essential elements (macro nutrients): These are the elements which are required to be present in the diet in amounts more than 1 mg. These elements form nearly 60-80% of all inorganic material in the body. Macro elements include twelve elements such as carbon, hydrogen, oxygen, nitrogen, sodium, potassium, calcium, magnesium, iron, phosphorous, sulphur and chlorine. Among these first four elements occur in substantial amount in energy tissue and get derived from dietary carbohydrates, lipids and proteins. The body gets oxygen directly from atmosphere. Nearly 85% of total oxygen and 70% of total hydrogen occur in the form of water which makes 3/5 of the total body weight. The remaining amount of O, H, all N, C, S and others are derived from carbohydrates, lipids and proteins which help to fulfill the basic requirements of tissue structure and synthesis of various biochemical substances within these structures.

(b) Micro essential elements (micro nutrients): These are the essential elements which are needed by the body in very small amounts almost in micro grams and nano grams e.g. copper, zinc, cobalt, manganese, molybdenum, iodine, fluorine, etc.

(2) Non-essential elements: These include remaining 10 elements which are not actually non-essential but their function in the body is not yet known e.g. boron, silicon, arsenic, nickel, aluminium, lead etc given in Scheme 8.1.

Elements in biological system
- Essential
  - Macro: C, H, N, O, Na, K, Ca, Mg, P, S, Cl, Fe
  - Micro: Cu, Zn, Co, Mn, Mo, I, F
- Non Essential: B, Si, As, Li, Al, Pb

Scheme 8.1

We can also classify the elements in a way that suggest their function in complex dynamic system like this

Table 8.1

Extra cellular fluid	Inside the cell	Inside the cyto plasma
Na, Ca	K, Mg	K, Mg
Cu, Mo	Fe, Ca	Ca
Cl, Si	Zn, Ali, Mn	Zn
Si	P, S	P, S
	Se	Se

The very important fact in bioinorganic chemistry is the functional value of the chemical elements in the bio-system. The chemical quality and peculiarities of the element for the partial biological activity is also an important factor. It will be assumed that a peculiarity is the result of evolutionary drive toward the best-chemical system for a living organism.

Table 8.2 : Classification of essential elements

Bulk structural element	Mineral element	Trace element	Ultra trace metals	Non-metals elements
H	Na	Fe	Mn	F
C	K	Cu	Mo	I
N	Mg	Zn	Cr	B
O	Ca	V	Si	
P	Cl	Ni	As	
S		Cd, Li, Pb	Se	
		Sn		

Table 8.3 : Division of metals in Biology

Group IA	Group IIA	Group IIB	Transition metals
Na+, K+	Mg2+, Ca2+_	Zn2+, Ni2+	Mn, Fe, Co, Lu, Mo
Osmotic can for all electrolytes ion currents	Triggers and conformational control	Acid catalysis	Redox catalysis

❑ MAJOR CHEMICAL PROPERTIES OF ELEMENTS IN AQUEOUS SOLUTION

(a) Major Properties of Metals in Aqueous Solutions are :

(i) the transport of positive charge by stable ions,

(ii) ready, often strong and selective interaction with organic ligands,

(iii) easy bond breaking of ionic bonds in low positive oxidation state,

(iv) considerable polarizing power of the ions of high electron affinity,

(v) readily adjustable bond directions and length of some but not all elements,

(vi) easy change of stable oxidation state of some transition elements,

(vii) in high oxidation states, some properties closely related to those of non-metals,

(viii) good p electron donor properties of heavier elements in low oxidation state.

(b) Properties of non-metals in water: The main properties of non-metals in water are:

(i) the transport of negative-charge by stable anions e.g. Cl^-, HPO_4^{2-} etc.;

(ii) strong kinetic control of homolytic and heterolytic breaking and making of covalent bonds which are thermodynamically unstable;

(iii) weak but selective interaction between their anions and cations including organic cationic side chains of proteins;

(iv) high electro-negativity, especially of the light non metals, providing good Lewis base,

(v) more fixed bond lengths and bond angles, giving stereo chemistry of high precision, especially for light elements.

(vi) difficult single unit changes of oxidation state and thus a restricted radical chemistry since one electron non metal reactions are rarely easy.

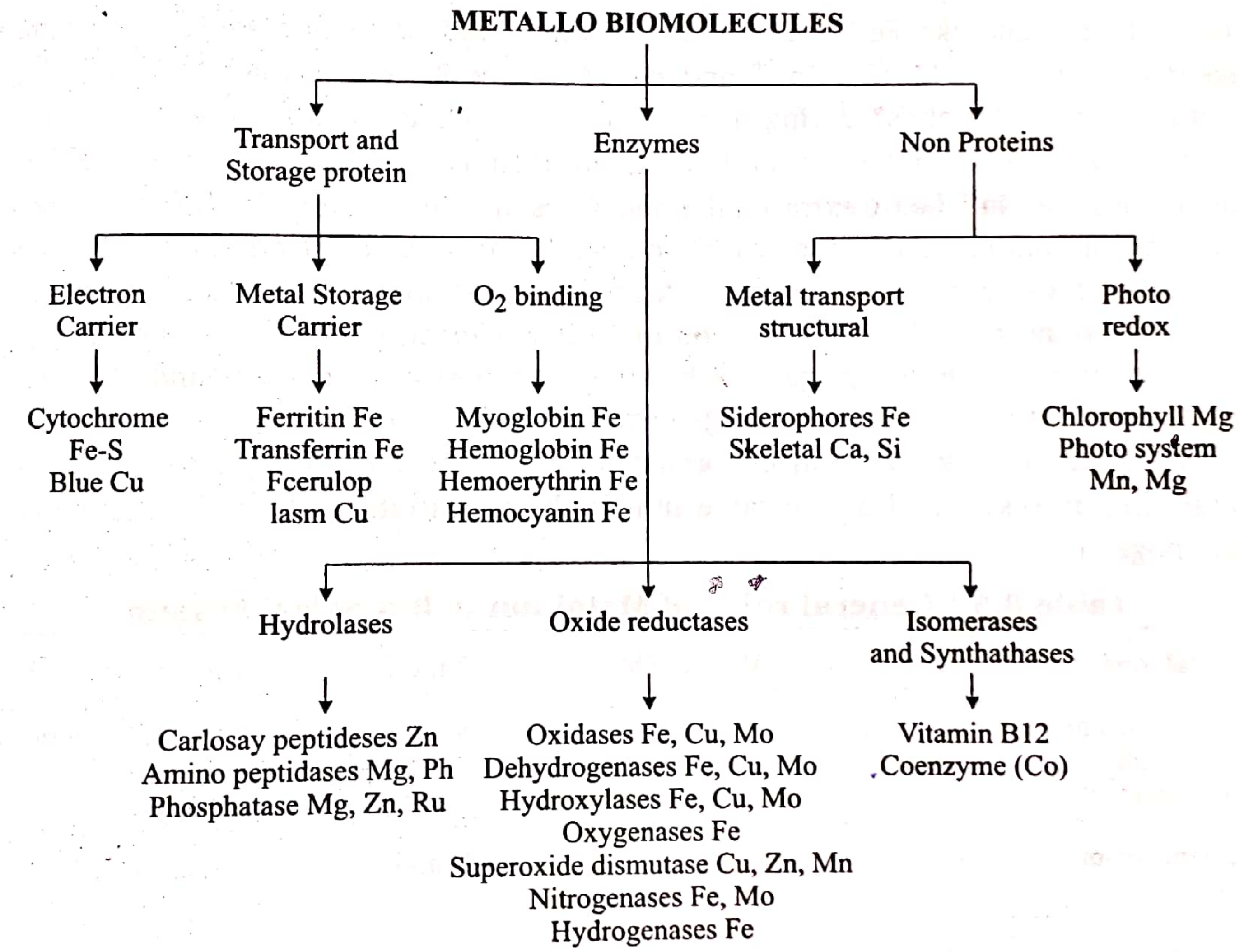
Now we can infer that in presence of water, non metals are the basis of most thermodynamically unstable but kinetically stable compounds like all major polymers and substrates, while metals are the best example of electron transfer agents, catalyst, conduction device etc. It is important to know the use of element functionality in biology. A brief summarized table is given below. It is based on our knowledge over last four decades. Among important elements the C, H, O, N, S, P are the central constructor of life. The metals and metalloids play an important role in catalytic activity and enzyme reactions teeth bones, shell etc. are fully inorganic materials. Some of the metal .... are essential as information carrier and in the coordination of activities.

