KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed University Established Under Section 3 of UGC Act 1956)

COIMBATORE-21

DEPARTMENT OF CHEMISTRY

B.Sc Chemistry Syllabus

	MAJOR ELECTIVE-I	**Semester -V**
15CHU505C	**BIOINORGANIC CHEMISTRY**	**5H-5C**

Instruction Hours/week:L: 5 T:0 P:0 Marks: Internal:40 External: 60 Total:100

Scope

The course provides the applications of Chemistry in the medical sciences. The course allows one to get a fundamental idea about the bioinorganic Chemistry. The course helps the students in improving their diverse skills in various areas such as laboratory skills, numerical and computing skills, ability to approach to the problems both analytically and logically, time management skills, etc.

Programme outcome

The students will be able

1. To acquaint the students with the applications of Bioinorganic Chemistry to the medicinal chemisty.
2. To Identify key structural molecules for metal bonding in biological molecules.
3. To learn about the metals in life process and oxygen carrier systems.
4. To understand about the metals used in plant life and about metal poisoning.

Programme learning outcome

Students will be capable to know the new knowledge in recognizing the requirement of metals and also its risk in our daily life. They will be able to learnt different environmental cycles. Student will have an ability to read the types, properties and reactivity of different type of metal toxicity. At the end of this course, the student will be able to view the world around them in chemical terms.

Methodology

Black board teaching and Group discussion.

UNIT-I

Metals in Life Processes

Na-K-charge carriers & osmotic pressure, relation to sensitivity of nerves and control on muscles, Mg-Ca complexes with nucleic acid, nerve impulse transmission, trigger reaction, Mn, Fe, Co, Cu, Mo, ferridoxins, Zn-super acid catalysis.

UNIT-II

Oxygen Carrier Systems

Structure and mechanism of hemoglobin, vitamin B12, B12 co-enzyme myoglobin, synthesis of oxygen carriers.
Photosynthesis : Porphyrins ring complexes and redox mechanism.

UNIT-III

Nitrogen Fixation

Nitrogen in biosphere, nitrogen cycle, nitrification role of microorganisms, nitrogen fixation in soils

UNIT-IV

Metal poisoning and drug action of Inorganic complexes compounds

Metal poisoning, treatment by using chelating agent, mercury, lead & cadmium poisoning & treatment. Platinum complexes in treatment of cancer, metal deficiency and use of metal chelates.

UNIT-V

Trace Metals in Plant Life

Micronutrients in soil, role of micronutrients in plant life
Biogeochemistry : Biodegradation of minerals bacteria leaching and its applications.

TEXT BOOK:

1. A.K.De , 2001 Environmental chemistry, Rohan Ahmed Publishers.
2. Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata.
3. Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

REFERENCES :

1. Ochiai E-I 1977. Bioinorganic Chemistry. Allyn and Bacon, Inc., Massachusetts, Boston.
2. Williams, 1983. An Introduction to Bioinorganic Chemistry, C.C. Thomos Spring III.
3. Wallace, 1962. Decade on synthetic chelating agent in Inorganic plant nutrition.
4. E. Crabb and E.Moore, 1995. Metals in Life , Royal Chemical Society, Washington.
5. Zagic J.E., 1969. Microbial Biogeochemistry, Academic press, New York.
6. Ahuja S and E.M. Cohen, 1973. Chemical Analysis of the Environment and other modern techniques, Plenum press, New York.

KARPAGAM ACADEMY OF HIGHER EDUCATION

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Coimbatore-641021

DEPARTMENT OF CHEMISTRY

LECTURE PLAN

BIO-INORGANIC CHEMISTRY

Name of the Faculty: R Kumar Department : CHEMISTRY
Semester : V Year : III
Course Code : 15CHU505C Section : B

UNIT-1 **METALS IN LIFE PROCESSES** **Total hours: 15**

S.NO	LECTURE DURATION	TOPICS TO BE COVERED	SUPPORT MATERIALS
1.	**1**	Na-K Charge carriers (function)	**T1: 109-112**
2.	**1**	Na-K Charge carriers (selectivity)	**T1: 109-112**
3.	**1**	Osmotic Pressure	**T1: 109-112**
4.	**1**	Relation to sensitivity of nerves and control on muscles	**T1: 112-114**
5.	**1**	Mg-Ca complexes with nucleic acid	**T1: 24-25, 51-55**
6.	**1**	Mg-Ca complexes with nucleic acid	**T1: 24-25, 51-55**
7.	**1**	Nerve impulse transmission	**T1: 86-88**
8.	**1**	Trigger reaction	**T1: 114**
9.	**1**	Cu	**T1: 70-74**
10.	**1**	Mn , Co	**T1: 82**
11.	**1**	Fe	**T1: 61-64**
12.	**1**	Mo, Ferridoxins	**T1:82-83; 64-66**
13.	**1**	Zn-super acid catalysis	**T1: 75-79**
14.	**1**	Revision and discussion of possible questions	
15.	**1**	Revision and discussion of possible questions	

Text book

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

UNIT-2

OXYGEN CARRIER SYSTEM **Total no. of hours: 15**

S.NO	LECTURE DURATION	TOPIC TO BE COVERED	SUPPORT MATERIALS
1.	**1**	Biological oxygen carriers	**T1: 123**
2.	**1**	Structure of Hemoglobin	**T1: 124-132**
3.	**1**	Mechanism of Hemoglobin	**T1: 124-132**
4.	**1**	Structure of Myoglobin	**T1: 124-132**
5.	**1**	Mechanism of Myoglobin	**T1: 124-132**
6.	**1**	Structure of Vitamin B12	**T1: 305 - 307,**
7.	**1**	Mechanism of Vitamin B12	**T1: 309- 314**
8.	**1**	B 12 co-enzyme	**T1: 316 - 320**
9.	**1**	Synthesis of oxygen carriers	**T1: 148 - 151**
10.	**1**	Photo synthesis	**T1: 256-258**
11.	**1**	Porphyrin ring complexes	**T1: 258- 260**
12.		Redox reaction	**T1: 260-264**
13.		Redox reaction	**T1: 260-264**
14.	**1**	Revision and Discussion of possible questions	
15.	**1**	Revision and Discussion of possible questions	

Text book

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T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

UNIT -3

NITROGEN FIXATION **Total no. of hours: 15**

S.NO	LECTURE DURATION	TOPIC TO BE COVERED	SUPPORT MATERIALS
1	**1**	Nitrogen in biosphere	**T2: 182-183**
2	**1**	Inorganic minerals of soil	**T2: 144-145**
3	**1**	Nitrogen in soil	**T2: 167**
4	**1**	Biosphere and Natural Cycles	**T2: 182-183**
5	**1**	Nitrogen cycle- Introduction	**T2: 189-192**
6	**1**	Importance of Nitrogen cycle	**T2: 189-192**
7	**1**	Nitrification role of micro-organism	**T2: 148-149, 167**
8	**1**	Nitrogen fixation	**T2 : 34**
9	**1**	Nitrogen fixation in soils (biological)	**T1: 246, T2:189-190**
10	**1**	Nitrogen fixation in soils (abiological)	**T1: 243, 255, T2: 190**
11	**1**	Nitrogen fixation in soils (abiological)	**T1: 243, 255, T2: 190**
12	**1**	Importance of nitrogen in environment	**T2: 182**
13	**1**	Revision and Discussion of possible questions	
14	**1**	Revision and Discussion of possible questions	
15	**1**	Recapitulation and discussion of previous year questions	

Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

UNIT -4

METAL POISONING AND DRUG ACTION OF INORGANIC COMPLEXES COMPOUNDS

Total no. of hours: 15

S.NO	LECTURE DURATION	TOPIC TO BE COVERED	SUPPORT MATERIALS
1	**1**	Metal Poisoning	**T2: 222-227**
2	**1**	Metal Poisoning	**T2: 222-227**
3	**1**	Chelating agent- Introduction	**T1: 372**
4	**1**	Treatment by using chelating agent	**T2: 257-263**
5	**1**	Treatment by using chelating agent	**T2: 257-263**
6	**1**	Poisoning and treatment of Mercury (Hg)	**T2: 241-242**
7	**1**	Poisoning and treatment of Lead (Pb)	**T2: 242-245**
8	**1**	Poisoning and treatment of Cadmium (Cd)	**T2: 245- 246**
9	**1**	Platinum complexes and its treatment in cancer	**T1: 385-386**
10	**1**	Metal deficiency	**T2: 223-224**
11	**1**	Uses of metal chelates	**T1: 372-380**
12	**1**	Uses of metal chelates	**T1: 372-380**
13	**1**	Revision and Discussion of possible questions	
14	**1**	Revision and Discussion of possible questions	
15	**1**	Recapitulation and Discussion of previous year question paper	

Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

UNIT -5

TRACE METALS IN PLANT LIFE **Total no. of hours: 15**

S.NO	LECTURE DURATION	TOPIC TO BE COVERED	SUPPORT MATERIALS
1	**1**	Micronutrients in soil	**T2: 169-170**
2	**1**	Micronutrients in soil	**T2: 170**
3	**1**	Role of micronutrients in plant life	**W_1**
4	**1**	Role of micronutrients in plant life	**W_1**
5	**1**	Bio-geo chemistry	**W_2**
6	**1**	Bio-degradation	**T2: 142**
7	**1**	Bio-degradation of minerals	**W_2**
8	**1**	Bio-degradation of minerals by bacteria leaching	**W_2**
9	**1**	Bio-degradation of minerals by bacteria leaching	**W_2**
10	**1**	Application of minerals bio-degradation by bacteria	**W_2**
11	**1**	Application of minerals bio-degradation by bacteria	**W_2**
12	**1**	Revision and Discussion of possible questions	
13	**1**	Revision and Discussion of possible questions	
14	**1**	Recapitulation and Discussion of previous year question papers	
15	**1**	Recapitulation and Discussion of previous year question papers	

Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

Website

W1: https://micronutrients.co.in//

W2: https: // bacteria leaching/ Wikipedia.co.in//

BIOINORGANIC CHEMISTRY

Introduction

Bioinorganic chemistry is a field that examines the role of metals in biology. Bioinorganic chemistry includes the study of both natural phenomena such as the behavior of metalloproteins as well as artificially introduced metals, including those that are non-essential, in medicine and toxicology. Many biological processes such as respiration depend upon molecules that fall within the realm of inorganic chemistry. The discipline also includes the study of inorganic models or mimics that imitate the behaviour of metalloproteins.

As a mix of biochemistry and inorganic chemistry, bioinorganic chemistry is important in elucidating the implications of electron-transfer proteins, substrate bindings and activation, atom and group transfer chemistry as well as metal properties in biological chemistry.

Composition of living organisms

About 99% of mammals' mass are the elements carbon, nitrogen, calcium, sodium, chlorine, potassium, hydrogen, phosphorus, oxygen and sulfur. The organic compounds (proteins, lipids and carbohydrates) contain the majority of the carbon and nitrogen and most of the oxygen and hydrogen is present as water. The entire collection of metal containing biomolecules in a cell is called the metallome.

History

Paul Ehrlich used *organoarsenic* ("arsenicals") for the treatment of syphilis, demonstrating the relevance of metals, or at least metalloids, to medicine, that blossomed with *Rosenberg's* discovery of the anti-cancer activity of *cisplatin* (cis-$PtCl_2(NH_3)_2$). The first protein ever crystallized (see James B. Sumner) was urease, later shown to contain nickel at its active site. Vitamin B_{12}, the cure for pernicious anemia was shown crystallographically by Dorothy Crowfoot Hodgkin to consist of a cobalt in a corrin macrocycle. The Watson-Crick structure for DNA demonstrated the key structural role played by phosphate-containing polymers.

Theme in Bio-inorganic chemistry

Metal ion transport and storage

It covers a diverse collection of ion channels, ion pumps (e.g. NaK ATPase), vacuoles, siderophores, and other proteins and small molecules which control the concentration of metal ions in the cells. One issue is that many metals that are metabolically required are not readily available owing to solubility or scarcity. Organisms have developed a number of strategies for collecting such elements and transporting them.

Oxygen transport and activation proteins

Aerobic life make extensive use of metals such as iron, copper, and manganese. Heme is utilized by red blood cells in the form of hemoglobin for oxygen transport and is perhaps the most recognized metal system in biology. Other oxygen transport systems include myoglobin, hemocyanin, and hemerythrin. Oxidases and oxygenases are metal systems found throughout nature that take advantage of oxygen to carry out important reactions such as

energy generation in cytochrome c oxidase or small molecule oxidation in cytochrome P450 oxidases or methane monooxygenase. Some metalloproteins are designed to protect a biological system from the potentially harmful effects of oxygen and other reactive oxygen-containing molecules such as hydrogen peroxide. These systems include peroxidases, catalases, and superoxide dismutases. A complementary metalloprotein to those that react with oxygen is the oxygen evolving complex present in plants. This system is part of the complex protein machinery that produces oxygen as plants perform photosynthesis.

Environmental chemistry

Environmental chemistry traditionally emphasizes the interaction of heavy metals with organisms. Methylmercury has caused major disaster called Minamata disease. Arsenic poisoning is a widespread problem owing largely to arsenic contamination of groundwater, which affects many millions of people in developing countries. The metabolism of mercury- and arsenic-containing compounds involves cobalamin-based enzymes.

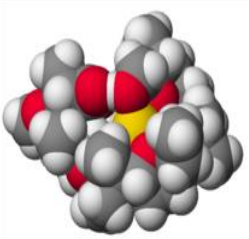
Metals in medicine

A number of drugs contain metals. This theme relies on the study of the design and mechanism of action of metal-containing pharmaceuticals, and compounds that interact with endogenous metal ions in enzyme active sites. The most widely used anti-cancer drug is cisplatin. MRI contrast agent commonly contain gadolinium. Lithium carbonate has been used to treat the manic phase of bipolar disorder. Gold antiarthritic drugs, e.g. auranofin have been commerciallized. Carbon monoxide-releasing molecules are metal complexes have been developed to suppress inflammation by releasing small amounts of carbon monoxide. The cardiovascular and neuronal importance of nitric oxide has been examined, including the enzyme nitric oxide synthase.

Biomineralization

Biomineralization is the process by which living organisms produce minerals, often to harden or stiffen existing tissues. Such tissues are called mineralized tissues. Examples include silicates in algae and diatoms, carbonates in invertebrates, and calcium phosphates and carbonates in vertebrates.Other examples include copper, iron and gold deposits involving bacteria. Biologically-formed minerals often have special uses such as magnetic sensors in magnetotactic bacteria (Fe_3O_4), gravity sensing devices ($CaCO_3$, $CaSO_4$, $BaSO_4$) and iron storage and mobilization ($Fe_2O_3 \cdot H_2O$ in the protein ferritin). Because extracellular[7] iron is strongly involved in inducing calcification,[8][9] its control is essential in developing shells; the protein ferritin plays an important role in controlling the distribution of iron.

Types of inorganic elements in biology



Like many antibiotics, monensin-A is an ionophore that tighlty bind Na^+(shown in yellow).

Alkali and alkaline earth metals

The abundant inorganic elements act as ionic electrolytes. The most important ions are sodium, potassium, calcium, magnesium, chloride, phosphate, and the organic ion bicarbonate. The maintenance of precise gradients across cell membranes maintains osmotic pressure and pH. Ions are also critical for nerves and muscles, as action potentials in these tissues are produced by the exchange of electrolytes between the extracellular fluid and the cytosol. Electrolytes enter and leave cells through proteins in the cell membrane called ion channels. For example, muscle contraction depends upon the movement of calcium, sodium and potassium through ion channels in the cell membrane and T-tubules.

Transition metals

The transition metals are usually present as trace elements in organisms, with zinc and iron being most abundant. These metals are used in some proteins as cofactors and are essential for the activity of enzymes such as catalase and oxygen-carrier proteins such as hemoglobin. These cofactors are bound tightly to a specific protein; although enzyme cofactors can be modified during catalysis, cofactors always return to their original state after catalysis has taken place. The metal micronutrients are taken up into organisms by specific transporters and bound to storage proteins such as ferritin or metallothionein when not being used. Cobalt is essential for the functioning of vitamin B12.

Main group compounds

Many other elements aside from metals are bio-active. Sulfur and phosphorus are required for all life. Phosphorus almost exclusively exists as phosphate and its various esters. Sulfur exists in a variety of oxidation states, ranging from sulfate (SO_4^{2-}) down to sulfide (S^{2-}). Selenium is a trace element involved in proteins that are antioxidants. Cadmium is important because of its toxicity.

UNIT-1

Metals in Life Processes

Na-K-charge carriers & osmotic pressure, relation to sensitivity of nerves and control on muscles, Mg-Ca complexes with nucleic acid, nerve impulse transmission, trigger reaction, Mn, Fe, Co, Cu, Mo, ferridoxins, Zn-super acid catalysis.

Na+/K+-ATPase

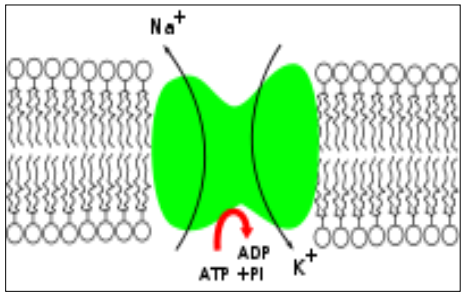
(sodium-potassium adenosine triphosphatase, also known as the **Na+/K+ pump** or **sodium-potassium pump**) is an enzyme (an electrogenic transmembrane ATPase) found in the plasma membrane of all animal cells.

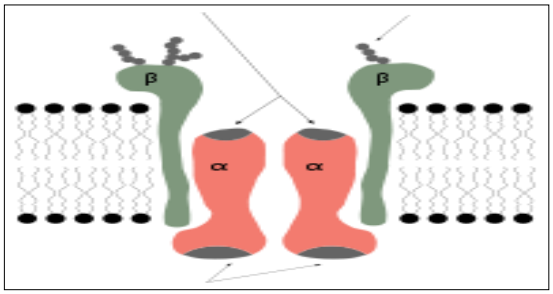
The Na+/K+-ATPase enzyme is a solute pump that pumps sodium out of cells while pumping potassium into cells, both against their concentration gradients. This pumping is active (i.e. it uses energy from ATP) and is important for cell physiology. An example application is nerve conduction.

It has antiporter-like activity, but since it moves both molecules against their concentration gradients it is not a true antiporter, which would require one solute to move with its gradient.

Sodium-potassium pumps

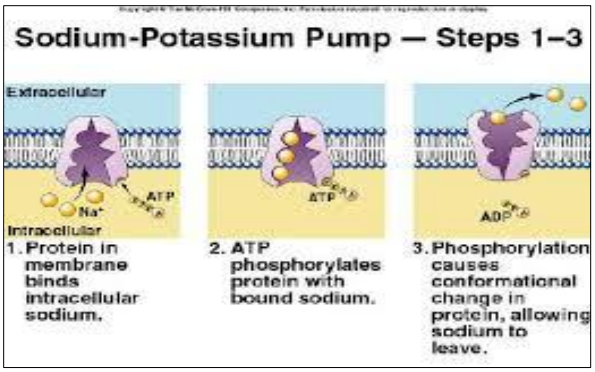
Active transport is responsible for the fact that cells contain a relatively high concentration of potassium ions but low concentrations of sodium ions. The mechanism responsible for this is the sodium-potassium pump, which moves these two ions in opposite directions across the plasma membrane. This was investigated by following the passage of radioactively labeled ions across the plasma membrane of certain cells. It was found that the concentrations of sodium and potassium ions on the two sides of the membrane are interdependent, suggesting that the same carrier transports both ions. It is now known that the carrier is an ATP-ase and that it pumps three sodium ions out of the cell for every two potassium ions pumped in.

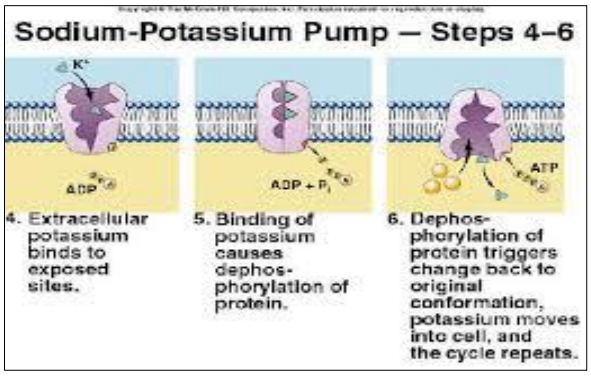




Function

The Na+/K+-ATPase helps maintain resting potential, effect transport, and regulate cellular volume. It also functions as a signal transducer/integrator to regulate MAPK pathway, ROS, as well as intracellular calcium. In most animal cells, the Na+/K+ -ATPase is responsible for about 1/5 of the cell's energy expenditure. For neurons, the Na+/K+-ATPase can be responsible for up to 2/3 of the cell's energy expenditure.





Resting potential

The Na+/K+-ATPase, as well as effects of diffusion of the involved ions maintain the resting potential across the membranes.

In order to maintain the cell membrane potential, cells keep a low concentration of sodium ions and high levels of potassium ions within the cell (intracellular). The sodium-potassium pump mechanism moves 3 sodium ions out and moves 2 potassium ions in, thus, in total, removing one positive charge carrier from the intracellular space. It contributes -6mV to resting potential but does not in fact generate it.

Transport

Export of sodium from the cell provides the driving force for several secondary active transporters membrane transport proteins, which import glucose, amino acids, and other nutrients into the cell by use of the sodium gradient.

Another important task of the Na^+-K^+ pump is to provide a Na^+ gradient that is used by certain carrier processes. In the gut, for example, sodium is transported out of the reabsorbing cell on the blood (interstitial fluid) side via the Na^+-K^+ pump, whereas, on the reabsorbing (lumenal) side, the Na^+-glucose symporter uses the created Na^+ gradient as a source of energy to import both Na^+ and glucose, which is far more efficient than simple diffusion. Similar processes are located in the renal tubular system.