Table 8.4 :

	General function	Elements	Chemical form	Examples of specific functions
(a)	Structural function	H, O, C, N, P, S, Si, B, F, Ca (Mg, (Zn)	Combined in organic compounds or sparingly soluble inorganic compounds	Components of biological molecules formation of tissues membranes, skeleton shells, teeth, internal structure.
(b)	Electro chemical function	H, Na, K, Cl (Mg), (Ca), HPO_4^{2-}	As per ions	Transmission of messages (nerves) production of metabolic activities
(c)	Mechanical effects	Ca (Mg, HPO_4^{2-}	As free ions exchanging with bound ions	Triggering of muscle contraction, lysis of vesicles.
(d)	Acid-base catalysis	Zn (Ni) Fe (Mn)	Combined in enzymes	Food digests on (Zn) hydrolysis of urea (Ni) phosphate removal in acid media (Fe/Mn)
(e)	Redox catalysis	Fe, Cu, Mn, Mo, Se (Co, (Ali), (V)	Combined in enzymes	Reduction with O_2 (Fe, Cu) oxygen evolution (Mn) Nitrogen fixation (Mn) reduction of nucleotides (Co)

(f)	Various specific function	Mg Fe, Cu Fe, Co, Si O_2, Mg, CO_2 .	In chlorophyll, in Protient special covalent compounds Mineral compounds Gases	Photo synthesis transpost of 2 Hormonal action sensors flotation.

Scheme 8.2 : A Schematic diagram of various functions of metallo biomolecules



(b) Availability of bio-element: An animal must adopt to its environment using raw material available to it. Metal ions are made available and of proper compounds type through the formation of metal complex. The Iron is less abundant in sea water. Plants can synthesize chelating agent to form soluble iron-complexes for the transport of metal ion through cell membrane. The treatment for toxic metals such as lead, is to inject a chelating agent such as EDTA to form a soluble complex that can be extracted. Although phosphorous is not abundant in earths crust or in sea water, it serves essential function in plant and animal life. The primary means for energy storage and release in cells involves the formation and hydrolysis of pyrophosphate. The DNA and RNA consists of long chains of cyclic five carbon sugars linked by heterocyclic nitrogen bases, the sequence of which constitute genetic code.

The ratio of the chemical elements in living organism is not in a simple relationship with their abundance on the eartn crust. The most abundant element, oxygen is a major component of the compounds constituting animal and plants organism. Most abundant silicon and aluminium plays no role whereas Co, Cu, Mo performs important biological function. It should be pointed out that among the bio elements there are metals and non-metals of widely varying chemical properties, particle sizes and electronic structure e.g. the bio metals include Na^+, K^+, Mg^{2+}, Ca^{2+} as well as includes Zn^{2+}, Fe^{2+}, Cu^{2+}, Fe^{3+}, Mo^V, Mo^{-V}. Some of them may change their oxidation state in course of metabolic processes. They may have ionic and covalent bonds. Some of them are strong complexing agent like Fe^{3+}, Co^{2+}, Cu^{2+}, Zn^{2+} and other one weak complexing agent-such as Ca^{2+}, Mg^{2+}, Mn^{2+} and even Na^+ and K^+ also involve in complexing (with macrocylic ligands) during metabolism. The significant difference in the ionic radii of Na^+ 0.98 Å and K^+ 1.33 Å results in dissimilar function of Na^+ and K^+ in metabolism i.e. Na^+ being extracellular and K^+ is intracellular one. It is the size of ion and type of bonding determines which ion can be substituted for others in metabolic processes. It is extremely important that Mg^{2+} and Ca^{2+} ions do not substitute for each other in bio system. The concentration of various elements and their compounds in living organism is very important. It has been demonstrated that one and the same element may produce effect on the organism as a whole yet be a strong poison if present in excess amount e.g. Zn is an important bio-metal, the Zn^{2+} form a part of many catalyzing processes and at the same time high concentration of Zn^{2+} in tissues is carcinogenic.

Table 8.5 : General roles of Metal ion in Biological System

Metal ions	Na, K	Mg, Ca, (Mn)	Zn, Cd (Co)	Cu, Fe, Mo (Mn)
Type of Complex biological function	Weak charge transfer nerves	Moderate trigger reactions hydrolysis phosphate transfer	Strong hydrolysis pH control	Strong oxidation and reduction reactions
Ligand atom preferred	0	0	N and S	N and S

The importance of bio-inorganic chemistry is that it is not a part of organic or bio chemistry that is the chemistry of C, H, N, O, etc. Since the combinations of these elements alone do not represent analytical make up observed in a living system, on the contrary, life seems to have evolved from a much wider use of elements in periodic table. A few examples of the uses of inorganic elements in bio systems are given as follows :

(i) The hard structure of animals are largely minerals, most frequently calcium salts.

(ii) Electrolytic connection in and between cells e.g. nerve messages, rests largely on the concentration gradients of sodium, potassium and calcium amongst the metal ions and chloride amongst non-metals.

(iii) Phosphate transfer, essential in bio energetics, is almost invariably linked with magnesium reaction in enzymes.

(iv) Mechanical changes in cells are frequently initiated by calcium concentration changes.

(v) Extra triggering in digestion, blood clotting, fertilization, muscle contraction, cell surface interaction depends largely on calcium concentration change.