Controlling cell volume

Failure of the Na^+-K^+ pumps can result in swelling of the cell. A cell's osmolarity is the sum of the concentrations of the various ion species and many proteins and other organic compounds inside the cell. When this is higher than the osmolarity outside of the cell, water flows into the cell through osmosis. This can cause the cell to swell up and lyse. The Na^+ - K^+ pump helps to maintain the right concentrations of ions. Furthermore, when the cell begins to swell, this automatically activates the Na+-K+ pump.

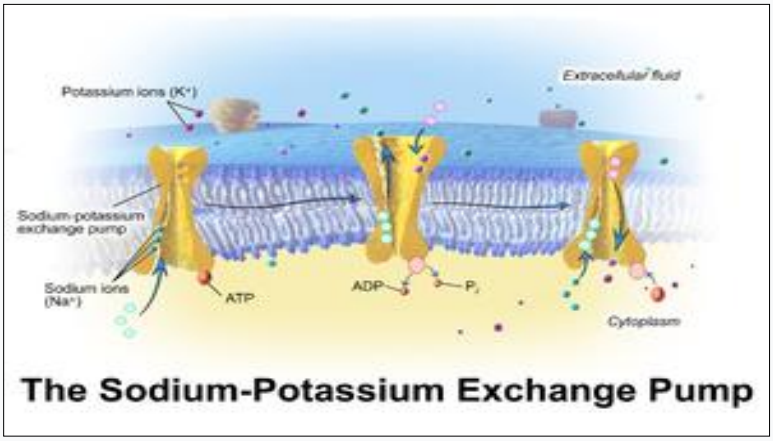
Functioning as signal transducer

Within the last decade, many independent labs have demonstrated that, in addition to the classical ion transporting, this membrane protein can also relay extracellular ouabain-binding signalling into the cell through regulation of protein tyrosine phosphorylation. The downstream signals through ouabain-triggered protein phosphorylation events include activation of the mitogen-activated protein kinase (MAPK) signal cascades, mitochondrial reactive oxygen species (ROS) production, as well as activation of phospholipase C (PLC) and inositol triphosphate (IP3) receptor (IP3R) in different intracellular compartments.

Protein-protein interactions play a very important role in Na+-K+ pump-mediated signal transduction. For example, Na+ -K+ pump interacts directly with Src, a non-receptor tyrosine kinase, to form a signaling receptor complex. Src kinase is inhibited by Na+ -K+ pump, while, upon ouabain binding, the Src kinase

domain will be released and then activated. Based on this scenario, NaK tide, a peptide Src inhibitor derived from Na+ -K+ pump, was developed as a functional ouabain-Na+ -K+ pump-mediated signal transduction. Na+ -K+ pump also interacts with ankyrin, IP3R, PI3K, PLC-gamma and cofilin.

Mechanism



- The pump, after binding ATP, binds 3 intracellular Na+ ions.
- ATP is hydrolyzed, leading to phosphorylation of the pump at a high conserved aspartate residue and subsequent release of ADP.
- A conformational change in the pump exposes the Na+ ions to the outside. The phosphorylated form of the pump has a low affinity for Na+ ions, so they are released.
- The pump binds 2 extracellular K^+ ions. This causes the dephosphorylation of the pump, reverting it to its previous conformational state, transporting the K+ ions into the cell.
- The unphosphorylated form of the pump has a higher affinity for Na+ ions than K+ ions, so the two bound K+ ions are released. ATP binds, and the process starts again.

Regulation

Endogenous

The Na+/K+ -ATPase is upregulated by cAMP. Thus, substances causing an increase in cAMP upregulate the Na+/K+-ATPase. These include the ligands of the G_s-coupled GPCRs. In contrast, substances causing a decrease in cAMP downregulate the Na+/K+-ATPase. These include the ligands of the G_i-coupled GPCRs.

Transmission of Nerve Impulses

The transmission of a nerve impulse along a neuron from one end to the other occurs as a result of electrical changes across the membrane of the neuron. The membrane of an unstimulated neuron is polarized—that is, there is a difference in electrical charge between the outside and inside of the membrane. The inside is negative with respect to the outside.

Polarization is established by maintaining an excess of sodium ions (Na^+) on the outside and an excess of potassium ions (K^+) on the inside. A certain amount of Na^+ and K^+ is always leaking across the membrane through leakage channels, but Na^+/K^+ pumps in the membrane actively restore the ions to the appropriate side.

The main contribution to the resting membrane potential (a polarized nerve) is the difference in permeability of the resting membrane to potassium ions versus sodium ions. The resting membrane is much more permeable to potassium ions than to sodium ions resulting in slightly more net potassium ion diffusion (from the inside of the neuron to the outside) than sodium ion diffusion (from the outside of the neuron to the inside) causing the slight difference in polarity right along the membrane of the axon.

Other ions, such as large, negatively charged proteins and nucleic acids, reside within the cell. It is these large, negatively charged ions that contribute to the overall negative charge on the inside of the cell membrane as compared to the outside.

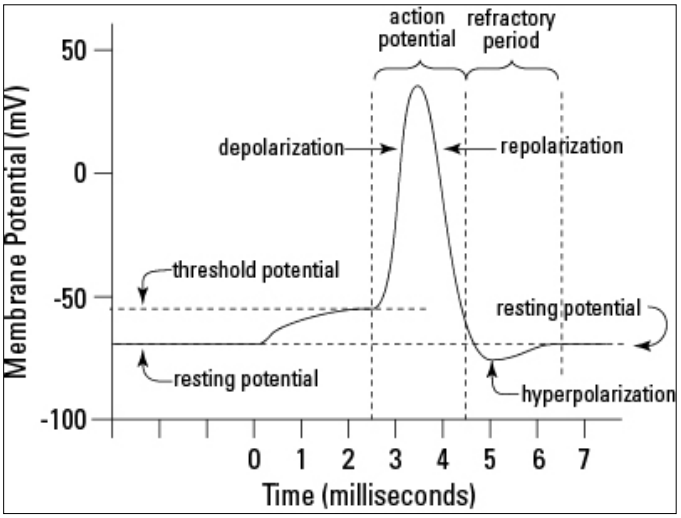
In addition to crossing the membrane through leakage channels, ions may cross through **gated channels.** Gated channels open in response to neurotransmitters, changes in membrane potential, or other stimuli.

The following events characterize the transmission of a nerve impulse (see Figure 1):

- **Resting potential.** The resting potential describes the unstimulated, polarized state of a neuron (at about –70 millivolts).

- **Graded potential.** A graded potential is a change in the resting potential of the plasma membrane in the response to a stimulus. A graded potential occurs when the stimulus causes Na^+ or K^+ gated channels to open. If Na^+ channels open, positive sodium ions enter, and the membrane depolarizes (becomes more positive). If the stimulus opens K^+ channels, then positive potassium ions exit across the membrane and the membrane**hyperpolarizes** (becomes more negative). A graded potential is a local event that does not travel far from its origin. Graded potentials occur in cell bodies and dendrites. Light, heat, mechanical pressure, and chemicals, such as neurotransmitters, are examples of stimuli that may generate a graded potential (depending upon the neuron).

Figure 1.Events that characterize the transmission of a nerve impulse.



The following four steps describe the initiation of an impulse to the "resetting" of a neuron to prepare for a second stimulation:

1. **Action potential.** Unlike a graded potential, an action potential is capable of traveling long distances. If a depolarizing graded potential is sufficiently large, Na^+ channels in the trigger zone open. In response, Na^+ on the outside of the membrane becomes depolarized (as in a graded potential). If the stimulus is strong enough—that is, if it is above a certain threshold level—additional Na^+ gates open, increasing the flow of Na^+ even more, causing an action potential, or complete depolarization (from –70 to about +30 millivolts). This in turn stimulates neighboring Na^+ gates, farther down the axon, to open. In this manner, the action potential travels down the length of the axon as opened Na^+ gates stimulate neighboring Na^+ gates to open. The action potential is an all-or-nothing event: When the stimulus fails to produce depolarization that exceeds the threshold value, no action potential results, but when threshold potential is exceeded, complete depolarization occurs.
2. Repolarization. In response to the inflow of Na^+, K^+ channels open, this time allowing K^+ on the inside to rush out of the cell. The movement of K^+ out of the cell causes repolarization by restoring the original membrane polarization. Unlike the resting potential, however, in repolarization the K^+ are on the outside and the Na^+ are on the inside. Soon after the K^+ gates open, the Na^+ gates close.
3. **Hyperpolarization.** By the time the K^+ channels close, more K^+ have moved out of the cell than is actually necessary to establish the original polarized potential. Thus, the membrane becomes hyperpolarized (about –80 millivolts).
4. Refractory period. With the passage of the action potential, the cell membrane is in an unusual state of affairs. The membrane is polarized, but the Na^+ and K^+ are on the wrong sides of the membrane. During this refractory period, the axon will not respond to a new stimulus. To reestablish the original distribution of these ions, the Na^+ and K^+ are returned to their resting potential location by Na^+/K^+ pumps in the cell membrane. Once these ions are completely returned to their resting potential location, the neuron is ready for another stimulus.

Nerve Impulse and Calcium

It is well-known that calcium is another positive molecule useful for the conduction of a nerve impulse to a muscle fiber. However, Clay Armstrong, a neurobiologist, believes that calcium may play a larger role. Armstrong suspects that calcium is in charge of the gated channels that release potassium and sodium to facilitate a nerve impulse. Armstrong's theory proposes that calcium ions are like a door to these gated channels. Calcium must move to release the ions and calcium must return before the impulse will stop and homeostasis is returned.

Calcium and Muscle Contractions

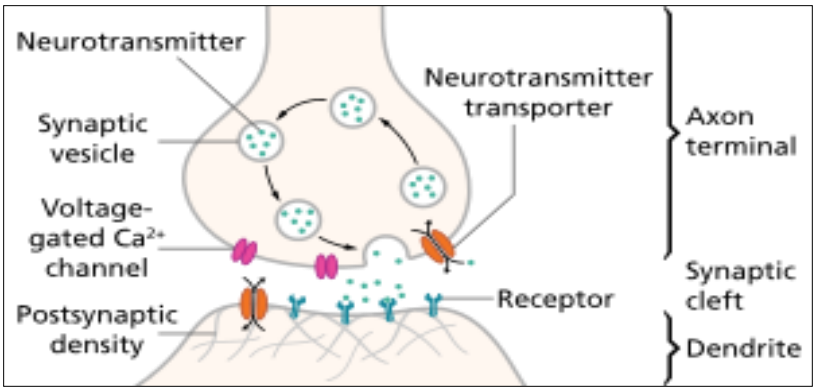
When a nerve impulse reaches a muscle cell, movement of the muscle requires calcium as well. Your muscle cells store calcium and upon nerve impulse, the cell is flooded with calcium. In order for a skeletal muscle to move, two myofilaments, actin and myosin, inside a muscle fiber must bind to one another to create a pulling action which shortens the muscle. However, a molecule known as tropomyosin blocks the binding site and must be moved to create a contraction. Calcium binds to troponin which is attached to

tropomyosin. Upon binding with calcium, troponin moves tropomyosin, exposing the binding site and creating movement.

Dynamics

Action potentials are most commonly initiated by excitatory postsynaptic potentials from a presynaptic neuron. Typically, neurotransmitter molecules are released by the presynaptic neuron. These neurotransmitters then bind to receptors on the postsynaptic cell. This binding opens various types of ion channels. This opening has the further effect of changing the local permeability of the cell membrane and, thus, the membrane potential. If the binding increases the voltage (depolarizes the membrane), the synapse is excitatory. If, however, the binding decreases the voltage (hyperpolarizes the membrane), it is inhibitory. Whether the voltage is increased or decreased, the change propagates passively to nearby regions of the membrane (as described by the cable equation and its refinements). Typically, the voltage stimulus decays exponentially with the distance from the synapse and with time from the binding of the neurotransmitter. Some fraction of an excitatory voltage may reach the axon hillock and may (in rare cases) depolarize the membrane enough to provoke a new action potential. More typically, the excitatory potentials from several synapses must work together at nearly the same time to provoke a new action potential. Their joint efforts can be thwarted, however, by the counteracting inhibitory postsynaptic potentials.

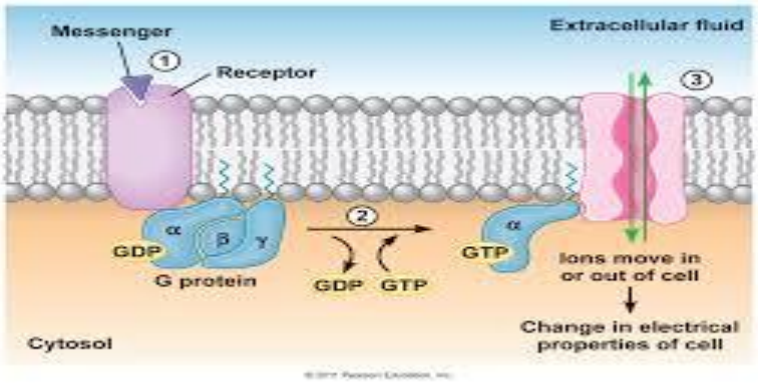
Neurotransmission can also occur through electrical synapses. Due to the direct connection between excitable cells in the form of gap junctions, an action potential can be transmitted directly from one cell to the next in either direction. The free flow of ions between cells enables rapid non-chemical-mediated transmission. Rectifying channels ensure that action potentials move only in one direction through an electrical synapse. Electrical synapses are found in all nervous systems, including the human brain, although they are a distinct minority.



Ion Channels

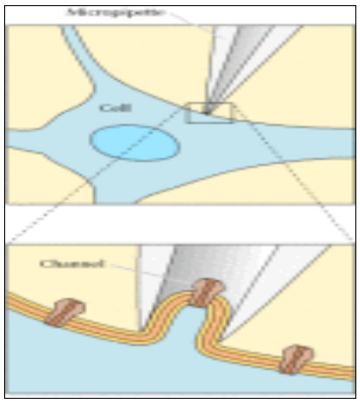
In contrast to carrier proteins, channel proteins simply form open pores in the membrane, allowing small molecules of the appropriate size and charge to pass freely through the lipid bilayer. One group of channel proteins, discussed earlier, is the porins, which permit the free passage of ions and small polar molecules through the outer membranes of bacteria. Channel proteins also permit the passage of molecules between cells connected at gap junctions, which are discussed later in the chapter. The plasma membranes of many cells also contain water channel proteins (aquaporins), through which water molecules are able to cross the membrane much more rapidly than they can diffuse through the phospholipid bilayer. The best-characterized channel proteins, however, are the ion channels, which mediate the passage of ions across plasma membranes. Although ion channels are present in the membranes of all cells, they have been especially well studied in nerve and muscle, where their regulated opening and closing is responsible for the transmission of electric signals.

Three properties of ion channels are central to their function (Figure). First, transport through channels is extremely rapid. More than a million ions per second flow through open channels—a flow rate approximately a thousand times greater than the rate of transport by carrier proteins. Second, ion channels are highly selective because narrow pores in the channel restrict passage to ions of the appropriate size and charge. Thus, specific channel proteins allow the passage of Na^+, K^+, Ca^{2+}, and Cl^- across the membrane. Third, most ion channels are not permanently open. Instead, the opening of ion channels is regulated by "gates" that transiently open in response to specific stimuli. Some channels (called **ligand-gated channels**) open in response to the binding of neurotransmitters or other signaling molecules; others (**voltage-gated channels**) open in response to changes in electric potential across the plasma membrane.



Model of an ion channel. In the closed conformation, the flow of ions is blocked by a gate. Opening of the gate allows ions to flow rapidly through the channel. The channel contains a narrow pore that restricts passage to ions of the appropriate size.

The fundamental role of ion channels in the transmission of electric impulses was elucidated through a series of elegant experiments reported by Alan Hodgkin and Andrew Huxley in 1952. These investigators used the giant nerve cells of the squid as a model. The axons of these giant neurons have a diameter of about 1 mm, making it possible to insert electrodes and measure the changes in membrane potential that take place during the transmission of nerve impulses. Using this approach, Hodgkin and Huxley demonstrated that these changes in membrane potential result from the regulated opening and closing of Na^+ and K^+ channels in the plasma membrane. It subsequently became possible to study the activity of individual ion channels, using the **patch clamp technique** developed by Erwin Neher and Bert Sakmann in 1976 (Figure). In this method, a micropipette with a tip diameter of about 1 μm is used to isolate a small patch of membrane, allowing the flow of ions through a single channel to be analyzed and greatly increasing the precision with which the activities of ion channels can be studied.



The patch clamp technique. A small patch of membrane is isolated in the tip of a micropipette. Stimuli can then be applied from within the pipette, allowing the behavior of the trapped channel to be measured. (Adapted from E. Neher and B. Sakmann, 1992.

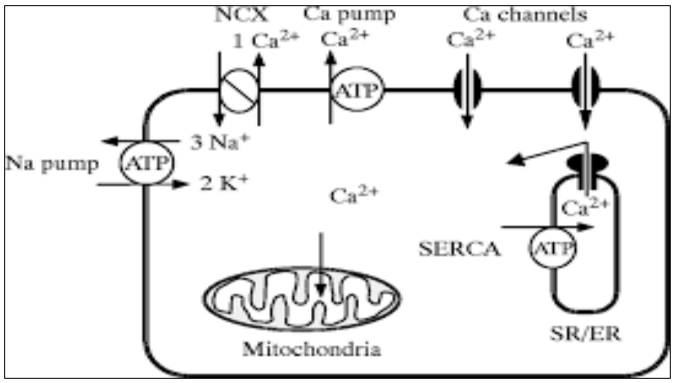
The flow of ions through membrane channels is dependent on the establishment of ion gradients across the plasma membrane. All cells, including nerve and muscle, contain ion pumps (discussed in the next section) that use energy derived from ATP hydrolysis to actively transport ions across the plasma membrane. As a result, the ionic composition of the cytoplasm is substantially different from that of extracellular fluids (Table). For example, Na^+ is actively pumped out of cells while K^+ is pumped in. In the squid axon, therefore, the concentration of Na^+ is about 10 times higher in extracellular fluids than inside the cell, whereas the concentration of K^+ is approximately 20 times higher in the cytosol than in the surrounding medium.

Table 12.1 Extracellular and Intracellular Ion Concentrations

	Concentration (mM)	
Ion	**Intracellular**	**Extracellular**
Squid axon		
K^+	400	20
Na^+	50	440
Cl^-	40–150	560
Ca^{2+}	0.0001	10
Mammalian cell		
K^+	140	5
Na^+	5–15	145
Cl^-	4	110
Ca^{2+}	0.0001	2.5–5

Extracellular and Intracellular Ion Concentrations.

Because ions are electrically charged, their transport results in the establishment of an electric gradient across the plasma membrane. With resting squid axons there is an electric potential of about 60 mV across the plasma membrane, with the inside of the cell negative with respect to the outside (Figure). This electric potential arises both from ion pumps and from the flow of ions through channels that are open in the resting cell plasma membrane. The plasma membrane of resting squid axons contains open K^+ channels, so it is more permeable to K^+ than to Na^+ or other ions. Consequently, the flow of K^+ makes the largest contribution to the resting membrane potential.



Ion gradients and resting membrane potential of the giant squid axon. Only the concentrations of Na^+ and K^+ are shown, because these are the ions that function in the transmission of nerve impulses. Na^+ is pumped out of the cell while K^+ is pumped in,

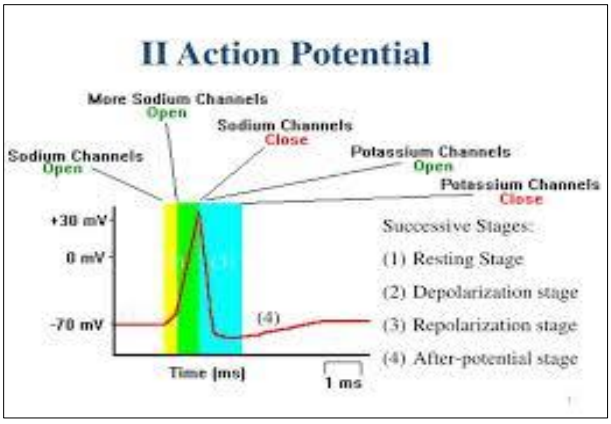
The flow of ions across a membrane is driven by both the concentration and voltage components of an electrochemical gradient. For example, the 20-fold higher concentration of K^+ inside the squid axon as compared to the extracellular fluid drives the flow of K^+ out of the cell. However, because K^+ is positively charged, this efflux of K^+ from the cell generates an electric potential across the membrane, with the inside of the cell becoming negatively charged. This membrane potential opposes the continuing flow of K^+ out of the cell, and the system approaches the equilibrium state, in which the membrane potential balances the K^+ concentration gradient.

Quantitatively, the relationship between ion concentration and membrane potential is given by the Nernst equation:

$$V = \frac{RT}{zF} \ln \frac{C_o}{C_i}$$

where V is the equilibrium potential in volts, R is the gas constant, T is the absolute temperature, z is the charge of the ion, F is Faraday's constant, and C_o and C_i are the concentrations of the ion outside and inside of the cell, respectively. An equilibrium potential exists separately for each ion, and the membrane potential is determined by the flow of all the ions that cross the plasma membrane. However, because resting squid axons are more permeable to K^+ than to Na^+ or other ions (including Cl^-), the resting membrane potential (-60 mV) is close to the equilibrium potential determined by the intracellular and extracellular K^+ concentrations (-75 mV).

As nerve impulses (**action potentials**) travel along axons, the membrane depolarizes (Figure). The membrane potential changes from -60 mV to approximately +30 mV in less than a millisecond, after which it becomes negative again and returns to its resting value. These changes result from the rapid sequential opening and closing of voltage-gated Na^+ and K^+ channels. Relatively small initial changes in membrane potential (from -60 to about -40 mV) lead to the rapid opening of Na^+ channels. This allows Na^+ to flow into the cell, driven by both its concentration gradient and the membrane potential. The sudden entry of Na^+ leads to a large change in membrane potential, which increases to nearly +30 mV, approaching the Na^+ equilibrium potential of approximately +50 mV. At this time, the Na^+ channels are inactivated and voltage-gated K^+ channels open, substantially increasing the permeability of the membrane to K^+. K^+then flows rapidly out of the cell, driven by both the membrane potential and the K^+ concentration gradient, leading to a rapid decrease in membrane potential to about -75 mV (the K^+ equilibrium potential). The voltage-gated K^+ channels are then inactivated and the membrane potential returns to its resting level of -60 mV, determined by the flow of K^+ and other ions through the channels that remain open in unstimulated cells.



Membrane potential and ion channels during an action potential. (A) Changes in membrane potential at one point on a squid giant axon following a stimulus. E_{Na} and E_K are the equilibrium potentials for Na^+ and K^+, respectively. (B) The membrane potential.

Depolarization of adjacent regions of the plasma membrane allows action potentials to travel down the length of nerve cell axons as electric signals, resulting in the rapid transmission of nerve impulses over long distances. For example, the axons of human motor neurons can be more than a meter long. The arrival of action potentials at the terminus of most neurons then signals the release of neurotransmitters, such as acetylcholine, which carry signals between cells at a synapse (Figure 12.22). Neurotransmitters released from presynaptic cells bind to receptors on the membranes of postsynaptic cells, where they act to open ligand-gated ion channels. One of the best-characterized of these channels is the acetylcholine receptor of muscle cells. Binding of acetylcholine opens a channel that is permeable to both Na^+ and K^+. This permits the rapid influx of Na^+, which depolarizes the muscle cell membrane and triggers an action potential. The action potential then results in the opening of voltage-gated Ca^{2+} channels, leading to the increase in intracellular Ca^{2+} that signals contraction.

Metal ions

Magnesium

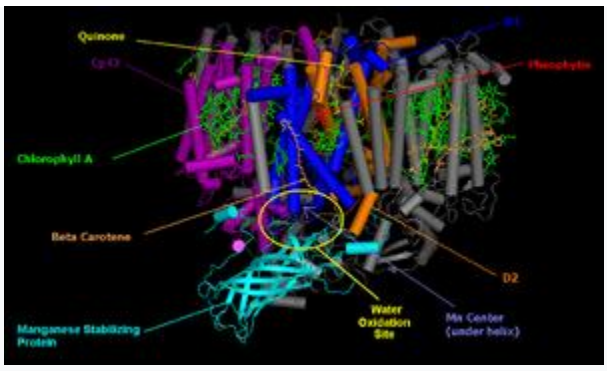
Magnesium is the eighth most abundant element on earth. It is the fourth most abundant element in vertebrates and the most abundant divalent cation within cells. The most available form of magnesium (Mg^{2+}) for living organisms can be found in the hydrosphere. The concentration of Mg^{2+} in seawater is around 55 mM. Mg^{2+} is readily available to cells during early evolution due to its high solubility in water. Other transition metals like calcium precipitate from aqueous solutions at much lower concentrations than the corresponding Mg^{2+} salts.

Since magnesium was readily available in early evolution, it can be found in every cell type living organism. Magnesium in anaerobic prokaryotes can be found in MgATP. Magnesium also has many functions in prokaryotes such as glycolysis, all kinases, NTP reaction, signalling, DNA/RNA structures and light capture. In aerobic eukaryotes, magnesium can be found in cytoplasm and chloroplasts. The reactions in these cell compartments are glycolysis, photophosphorylation and carbon assimilation.

ATP, the main source of energy in almost all living organisms, must bind with metal ions such as Mg^{2+} or Ca^{2+} to function. Examination of cells with limited magnesium supply has shown that a lack of magnesium can cause a decrease in ATP. Magnesium in ATP hydrolysis acts as a co-factor to stabilize the high negative charge transition state. MgATP can be found in both prokaryotes and eukaryotes cells.

However, most of the ATP in cells is MgATP. Following the Irving–Williams series, magnesium has a higher binding constant than the Ca^{2+}. Therefore, the dominant ATP in living organisms is MgATP. A greater binding constant also given magnesium the advantage as a better catalyst over other competing transition metals.

Manganese



Magnesium Center in Cyanobacterial photosystem II. Incorporation of manganese sparked evolution of complex plant life.

Evidence suggests that manganese (Mn) was first incorporated into biological systems roughly 3.2 - 2.8 billion years ago, during the Archean Period. Together with calcium, it formed the manganese-calcium oxide complex (determined by X-ray diffraction) which consisted of a manganese cluster, essentially an inorganic cubane (cubical) structure. The incorporation of a manganese center in photosystem II was highly significant, as it allowed for photosynthetic oxygen evolution of plants. The oxygen-evolving complex (OEC) is a critical component of photosystem II contained in the thylakoid membranes of chloroplasts; it is responsible for terminal photooxidation of water during light reactions.

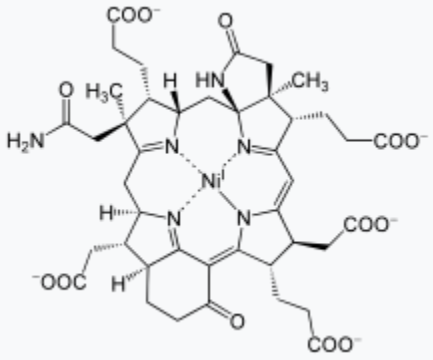
The incorporation of Mn in proteins allowed the complexes the ability to reduce reactive oxygen species in Mn-superoxide dismutatse (MnSOD) and catalase, in electron transfer-dependent catalysis (for instance in certain class I ribonucleotide reductases) and in the oxidation of water by photosystem II (PSII), where the production of thiobarbituric acid-reactive substances is decreased. This is due to manganese's ability to reduce superoxide anion and hydroxyl radicals as well as its chain-breaking capacity.

Iron

Iron (Fe) is the most abundant element in the Earth and the fourth most abundant element in the crust, approximately 5 percent by mass. Due to the abundance of iron and its role in biological systems, the transition and mineralogical stages of iron have played a key role in Earth surface systems. It played a larger role in the geological past in marine geochemistry, as evidenced by the deposits of Precambrian iron-rich sediments. The redox transformation of Fe(II) to Fe(III), or vice versa, is vital to a number of biological and element cycling processes. The reduction of Fe(III) is seen to oxidize sulfur (from H_2S to SO_4^{-2}), which is a central process in marine sediments. Many of the first metalloproteinsconsisted of iron-sulphur complexes formed during photosynthesis. Iron is the main redox metal in biological systems. In proteins, it is found in a variety of sites and cofactors, including, for instance, haem groups, Fe–O–Fe sites, and iron–sulfur clusters.

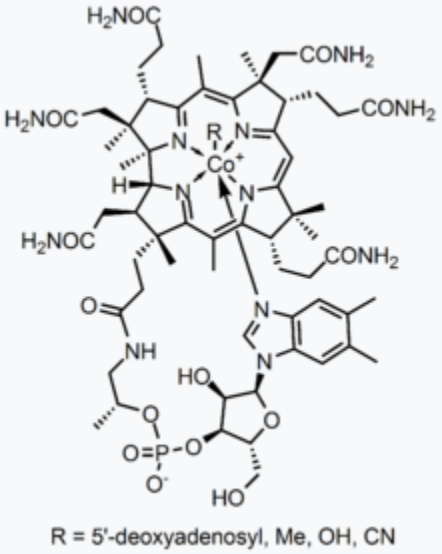
The prevalence of iron is apparently due to the large availability of Fe(II) in the initial evolution of living organisms, before the rise of photosynthesis and an increase in atmospheric oxygen levels which resulted in the precipitation of iron in the environment as $Fe(OH)_3$. It has flexible redox properties because such properties are sensitive to ligand coordination, including geometry. Iron can be also used in enzymes due to its Lewis acid properties, for example in nitrile hydratase. Iron is frequently found in mononuclear sites

in the reduced Fe(II) form, and functions in dioxygen activation; this function is used as a major mechanism adopted by living organisms to avoid the kinetic barrier hindering the transformation of organic compounds by O_2. Iron can be taken up selectively as ferredoxins, Fe-O-Fe (hemerythrin and ribonucleotide reductase), Fe (many oxidases), apart from iron porphyrin. Variation in the related proteins with any one of these chemical forms of iron has produced a wide range of enzymes. All of these arrangements are modified to function both in the sense of reactivity and the positioning of the protein in the cell. Iron can have various redox and spin states, and it can be held in many stereochemistries.



Coenzyme F430- Theorized as the first occurrence of nickel in biological systems

Nickel and cobalt



Coenzyme B12- Theorized as the first occurrence of cobalt in a biological system

Around 4-3 Ga, anaerobic prokaryotes began developing metal and organic cofactors for light absorption. They ultimately ended up making chlorophyll from Mg(II), as is found in cyanobacteria and plants, leading to modern photosynthesis. However, chlorophyll synthesis requires numerous steps. The process starts with uroporphyrin, a primitive precursor to the porphyrin ring which may be biotic or abiotic in origin, which is then modified in cells differently to make Mg, Fe, nickel (Ni), and cobalt (Co) complexes. The centers of these rings are not selective, thus allowing the variety of metal ions to be incorporated. Mg porphyrin gives rise to chlorophyll, Fe porphyrin to heme proteins, Ni porphyrin yields factor F-430, and Co porphyrin Coenzyme B12.

Copper

Before the Great Oxygenation Event, copper was not readily available for living organisms. Most early copper was Cu^{+} and Cu. This oxidation state of copper is not very soluble in water. One billion years ago, after the great oxidation event the oxygen pressure rose sufficiently to oxidise Cu^{+} to Cu^{2+}, increasing its solubility in water. As a result, the copper became much more available for living organisms.

Most copper-containing proteins and enzymes can be found in eukaryotes. Only a handful of prokaryotes such as aerobic bacteria and cyanobacteria contain copper enzymes or proteins. Copper can be found in both prokaryotes and eukaryotes superoxide dismutase (SOD)enzyme. There are three distinct types of SOD, containing Mn, Fe and Cu respectively. Mn-SOD and Fe-SOD are found in most prokaryotes and mitochondria of the eukaryotic cell. Cu-SOD can be found in the cytoplasmic fraction of the eukaryotic cells. The three elements, copper, iron and manganese, can all catalyze superoxide to ordinary molecular oxygen or hydrogen peroxide. However, Cu-SOD is more efficient than Fe-SOD and Mn-SOD. Most prokaryotes only utilize Fe-SOD or Mn-SOD due to the lack of copper in the environment. Some organisms did not develop Cu-SOD due to the lack of a gene pool for the Cu-SOD adoption.

Zinc

Zinc (Zn) was incorporated into living cells in two waves. Four to three Ga, anaerobic prokaryotes arose, and the atmosphere was full of $H_2S$and highly reductive. Thus most zinc was in the form of insoluble ZnS. However, because seawater at the time was slightly acidic, some Zn(II) was available in its ionic form and became part of early anaerobic prokaryotes' external proteases, external nucleases, internal synthetases and dehydrogenases.

During the second wave, once the Great Oxygenation Event occurred, more Zn(II) ions were available in the seawater. This allowed its incorporation in the single-cell eukaryotes as they arose at this time. It is believed that the later addition of ions such as zinc and copper allowed them to displace iron and manganese from the enzyme superoxide dismutase (SOD). Fe and Mn complexes dissociate readily (Irving-Williams series) while Zn and Cu do not. This is why eukaryotic SOD contains Cu or Zn and its prokaryotic counterpart contains Fe or Mn.

Zn (II) doesn't pose an oxidation threat to the cytoplasm. This allowed it to become a major cytoplasmic element in the eukaryotes. It became associated with a new group of transcription proteins, zinc fingers. This could only have occurred due to the long life of eukaryotes, which allowed time for zinc to exchange and hence become an internal messenger coordinating the action of other transcription factors during growth.

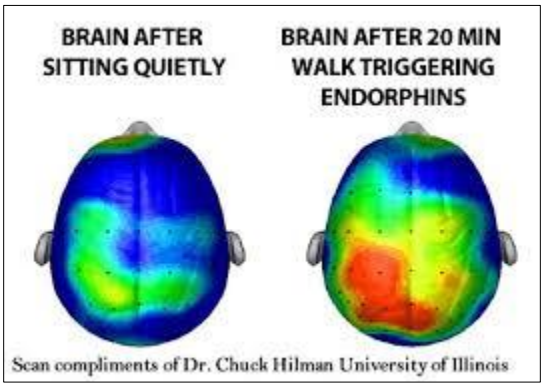
Molybdenum

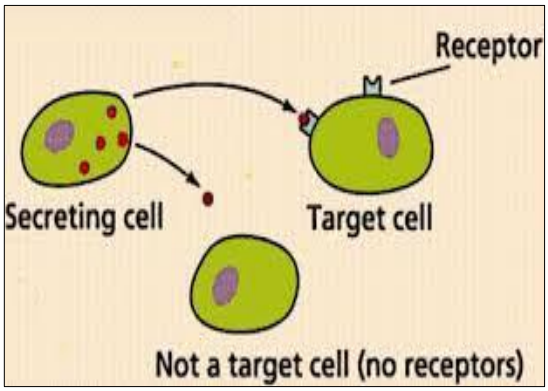
Molybdenum (Mo) is the most abundant transition element in solution in the sea (mostly as dianionic molybdate ion) and in living organisms, its abundance in the Earth's crust is quite low. Therefore, the use of Mo by living organisms seems surprising at first glance. Archaea, bacteria, fungi, plants, and animals, including humans, require molybdenum. It is also found in over 50 different enzymes. Its hydrolysis to water-soluble oxo-anionic species makes Mo readily accessible. Mo is found in the active sites of metalloenzymes that perform key transformations in the metabolism of carbon, nitrogen, arsenic, selenium, sulfur, and chlorine compounds. The mononuclear Mo enzymes are widely distributed in the biosphere; they catalyze many significant reactions in the metabolism of nitrogen and sulfur-containing compounds as well as various carbonyl compounds (e.g., aldehydes, CO, and CO_2). Nitrate reductases enzymes are important for the nitrogen cycle. They belong to a class of enzymes with a mononuclear Mo center and they catalyze the metabolism reaction of C, N, S, etc., in bacteria, plants, animals, and humans. Due to the oxidation of sulfides, The first considerable development was that of aerobic bacteria which could now utilize Mo. As oxygen began to accumulate in the atmosphere and

oceans, the reaction of MoS_2 to MoO_4 also increased. This reaction made the highly soluble molybdate ion available for incorporation into critical metalloenzymes, and may have thus allowed life to thrive. It allowed organisms to occupy new ecological niches. Mo plays an important role in the reduction of dinitrogen to ammonia, which occurs in one type of nitrogenases. These enzymes are used by bacteria that usually live in a symbiotic relationship with plants; their role is nitrogen fixation, which is vital for sustaining life on earth. Mo enzymes also play important roles in sulfur metabolism of organisms ranging from bacteria to humans.

Trigger reaction

A **trigger** is an experience that causes someone to recall a previous traumatic memory, although the trigger itself need not be frightening or traumatic and can be indirectly or superficially reminiscent of an earlier traumatic incident. Trauma triggers are related to posttraumatic stress disorder (PTSD), a condition in which people often cannot control the recurrence of emotional or physical symptoms, or of repressed memory. Triggers can be subtle and difficult to anticipate, and can sometimes exacerbate PTSD. A trauma trigger may also be referred to as a trauma stimulus or a trauma stressor.





Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

POSSIBLE QUESTIONS

MULTIPLE CHOICE QUESTIONS

Section-A **20X1=20**

1. The sodium-potassium pump passes
a. **more Na+ out than K+ in** b. K+ out and Na+ in on a one-for-one basis
c. Na+ out and K+ in on a one-for-one basis d. K+ and Na+ in the same direction
2. Which of the following are not components of the cell membrane?
a. cell surface markers b. transmembrane proteins c. interior protein network
d. plasmodesmata
3. Red blood cells have a characteristic concave shape because of
a. **Spectrin** b. dextrin c. hemoglobin d. hemocyanin
4. ATP is required in the transport of
a. water molecules b. all molecules across a membrane c. molecules to areas of lower concentrations
d. molecules to areas of higher concentrations
5. Sodium and potassium ions are transported across the plasma membrane by a _____ protein.
a. **Carrier** b. channel c. receptor d. enzymatic
6. _____ is the net movement of any type of molecule from a region of higher concentration to a region of lower concentration.
a. Osmosis **b. Diffusion** c. Active transport d. Facilitated diffusion
7. The diffusion of water across a differentially permeable membrane is called _____.
a. simple diffusion b. facilitated diffusion **c. osmosis** d. exocytosis
8. Which of the following processes uses a carrier protein and ATP?
a. Osmosis b. Diffusion **c. Active transport** d. Facilitated diffusion
9. Nucleotide bases and aromatic amino acids absorb light respectively at
a. **260 and 280 nm** b. 270 and 280 nm c. 280 and 260 nm d. 260 and 270 nm
10. Nucleic acids can be analyzed experimentally by their
a. molecular weight b. absorption of visible light c. a**bsorption of uv light**
d. equivalent weight
11. The most stabilizing force for nucleic acids is
a. **Van der Waals** b. electrostatic bond c. hydrogen bonds
d. conformational entropy
12. The basic unit of nucleic acid is
a. pentose sugar **b. nucleotide.** C. nucleoid d. nucleoside
13. NAD^+ is a(n)
a. Enzyme **b. Coenzyme** c. active site d. high-energy bond
14. Which of the following is a reduced compound?
a. CO_2 b. O_2 c. N_2 **d. NADH**

15. The initial steps in breaking down glucose are called
a. **Glycolysis** b. intramolecular catalysis c. chemiosmosis
d. intermolecular catalysis
16. Cofactors
a. break hydrogen bonds in proteins **b. help facilitate enzyme activity**
c. increase activation energy d. decrease activation energy
17. The actions of an enzyme can be affected by all of the following except
a. p/PH b. allosteric inhibitors c. temperature **d. availability ATP**
18. Which of the following are mismatched
a. anabolic reactions-expend energy b. reduction-gain of an electron
c. activation energy-entropy d. exergonic reaction-catabolism
19. The activation energy of a chemical reaction is the energy that
a. **initiates the reaction** b. activates the catalyst c. must be removed from the mixture
d. must be released from the mixture
20. In a catalyzed chemical reaction, one function of a catalyst is to
a. increase the number of successful reactant collisions.
b. decrease the concentration of reactants.
c. change the equilibrium concentrations of the products and reactants
d. increase the energy given off during the reaction

8- MARKS

1. Explain the ion channel of Na^+-K^+ charge carriers?
2. What are the biochemical importance of Fe, Mo, Cu and Ca?
3. Explain the ion channel of Ca^+-Mg^+ charge carriers in muscle contraction of bones?
4. What is Zn-acid catalyst? And discuss it role in biological system?
5. Compare the mechanism of activity of Na^+-K^+ pump and Ca^{2+} pump?
6. What is nerve impulse? Discuss the properties of the Ca^{2+} pump involved in nerve impule transmission?
7. Discuss the role of osmosis in ion-channels?
8. What is nerve impulse? How it creates?
9. What is Na^+-K^+ ATP ase? Explain it function?
10. What are the biochemical importance of Co and Zn?