(vi) The capture of light in photosynthesis depends on magnesium containing pigment chlorophyll.

(vii) Electron transfer in energy transduction is very largely dependent on iron proteins.

(viii) Oxidative metabolism is almost always dependent on iron and copper catalysis.

(ix) The capture of combined nitrogen from nitrate or dinitrogen relies almost totally on a molybdenum containing catalyst centre and in some cases also on Fe and V.

(x) The release of oxygen from water, that maintains our present atmosphere is absolutely dependent on Manganese.

(xi) Transport of oxygen requires iron or copper proteins.

(xii) The synthesis of some DNA and RNA, the activation of water as a leaving or attacking unit in condensation and hydrolysis reactions etc. depend on intervention of more than 150 zinc and (Mg) enzymes involved in biological reactions. The DNA synthesis also require either Co, Mn or Fe in ribonucleotide reductase.

(xiii) Bound pyrophosphate (ATP) is the major carrier or chemical free energy for driving reactions.

The above list of activities clearly indicate the involvement of inorganic elements in structural and mechanical function, electrochemical control, acid base and redox catalysis, generation transmission and storage of energy etc. Although various metal ions are essential. They become hazardous when present in excess. As a result there are metabolic disorders connected with both deficiency and excess amounts of these metal ion as given in table 8.6

Table 8.6

Essential or beneficial element		**Disease arising from deficiency**	**Disease associated with an excess of the element**
1	Calcium	Bone deformities, tetary	Cataracts, gall stones atheroscierosis
2	Cobalt	Aneamia	Coronary failure polycythaemia
3	Copper	Aneamia, kinky hair syndrome	S.A.K. Wilson's disease
4	Chromium	In correct glucose metabolism	
5	Iron	Anaemia	Haernochomatosis Siderosis
6	Lithium	Manic depression	Anaesthesia
7	Magnesium	Covulsions	
8	Manganese	Skeletal deformities, gonadal dysfunction	Ataxia

9	Potassium		Addison's disease
10	Selenium	Necrosis of liver, white muscle disease	Blind staggers in cattle
11	Sodium	Addison's disease stroker's cranks	
12	Zinc	Dwarfirm, hypogonadism	Metal fume fenear
13	Cadmium		Nephritis Anaemia
14	Lead		Encephalitis neuritis
15	Mercury		Encephalitis and neuritis

PART II

Bio importance of Alkali and Alkaline Earth Metals

The role of group IA and group IIA metal ions is well known in biological process. The main elements in this category are sodium, potassium, calcium and magnesium. The aim of this chapter is to high light important role of these metal ions.

In general magnesium and potassium ions are present in high concentration in bacterial cells, while Ca^{2+} is present to a lesser extent. It has been found that growth of bacteria is directly proportional to $[Mg^{2+}]$. It appears that Mg^{2+} is an integral part of ribsome structure and is also found in the outer membrane of the cell. The growth rate of bacteria is similarly dependent on $[K^+]$. Ca^{2+} is found in large amount in bacterial spores. All the higher members require proper amount of all the four cations.

Table 8.7 : Concentration of ions in living cell and their environment ($mmol^{-1}$)

System	Na^+	K^+	Ca^{2+}	Mg^{2+}
Sea water	460	10	10	52
Valonia (single a valgae)	80	400	1-5	50
R.B.C.	11	92	10–4	2.5
Blood plasma	160	10	2	2

A. Role of Sodium and Potassium

There are large amounts of sodium, potassium and chloride ions in sea water but not very much in fresh water, yet life abounds in both media keeping concentration of these element constant. Even small deviation from normal level creates problem in life. Both Na^+ and K^+ can bind weakly to all organic molecules (chelate). Binding by cyclic ligands can be used as drugs or poison. The supra molecular chemistry include these types of drugs.

The main source of sodium is diet. It is the common table salt. In general food from plant source is generally low in sodium. Potassium occurs in almost all foods both plants and animals. The good sources it potassium include coffee, tea, cocoa, dried linear, vegetables, milk, fish, chicken, beef, linear, pork, dry fruits, bananas, orange, pineapples, broccoli, potatoes etc.

Under certain health conditions like congestive heart disease, hypertensive high blood pressure, kidney disease a restricted sodium diet is preferred. As sodium in the blood and interstitial fluid is a major factor in determining the osmotic pressure of these fluids, a reduction of sodium causes the transfer of water into the cell and loss of NaCl in urine.

General function of Na^+ and K^+ ions are as follows :

(i) The main function of Na^+, K^+ has been to maintain normal osmotic pressure of different body fluids and thereby protect the body against excessive loss of fluids which otherwise will disturb normal hydration.

(ii) The salts of Na+ and K+ with weak acids are known to form the chief buffer system respectively of extracellular and intracellular fluids. This buffer system regulates pH of various fluids.

(iii) Na and K plays an important role in normal neuro muscular irritability and excitability.

$$\text{Irritability} \propto \frac{Na^+ \; K^+}{Ca^{2+},\; Mg^{2+},\; H^+}$$

(iv) Both Na and K maintain proper viscosity of blood by regulating degree of hydration of the plasma protein.

(v) Various digestive fluids are secreted with the help of the Na and K. Gastric HCl gets derived from NaCl of blood and pancreatic juice, bile etc. are derived from blood K and Na salts.

(vi) An important role is played by K^+ in storage of protein and glycogen. Potassium enters in extra cellular fluid during the period of cell growth and repair, during this time increased protein anabolism taking place spontaneously or induced by such agents as growth hormone. Deposition of 1 gm of cell protein needs retention of about 0.4 mg of K. Similarly storage of 1 gm of glycogen in linear muscle causes the passage of about 0.15 mg of K in intra cellular fluid.

(vii) The alkali metal ions are weak lewis acid and form weak complexes. The complex formation with oxygen and N donor drugs make them very important in various drugs in bio system. The encapsulation of cation by crown ether is selectively depending on cation size. The size of the Na^+ and K^+ is appropriate to from bond in hole of macrocycles.

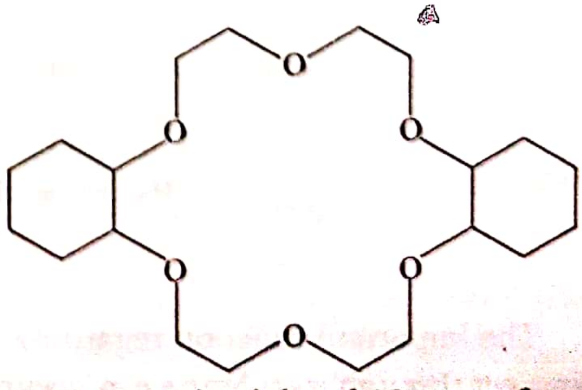
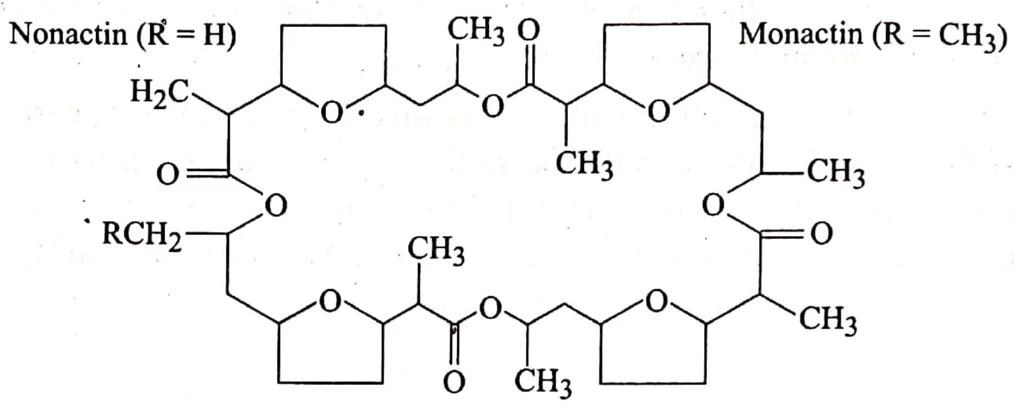
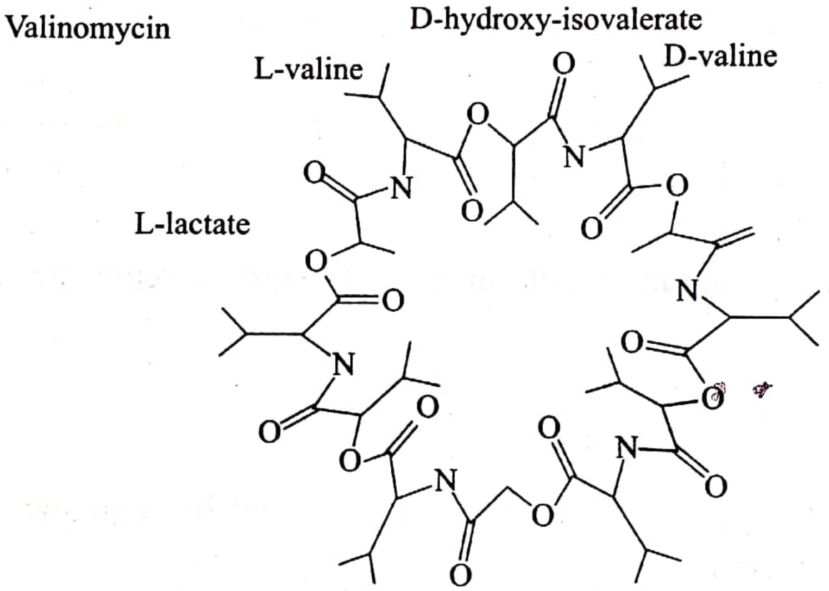


Fig. 8.1 Dicyclohexyl 18 crown-6

The ligand form complex selectively with K^+ than Na^+. Some macrocyclic antibiotics such as Nonactin, Valinomycin have high degree of cation specificity for K^+ and Rb^+.



(a)



(b)

Fig. 8.2

A synthetic peptide has been prepared which binds K^+ structure of the molecule as given below :

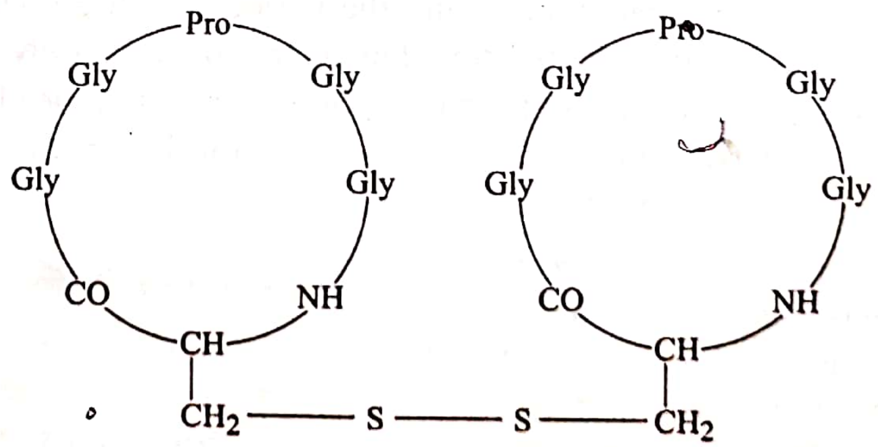


Fig. 8.3

The important function regarding alkali earth metal is pump system by which ion transport through membrane can occur. Sodium Na^+/K^+ pump is associated with the active transport of the ions across the cell membrane. The permeability properties of cell membrane are dependent upon the structure of the membrane and the presence of enzyme system that operate ion pump. In the mechanistic system the cell are outer membranes as well as the membranes that separate internal component of the cell also involved. The control of cell permeability is a most important aspect of medicine. Drugs may act by conferring liposolubility upon the other species or by preventing the transport of ions.

Na/K Pump : The sodium pump is associated with the active transport of sodium and potassium across the cell membrane. With the possible exception of certain plant cells, ion transport is associated with phosphorylation. Cells are enclosed by a membrane about 70 Å thick and composed of double layer of protein separated by lipids. Cation cannot pass through the lipid layer without encapsulation. Thus the enclosed cation presents an organic lipid soluble surface to the membrane. In most-animals cells the concentration of K^+ is about 0.15 M and Na^+ is about 0.01 M. In fluid outside the cells the concentration of Na^+ is about 0.15 M and K^+ is less than 0.004 M. Maintenance of these large concentration gradient require a sodium pumps. The energy of transport of ion is provided by hydrolysis of ATP. Kidney and brain cells use about 70% of the energy from ATP for this transport. In some cells each ATP molecule hydrolyzes transport of 3 Na^+ out of the cell and $2K^+$ into the cell. The K^+ is required in the cell for glucose metabolism, protein synthesis and activation of some enzymes. The transport of glucose and amino acid into the cell is coupled with Na^+ transport which is favoured by great concentration gradient. The Na^+ entering cell in this way must be pumped out again. The carrier of the ions is now regarded as phospho protein (in which phosphate is bound to a serine group) which binds K^+ not Na^+. On phosporylation it will bind Na^+ not K^+. The phosphorylation and Na^+ binding occurs at inner surface of the membrane (where ATP $\rightarrow$ ADP). The system is then transported to outer cell where it is dephosphorylated giving original phosphoprotein which releases Na^+ and binds K^+ prior to its return to inner surface. It is then phosphorylated. K^+ is released into the cell and Na^+ is bound to efflux from the cell.