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Karpagam Academy of Higher Education
Coimbatore-21
(For the candidate admitted on 2015 onwards)
Department of Chemistry
V- semester
Bio-Inorganic Chemistry

UNIT I- Objective Questions for online examination
(Each carry 1 Marks)

Questions	Option A	Option B	Option C	Option D	Answer
The sodium-potassium pump passes	more Na+ out than K+ in	K+ out and Na+ in on a one-for-one basis	Na+ out and K+ in on a one-for-one basis	K+ and Na+ in the same direction	more Na+ out than K+ in
Which of the following are not components of the cell membrane?	cell surface markers	transmembrane proteins	interior protein network	plasmodesmata	plasmodesmata
Red blood cells have a characteristic concave shape because of	spectrin	dextrin	hemoglobin	hemocyanin	spectrin
ATP is required in the transport of	water molecules	all molecules across a membrane	molecules to areas of lower concentrations	molecules to areas of higher concentrations	molecules to areas of higher concentrations
The sodium-potassium pump establishes concentration gradients	of higher potassium concentrations inside the cell and higher sodium concentrations outside the cell	of ATP inside the cell where it is needed	by pumping sodium outside the cell and potassium is cotransported out as well	of higher sodium concentrations inside the cell and higher potassium concentrations outside the cell	of higher potassium concentrations inside the cell and higher sodium concentrations outside the cell
A _____ protein combines with a substance and helps to move it across the membrane.	carrier	channel	receptor	enzymatic	carrier
Sodium and potassium ions are transported across the plasma membrane by a _____ protein.	carrier	channel	receptor	enzymatic	carrier
_____ is the net movement of any type of molecule from a region of higher concentration to a region of lower concentration.	Osmosis	Diffusion	Active transport	Facilitated diffusion	Diffusion
The diffusion of water across a differentially permeable membrane is called _____.	simple diffusion	facilitated diffusion	osmosis	exocytosis	osmosis
Which of the following processes uses a carrier protein and ATP?	Osmosis	Diffusion	Active transport	Facilitated diffusion	Active transport
Which of the following conditions does NOT apply to active transport?	requires ATP	transports molecules from a high to low concentration area	requires a carrier protein	carrier proteins bind reversibly to transported substances	transports molecules from a high to low concentration area
Why are proteins involved in active transport often called "pumps"?	They use energy to move a substance with its concentration gradient.	They use energy to move a substance against its concentration gradient.	They use energy to bind the substance to the carrier.	They use energy to dislodge the substance from the carrier.	They use energy to move a substance against its concentration gradient.
The principal intracellular cation is:	Na+	Cl-	K+	Ca2+	K+
Which of the following is an example of primary active transport	Cl--HCO3- exchange	Na+ - H+ exchange	Na+-Ca2+ exchange	The Na+, K+ ATPase	The Na+, K+ ATPase

The sodium pump	Exchanges extracellular Na+ for intracellular K+	Is important for maintaining a constant cell volume	Can only be inhibited by metabolic poisons	Is an ion channel	Is important for maintaining a constant cell volume
Which of the following values is closest to the resting membrane potential of mammalian cells:	-20 mV	-60 mV	+60 mV	+20 mV	-60 mV
The principal extracellular cation is	Sodium (Na+)	Potassium (K+)	Chloride (Cl-)	Calcium (Ca2+)	Sodium (Na+)
The resting membrane potential is mainly determined by	the Cl- gradient	the Ca2+ gradient	the Na+ gradient	the K+ gradient	the K+ gradient
Nucleoside is a pyrimidine or purine base	covalently bonded to a sugar	ionically bonded to a sugar	hydrogen bonded to a sugar	none of the above	covalently bonded to a sugar
Which pyrimidine base contains an amino group at carbon 4?	Thymine	Cytosine	Adenine	Uracil	Cytosine
Nucleotide bases and aromatic amino acids absorb light respectively at	260 and 280 nm	270 and 280 nm	280 and 260 nm	260 and 270 nm	260 and 280 nm
Nucleic acids can be analyzed experimentally by their	molecular weight	absorption of visible light	absorption of uv light	equivalent weight	absorption of uv light
The most stabilizing force for nucleic acids is	Van der Waals	electrostatic bond	hydrogen bonds	conformational entropy	Van der Waals
The basic unit of nucleic acid is	pentose sugar	nucleotide.	nucleoid	nucleoside	nucleotide.
Adenine is	purine	pyrimidine	nucleoside	nucleotide.	purine
Living cell contains 60 – in human body is	65 – 70%.	50 – 55%	75 – 80%	65 – 70%.	65 – 70%.
Amino acids are produced from	fatty acids	essential oils	proteins	a-keto acids.	proteins
Amino acids are mostly synthesised from	a-ketoglutaric acid.	mineral salts	fatty acids	volatile acids	a-ketoglutaric acid.
What are the most diverse molecules in the cell?	proteins	lipids	mineral salts	carbohydrates.	proteins
ATP is	nucleoside	vitamin.	nucleic acid	nucleotide	nucleotide
The major role of minor elements inside living organisms is to act as	co-factors of enzymes	building blocks of important amino acids	constituent of hormones	binder of cell structure	co-factors of enzymes
nucleic acid is one of the	pentose sugar unit	nucleotide uit	nucleoid unit	nucleoside unit	nucleotide unit
purine base with nucleoside is	covalently bonded to a sugar	ionically bonded to a sugar	hydrogen bonded to a sugar	none of the above	covalently bonded to a sugar
pyrimidine base with nucleoside is	covalently bonded to a sugar	ionically bonded to a sugar	hydrogen bonded to a sugar	none of the above	covalently bonded to a sugar
Hydrogenation involve the saturation of which type of linkage?	Carbon-carbon	Carboxyl group	Hydroxyl group	All of the mentioned	All of the mentioned
Which catalyst carry hydrogenation to the maximum?	Mild Catalyst	Vigorous catalyst	All the above	Both mild and vigorous catalyst	Vigorous catalyst
Which of the following is a vigorous catalyst?	Nickel	gold	copper	Zinc	Nickel
Which of the following is mild hydrogenation catalyst?	Nickel	gold	copper	Zinc oxide	Zinc oxide
What are the hydrogenation reactions catalysed by molybdenum compounds?	Reduction in unsaturated	Cleavage of C-C	Dehydroisomerization	All the above	All the above
Which of the following is a Nobel-metal catalyst?	Nickel	gold	copper	Platinum	Platinum
What are the commonly used catalysts for the Fischer Tropsch synthesis?	Nickel	gold	copper	Zinc	Nickel
Cobalt catalyst is used when which type of products are desired?	Solid	Liquid	vapour	both solid and liquid	Liquid
Complete the following reaction: 3Fe2C + 4H20 —–> 2_____ + 3C + 4H2.	Fe3O4	Fe3O6	Fe3O2	Fe3O5	Fe3O4
Which catalyst is prepared by precipitation from a nitrate solution with potassium carbonate?	Nickel	gold	copper	Zinc	Nickel
The magnetite catalysts are reduced to what?	Metallic iron	Metallic zinc	Metallic cobalt	Metallic nickel	Metallic iron

By which process Iron can not be prepared?	From magnetite	Iron oxide	Oxidation of metals	Reduction of metals	Reduction of metals
By which process Iron can be prepared?	From magnetite	Iron oxide	Oxidation of metals	All the above	All the above
Which of the following is uncharacteristic of ATP?	It is formed by attaching a phosphate group to ADP with a high-energy bond.	In most reactions involving ATP, only the outer, high-energy bond is hydrolized.	anaerobic respiration	It is a good long-term energy storage molecule.	It is a good long-term energy storage molecule.
The universal energy currency for all cells is	ATP	Enzyme	NAD+	ADP	ATP
Enzymes	make endergonic reactions proceed spontaneously	lower the activation energy of a reaction	are not very specific in their choice of substrates	are needed in large quantities because they are used up during catalysis	lower the activation energy of a reaction
NAD+ is a(n)	Enzyme	CoEnzyme	active site	high-energy bond	CoEnzyme
Which of the following is a reduced compound?	CO2	O2	N2	NADH	NADH
The initial steps in breaking down glucose are called	glycolysis	intramolecular catalysis	chemiosmosis	intermolecular catalysis	glycolysis
Cofactors	break hydrogen bonds in proteins	help facilitate enzyme activity	increase activation energy	decrease activation energy	help facilitate enzyme activity
Enzyme B requires Zn2+ in order to catalyze the conversion of substrate X. The zinc is best identified as a(n)	coenzyme	enzyme	Cofactor	Substrate	Cofactor
Redox reactions (oxidation-reduction)	do not occur in living systems	involve the loss of electrons termed oxidation	involve the gaining of energy by an oxidized substance	require the presence of oxygen	involve the loss of electrons termed oxidation
The actions of an enzyme can be affected by all of the following except	p/PH	allosteric inhibitors	temperature	availability ATP	availability ATP
Which of the following are mismatched	anabolic reactions-expend energy	reduction-gain of an electron	activation energy-entropy	exergonic reaction-catabolism	activation energy-entropy
The activation energy of a chemical reaction is the energy that	initiates the reaction	activates the catalyst	must be removed from the mixture	must be released from the mixture	initiates the reaction
In a catalyzed chemical reaction, one function of a catalyst is to	increase the number of successful reactant collisions.	decrease the concentration of reactants.	change the equilibrium concentrations of the products and reactants	increase the energy given off during the reaction	increase the number of successful reactant collisions.

UNIT-2

Oxygen Carrier Systems

Structure and mechanism of Hemoglobin, Vitamin B-12, B-12 co-enzyme, Myoglobin, Synthesis of oxygen carriers.

Photosynthesis: Porphyrins ring complexes and redox mechanism.

Oxygen carrier systems

The interaction of molecular dioxygen (O_2) with metalloporphyrin species has intrigued scientists of all disciplines ever since such species were recognized as being important centers in some naturally occurring oxygen- storage and transport systems. The iron porphyrin moiety (the heme unit) is the prosthetic group present in myoglobin and hemoglobin (oxygen carriers) and various oxygenases (Which are a class of enzymes that incorporate one or two O_2 to a substrate).

Heme unit are also components of cytochrome c oxidase, the terminal enzyme in the respiratory redox chain that reduces O_2 to water. Oxidases are enzymes that convert both atoms of O_2 to water of hydrogen peroxide.

Heavy medical interventions in severely injured patients and complex transplantation surgery are currently performed with success, but they have increased the need of human blood. At the same time, the risk of transmission of viral diseases, the risk of errors in blood transfusion and the insufficiency of palliative treatments (blood predonation, pre- and perioperative hemodilution, perioperative blood sparing, lowering of transfusion trigger) accelerated the development of blood substitutes as alternatives to human blood.

- Together with the property of carrying O2 , a blood substitute must have at least the following properties: Free of toxicity and side effects
- Adequate O_2 uptake in the lungs and adequate delivery to tissues
- Sufficient half
- Life time in the circulation to avoid repeated administrations
- Harmful and rapid excretion
- Stable at room temperature, easy to store and easy to use
- Easy to sterilize (to assure the absence of pathogens and viruses transmission)
- Cheap to manufacture.

Structure and mechanism of Hemoglobin

Hemoglobin (American) or **haemoglobin** (British); abbreviated **Hb** or **Hgb**, is the iron-containing oxygen-transport metalloprotein in the red blood cells of all vertebrates (with the exception of

the fish family Channichthyidae) as well as the tissues of some invertebrates. It has the formula $C_{2952}H_{4664}O_{832}N_{812}S_8Fe_4$. Hemoglobin in the blood carries oxygen from the respiratory organs (lungs or gills) to the rest of the body (i.e. the tissues). There it releases the oxygen to permit aerobic respiration to provide energy to power the functions of the organism in the process called metabolism.

In mammals, the protein makes up about 96% of the red blood cells' dry content (by weight), and around 35% of the total content (including water). Hemoglobin has an oxygen-binding capacity of 1.34 mL O_2 per gram, which increases the total blood oxygen capacity seventy-fold compared to dissolved oxygen in blood. The mammalian hemoglobin molecule can bind (carry) up to four oxygen molecules.

Hemoglobin is involved in the transport of other gases: It carries some of the body's respiratory carbon dioxide (about 20–25% of the total) as carbaminohemoglobin, in which CO_2 is bound to the globin protein. The molecule also carries the important regulatory molecule nitric oxide bound to a globin protein thiol group, releasing it at the same time as oxygen.

Hemoglobin is also found outside red blood cells and their progenitor lines. Other cells that contain hemoglobin include the A9 dopaminergic neurons in the substantia nigra, macrophages, alveolar cells, and mesangial cells in the kidney. In these tissues, hemoglobin has a non-oxygen-carrying function as an antioxidant and a regulator of iron metabolism.

Hemoglobin and hemoglobin-like molecules are also found in many invertebrates, fungi, and plants. In these organisms, hemoglobins may carry oxygen, or they may act to transport and regulate other small molecules and ions such as carbon dioxide, nitric oxide, hydrogen sulfide and sulfide. A variant of the molecule, called leghemoglobin, is used to scavenge oxygen away from anaerobic systems, such as the nitrogen-fixing nodules of leguminous plants, before the oxygen can poison (deactivate) the system.

Discovery

In 1825 J. F. Engelhard discovered that the ratio of Fe to protein is identical in the hemoglobins of several species. From the known atomic mass of iron he calculated the molecular mass of hemoglobin to $n \times 16000$ (n = number of iron atoms per hemoglobin, now known to be 4), the first determination of a protein's molecular mass. This "hasty conclusion" drew a lot of ridicule at the time from scientists who could not believe that any molecule could be that big. Gilbert Smithson Adair confirmed Engelhard's results in 1925 by measuring the osmotic pressure of hemoglobin solutions.

The oxygen-carrying protein hemoglobin was discovered by Hünefeld in 1840 and 1851 German physiologist Otto Funke published a series of articles in which he described growing hemoglobin crystals by successively diluting red blood cells with a solvent such as pure water, alcohol or ether, followed by slow evaporation of the solvent from the resulting protein solution. Hemoglobin's reversible oxygenation was described a few years later by Felix Hoppe-Seyler.

In 1959, Max Perutz determined the molecular structure of hemoglobin by X-ray crystallography. This work resulted in his sharing with John Kendrew the 1962 Nobel Prize in Chemistry for their studies of the structures of globular proteins.

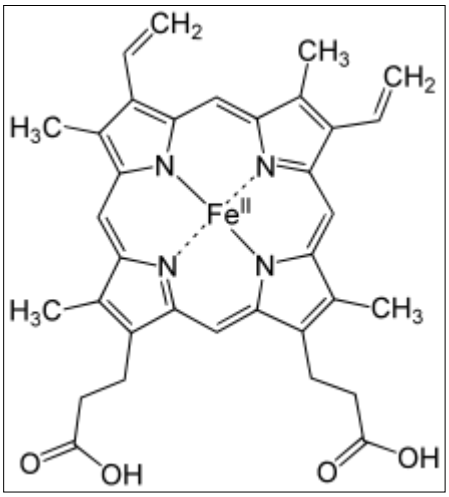
The role of hemoglobin in the blood was elucidated by French physiologist Claude Bernard. The name *hemoglobin* is derived from the words *heme*and *globin*, reflecting the fact that each subunit of hemoglobin is a globular protein with an embedded heme group. Each heme group contains one iron atom, that can bind one oxygen molecule through ion-induced dipole forces. The most common type of hemoglobin in mammals contains four such subunits.

Synthesis

Hemoglobin (Hb) is synthesized in a complex series of steps. The heme part is synthesized in a series of steps in the mitochondria and the cytosol of immature red blood cells, while the globin protein parts are

synthesized by ribosomes in the cytosol.[30] Production of Hb continues in the cell throughout its early development from the proerythroblast to the reticulocyte in the bone marrow. At this point, the nucleus is lost in mammalian red blood cells, but not in birds and many other species. Even after the loss of the nucleus in mammals, residual ribosomal RNA allows further synthesis of Hb until the reticulocyte loses its RNA soon after entering the vasculature (this hemoglobin-synthetic RNA in fact gives the reticulocyte its reticulated appearance and name).

Structure



Heme b group

Hemoglobin has a quaternary structure characteristic of many multi-subunit globular proteins. Most of the amino acids in hemoglobin form alpha helices, and these helices are connected by short non-helical segments. Hydrogen bonds stabilize the helical sections inside this protein, causing attractions within the molecule, which then causes each polypeptide chain to fold into a specific shape. Hemoglobin's quaternary structure comes from its four subunits in roughly a tetrahedral arrangement.

In most vertebrates, the hemoglobin molecule is an assembly of four globular protein subunits. Each subunit is composed of a protein chain tightly associated with a non-protein prosthetic heme group. Each protein chain arranges into a set of alpha-helix structural segments connected together in a globin fold arrangement. Such a name is given because this arrangement is the same folding motif used in other heme/globin proteins such as myoglobin. This folding pattern contains a pocket that strongly binds the heme group.

A heme group consists of an iron (Fe) ion (charged atom) held in a heterocyclic ring, known as a porphyrin. This porphyrin ring consists of four pyrrole molecules cyclically linked together (by methine bridges) with the iron ion bound in the center. The iron ion, which is the site of oxygen binding, coordinates with the four nitrogen atoms in the center of the ring, which all lie in one plane. The iron is bound strongly (covalently) to the globular protein via the N atoms of the imidazole ring of F8 histidine residue (also known as the proximal histidine) below the porphyrin ring. A sixth position can reversibly bind oxygen by a coordinate covalent bond, completing the octahedral group of six ligands. Oxygen binds in an "end-on bent" geometry where one oxygen atom binds to Fe and the other protrudes at an angle. When oxygen is not bound, a very weakly bonded water molecule fills the site, forming a distorted octahedron.

Even though carbon dioxide is carried by hemoglobin, it does not compete with oxygen for the iron-binding positions but is bound to the protein chains of the structure.

The iron ion may be either in the Fe^{2+} or in the Fe^{3+} state, but ferrihemoglobin (methemoglobin) (Fe^{3+}) cannot bind oxygen. In binding, oxygen temporarily and reversibly oxidizes (Fe^{2+}) to (Fe^{3+}) while oxygen temporarily turns into the superoxide ion, thus iron must exist in the +2 oxidation state to bind oxygen. If superoxide ion associated to Fe^{3+} is protonated, the hemoglobin iron will remain oxidized and incapable of binding oxygen. In such cases, the enzyme methemoglobin reductase will be able to eventually reactivate methemoglobin by reducing the iron center.

In adult humans, the most common hemoglobin type is a tetramer (which contains four subunit proteins) called *hemoglobin A*, consisting of two α and two β subunits non-covalently bound, each made of 141 and 146 amino acid residues, respectively. This is denoted as $\alpha_2\beta_2$. The subunits are structurally similar and about the same size. Each subunit has a molecular weight of about 16,000 daltons, for a total molecular weight of the tetramer of about 64,000 daltons (64,458 g/mol).[40] Thus, 1 g/dL = 0.1551 mmol/L. Hemoglobin A is the most intensively studied of the hemoglobin molecules.

In human infants, the hemoglobin molecule is made up of 2 α chains and 2 γ chains. The gamma chains are gradually replaced by β chains as the infant grows.

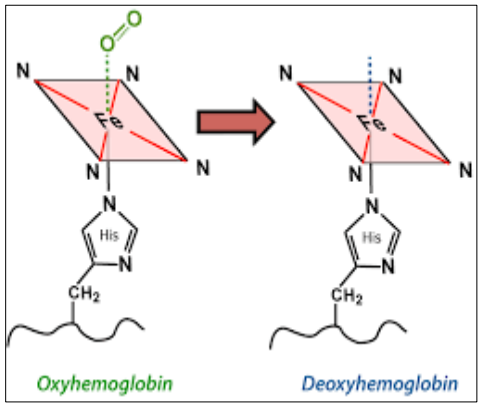
The four polypeptide chains are bound to each other by salt bridges, hydrogen bonds, and the hydrophobic effect.

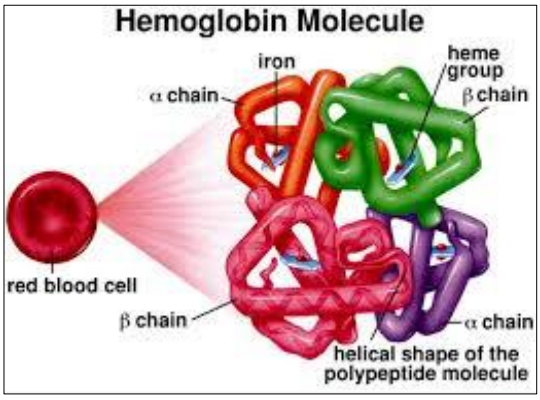
Oxygen saturation

In general, hemoglobin can be saturated with oxygen molecules (oxyhemoglobin), or desaturated with oxygen molecules (deoxyhemoglobin).

Oxyhemoglobin

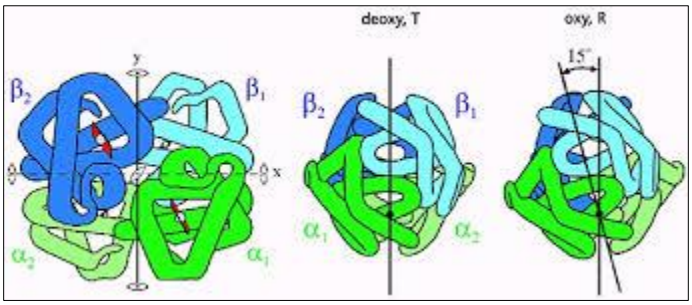
Oxyhemoglobin is formed during physiological respiration when oxygen binds to the heme component of the protein hemoglobin in red blood cells. This process occurs in the pulmonary capillaries adjacent to the alveoli of the lungs. The oxygen then travels through the blood stream to be dropped off at cells where it is utilized as a terminal electron acceptor in the production of ATP by the process of oxidative phosphorylation. It does not, however, help to counteract a decrease in blood pH. Ventilation, or breathing, may reverse this condition by removal of carbon dioxide, thus causing a shift up in pH.





Hemoglobin exists in two forms, a *taut (tense) form* (T) and a *relaxed form* I. Various factors such as low pH, high CO_2 and high 2,3 BPG at the level of the tissues favor the taut form, which has low oxygen affinity and releases oxygen in the tissues. Conversely, a high pH, low CO_2, or low 2,3 BPG favors the relaxed form, which can better bind oxygen. The partial pressure of the system also affects O_2 affinity where, at high partial pressures of oxygen (such as those present in the alveoli), the relaxed (high affinity, R) state is favoured. Inversely, at low partial pressures (such as those present in respiring tissues), the (low affinity, T) tense state is favoured. Additionally, the binding of oxygen to the iron(II) heme pulls the iron into the plane of the porphyrin ring, causing a slight conformational shift. The shift encourages

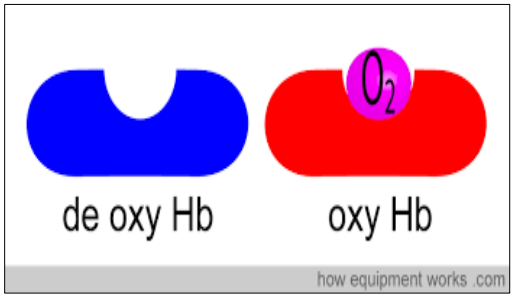
oxygen to bind to the three remaining heme units within hemoglobin (thus, oxygen binding is cooperative).



Deoxygenated hemoglobin

Deoxygenated hemoglobin is the form of hemoglobin without the bound oxygen. The absorption spectra of oxyhemoglobin and deoxyhemoglobin differ. The oxyhemoglobin has significantly lower absorption of the 660 nm wavelength than deoxyhemoglobin, while at 940 nm its absorption is slightly higher. This difference is used for the measurement of the amount of oxygen in a patient's blood by an instrument called a pulse oximeter. This difference also accounts for the presentation of cyanosis, the blue to purplish color that tissues develop during hypoxia.

Deoxygenated hemoglobin is paramagnetic; it is weakly attracted to magnetic fields. In contrast, oxygenated hemoglobin exhibits diamagnetism, a weak repulsion from a magnetic field.



Iron's oxidation state in oxyhemoglobin

Assigning oxygenated hemoglobin's oxidation state is difficult because oxyhemoglobin (Hb-O_2), by experimental measurement, is diamagnetic (no net unpaired electrons), yet the lowest-energy (ground-state) electron configurations in both oxygen and iron are paramagnetic (suggesting at least one unpaired electron in the complex). The lowest-energy form of oxygen and the lowest energy forms of the relevant oxidation states of iron, are these:

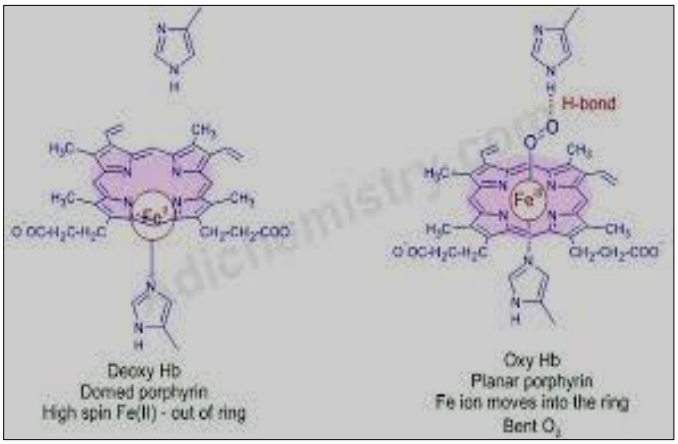
- Triplet oxygen, the lowest-energy molecular oxygen species, has two unpaired electrons in antibonding π* molecular orbitals.
- Iron(II) tends to exist in a high-spin $3d^6$ configuration with four unpaired electrons.
- Iron(III) ($3d^5$) has an odd number of electrons, and thus must have one or more unpaired electrons, in any energy state.

All of these structures are paramagnetic (have unpaired electrons), not diamagnetic. Thus, a non-intuitive (e.g., a higher-energy for at least one species) distribution of electrons in the combination of iron and oxygen must exist, in order to explain the observed diamagnetism and no unpaired electrons.

The two logical possibilities to produce diamagnetic (no net spin) Hb-O_2 are:

1. Low-spin Fe^{2+} binds to singlet oxygen. Both low-spin iron and singlet oxygen are diamagnetic. However, the singlet form of oxygen is the higher-energy form of the molecule.
2. Low-spin Fe^{3+} binds to $O_2^{\bullet-}$ (the superoxide ion) and the two unpaired electrons couple antiferromagnetically, giving observed diamagnetic properties. Here, the iron has been oxidized (has lost one electron), and the oxygen has been reduced (has gained one electron).

Another possible model in which low-spin Fe^{4+} binds to peroxide, O_2^{2-}, can be ruled out by itself, because the iron is paramagnetic (although the peroxide ion is diamagnetic). Here, the iron has been oxidized by two electrons, and the oxygen reduced by two electrons.



Direct experimental data:

- X-ray photoelectron spectroscopy suggests iron has an oxidation state of approximately 3.2.
- Infrared vibrational frequencies of the O-O bond suggests a bond length fitting with superoxide (a bond order of about 1.6, with superoxide being 1.5).
- X-ray Absorption Near Edge Structures at the iron K-edge. The energy shift of 5 eV between deoxyhemoglobin and oxyhemoglobin, as for all the methemoglobin species, strongly suggests an actual local charge closer to Fe^{3+} than Fe^{2+}.

Thus, the nearest formal oxidation state of iron in Hb-O_2 is the +3 state, with oxygen in the −1 state (as superoxide $\cdot O_2^-$). The diamagnetism in this configuration arises from the single unpaired electron on superoxide aligning antiferromagnetically with the single unpaired electron on iron (in a low-spin d^5 state), to give no net spin to the entire configuration, in accordance with diamagnetic oxyhemoglobin from experiment.

The second choice of the logical possibilities above for diamagnetic oxyhemoglobin being found correct by experiment, is not surprising: singlet oxygen (possibility #1) is an unrealistically high energy state. Model 3 leads to unfavorable separation of charge (and does not agree with the magnetic data), although it could make a minor contribution as a resonance form. Iron's shift to a higher oxidation state in Hb-O_2 decreases the atom's size, and allows it into the plane of the porphyrin ring, pulling on the coordinated histidine residue and initiating the allosteric changes seen in the globulins.

Early postulates by bio-inorganic chemists claimed that possibility #1 (above) was correct and that iron should exist in oxidation state II. This conclusion seemed likely, since the iron oxidation state III as methemoglobin, when *not* accompanied by superoxide $\cdot O_2^-$ to "hold" the oxidation electron, was known to render hemoglobin incapable of binding normal triplet O_2 as it occurs in the air. It was thus assumed that iron remained as Fe(II) when oxygen gas was bound in the lungs. The iron chemistry in this previous classical model was elegant, but the required presence of the diamagnetic, high-energy, singlet oxygen molecule was never explained. It was classically argued that the binding of an oxygen molecule

placed high-spin iron(II) in an octahedral field of strong-field ligands; this change in field would increase the crystal field splitting energy, causing iron's electrons to pair into the low-spin configuration, which would be diamagnetic in Fe(II). This forced low-spin pairing is indeed thought to happen in iron when oxygen binds, but is not enough to explain iron's change in size. Extraction of an additional electron from iron by oxygen is required to explain both iron's smaller size and observed increased oxidation state, and oxygen's weaker bond.

The assignment of a whole-number oxidation state is a formalism, as the covalent bonds are not required to have perfect bond orders involving whole electron transfer. Thus, all three models for paramagnetic Hb-O_2 may contribute to some small degree (by resonance) to the actual electronic configuration of Hb-O_2. However, the model of iron in Hb-O_2 being Fe(III) is more correct than the classical idea that it remains Fe(II).

Binding for ligands other than oxygen

Besides the oxygen ligand, which binds to hemoglobin in a cooperative manner, hemoglobin ligands also include competitive inhibitors such as carbon monoxide (CO) and allosteric ligands such as carbon dioxide (CO_2) and nitric oxide (NO). The carbon dioxide is bound to amino groups of the globin proteins to form carbaminohemoglobin; this mechanism is thought to account for about 10% of carbon dioxide transport in mammals. Nitric oxide can also be transported by hemoglobin; it is bound to specific thiol groups in the globin protein to form an S-nitrosothiol, which dissociates into free nitric oxide and thiol again, as the hemoglobin releases oxygen from its heme site. This nitric oxide transport to peripheral tissues is hypothesized to assist oxygen transport in tissues, by releasing vasodilatory nitric oxide to tissues in which oxygen levels are low.

Competitive for O_2 Binding

The binding of oxygen is affected by molecules such as carbon monoxide (for example, from tobacco smoking, exhaust gas, and incomplete combustion in furnaces). CO competes with oxygen at the heme binding site. Hemoglobin's binding affinity for CO is 250 times greater than its affinity for oxygen, meaning that small amounts of CO dramatically reduce hemoglobin's ability to transport oxygen. Since carbon monoxide is a colorless, odorless and tasteless gas, and poses a potentially fatal threat, carbon monoxide detectors have become commercially available to warn of dangerous levels in residences. When hemoglobin combines with CO, it forms a very bright red compound called carboxyhemoglobin, which may cause the skin of CO poisoning victims to appear pink in death, instead of white or blue. When inspired air contains CO levels as low as 0.02%, headache and nausea occur; if the CO concentration is increased to 0.1%, unconsciousness will follow. In heavy smokers, up to 20% of the oxygen-active sites can be blocked by CO.

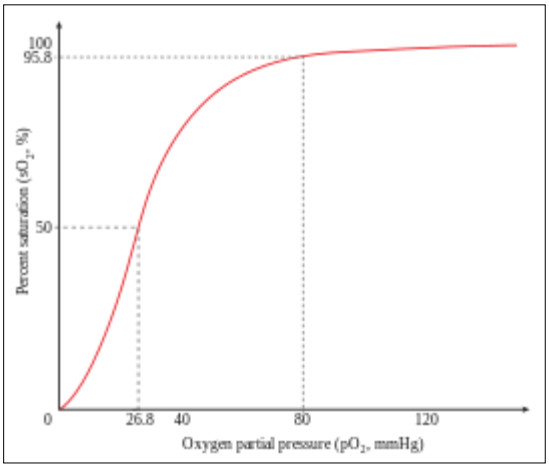
In similar fashion, hemoglobin also has competitive binding affinity for cyanide (CN^-), sulfur monoxide (SO), and sulfide (S^{2-}), including hydrogen sulfide (H_2S). All of these bind to iron in heme without changing its oxidation state, but they nevertheless inhibit oxygen-binding, causing grave toxicity.

The iron atom in the heme group must initially be in the ferrous (Fe^{2+}) oxidation state to support oxygen and other gases' binding and transport (it temporarily switches to ferric during the time oxygen is bound, as explained above). Initial oxidation to the ferric (Fe^{3+}) state without oxygen converts hemoglobin into "7emoglobin" or methemoglobin, which cannot bind oxygen. Hemoglobin in normal red blood cells is protected by a reduction system to keep this from happening. Nitric oxide is capable of converting a small fraction of hemoglobin to methemoglobin in red blood cells. The latter reaction is a remnant activity of the more ancient nitric oxide dioxygenase function of globins.

Allosteric

Carbon *di*oxide occupies a different binding site on the hemoglobin. Carbon dioxide is more readily dissolved in deoxygenated blood, facilitating its removal from the body after the oxygen has been released to tissues undergoing metabolism. This increased affinity for carbon dioxide by the venous blood is known as the Haldane effect. Through the enzyme carbonic anhydrase, carbon dioxide reacts with water to give carbonic acid, which decomposes into bicarbonate and protons:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$$



The sigmoidal shape of hemoglobin's oxygen-dissociation curve results from cooperative binding of oxygen to hemoglobin

Hence, blood with high carbon dioxide levels is also lower in pH (more acidic). Hemoglobin can bind protons and carbon dioxide, which causes a conformational change in the protein and facilitates the release of oxygen. Protons bind at various places on the protein, while carbon dioxide binds at the α-amino group. Carbon dioxide binds to hemoglobin and forms carbaminohemoglobin. This decrease in hemoglobin's affinity for oxygen by the binding of carbon dioxide and acid is known as the Bohr effect The Bohr effect favors the T state rather than the R state. (shifts the O_2-saturation curve to the *right*). Conversely, when the carbon dioxide levels in the blood decrease (i.e., in the lung capillaries), carbon dioxide and protons are released from hemoglobin, increasing the oxygen affinity of the protein. A reduction in the total binding capacity of hemoglobin to oxygen (i.e. shifting the curve down, not just to the right) due to reduced pH is called the root effect. This is seen in bony fish.

It is necessary for hemoglobin to release the oxygen that it binds; if not, there is no point in binding it. The sigmoidal curve of hemoglobin makes it efficient in binding (taking up O_2 in lungs), and efficient in unloading (unloading O_2 in tissues).

In people acclimated to high altitudes, the concentration of 2,3-Bisphosphoglycerate (2,3-BPG) in the blood is increased, which allows these individuals to deliver a larger amount of oxygen to tissues under conditions of lower oxygen tension. This phenomenon, where molecule Y affects the binding of molecule X to a transport molecule Z, is called a *heterotropic* allosteric effect. Hemoglobin in organisms at high altitudes has also adapted such that it has less of an affinity for 2,3-BPG and so the protein will be shifted more towards its R state. In its R state, hemoglobin will bind oxygen more readily, thus allowing organisms to perform the necessary metabolic processes when oxygen is present at low partial pressures.

Animals other than humans use different molecules to bind to hemoglobin and change its O_2 affinity under unfavorable conditions. Fish use both ATP and GTP. These bind to a phosphate "pocket" on the fish hemoglobin molecule, which stabilizes the tense state and therefore decreases oxygen affinity. GTP reduces hemoglobin oxygen affinity much more than ATP, which is thought to be due

to an extra hydrogen bond formed that further stabilizes the tense state. Under hypoxic conditions, the concentration of both ATP and GTP is reduced in fish red blood cells to increase oxygen affinity.

A variant hemoglobin, called fetal hemoglobin (HbF, $\alpha_2\gamma_2$), is found in the developing fetus, and binds oxygen with greater affinity than adult hemoglobin. This means that the oxygen binding curve for fetal hemoglobin is left-shifted (i.e., a higher percentage of hemoglobin has oxygen bound to it at lower oxygen tension), in comparison to that of adult hemoglobin. As a result, fetal blood in the placenta is able to take oxygen from maternal blood.

Hemoglobin also carries nitric oxide (NO) in the globin part of the molecule. This improves oxygen delivery in the periphery and contributes to the control of respiration. NO binds reversibly to a specific cysteine residue in globin; the binding depends on the state (R or T) of the hemoglobin. The resulting S-nitrosylated hemoglobin influences various NO-related activities such as the control of vascular resistance, blood pressure and respiration. NO is not released in the cytoplasm of erythrocytes but transported by an anion exchanger called AE1 out of them.

Types in humans

Hemoglobin variants are a part of the normal embryonic and fetal development. They may also be pathologic mutant forms of hemoglobin in a population, caused by variations in genetics. Some well-known hemoglobin variants, such as sickle-cell anemia, are responsible for diseases and are considered hemoglobinopathies. Other variants cause no detectable pathology, and are thus considered non-pathological variants.

In the embryo:

- Gower 1 ($\zeta_2\varepsilon_2$)
- Gower 2 ($\alpha_2\varepsilon_2$)
- Hemoglobin Portland I ($\zeta_2\gamma_2$)
- Hemoglobin Portland II ($\zeta_2\beta_2$).

In the fetus:

- Hemoglobin F ($\alpha_2\gamma_2$)

After birth:

- Hemoglobin A ($\alpha_2\beta_2$) – The most common with a normal amount over 95%

- Hemoglobin A_2 ($\alpha_2\delta_2$) – δ chain synthesis begins late in the third trimester and, in adults, it has a normal range of 1.5–3.5%
- Hemoglobin F ($\alpha_2\gamma_2$) – In adults Hemoglobin F is restricted to a limited population of red cells called F-cells. However, the level of Hb F can be elevated in persons with sickle-cell disease and beta-thalassemia.
- Hemoglobin D-Punjab – ($\alpha_2\beta^D{}_2$) – A variant form of hemoglobin.
- Hemoglobin H (β_4) – A variant form of hemoglobin, formed by a tetramer of β chains, which may be present in variants of α thalassemia.
- Hemoglobin Barts (γ_4) – A variant form of hemoglobin, formed by a tetramer of γ chains, which may be present in variants of α thalassemia.
- Hemoglobin S ($\alpha_2\beta^S{}_2$) – A variant form of hemoglobin found in people with sickle cell disease. There is a variation in the β-chain gene, causing a change in the properties of hemoglobin, which results in sickling of red blood cells.

- Hemoglobin C ($\alpha_2\beta^C_2$) – Another variant due to a variation in the β-chain gene. This variant causes a mild chronic hemolytic anemia.
- Hemoglobin E ($\alpha_2\beta^E_2$) – Another variant due to a variation in the β-chain gene. This variant causes a mild chronic hemolytic anemia.
- Hemoglobin AS – A heterozygous form causing sickle cell trait with one adult gene and one sickle cell disease gene
- Hemoglobin SC disease – A compound heterozygous form with one sickle gene and another encoding Hemoglobin C.
- Hemoglobin Hopkins-2 – A variant form of hemoglobin that is sometimes viewed in combination with Hemoglobin S to produce sickle cell disease.

Concentration

Hemoglobin concentration measurement is among the most commonly performed blood tests, usually as part of a complete blood count. For example, it is typically tested before or after blood donation. Results are reported in g/L, g/dL or mol/L. 1 g/dL equals about 0.6206 mmol/L, although the latter units are not used as often due to uncertainty regarding the polymeric state of the molecule. This conversion factor, using the single globin unit molecular weight of 16,000 Da, is more common for hemoglobin concentration in blood. For MCHC (mean corpuscular hemoglobin concentration) the conversion factor 0.155, which uses the tetramer weight of 64,500 Da, is more common. Normal levels are:

- **Men: 13.8 to 18.0 g/dL (138 to 180 g/L, or 8.56 to 11.17 mmol/L)**
- **Women: 12.1 to 15.1 g/dL (121 to 151 g/L, or 7.51 to 9.37 mmol/L)**
- **Children: 11 to 16 g/dL (111 to 160 g/L, or 6.83 to 9.93 mmol/L)**
- **Pregnant women: 11 to 14 g/dL (110 to 140 g/L, or 6.83 to 8.69 mmol/L) (9.5 to 15 usual value during pregnancy)**

Normal values of hemoglobin in the 1st and 3rd trimesters of pregnant women must be at least 11 g/dL and at least 10.5 g/dL during the 2nd trimester.

Dehydration or hyperhydration can greatly influence measured hemoglobin levels. Albumin can indicate hydration status.

If the concentration is below normal, this is called anemia. Anemias are classified by the size of red blood cells, the cells that contain hemoglobin in vertebrates. The anemia is called "microcytic" if red cells are small, "macrocytic" if they are large, and "normocytic" otherwise.

Hematocrit, the proportion of blood volume occupied by red blood cells, is typically about three times the hemoglobin concentration measured in g/dL. For example, if the hemoglobin is measured at 17 g/dL, that compares with a hematocrit of 51%.

Laboratory hemoglobin test methods require a blood sample (arterial, venous, or capillary) and analysis on hematology analyzer and CO-oximeter. Additionally, a new noninvasive hemoglobin (SpHb) test method called Pulse CO-Oximetry is also available with comparable accuracy to invasive methods.

Concentrations of oxy- and deoxyhemoglobin can be measured continuously, regionally and noninvasively using NIRS. NIRS can be used both on the head as on muscles. This technique is often used for research in e.g. elite sports training, ergonomics, rehabilitation, patient monitoring, neonatal research, functional brain monitoring, brain computer interface, urology (bladder contraction), neurology (Neurovascular coupling) and more.

Long-term control of blood sugar concentration can be measured by the concentration of Hb A_{1c}. Measuring it directly would require many samples because blood sugar levels vary widely through the day. Hb A_{1c} is the product of the irreversible reaction of hemoglobin A with glucose. A higher glucose concentration results in more Hb A_{1c}. Because the reaction is slow, the Hb A_{1c} proportion represents glucose level in blood averaged over the half-life of red blood cells, is typically 50–55 days. An Hb A_{1c} proportion of 6.0% or less show good long-term glucose control, while values above 7.0% are elevated. This test is especially useful for diabetics.

The functional magnetic resonance imaging (fMRI) machine uses the signal from deoxyhemoglobin, which is sensitive to magnetic fields since it is paramagnetic. Combined measurement with NIRS shows good correlation with both the oxy- and deoxyhemoglobin signal compared to the BOLD signal.

Athletic tracking and self tracking uses

Hemoglobin can be tracked noninvasively, to build an individual data set tracking the hemoconcentration and hemodilution effects of daily activities for better understanding of sports performance and training. Athletes are often concerned about endurance and intensity of exercise. Using the scientific technique of absorption spectroscopy with eight wavelengths of light. This method is similar to a pulse oximeter, which consists of a small sensing device that clips to the finger. The sensor uses light-emitting diodes that emit red and infrared light through the tissue to a light detector, which then sends a signal to a processor to calculate the absorption of light by the hemoglobin protein.

Myoglobin

Myoglobin (symbol **Mb** or **MB**) is an iron- and oxygen-binding protein found in the muscle tissue of vertebrates in general and in almost all mammals. It is related to hemoglobin, which is the iron- and oxygen-binding protein in blood, specifically in the red blood cells. In humans, myoglobin is only found in the bloodstream after muscle injury. It is an abnormal finding, and can be diagnostically relevant when found in blood.

Myoglobin is the primary oxygen-carrying pigment of muscle tissues. High concentrations of myoglobin in muscle cells allow organisms to hold their breath for a longer period of time. Diving mammals such as whales and seals have muscles with particularly high abundance of myoglobin. Myoglobin is found in Type I muscle, Type II A and Type II B, but most texts consider myoglobin not to be found in smooth muscle.

Myoglobin was the first protein to have its three-dimensional structure revealed by X-ray crystallography. This achievement was reported in 1958 by John Kendrew and associates. For this discovery, John Kendrew shared the 1962 Nobel Prize in chemistry with Max Perutz. Despite being one of the most studied proteins in biology, its physiological function is not yet conclusively established: mice genetically engineered to lack myoglobin can be viable and fertile but show many cellular and physiological adaptations to overcome the loss. Through observing these changes in myoglobin-deplete mice, it is hypothesised that myoglobin function relates to increased oxygen transport to muscle, oxygen storage and as a scavenger of reactive oxygen species.

In humans myoglobin is encoded by the *MB* gene.

Hemoglobin can take the forms of oxyhemoglobin (HbO_2), carboxyhemoglobin (HbCO), and methemoglobin (met-Hb); similarly, myoglobin can take the forms of oxymyoglobin (MbO_2), carboxymyoglobin (MbCO), and metmyoglobin (met-Mb).

Differences from hemoglobin

Like hemoglobin, myoglobin is a cytoplasmic protein that binds oxygen on a heme group. It harbors only one heme group, whereas hemoglobin has four. Although its heme group is identical to those in Hb, Mb has a higher affinity for oxygen than does hemoglobin. This difference is related to its different role: whereas hemoglobin transports oxygen, myoglobin's function is to store oxygen.

Structure and bonding

Myoglobin belongs to the globin superfamily of proteins, and as with other globins, consists of eight alpha helices connected by loops. Human globin contains 154 amino acids.

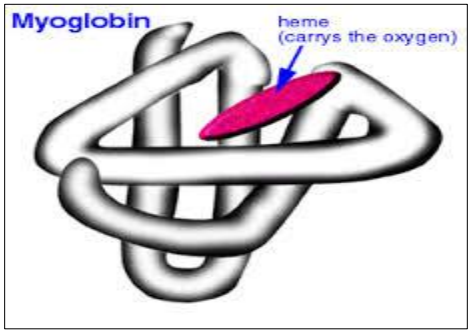
Myoglobin contains a porphyrin ring with an iron at its center. A *proximal* histidine group (His-93) is attached directly to iron, and a *distal* histidine group (His-64) hovers near the opposite face.The distal imidazole is not bonded to the iron but is available to interact with the substrate O_2. This interaction encourages the binding of O_2, but not carbon monoxide (CO), which still binds about 240× more strongly than O_2.