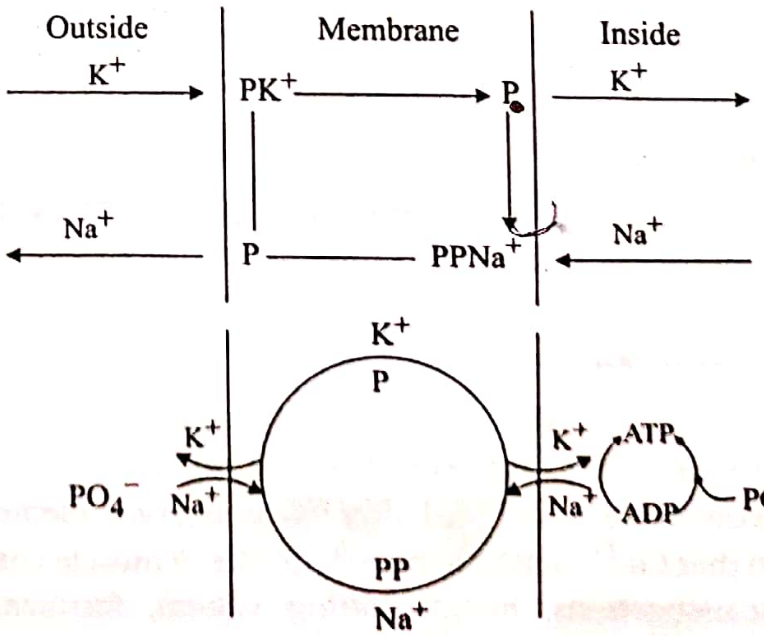


Fig. 8.4

The energy involved in pump system is Na^+, K^+ activated ATPase. When the outer sites are filled with K^+ and inner one with Na^+ a conformational change occurs rotating the sites and alternating the site preference. This releases K^+ inside the cell and Na^+ outside the cell. This is a revolving door for transport of Na^+ and K^+ in opposite direction. It is called eversion like motions through a revolving door. Three sodium ions are replace by $2K^+$ ions. The attachment of K^+ ion triggers dephosphorylation. The figure can be given as follows :

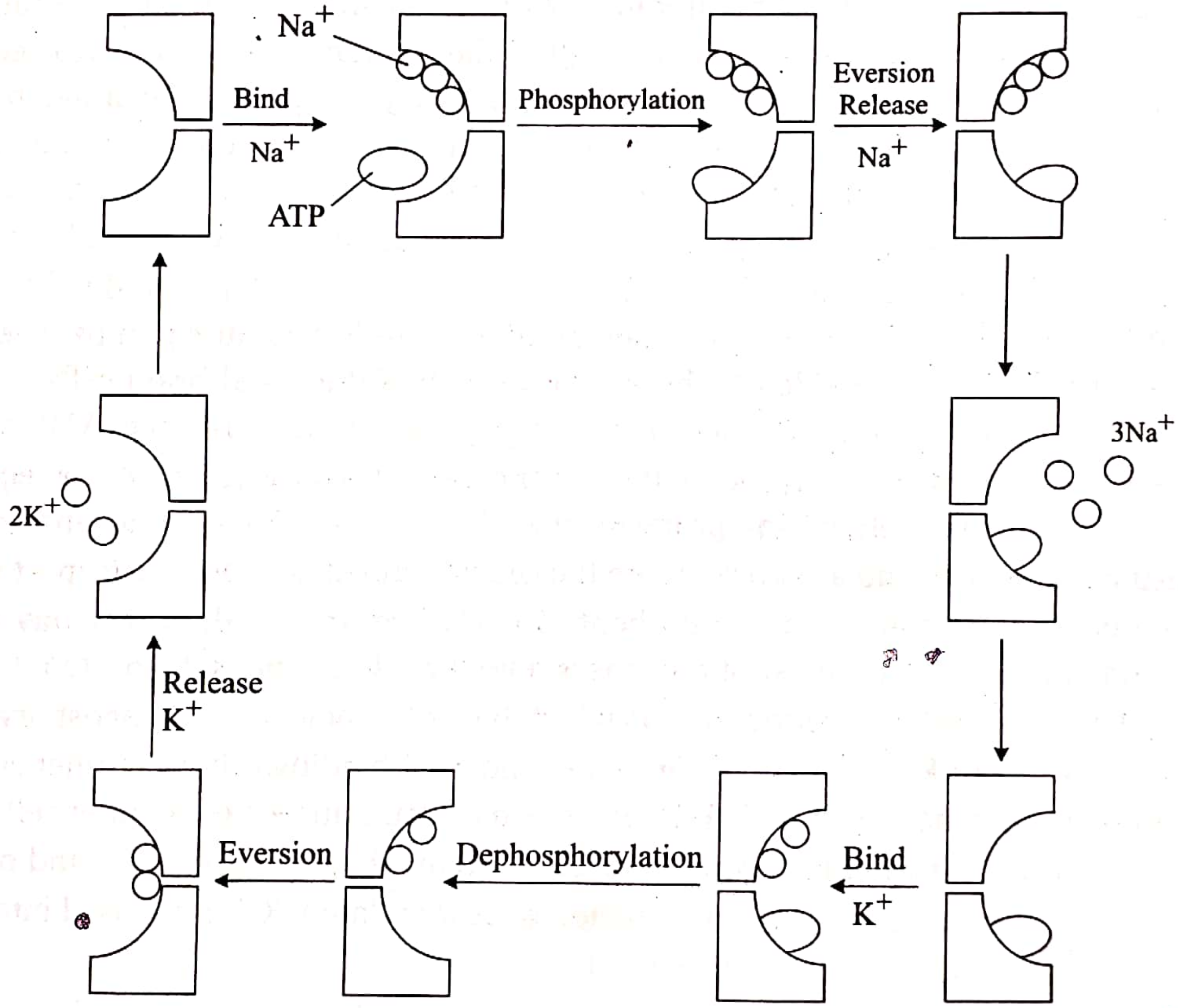


Fig. 8.5

The overall reaction is

$$ATP + H_2O + 3Na^+ \text{ (inside)} + 2K+ \text{ (outside)} \rightarrow ADP + Pi + H_2O + 3Na^+ \text{ (outside)} + 2K+ \text{ (inside)}$$

B. Role of Ca^{2+} and Mg^{2+}

(i) Calcium : Calcium like many other inorganic elements is important in biological system. The presence and central role of calcium in mammalian bones and other mineralized tissue were recognized after its discovery as element by lavy. Today it is widely recognized that Ca^{2+} plays an important role in muscle contraction, secretion, glycolysis and gluconeogenesis, blood clotting system, fertilization, cell division, hormonal activities and also as dominant biomineral.

Table 8.8 : Calcium Controlled Events In cells

	Activity	Controlled events or systems
1	Photo synthesis	Dioxygen release
2	Oxidative phosphorylation	Dehydrogenases
3	Receptor responses	(a) Nerve synapse
		(b) IP3 - linked reaction
4	Contractive devices	(a) Muscle triggering
		(b) Cell filament control
5	Phosphorylation	Activation of kinases
6	Metabolism	Numerous enzyme

Muscle contraction : The major constituents of muscle fibres are the proteins that is 54% myosin and 27% actin. 0.12% tropomyosin and tropanin and actinin.

Each muscle fibre is made up of some 1000 fibrits. Myosin and actin one organised in the form of true types of filament one thick and other thin. Myosin is a long, thin molecule of overall length 150 nm and includes a thicker portion (Head) 20 nm long and 4 nm breadth. The thick filaments are made up of either 180 or 360 myosin molecules. The actin molecule is a globular protein: having 5.5 nm diameter. The thin filaments are made up of double stranded chains of these actin molecules. The two proteins differ very much in their primary structure Muscle contraction and relaxation results from the sliding of one filament over the other. The fig is as follows :

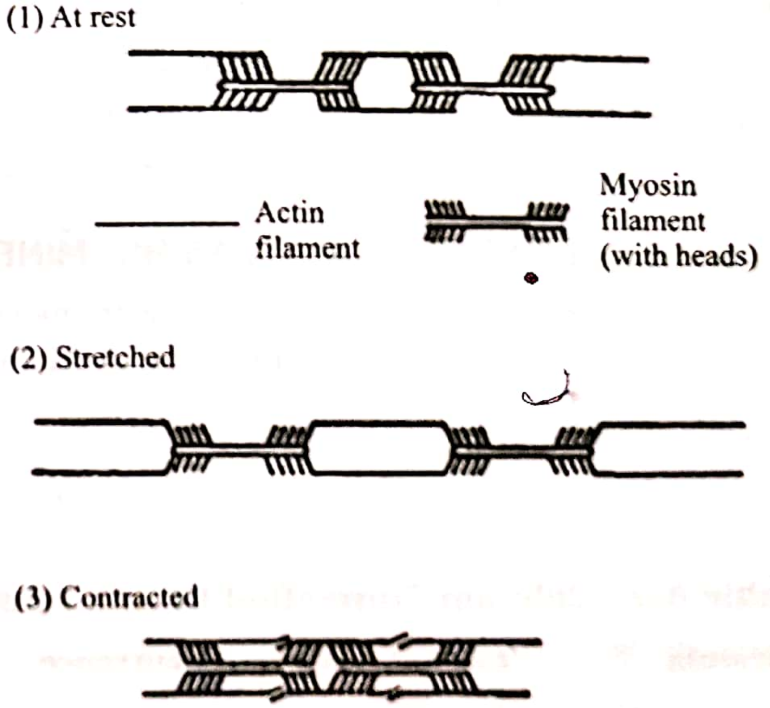


Fig. 8.6 Sliding filament model of muscle Contraction

The muscle contraction is based on interaction between the two types of filaments. Myosin heads and ATPase site of myosim is activated by Ca^{2+}. Here ATP hydrolysis takes place. This is the reaction that provides the energy for contraction. Here it is important that Mg^{2+} cannot activate this, but Mg^{2+} must be present. When ATP is hydrolyzed, interaction can occur between the filaments resulting in the sliding of one filament against another and contraction of muscle takes place. It appears that myosin readily binds Ca^{2+} and ATP.

Ca^{2+} in intracellular process : In order to influence the cellular machinery the Ca^{2+} must act with different proteins called intracellular calcium receptor e.g. Calmodulin, Troponinc, Protein kinase C etc. These intracellular calcium receptors must have certain properties in order to function :

(i) Their Ca^{2+} affinity must be such that their Ca^{2+} binding sites are essentially unoccupied at resting level.

(ii) Receptor must have adequate selectivity for Ca^{2+}.

(iii) In response to Ca^{2+} binding, a Ca^{2+} receptor must undergo some kind of conformation change.

(iv) There are some kinetic considerations. In many cells rapid response is essential so to interact swiftly within milliseconds.

Ca^{2+} in extra cellular binding proteins : The calcium concentration in extra cellular fluid is higher than intracellular concentration. In mammalian body fluid the free Ca^{2+} concentration is upto 1.25 mm. (Total is 2.45 mm). We would thus except that Ca^{2+} in extra cellular fluid play a very different role from that inside cell. One particularly important aspect of Ca^{2+} is its role in blood coagulation system. Here two new type of amino acid S-carboxy glutamic acid ("Gla") and ("Hya") bind to Calcium.

This seems to have been designed by nature as a Ca^{2+} ligand with rather special function. Ca^{2+} plays more structure role rather than enzymatic activity. It appears likely that Ca^{2+} form a link between the protein and membrane surface.

❑ CALCIUM IN MINERALIZED TISSUE (Ca AS BIO-MINERAL)

Calcium along with iron, silicon and alkaline earth metal is an important constituent of mineralized biological tissue. The formation of calcified bio-minerals is a highly regulated process and human bone is constantly being dissolved and rebuilt. When the rates of these two counter acting processes are not in balance the result may be calcification or osteoporosis which seriously reduces the strength of bone. A brief idea of calcium as bio mineral is given in table as follows :

Table 8.9 : Calcium Controlled Events In cells

Anion	Formula	Crystal form	Occurrence	Main function
Carbonate	$CaCO_3$	Calcite Argonite valerite	Sea corals molluscs and many animals and plants	Exo-skeleton Ca, Storage eye lense

Oxalate	$Ca(COO)_2H_2O$	Wheovellite wedillite	Insect eggs vertebrate store	Deterrant cyto skeleton, Ca-storage
Phosphate	$(Ca)_{10}(PO_4)_6(OH)_2$	Hydroxy apatile	Bones teeth, shells	Skeletal Ca Storage
Sulfate	$CaSO_4H_2O$	Gypsum	Jelly fish plants	Ca Storage

(ii) Magnesium : Magnesium in bio inorganic chemistry is a "Cinderalla" element. The general involvement of Mg is with phosphate compounds and phosphate metabolism. The binding of Mg in chlorophyll pigment in plants is another important role. These two roles are quite different since in the first, Mg is a freely diffusible cation in aqueous solution involved not only in catalysis but in a multitude of controls, while in second magnesium is an immobilized element in a light capture device in a membrane.

The charge density of Mg^{2+} and its radius 0.6 Å is higher than that on any other freely available charge centre in biology, so it dominates binding to negative centres of high charge density e.g. pyrophosphate.

Magnesium is found in surrounding membrane of protein, polysaccharide and lipid. It is used here to cross link the carboxylated and phosphorylated anionic polymer and shares this role with calcium. They use to stabilize external structure of cells. In biology binding of Mg^{2+} with pyrophosphate and polyphosphate is observed. Most of the energy transfer due to NATP and the phosphate transfer of kinases depends on Mg^{2+}.

The requirement of Mg rather than any another metal ion in this light capturing system (chlorophyll) is that it is perhaps an element with such low atomic number, does not enhance fluorescence and also does not possess redox properties; Mg does not interfere with photo and free radical reaction of chlorine. Moreover the presence of Mg in ring gives the ring an approximate tetragonal symmetry and hence enhances the molecular extinction coefficient e around 650 - 700 nm relative to the low symmetry metal free molecule while moving absorption maximum to longer wave length.