The binding of O_2 causes substantial structural change at the Fe center, which shrinks in radius and moves into the center of N4 pocket. O_2-binding induces "spin-pairing": the five-coordinate ferrous deoxy form is high spin and the six coordinate oxy form is low spin and diamagnetic.

Function

The binding affinities for oxygen between myoglobin and hemoglobin are important factors for their function. Both myoglobin and hemoglobin binds oxygen well when the concentration of oxygen is really high (E.g. in Lung), however, hemoglobin is more likely to release oxygen in areas of low concentration (E.g. in tissues). Since hemoglobin binds oxygen less tightly than myoglobin in muscle tissues, it can effectively transport oxygen throughout the body and deliver it to the cells. Myoglobin, on the other hand, would not be as efficient in transferring oxygen. It does not show the cooperative binding of oxygen because it would take up oxygen and only release in extreme conditions. Myoglobin has a strong affinity for oxygen that allows it to store oxygen in muscle effectively. This is important when the body is starved for oxygen, such as during anaerobic exercise. During that time, carbon dioxide level in blood streams is extremely high and lactic acid concentration builds up in muscles. Both of these factors cause myoglobin (and hemoglobins) to release oxygen, for protecting the body tissues from getting damaged under harsh conditions. If the concentration of myoglobin is high within the muscle cells, the organism is able to utilize the oxygen in its lungs for a much longer period of time.

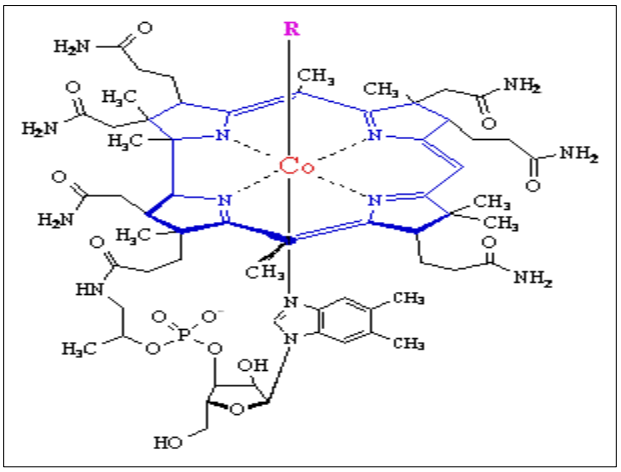
Myoglobin, an iron-containing protein in muscle, receives oxygen from the red blood cells and transports it to the mitochondria of muscle cells, where the oxygen is used in cellular respiration to produce energy. Each myoglobin molecule has one heme prosthetic group located in the hydrophobic cleft in the protein. The function of myoglobin is notable from Millikan's review (1) in which he put together an accomplished study to establish that myoglobin is formed adaptively in tissues in response to oxygen needs and that myoglobin contributes to the oxygen supply of these tissues. Oxymyoglobin regulates both oxygen supply and utilization by acting as a scavenger of the bioactive molecule nitric oxide. Nitric oxide is generated continuously in the myocyte. Oxymyoglobin reacts with NO to form harmless nitrates, with concomitant formation of ferric myoglobin, which is recycled through the action of the intracellular enzyme metmyoglobin reductase. Flogel (2) conducted a study that showed how the interaction of NO and oxymyoglobin controls cardiac oxygen utilization.



Vitamin B-12

Vitamin B_{12} is the only known essential biomolecule with a stable metal-carbon bond, that is, it is an organometallic compound. The cobalt can link to:

1. a methyl group - as in methylcobalamin
2. a 5'-deoxyadenosine at the the 5' positon - as in adenosylcobalamin (coenzyme B_{12}
3. a cyanide group - as in Vitamin B_{12} - as supplied from drug companies.

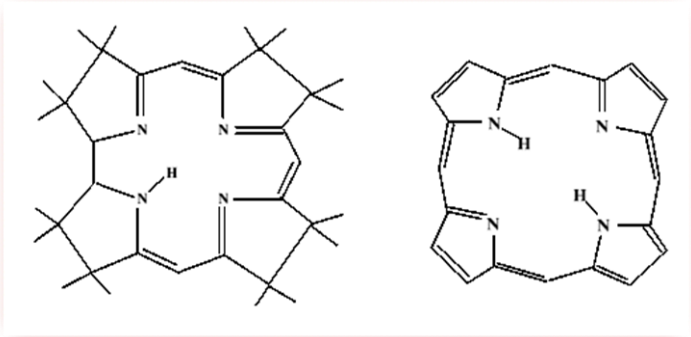


The particular link in the cobalamin has a profound effect upon the mechanism of the enzyme reaction.

A methyl-nickel intermediate on acetyl-CoA synthase is also known, but only as an intermediate rather than a stable, isolable compound as the three cobalamins. Other organometals such as the methylmercury ion are highly toxic, it is interesting that there is an unfortunate connection between CH_3Hg^+ and methylcobalamin.

Chime enhanced structures

The core of the molecule is a corrin ring with various attached sidegroups. The ring consists of 4 pyrrole subunits, joined on opposite sides by a C-CH_3 methylene link, on one side by a C-H methylene link, and with the two of the pyrroles joined directly. It is thus like a porphyrin, but with one of the bridging methylene groups removed. The nitrogen of each pyrolle is coordinated to the central cobalt atom.



Links are to Chime pbd files to enable comparisons of the structures

The sixth ligand below the ring is a nitrogen of a 5,6-dimethylbenzimidazole. The other nitrogen of the 5,6-dimethylbenzimidazole is linked to a five-carbon sugar, which in turn connects to a phosphate group, and thence back onto the corrin ring via one of the seven amide groups attached to the periphery of the corrin ring. The base ligand thus forms a 'strap' back onto the corrin ring. An important aspect of the corrin ring, when compared to the porphyrin, is the relative flexibility of the corrin system, the corrin ring is also less flat when viewed from the side than is a porphyrin ring. This adds up to some considerable differences between the chemistry of a cobalt porphyrin and a cobalt corrin. In addition, the corrin only has a conjugated chain around part of the ring system, whereas a porphyrin is delocalised around the whole four pyrolle rings.

The center-piece in the structure is of course the cobalt(III), the octahedral coordination to five nitrogens and a carbon is common to all three cobalamins, and can be found in a number of simple coordination complexes. The simple complexes have attracted wide interest as models for cobalamins.

Chemistry

B_{12} is the most chemically complex of all the vitamins. The structure of B_{12} is based on a corrin ring, which is similar to the porphyrin ring found in heme, chlorophyll, and cytochrome. The central metal ion is cobalt. Four of the six coordination sites are provided by the corrin ring, and a fifth by a dimethylbenzimidazole group. The sixth coordination site, the center of reactivity, is variable, being a cyano group (–CN), a hydroxyl group (–OH), a methyl group ($–CH_3$) or a 5′-deoxyadenosyl group (here the C5′ atom of the deoxyribose forms the covalent bond with cobalt), respectively, to yield the four B_{12} forms mentioned below. Historically, the covalent C-Co bond is one of the first examples of carbon-metal bonds to be discovered in biology. The hydrogenases and, by necessity, enzymes associated with cobalt utilization, involve metal-carbon bonds.

Vitamin B_{12} is a generic descriptor name referring to a collection of cobalt and corrin ring molecules which are defined by their particular vitamin function in the body. All of the substrate cobalt-corrin molecules from which B_{12} is made must be synthesized by bacteria. After this synthesis is complete, the human body has the ability (except in rare cases) to convert any form of B_{12} to an active form, by means of enzymatically removing certain prosthetic chemical groups from the cobalt atom and replacing them with others.

The four forms (vitamers) of B_{12} are all deeply red colored crystals and water solutions, due to the color of the cobalt-corrin complex.

- **Cyanocobalamin** is one such form, i.e. "vitamer", of B_{12} because it can be metabolized in the body to an active coenzymeform. The cyanocobalamin form of B_{12} does not occur in nature normally, but is a byproduct of the fact that other forms of $B_{12}$are avid binders of cyanide (–CN) which they pick up in the process of activated charcoal purification of the vitamin after it is made by bacteria in the commercial process. Since the cyanocobalamin form of B_{12} is easy to crystallize and is not sensitive to air-oxidation, it is typically used as a form of B_{12} for food additives and in many common multivitamins. Pure cyanocobalamin possesses the deep pink color associated with most octahedral cobalt(II) complexes and the crystals are well formed and easily grown up to millimeter size.

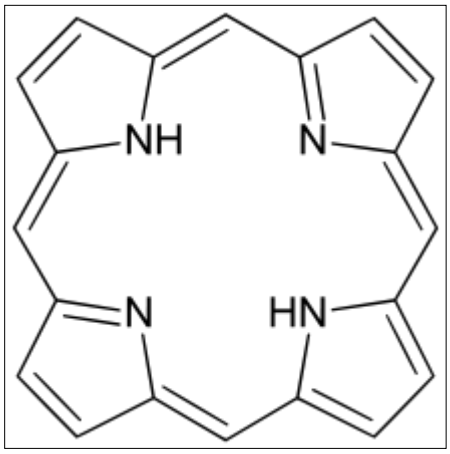
- **Hydroxocobalamin** is another form of B_{12} commonly encountered in pharmacology, but which is not normally present in the human body. Hydroxocobalamin is sometimes denoted B_{12a}. This form of B_{12} is the form produced by bacteria, and is what is converted to cyanocobalmin in the commercial charcoal filtration step of production. Hydroxocobalamin has an avid affinity for cyanide ions and has been used as an antidote to cyanide poisoning. It is supplied typically in water solution for injection. Hydroxocobalamin is thought to be converted to the active enzymic forms of B_{12} more easily than cyanocobalamin, and since it is little more expensive than cyanocobalamin, and has longer retention times in the body, has been used for vitamin replacement in situations where added reassurance of activity is desired. Intramuscular administration of hydroxocobalamin is also the preferred treatment for pediatric patients with intrinsic cobalamin metabolic diseases, for vitamin B_{12} deficient patients with tobacco amblyopia (which is thought to perhaps have a component of cyanide poisoning from cyanide in cigarette smoke); and for treatment of patients with pernicious anemia who have optic neuropathy.

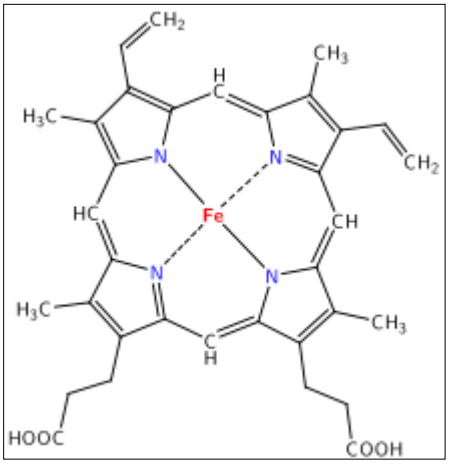
- **Adenosylcobalamin** (adoB_{12}) and **methylcobalamin** (MeB_{12}) are the two enzymatically active cofactor forms of B_{12} that naturally occur in the body. Most of the body's reserves are stored as adoB_{12} in the liver. These are converted to the other methylcobalamin form as needed.

Porphyrin

Porphyrins are a group of heterocyclic macrocycle organic compounds, composed of four modified pyrrole subunits interconnected at their α carbon atoms via methine bridges (=CH−). The parent porphyrin is porphin, and substituted porphines are called porphyrins. The porphyrin ring structure is aromatic, with a total of 26 electrons in the conjugated system. Various analyses indicate that not all atoms of the ring are involved equally in the conjugation or that the molecule's overall nature is substantially based on several smaller conjugated systems. One result of the large conjugated system is that porphyrin molecules typically have very intense absorption bands in the visible region and may be deeply colored; the name "porphyrin" comes from the Greek word πορφύρα (*porphyra*), meaning *purple*.

Many porphyrins are naturally occurring; one of the best-known porphyrins is heme, the pigment in red blood cells, a cofactor of the protein hemoglobin.





Complexes of porphyrins

Porphyrins are the conjugate acids of ligands that bind metals to form complexes. The metal ion usually has a charge of 2+ or 3+. A schematic equation for these syntheses is shown:

$$H_2\text{porphyrin} + [ML_n]^{2+} \rightarrow M(\text{porphyrinate})L_{n-4} + 4\ L + 2\ H^+$$ where M = metal ion and L = a ligand

A porphyrin without a metal-ion in its cavity is a *free base*. Some iron-containing porphyrins are called hemes. Heme-containing proteins, or *hemoproteins*, are found extensively in nature. Hemoglobin and myoglobin are two O_2-binding proteins that contain iron porphyrins. Various cytochromes are also hemoproteins.

Introduction

Chlorophyll is a green compound found in leaves and green stems of plants. Initially, it was assumed that chlorophyll was a single compound but in 1864 Stokes showed by spectroscopy that chlorophyll was a mixture. If dried leaves are powdered and digested with ethanol, after concentration of the solvent, 'crystalline' chlorophyll is obtained, but if ether or aqueous acetone is used instead of ethanol, the product is 'amorphous' chlorophyll.

In 1912, Willstatter *et al*. showed that chlorophyll was a mixture of two compounds, chlorophyll-*a* and chlorophyll-*b*:

Chlorophyll *a*

Chlorophyll *a* is a specific form of chlorophyll used in oxygenic photosynthesis. It absorbs most energy from wavelengths of violet-blue and orange-red light. It also reflects green/yellow light, and as such contributes to the observed green color of most plants. This photosynthetic pigment is essential for photosynthesis in eukaryotes, cyanobacteria and prochlorophytes because of its role as primary electron donor in the electron transport chain. Chlorophyll *a* also transfers resonance energy in the antenna complex, ending in the reaction center where specific chlorophylls P680 and P700 are located.

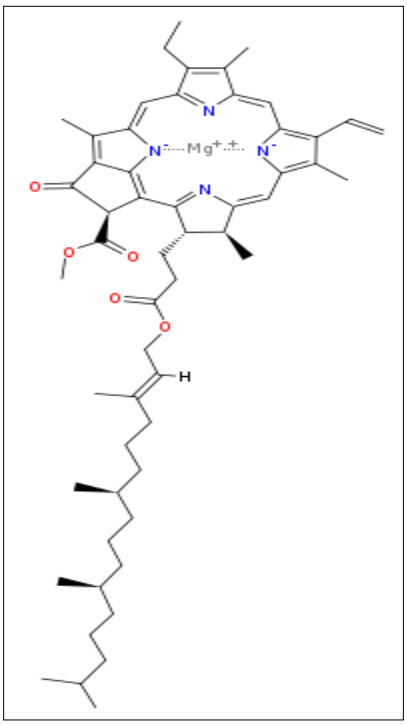


Photo synthesis in porphyrin ring complexes

The two components were separated by shaking a light petroleum solution of chlorophyll with aqueous methanol: chlorophyll-*a* remains in the light petroleum but chlorophyll-*b* is transferred into the aqueous methanol. Cholorophyll-*a* is a bluish-black solid and cholorophyll-*b* is a dark green solid, both giving a green solution in organic solutions. In natural chlorophyll there is a ratio of 3 to 1 (of *a* to *b*) of the two components.

The intense green colour of chlorophyll is due to its strong absorbencies in the red and blue regions of the spectrum, Because of these absorbencies the light it reflects and transmits appears green.

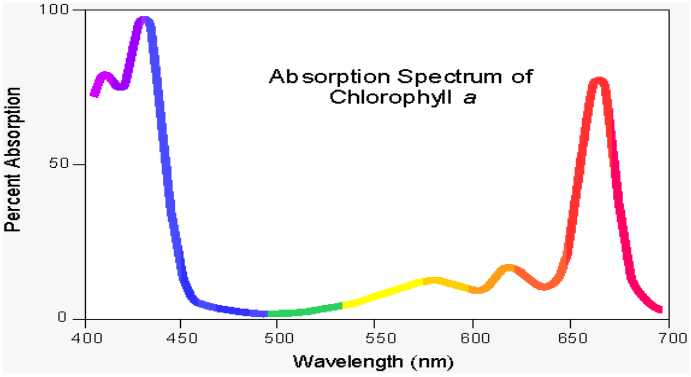


Fig. 1 - The uv/visible adsorption spectrum for chlorophyll.

Due to the green colour of chlorophyll, it has many uses as dyes and pigments. It is used in colouring soaps, oils, waxes and confectionary.

Chlorophyll's most important use, however, is in nature, in photosynthesis. It is capable of channelling the energy of sunlight into chemical energy through the process of photosynthesis. In this process the energy absorbed by chlorophyll transforms carbon dioxide and water into carbohydrates and oxygen:

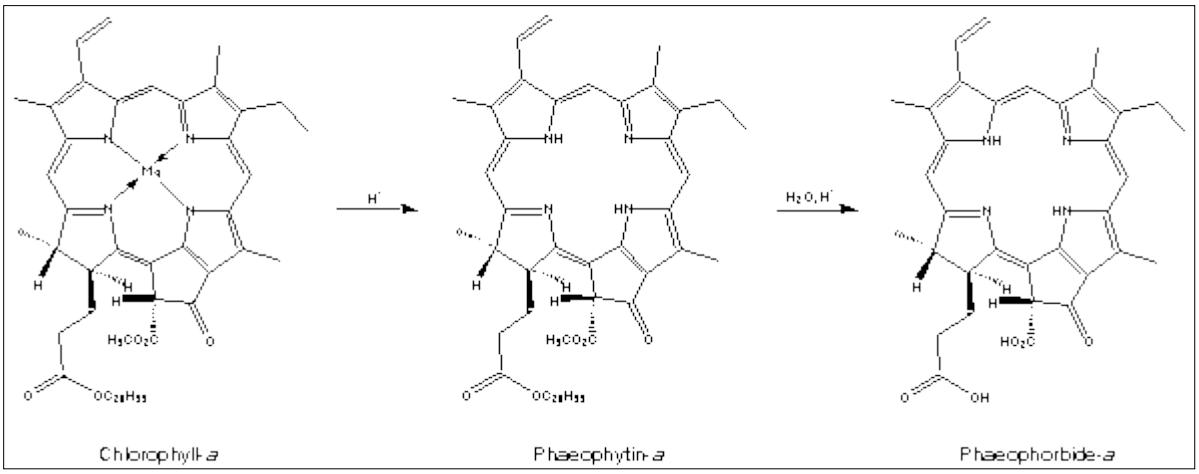
$$CO_2 + H_2O \longrightarrow (CH_2O) + O_2$$

The chemical energy stored by photosynthesis in carbohydrates drives biochemical reactions in nearly all living organisms.

In the photosynthetic reaction electrons are transferred from water to carbon dioxide, that is carbon dioxide is reduced by water. Chlorophyll assists this transfer as when chlorophyll absorbs light energy, an electron in chlorophyll is excited from a lower energy state to a higher energy state. In this higher energy state, this electron is more readily transferred to another molecule. This starts a chain of electron-transfer steps, which ends with an electron being transferred to carbon dioxide. Meanwhile, the chlorophyll which gave up an electron can accept an electron from another molecule. This is the end of a process which starts with the removal of an electron from water. Thus, chlorophyll is at the centre of the photosynthetic oxidation-reduction reaction between carbon dioxide and water.

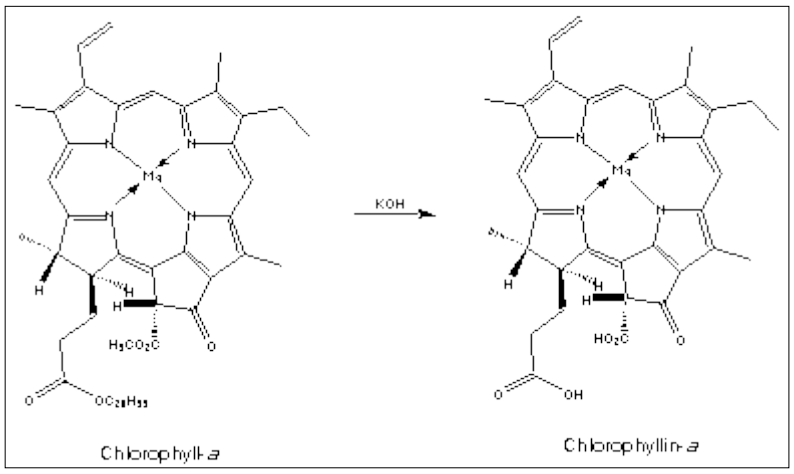
Simple reactions of chlorophyll

Treatment of cholorophyll-*a* with acid removes the magnesium ion replacing it with two hydrogen atoms giving an olive-brown solid, phaeophytin-*a*. Hydrolysis of this (reverse of esterification) splits off phytol and gives phaeophorbide-*a*. Similar compounds are obtained if chlorophyll-*b* is used.



Overall reaction scheme for the hydrolysis of chlorophyll.

Chlorophyll can also be reacted with a base which yields a series of phyllins, magnesium porphyrin compounds. Treatment of phyllins with acid gives porphyrins.



Overall scheme for the reaction of alkaline with chlorophyll.

Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

POSSIBLE QUESTIONS

MULTIPLE CHOICE QUESTIONS

Section A **20x1=20**

1. Which of the following is not a part of hemoglobin molecule?
a. Pyrrole rings b. Vinyl group c. Histidine **d. Ferric ions**
2. False statement about hemoglobin structure
a. **Hb has 2 polypeptides** b. Iron is present in ferrous state
c. Hb structurally similar to myoglobin
d. Ferrous ions are in porphyrin rings
3. In hemoglobin, iron is bound to
a. **Histidine** b. Leucine c. Iso-leucine d. Valine
4. In hemoglobin the innate affinity of heme for carbon monoxide is diminished by the presence of
a. His F9 **b. His E7** c. Thr C4 d. Gly B6
5. Heme in Hemoglobin is in the
a. **Hydrophobic Pocket** b. Positive region c. Negative region d. Polar region
6. Iron in the hemoglobin is held by-
a. **Polar bonds** b. Covalent bonds c. Co-ordinate bonds d. Non polar bonds
7. Heme in hemoglobin is-
a. Between Helix C and D **b. Surrounded by non- polar environment** c. Bonded to E7 histidine d. Proto-porphyrin IX
8. Which of the following statement characterize both Hemoglobin and Myoglobin?
a. Non helical b. Subunits which are held together by hydrogen bonds c. Binds with 2 Heme **d. Bind with 4 molecule of O_2**
9. At pH 7 the binding of 2.3-DPG to hemoglobin occurs at which site
a. Sulfhydryl group b. Carboxy terminal c. **Amino-terminal** d. Histidin
10. Decreased glycolytic activity impairs oxygen transport by hemoglobin due to
a. Reduced energy production **b. Decreased production of 2, 3-bisphsphoglycerate**
c. Reduced synthesis of hemoglobin d. Low levels of oxygen

11. There are more than how many variants of human hemoglobin gene?
a. **300** b. 330 c. 350 d. 400

12. Hemoglobin estimation is done by all except
a. Drabkin's method b. Sahli's method c. Spectro-photometry
d. Wintrobe's method

13. Bisphosphoglycerate (BPG) cannot bind to the oxygenated R state of hemoglobin because

a. It is displaced from the heme by oxygen
b. it is displaced from the heme by movement of the proximal histidine
c. its binding pocket becomes too small to accommodate BPG
d. BPG binds to the R state with the same affinity as the T state

14. The Hill coefficient (nH) for myoglobin and hemoglobin are respectively

a. 2.8 and 1.0 **b. 1.0 and 2.8** c. 1.2 and 4.5 d. 4.5 and 1.2

15. In hemoglobin, allosteric effects occur

a. Only in humans b. For maintaining Fe in the Fe2+ state
c. To minimize oxygen delivery to the tissue
d. To maximize oxygen delivery to the tissues

16. Small molecules affect hemoglobin (Hb) by

a. Decreasing Hb affinity for O2 b. Increasing Hb affinity for O2 c.Increasing [H+]
d. Increasing [H+] and decreasing Hb affinity for O_2

17. The oxidation state of an individual atom is

a. **Zero** b. One c. Two d. Three

18. Low counts of hemoglobin leads to

a. **Anemia** b. Pellagra c. Sterility d. Scurvey

19. Which one of the following has 153 amino acids residues?

a. Hemoglobin **b. Myoglobin** c. Oxyhemoglobin d. Coenzyme

20. Muscle injury is commonly associated with the release of

a. Hemoglobin **b. Myoglobin** c. Oxyhemoglobin d. Coenzyme

8-MARKS

1. What is Vitamin B-12? Name the important biological reactions?
2. What is porphyrin ring? Mention it occurrence in biological system?
3. Give an account of structure of hemoglobin and myoglobin?
4. How the photosynthesis occurred in porphyrin ring complexes?
5. Give the characteristic properties of B-12 co-enzyme?
6. Discuss the functions of hemoglobin in biological system?
7. Give an account of biological oxygen carriers?
8. Discuss the structural features of Vitamin B12?
9. Command on the different oxidation states of Co in vitamin B-12?
10. Name some important synthetic oxygen carriers and give the structural features?

15CHU505C
Karpagam Academy of Higher Education
Coimbatore-21
(For the candidate admitted on 2015 onwards)
Department of Chemistry
V- semester
Bio-Inorganic Chemistry

UNIT II- Objective Questions for online examination (Each carry 1 Marks)

Questions	Option A	Option B	Option C	Option D	Answer
Which of the following is not a part of hemoglobin molecule?	Pyrrole rings	Vinyl group	Histidine	Ferric ions	Ferric ions
False statement about hemoglobin structure	Hb has 2 polypeptides	Iron is present in ferrous state	Hb structurally similar to myoglobin	Ferrous ions are in porphyrin rings	Hb has 2 polypeptides
In hemoglobin, iron is bound to	Histidine	Leucine	Iso-leucine	Valine	Histidine
In hemoglobin the innate affinity of heme for carbon monoxide is diminished by the presence of	His F9	His E7	Thr C4	Gly B6	His E7
Heme in Hemoglobin is in the	Hydrophobic Pocket	Positive region	Negative region	Polar region	Hydrophobic Pocket
Iron in the hemoglobin is held by-	Polar bonds	Covalent bonds	Co-ordinate bonds	Non polar bonds	Polar bonds
Heme in hemoglobin is-	Between Helix C and D	Surrounded by non- polar environment	Bonded to E7 histidine	Proto-porphyrin IX	Surrounded by non- polar environment
Which of the following statement characterize both Hemoglobin and Myoglobin?	Non helical	Subunits which are held together by hydrogen bonds	Binds with 2 Heme	Bind with 1 molecule of O2	Bind with 1 molecule of O2
Which is an allosteric protein?	Transferrin	Ceruloplasmin	Hemoglobin	Myoglobin	Hemoglobin
Myoglobin	Contains four Hemes per molecule	Shows the Bohr Effect	Has an O2 dissociation curve that is unaffected by wide range of pH	Unaffected by wide range of pH	Has an O2 dissociation curve that is unaffected by wide range of pH
Hemoglobin is a buffer because of	Histidine residue	Glycoprotein nature	Weak acidic nature	Iron molecule	Histidine residue
At pH 7 the binding of 2.3-DPG to hemoglobin occurs at which site	Sulfhydryl group	Carboxy terminal	Amino-terminal	Histidine	Amino-terminal
Decreased glycolytic activity impairs oxygen transport by hemoglobin due to	Reduced energy production	Decreased production of 2, 3-bisphsphoglycerate	Reduced synthesis of hemoglobin	Low levels of oxygen	Decreased production of 2, 3-bisphsphoglycerate
There are more than how many variants of human hemoglobin gene?	300	330	350	400	300
Hemoglobin estimation is done by all except	Drabkin's method	Sahli's method	Spectro-photometry	Wintrobe's method	Wintrobe's method
Myoglobin and the subunits of hemoglobin have	no obvious structural relationship	Very similar primary and tertiary structures	Very similar primary structures, but different tertiary structures	Very similar tertiary structures, but different primary structures	very similar tertiary structures, but different primary structures
Vitamin B12 is also called as	Cobalamin	Retinol	Thiamine	Riboflavin	Cobalamine
Vitamin B12 contains the biochemically rare element	Cobalt	Nickle	Iron	Zinc	Cobalt
Which one of the following is an iron- and oxygen-binding protein	Myoglobin	Hemoglogin	Cobalt	Veins	Myoglobin
Which one of the following is a protein in red blood cells that carries oxygen throught the body	Myoglobin	Hemoglogin	Cobalt	Veins	Hemoglogin
Myoglobin's affinity for oxygen is	higher than hemoglobin	Lower than hemoglobin	Equal to hemoglobin	Much higher than hemoglobin	Higher than hemoglobin
The hemoglobin molecule is made up of	One polypeptide chains	Two polypeptide chains	Three polypeptide chains	four polypeptide chains	Four polypeptide chains
The binding of oxygen to hemoglobin is a	Reversible reaction	Irreversible reaction	Continuous reaction	Spontaneous reaction	reversible reaction
Hemoglobin is a tetramer consisting of	Two dimers	Three dimers	Four dimers	Five dimers	Two dimers
Hemoglobin is a	Trimer	Tetramer	Polymer	Dimer	Tetramer

Which one of the following helps in the transportation of carbon dioxide and hydrogen ions back to the lungs	Hemoglobin	Myoglobin	Cobalt	Veins	Hemoglobin
Which one of the following is a group of heterocyclic macrocycle organic compounds, composed of four modified pyrrole subunits interconnected at their α carbon atoms	Porphyrins	Hemoglobin	Myoglobin	Riboflavin	Porphyrins
Vitamin-B12 deficiency causes	Pernicious anemia	BeriBeri	Nightblindness	Scurvey	Pernicious anemia
Vitamin B12 acts as co-enzyme to which one of the following enzymes?	Isocitrate dehydrogenase	Homocysteine methyl transferase	Glycogen synthase	G-6-P dehydrogenase	Homocysteine methyl transferase
Cobalt contain vitamin is	Vit-B	Vit-B1	Vit-B9	Vit-B12	Vit-B12
Vitamin often acts as	Apoenzymes	Holoenzymes	Co-factors	Co-enzymes	Co-enzymes
The subunits of hemoglobin are arranged in a	Tetrahedral array	Trihedral array	Polygonal array	Monomer array	Tetrahedral array
In hemoglobin the arrangement of polypeptides is held together by	Double bonding	Carbon bonding	Triple bonding	Hydrogen bonding	Hydrogen bonding
Vitamin B12 is synthesized by	Fishes	micro-organisms	Plants	Animals	Micro-organisms
In the co-enzyme $B_{12}$the position occupied by a cyanide ion in vitamin B_{12} is bonded directly to the ?	Adenine	5-6 dimethylbenzimidazole	Hydroxycobalamin	Cyanocobalamin	Adenine
Which one of the following reactions is NOT a redox reaction?	HCl + NaOH --> NaCl + H_2O	$I_2 + 2Fe^{2+}$ --> $2I^- + 2Fe^{3+}$	Zn + Cu^{2+} --> Zn^{2+} + Cu	2Mg + O_2 --> 2MgO	HCl + NaOH --> NaCl + H_2O
Redox reactions involves exchange of	Electrons between atoms	Protons between atoms	Neutrons between atoms	Neurons between molecules	electrons between atoms
Redox reaction in living organisms involves gain and loss of	Carbon atoms	Nitrogen atoms	Hydrogen atoms	Oxygen atoms	hydrogen atoms
Which particles are gained and lost during a redox reaction?	Electrons	Neutron	Positron	Duetron	Electrons
In an oxidation-reduction reduction, reduction is defined as	Loss of protons	Loss of electrons	Loss of positron	Gain of electrons	Gain of electrons
Reducing agent	Donor of electrons	Acceptor of electrons	Loss of electrons	Gain of electrons	Donor of electrons
The primary process of reducing ore at high temperature to produce metals is known as	Smelting	Galvanization	Electroplating	Electrorefining	Smelting
Which of the following ETC components accepts only electrons?	Coenzyme Q	Cytochrome b	FAD	FMN	Cytochrome b
Oxidizing which of the following substances yields the most energy?	Proteins	Glucose	Fatty acids	Water	Fatty acids
The final electron acceptor in lactic acid fermentation is	Pyruvate	NAD^+	Lactic acid	O_2	Pyruvate
In sickle cell anemia, the basis of the malfunction of the hemoglobin molecule is	Incorrect secondary structure	Substitution of a single amino acid	Reduced affinity for oxygen	Insufficient iron in the diet	Substitution of a single amino acid
Deficiency of which one of these vitamins may lead to megaloblastic anaemia?	Vitamin B6	Vitamin B12	Vitamin E	Vitamin K	Vitamin B12
Vitamin B12 deficiency can give rise to all of the following, except	Myelopathy	Optic atrophy	Peripheral neuropathy	Myopathy	Myopathy
Bisphosphoglycerate (BPG) cannot bind to the oxygenated R state of hemoglobin because	It is displaced from the heme by oxygen	it is displaced from the heme by movement of the proximal histidine	its binding pocket becomes too small to accommodate BPG	BPG binds to the R state with the same affinity as the T state	Its binding pocket becomes too small to accommodate BPG
The Hill coefficient (n_H) for myoglobin and hemoglobin are respectively	2.8 and 1.0	1.0 and 2.8	1.2 and 4.5	4.5 and 1.2	1.0 and 2.8
In hemoglobin, allosteric effects occur	Only in humans	For maintaining Fe in the Fe^{2+} state	To minimize oxygen delivery to the tissues	To maximize oxygen delivery to the tissues	To maximize oxygen delivery to the tissues
Small molecules affect hemoglobin (Hb) by	Decreasing Hb affinity for O_2	Increasing Hb affinity for O_2	Increasing $[H^+]$	Increasing $[H^+]$ and decreasing Hb affinity for O_2	Increasing $[H^+]$ and decreasing Hb affinity for O_2
Myoglobin was the first protein to have its	Two-dimensional structure	Three-dimensional structure	Four-dimensional structure	Five-dimensional structure	Three-dimensional structure
Hydrogen fluoride is an example for	Redox reaction	Oxidation reaction	Reduction reaction	Reducing agent	Redox reaction

Which one of the following is a chemical species that undergoes a chemical reaction that removes one or more electrons from another atom	Oxidizing agent	Reducing agent	Redox agent	Divising agent	Oxidizing agent
The oxidation state of an individual atom is	Zero	One	Two	Three	Zero
Low counts of hemoglobin leads to	Anemia	Pellagra	Sterility	Scurvey	Anemia
Which one of the following has 153 amino acids residues?	Hemoglobin	Myoglobin	Oxyhemoglobin	Coenzyme	Myoglobin
Which one of the following has smaller monomer of polypeptide structure	Hemoglobin	Myoglobin	Oxyhemoglobin	Coenzyme	Myoglobin
Muscle injury is commonly associated with the release of	Hemoglobin	Myoglobin	Oxyhemoglobin	Coenzyme	myoglobin

UNIT 3

Nitrogen Fixation

Nitrogen in biosphere, nitrogen cycle, nitrification role of microorganisms, nitrogen fixation in soils

Nitrogen in Biosphere

Role of nitrogen in the biosphere

The growth of all organisms depends on the availability of mineral nutrients, and none is more important than nitrogen, which is required in large amounts as an essential component of proteins, nucleic acids and other cellular constituents. There is an abundant supply of nitrogen in the earth's atmosphere - nearly 79% in the form of N_2 gas. However, N_2 is unavailable for use by most organisms because there is a triple bond between the two nitrogen atoms, making the molecule almost inert. In order for nitrogen to be used for growth it must be "fixed" (combined) in the form of ammonium (NH_4) or nitrate (NO_3) ions. The weathering of rocks releases these ions so slowly that it has a neglible effect on the availability of fixed nitrogen. So, nitrogen is often the limiting factor for growth and biomass production in all environments where there is suitable climate and availability of water to support life.

Microorganisms have a central role in almost all aspects of nitrogen availability and thus for life support on earth:

- some bacteria can convert N_2 into ammonia by the process termed nitrogen fixation**;** these bacteria are either free-living or form symbiotic associations with plants or other organisms (e.g. termites, protozoa)
- other bacteria bring about transformations of ammonia to nitrate, and of nitrate to N_2 or other nitrogen gases
- Many bacteria and fungi degrade organic matter, releasing fixed nitrogen for reuse by other organisms.

All these processes contribute to the nitrogen cycle**.**

We shall deal first with the process of nitrogen fixation and the nitrogen-fixing organisms, then consider the microbial processes involved in the cycling of nitrogen in the biosphere.

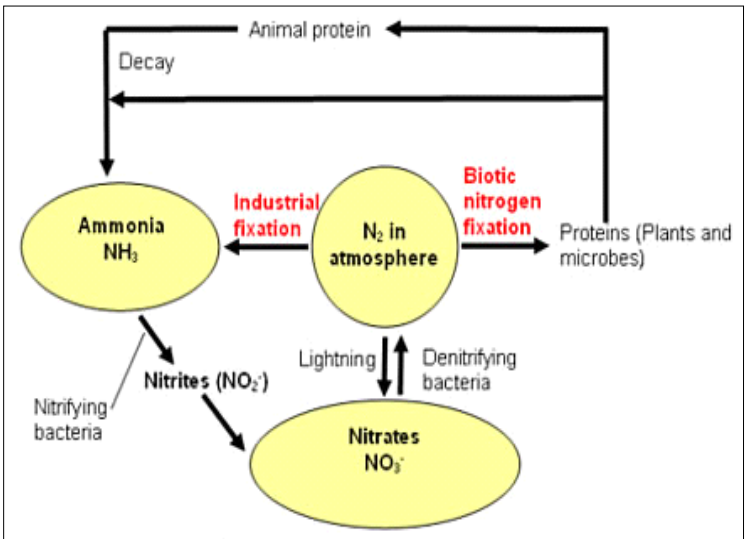
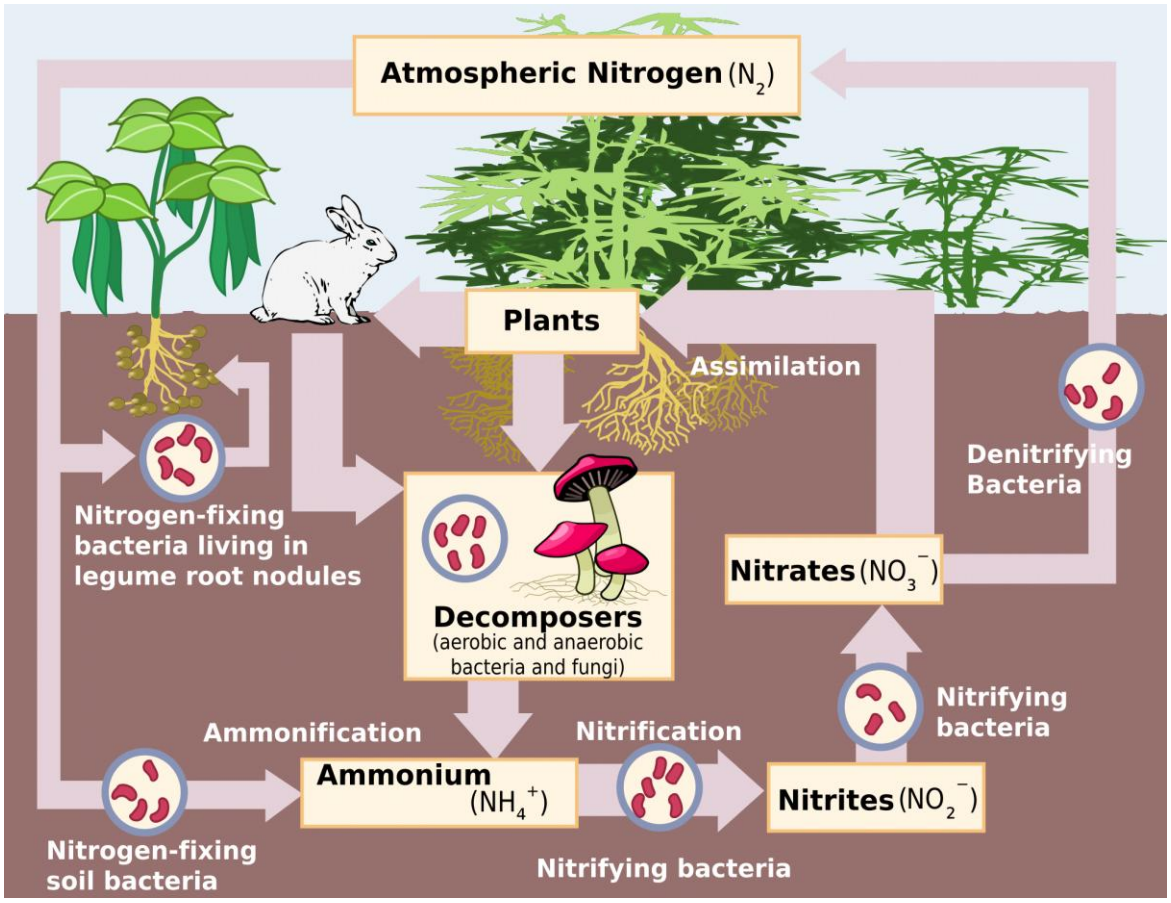


Figure 1: Nitrogen cycle in the biosphere

Nitrogen cycle

The nitrogen cycle is the biogeochemical cycle by which nitrogen is converted into various chemical forms as it circulates among the atmosphere, terrestrial, and marine ecosystems. The conversion of nitrogen can be carried out through both biological and physical processes. Important processes in the nitrogen cycle include fixation, ammonification, nitrification, and denitrification. The majority of Earth's atmosphere (78%) is nitrogen, making it the largest source of nitrogen. However, atmospheric nitrogen has limited availability for biological use, leading to a scarcity of usable nitrogen in many types of ecosystems. The nitrogen cycle is of particular interest to ecologists because nitrogen availability can affect the rate of key ecosystem processes, including primary production and decomposition. Human activities such as fossil fuel combustion, use of artificial nitrogen fertilizers, and release of nitrogen in wastewater have dramatically altered the global nitrogen cycle.



Schematic representation of the flow of nitrogen through the land environment. The importance of bacteria in the cycle is immediately recognized as being a key element in the cycle, providing different forms of nitrogen compounds assimilable by higher organisms.

Nitrogen is present in the environment in a wide variety of chemical forms including organic nitrogen, Ammonium (NH_4+), nitrite (NO_2−), nitrate (NO_3−), nitrous oxide (N_2O), Nitric oxide (NO) or inorganic nitrogen gas (N_2). Organic nitrogen may be in the form of a living organism, humus or in the intermediate products of organic matter decomposition. The processes of the nitrogen cycle transform nitrogen from one form to another. Many of those processes are carried out by microbes, either in their effort to harvest energy or to accumulate nitrogen in a form needed for their growth. For example, the nitrogenous wastes in animal urine are broken down by nitrifying bacteria in the soil to be used as new. The diagram besides shows how these processes fit together to form the nitrogen cycle.