Table 8.10 : Magnesium requiring enzymes and polynucleotides

Kinases	Phosphate transfer from ATP Mg
ATPases	ATP Mg is the substrate
Methyl as partase	Mg is bond to the enzyme
Ribulose bisphosphate carboxylase	Mg binds to intermediate and enzyme
Myosin ATPase	Mg, ATP is the substrate
tRNA	One strong site, fold stabilization Half crucifix structure
r-RNA	Stabilization of folds
m-RNA	Attachment to ribosome
DNA	Crucifix structure

❑ ROLE OF 'D' BLOCK ELEMENTS IN BIO-SYSTEM

(a) Vanadium : It is known that vanadium in extremely small amounts is a nutritional requirement for many types of organism including her animals. Vanadium containing haloperoxidases occurring in some brown and red algae containing V(V) bonded to oxygen and nitrogen donors. Vanadium having rich oxygen chemistry associated with oxyanion and oxycation species. It can be predicted to associate as oxidant in catalytic activities. Still the biological function in unknown. Vanadium in a sea squirt (a primitive vertebrate) is concentrated in blood cells as major cellular transition metal. It is expected to play a role in dixoygen transport. Some activity in nitrogen fixation is also predicted.

Chromium: It is an essential trace element in mammals having daily requirement of about 50-200 μg in the form of Cr(III). Its participation is expected in glucose and lipid metabolism. In low molecular weight Cr binding substance, an aligopeptide, a tetra nuclear Cr(III) carboxylate complex may be present. Cr(VI) is toxic and possesses mutagenic and carcinogenic activity. Chromate (CrO_4^{4-}) is taken up by the cell where it is converted to Cr(III). The special Cr(V) and Cr(VI) in reduction sequence coordinate to phosphate and thus may be involved in DNA damage.

Manganese : Mn plays a critical role in evaluation of oxygen which is catalyzed by the proteins of photo synthetic reaction center. Mn is the energy source for a series of redox reaction in photo system I and II. In photo system II a strong oxidizing agent is formed and is responsible for the production of molecular oxygen. This oxidizing agent is reduced and recycled for further use by interaction with a manganese complex.

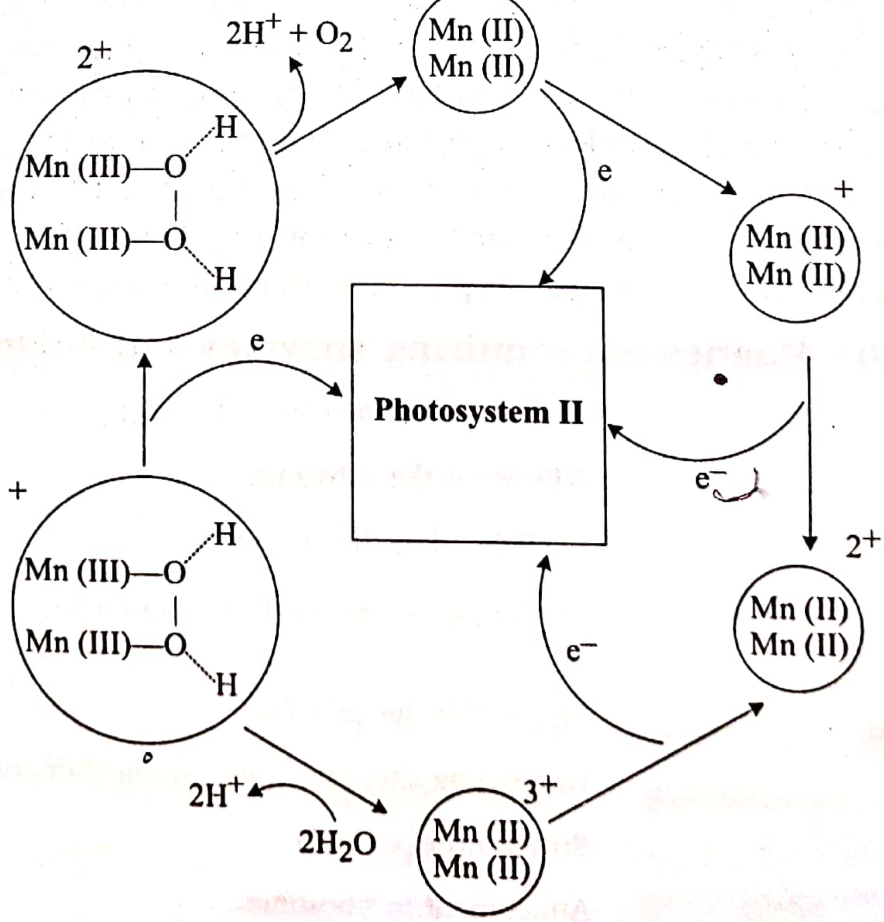


Fig. 8.7

The superoxide dismutase of bacteria and mitochondria as well as pyrunate carboxylase in mammals are also manganese proteins, responsible for various biological processes.

Iron : Iron is truly essential for living system. Its versatility is unique. It is at the active center of molecules responsible for oxygen transport and electron transport and it is found in or with, such diverse metalloenzymes as various oxidases, hydrogenases, reductases, dehydrogenases, deoxygenaous and dehydrases.

Iron is involved in the whole gamut of life forms from bacteria to man. Iron is extremely abundant in each crust and it has two readily inter converted oxidation states, in biological system there are three well characterized iron systems; proteins that contain one or more iron porphyrin units such as hemoglobin, myoglobin and cytochrome P450 and a diverse group of proteins that contain non heme iron like nitrogenase, rubridoxin, feridoxin and non home diron are bridged species such as hemerytrin, methanemonoxygenase, ribonuclotide reductase. A lot is known about the active sites by extensive spectral studies like Mossbauert, Infrared, Raman H, ^{17}O NMR, and X-ray crystallography.

Cobalt : Cobalt complex Co(III) of corrinoid ligands are found in many organisms including man and are known as cobalamine, they are naturally occurring organnometallic compound. The human body contains about 5 mg of cobalamine (vitamin B12) and its deficiencies causes diseases such as aneamia, Vitamin B_{12} can undergo one electron and two electron reduction leading to Co II and Co I respectively.

A cobalt III complex (d^6), cobalamines strictly adhere to an octahedral geometry, with an axial benzimidaole nitrogen ligand. It appears that in protein bound B_{12} this axial ligand is replaced by a histidine provided by the peptic chain, with consequent configuration change that influence the reactivity of cobalamine unit.

$$B_{12}(\text{CoIII})] \xrightarrow{\text{NaOH (le)or}} [B_{12}(\text{CoII})] \xrightarrow{\text{FAD (2e)}} [B_{12}(\text{CoI})]$$

Nickel : Ni(I) and Ni(II), (III) species are important because of the possible involvement of these oxidation state in nickel containing metalloenzyms Nickel is an essential component in at least four types of enzymes; urease, carbonmonoxide dehydrogenase, (COOH, acetyl coenzyme A) hydrogenase and methyl S coenzyme M reductase. Nickel containing enzymes of certain methanogenic organism also catalyze the synthesis of acetyl coenzyme A. Here Ni center is linked to an Fe4S4 cubane. The redox active Ni center in hydrogenases probably has a N3S2 coordination. Various mimics have been prepared with Ni to explain enzymatic activity.

Copper : Copper is the third most abundant metallic element in human body. It also occurs in all forms of life and it plays a role in the action of a multitude of enzymes that catalyze a great variety of reactions. There are many kinds of copper sties, which are enzyme active sites. Most common are those containing Cu(II) having tetragonally coordinated sites. Super oxide dismutase (CuZnSOD) is an example of normal site. Its function is to catalyze following reaction.

$$2O_2^- + 2H^+ \rightarrow H_2O_2 + O_2$$

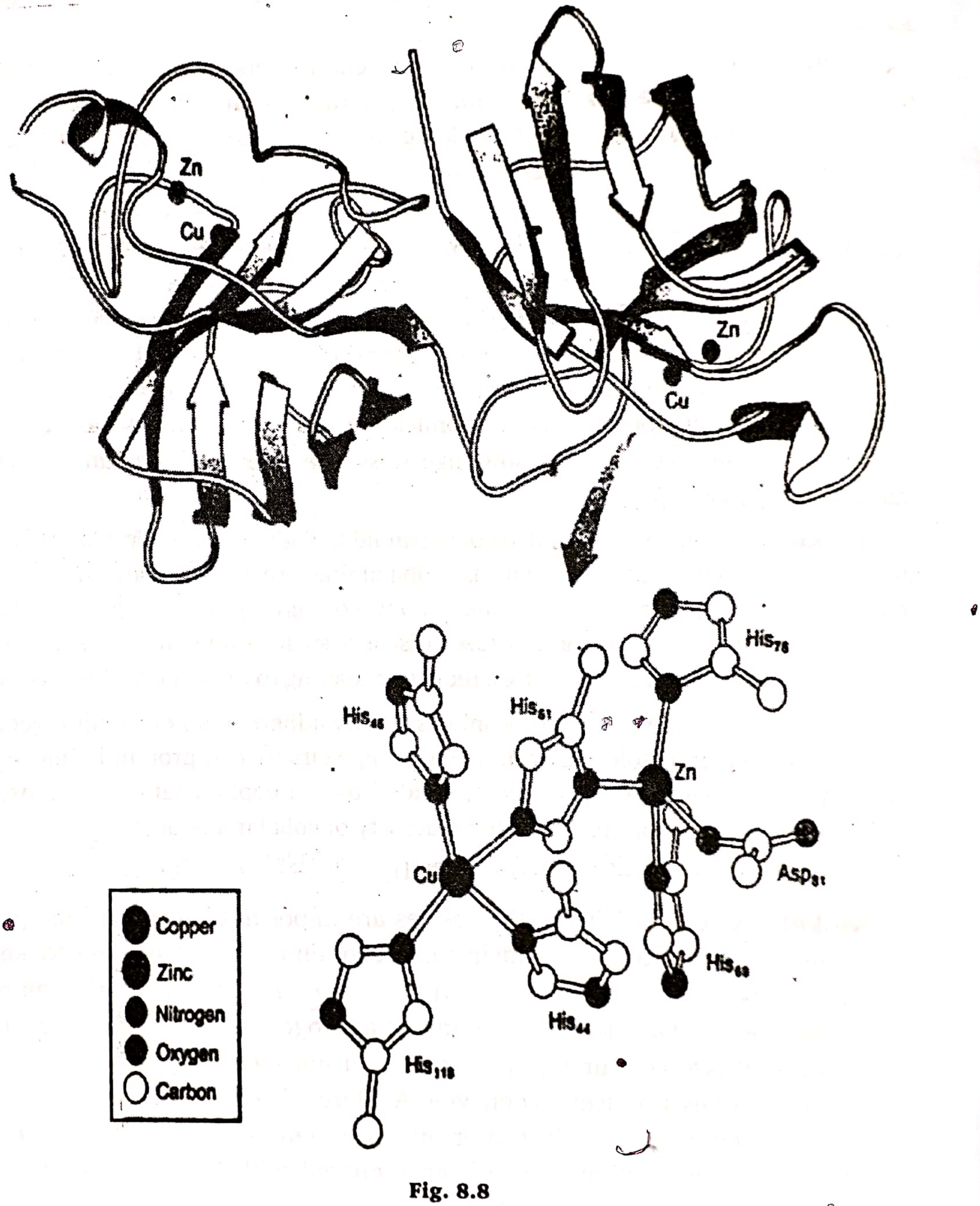


Fig. 8.8

Two Cu sites (Cu II (O_2^{2-}) - Cu II) is seen in hemocyanins. These are respiratory enzymes found in molluscs and arthropodes. They act cooperatively. The deoxy form is colourless containing Cu I while blue oxy has Cu II.

Similarly Cy to chrome C oxidase that catalyzes the terminal step in the four electron reduction of O_2 to $2H_2O$ contains both Fe and Cu (two kinds of sites CuA and CuB)

Zinc : It is not a 'd' block element but in active site it becomes the same. Zinc is an important metal in life processes. It is essential to all forms of life and a large number of diseases and congential disorders have been traced to zinc deficiency. In adult human body 2 to 3 gm of Zinc is required. In 1940 carbonic anhydrase was shown to be a zinc enzyme and in 1955 carboxypeptidases was recognized. Since then more than 300 other Zn-enzymes have been reported. In addition to its role at active sites of hundreds of enzymes, there are cases where zinc serves a purely structural role. The most notable of there are "zinc fingers", "twists" and "clusters". These occur in DNA binding proteins where they stabilize correct binding sites. Metavothioneins was discovered by B.L. Vallee in 1957 as storage protein for Zn.

Molybdenum : It has long been known as one of the biologically active transition elements in second series. It is intimately involved in the function of enzymes called nitrogenases which causes atmorpheric N_2 to be reduced to NH_3 or its derivatives, Mo occurs in more than 30 enzymes. Enzymes containing Mo are of two types (i) Nitrogenases which are required for converting atmospheric nitrogen to nitrogen compounds (ii) Molybdenum cofactor.

Tungusten : Tungusten is the only element in third transition series known to have natural biological functions. Not only found with Mo, there are some enzymes that are known only with W. In a tungusten containing enzyme, ferridexin aldehyde oxide reductase the metal site is shown in figure below:

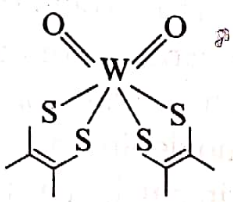


Fig. 8.9.

□□□