Nitrogen fixation

Conversion of nitrogen into nitrates and nitrites through atmospheric, industrial and biological processes is called as nitrogen fixation. Atmospheric nitrogen must be processed, or "fixed", in a usable form to be taken up by plants. Between $5x10^{12}$ and $10x10^{12}$ g per year are fixed by lightning strikes, but most fixation is done by free-living or symbiotic bacteria known as diazotrophs. These bacteria have the nitrogenase enzyme that combines gaseous nitrogen with hydrogen to produce ammonia, which is converted by the bacteria into other organic compounds. Most biological nitrogen fixation occurs by the activity of Mo-nitrogenase, found in a wide variety of bacteria and some Archaea. Mo-nitrogenase is a complex two-component enzyme that has multiple metal-containing prosthetic groups. An example of the free-living bacteria is *Azotobacter*. Symbiotic nitrogen-fixing bacteria such as *Rhizobium* usually live in the root nodules of legumes (such as peas, alfalfa, and locust trees). Here they form a mutualistic relationship with the plant, producing ammonia in exchange for carbohydrates. Because of this relationship, legumes will often increase the nitrogen content of nitrogen-poor soils. A few non-legumes can also form such symbioses. Today, about 30% of the total fixed nitrogen is produced industrially using the Haber-Bosch process, which uses high temperatures and pressures to convert nitrogen gas and a hydrogen source (natural gas or petroleum) into ammonia.

Assimilation

Plants take nitrogen from the soil by absorption through their roots as amino acids, nitrate ions, nitrite ions, or ammonium ions. Most nitrogen obtained by terrestrial animals can be traced back to the eating of plants at some stage of the food chain.

Plants can absorb nitrate or ammonium from the soil via their root hairs. If nitrate is absorbed, it is first reduced to nitrite ions and then ammonium ions for incorporation into amino acids, nucleic acids, and chlorophyll. In plants that have a symbiotic relationship with rhizobia, some nitrogen is assimilated in the form of ammonium ions directly from the nodules. It is now known that there is a more complex cycling of amino acids between *Rhizobia* bacteroids and plants. The plant provides amino acids to the bacteroids so ammonia assimilation is not required and the bacteroids pass amino acids (with the newly fixed nitrogen) back to the plant, thus forming an interdependent relationship. While many animals, fungi, and other heterotrophic organisms obtain nitrogen by ingestion of amino acids, nucleotides, and other small organic molecules,

other heterotrophs (including many bacteria) are able to utilize inorganic compounds, such as ammonium as sole N sources. Utilization of various N sources is carefully regulated in all organisms.

Ammonification

When a plant or animal dies or an animal expels waste, the initial form of nitrogen is organic. Bacteria or fungi convert the organic nitrogen within the remains back into ammonium (NH+ 4), a process called ammonification or mineralization.

Nitrification

The conversion of ammonium to nitrate is performed primarily by soil-living bacteria and other nitrifying bacteria. In the primary stage of nitrification, the oxidation of ammonium (NH_4+) is performed by bacteria such as the *Nitrosomonas* species, which converts ammonia to nitrites (NO_2−). Other bacterial species such as *Nitrobacter*, are responsible for the oxidation of the nitrites (NO_2−) into nitrates (NO_3−). It is important for the ammonia (NH_3) to be converted to nitrates or nitrites because ammonia gas is toxic to plants.

Due to their very high solubility and because soils are highly unable to retain anions, nitrates can enter groundwater. Elevated nitrate in groundwater is a concern for drinking water use because nitrate can interfere with blood-oxygen levels in infants and cause methemoglobinemia or blue-baby syndrome. Where groundwater recharges stream flow, nitrate-enriched groundwater can contribute to eutrophication, a process that leads to high algal population and growth, especially blue-green algal populations. While not directly toxic to fish life, like ammonia, nitrate can have indirect effects on fish if it contributes to this eutrophication. Nitrogen has contributed to severe eutrophication problems in some water bodies. Since 2006, the application of nitrogen fertilizer has been increasingly controlled in Britain and the United States. This is occurring along the same lines as control of phosphorus fertilizer, restriction of which is normally considered essential to the recovery of eutrophied waterbodies

Denitrification

Denitrification is the reduction of nitrates back into nitrogen gas (N_2), completing the nitrogen cycle. This process is performed by bacterial species such as *Pseudomonas* and *Clostridium* in

anaerobic conditions. They use the nitrate as an electron acceptor in the place of oxygen during respiration. These facultatively anaerobic bacteria can also live in aerobic conditions. Denitrification happens in anaerobic conditions e.g. waterlogged soils. The denitrifying bacteria use nitrates in the soil to carry out respiration and consequently produce nitrogen gas, which is inert and unavailable to plants.

Nitrifying Microorganisms

Ammonia-Oxidizing Bacteria

Nitrification is performed by two functionally defined groups of microbes, referred to together as nitrifiers. The first group of nitrifiers is the ammonia oxidizers, which oxidize ammonia to nitrite. In most natural waters, ammonium is present predominantly as the positively charged ion, ammonium (NH_4+), but the enzyme responsible for the first step of the reaction uses the gaseous form, NH_3, which is usually a minor component at equilibrium. We shall use the term ammonium when we are mainly concerned with the form that is important in the environment, and ammonia when referring to the enzymatic oxidation process of the specific substrate. There are two very different groups of ammonia-oxidizing microbes. One is the well-known bacterial group (ammonia- oxidizing bacteria, AOB), which includes a few different kinds of bacteria that all make a living by generating reducing power (ATP) from the oxidation of ammonia and using that energy to fix carbon dioxide. They are generally considered to be obligate autotrophs, that is, they are unable to utilize or grow on organic carbon to any important extent, and can grow only by fixing their own CO_2 using the Calvin cycle. Ammonia is their only energy source, and their main metabolic product is nitrite. Nitrous oxide is a minor product of ammonia oxidation, and is produced by two different pathways. AOB have been cultivated for over 100 years and their description played an important role in the discovery and early research on chemoautotrophy.

Ammonia-Oxidizing Archaea

A second distinct group of ammonia-oxidizing microbes has only recently been recognized and brought into culture only in 2005. These are not bacteria, but archaea (ammonia-oxidizing archaea, AOA). Like AOB, AOA oxidize ammonia to nitrite and produce nitrous oxide and nitrite from ammonia, but the enzymatic pathways are quite different. AOA are also thought to be predominantly autotrophic, but they fix CO_2 using the 3-hydroxypropionate /4-hydroxybutyrate pathway, rather than the Calvin Cycle. AOA are abundant in many

environments and in the ocean and many terrestrial systems, they far outnumber the AOB. In estuaries, the ratio of AOB to AOB varies widely, with AOB sometimes more abundant. Although the enzymes and pathways differ for the AOA and AOB, aerobic ammonia oxidation in both groups apparently proceeds by the same stoichiometry:

$$NH_3 + 1.5\ O_2 \text{----------} NO^- + H_2O + H^+$$

In addition to the net production of nitrite by the above equation, AOB are also capable of producing nitrous oxide (N_2O) by two distinct pathways. Most AOB investigated to date possess the genes and enzymes necessary for the partial denitrification pathway that reduces nitrite to nitric oxide (NO) and then to N_2O. The genes involved are homologous to those found in denitrifiers, and the process is often referred to as nitrifier denitrification. The result is the production of N_2O, whereas complete denitrification by the usual denitrifying bacteria produces N_2O only as a transient intermediate. A second pathway produces N_2O from hydroxylamine (NH_2OH), which is an intermediate in the oxidation of ammonia to nitrite by the AOB. The nitrifier denitrification pathway of N_2O production is favored during nitrification at low oxygen concentrations, implying that nitrifiers use this pathway for anaerobic respiration, just as in denitrifiers. AOA also produce N_2O, in approximately the same proportion to NO_2 as in AOB, and with similar isotopic fractionation. Nevertheless, the pathways of N_2O production in AOA are unknown, but almost certainly are different from the pathways in AOB. Significantly, AOA do not use NH2OH as an intermediate, so the production of N_2O from NH_2OH cannot occur in AOA, and AOA do not possess the reductive enzymes used in nitrifier denitrification by AOB.

Nitrite-Oxidizing Bacteria

The second functionally defined group of nitrifying microbes is the nitrite-oxidizing bacteria (NOB), which include several genera. The best-known cultivated members, in the genus Nitrobacter, are chemolithoautotrophic, like the AOB, using nitrite as an energy source and CO_2 as a carbon source via the Calvin cycle. However, the lesser known genus, Nitrospina, is apparently most abundant in the ocean, and uses the reductive tricarboxylic acid pathway for CO_2 fixation. Many strains are known to possess heterotrophic capabilities and are considered mixotrophic or facultative autotrophs. Although they have limited metabolic capabilities for uptake and degradation of organic molecules, they can supplement their growth with organic carbon and, in some cases, grow slowly in the absence of nitrite when certain organic substrates

are present. The oxidation of nitrite is even less energy yielding than ammonia oxidation, so perhaps this ability for heterotrophic growth is not surprising. Aerobic nitrite oxidation proceeds by the following stoichiometry:

$$NO_2 + 0.5\ O_2 \text{ ----------} NO_3$$

There are no other pathways, nor any different kinds of bacteria or archaea known to be capable of or involved in nitrite oxidation in the environment. The recent finding of greater diversity among ammonia-oxidizing microbes begs the question, however, of whether additional nitrite oxidation.

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There are no other pathways, nor any different kinds of bacteria or archaea known to be capable of or involved in nitrite oxidation in the environment. The recent finding of greater diversity among ammonia-oxidizing microbes begs the question, however, of whether additional nitrite oxidation pathways and organisms remain to be discovered.

Nitrogen fixation

A relatively small amount of ammonia is produced by lightning. Some ammonia also is produced industrially by the Haber-Bosch process, using an iron-based catalyst, very high pressures and fairly high temperature. But the major conversion of N_2 into ammonia, and thence into proteins, is achieved by microorganisms in the process called nitrogen fixation (or dinitrogen fixation).
The table below shows some estimates of the amount of nitrogen fixed on a global scale. The total biological nitrogen fixation is estimated to be twice as much as the total nitrogen fixation by non-biological processes.

To illustrate the importance of biological nitrogen fixation, the image below shows part of the Lower Sonoran desert in Arizona. Every plant that we see in this scene depends ultimately on biological nitrogen fixation. Both free-living cyanobacteria and the cyanobacterial associates of lichens initially contributed nitrogen to the soil by forming a cryptobiotic crust. Now numerous leguminous plants occur in this desert, with nitrogen-fixing *Rhizobium* in their root nodules.

Mechanism of biological nitrogen fixation

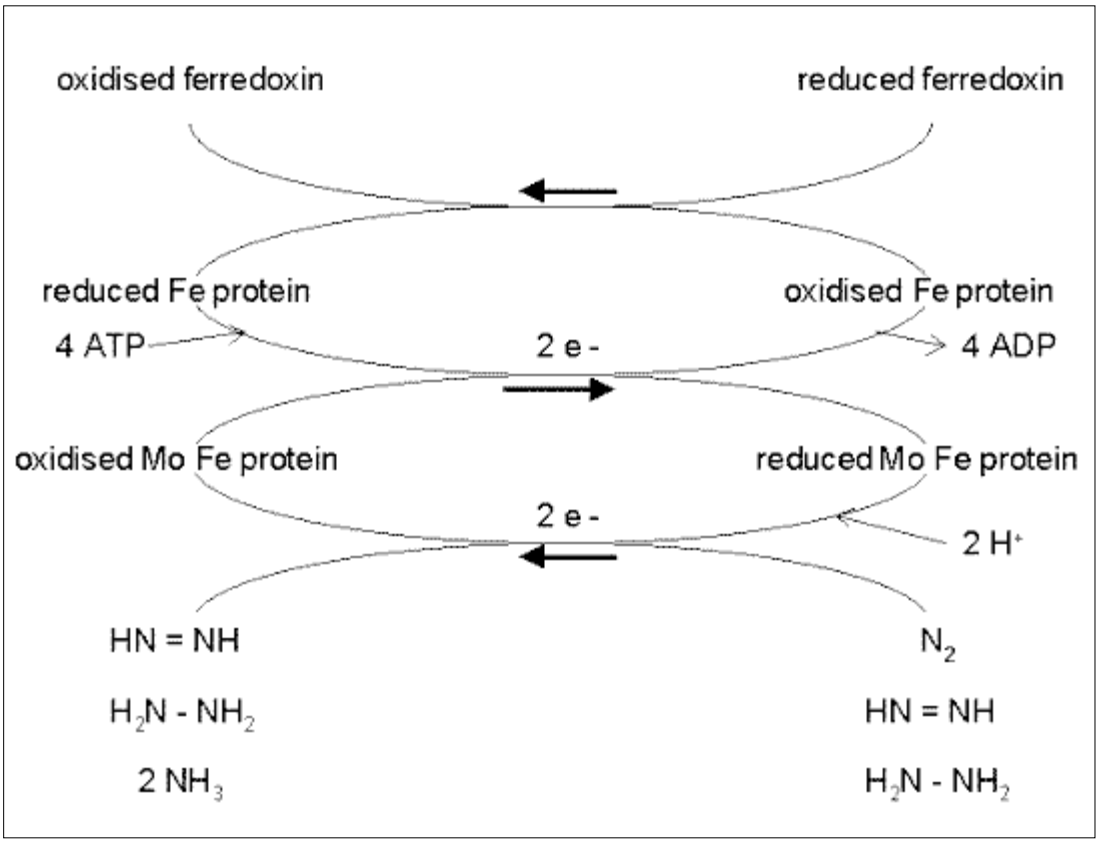
Biological nitrogen fixation can be represented by the following equation, in which two moles of ammonia are produced from one mole of nitrogen gas, at the expense of 16 moles of ATP and a supply of electrons and protons (hydrogen ions):

$$N_2 + 8H+ + 8e^- + 16\ ATP = 2NH_3 + H_2 + 16ADP + 16\ Pi$$

This reaction is performed exclusively by prokaryotes (the bacteria and related organisms), using an enzyme complex termed nitrogenase. This enzyme consists of two proteins - an iron protein and a molybdenum-iron protein, as shown below.

The reactions occur while N_2 is bound to the nitrogenase enzyme complex. The Fe protein is first reduced by electrons donated by ferredoxin. Then the reduced Fe protein binds ATP and reduces the molybdenum-iron protein, which donates electrons to N_2, producing HN=NH. In two further cycles of this process (each requiring electrons donated by ferredoxin) HN=NH is reduced to $H_2N\text{-}NH_2$, and this in turn is reduced to $2NH_3$.

Depending on the type of microorganism, the reduced ferredoxin which supplies electrons for this process is generated by photosynthesis, respiration or fermentation.



There is a remarkable degree of functional conservation between the nitrogenase proteins of all nitrogen-fixing bacteria. The Fe protein and the Mo-Fe protein have been isolated from many of these bacteria, and nitrogen fixation can be shown to occur in cell-free systems in a laboratory

when the Fe protein of one species is mixed with the Mo-Fe protein of another bacterium, even if the species are very distantly related.

Abiological Nitrogen Fixation

In abiological nitrogen fixation the nitrogen is reduced to ammonia without involving any living cell. Abiological fixation can be of two types: **industrial and natural**.

For example, in the Haber's process, synthetic ammonia is produced by passing a mixture of nitrogen and hydrogen through a bed of catalyst (iron oxides) at a very high temperature and pressure.

$$N_2 + 3H_2 \rightarrow 2NH_3$$

This is industrial fixation wherein nitrogen gets reduced to ammonia.

In natural process nitrogen can be fixed especially during electrical discharges in the atmosphere. It may occur during lightning storms when nitrogen in the atmosphere can combine with oxygen to form oxides of nitrogen.

$$N_2 + O_2 \rightarrow 2NO_2$$

These oxides of nitrogen may be hydrated and trickle down to earth as combined nitrite and nitrate.

Importance of Nitrogen in environment

- Nitrogen is an essential component of many organic molecules such as DNA, RNA and proteins, the building blocks of life. Air is the major reservoir of nitrogen that constitutes 79% of nitrogen gas (N_2). Although the majority of the air we breathe is N_2, most of this is unavailable for use. This is because of the strong triple bond between the N atoms in the N_2 molecules that make it relatively inert. Therefore, in order for the plants and animals to use nitrogen, N_2 gas must be converted to either ammonium (NH_4+) or nitrate (NO_3-) or organic nitrogen such as urea - $(NH_3)_2CO$.
- Nitrogen (N), a macronutrient, is most frequently found limiting for plant growth. This is due to the continual loss of nitrogen from the reserve of combined or fixed nitrogen, which is present in soil and available for use by plants. It is continually depleted by such processes as microbial denitrification, soil erosion, leaching, chemical volatilization, and

most important, removal of nitrogen-containing crop residues from the land. The nitrogen reserve in agricultural soils must therefore be replenished periodically in order to maintain an adequate (non-growth limiting) level for crop production. This replacement of soil nitrogen is generally accomplished by the addition of chemically fixed nitrogen in the form of commercial inorganic fertilizers or by the activity of biological nitrogen fixation (BNF) systems.

- Nitrogen is a versatile element that exists in both organic and inorganic forms as well as in many different oxidation states. The movement of nitrogen between the atmosphere, biosphere, and geosphere is described in the nitrogen cycle, one of the major biogeochemical cycles.

Effects of nitrogen on human health

- Reactive nitrogen (like NO_3- and NH_4+) present in surface waters and soils can also enter the atmosphere as the smog-component nitric oxide (NO). NO is also a major factor in the formation of smog, which is known to cause respiratory illnesses like asthma in both children and adults.
- Excess nitrate in the soil can leach into the groundwater supplies and contaminate wells. This nitrate is therefore a potential human health threat especially to infants, causing the condition known as methemoglobinemia, also called "blue baby syndrome". Nitrate is converted in the gut to nitrite, which then combines with hemoglobin to form methemoglobin, thus decreasing the ability of the blood to carry oxygen. Infants are more susceptible to nitrate toxicity than older children or adults.

Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata.

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

POSSIBLE QUESTIONS

MULTIPLE CHOICE QUESTIONS

Section A **20x1 = 20**

1. Which of the following is correct regarding nitrogen cycle?
a. N_2 cycle is a sedimentary cycle
b. b. N is the most abundant nutrient for plants
c. **The major reservoir of nitrogen is atmosphere** d. All of these
2. Majority of nitrogen fixation occurs by
a. **Biological nitrogen fixing organisms** b. Lightning c. Volcanic eruptions
d. Haber-Bosch process
3. Nitrogen accounts nearly 79% of the air.Still nitrogen is the most limiting nutrient for plant growth
a. N2 cannot be directly utilized by plants
b. High energy is required to break triple bond
c. Nitrogen is almost an inert gas as N involved reaction requires extreme conditions such as high temperature
d. All the above
4. Biological nitrogen fixation is the conversion of
a. **Conversion of N_2 to NH_3** b. Conversion of N_2 to N
c. Conversion of N to urea d. Conversion of N to nitrogen oxide

5. Which of the following is a symbiotic nitrogen fixing organism?
a. Azospirillum **b. Rhizobium** c. Clostridium d. Nitrococcus
6. The major enzymes involved in biological nitrogen fixation are?
a. Nitrogenase and hexokinase **b. Nitrogenase and hydrogenase** c. Nitrogenase and hydrolyase d. Nitrogenase and peptidase
7. Ammonification is the process of ?
a. Formation of ammonia from nitrogen by nitrogen fixers
b. Formation of ammonia from amino acids by decomposers
c. Formation of ammonia from nitrates by nitrogen fixers
d. Formation of ammonia from nitrates by decomposers
8. The conversion of ammonia to nitrite and then to nitrates is called?
a. **Nitrification** b. Ammonification c. Assimilation d. Denitrification
9. The conversion of ammonia to nitrite and then to nitrates is called?
a. **Nitrification** b. Ammonification c. Assimilation d. Denitrification
10. The process that convert nitrates back to nitrogen gas there by replenishing N_2 in the atmosphere is called
a. Nitrification b. Ammonification c. Assimilation **d. Denitrification**

11. Nitrogen fixation is the?
a. **Conversion of N_2 to NH_3** b. Conversion of N_2 to N
c. Conversion of N to urea d. Conversion of N_2 to nitrates and ammonia
12. In nitrogen cycle nitrite is converted to nitrate by
a. Azotobacter **b. Rhizobium** c. Nitrobacter d. Clostridium
13. What is the first step in the nitrogen cycle?
a. **Nitrogen fixation** b. Nitrification c. Assimilation d. Ammonification

14. Nitrogen is recycled in a process called the
a. Nitrogen cycle b. Assimilation c. Ammonification d. Nitrification
15. Plants use nitrogen by absorbing either nitrate or ammonium ions through the
a. Roots b. Flowers c. Stem d. Leaves
16. Plants absorb ammonium and nitrate during the
a. Assimilation process b. Mineralization c. Alchemical process
d. Haber-Bosch process
17. Which one of the following takes place under special conditions in both terrestrial and marine ecosystems
a. **Denitrification** b. Mineralization c. Ammonification d. Nitrification
18. Bacteria or fungi convert the organic nitrogen within the remains back into ammonium (NH_4^+), a process called
a. **Ammonification** b. Nitrofication c. Assimilation d. Nitrification
19. Plants absorb ammonium and nitrate during the
a. **Assimilation process** b. Nitrofication process c. Ammonification process
d. Nitrification process
20. The transformation of ammonia to nitrite is usually the rate limiting step of
a. **Nitrification** b. Nitrofication c. Assimilation d. Ammonification

8-MARKS

1. Write a note on Nitrogen in biosphere?
2. What is biological nitrogen fixation explain it detail?
3. Write a note on Nitrogen cycle?
4. What is nitrogenase ? What is its biological function?
5. Command on the prospect of abiological nitrogen fixation?
6. What is the role of the bacterias in nitrogen cycle?
7. What are the chemical barriers in the reduction of N_2 to NH_3?

8. How the Nitrogens are fixed in soil?

9. What is the importance of nitrogen cycle in atmosphere?

10. Differentiate biological and abiological nitrogen fixation?

15CHU505C
Karpagam Academy of Higher Education
Coimbatore-21
(For the candidate admitted on 2015 onwards)
Department of Chemistry
V- semester
Bio-Inorganic Chemistry

UNIT III- Objective Questions for online examination (Each carry 1 Marks)

Questions	Option A	Option B	Option C	Option D	Answer
Which of the following is correct regarding nitrogen cycle?	N2 cycle is a sedimentary cycle	N is the most abundant nutrient for plants	The major reservoir of nitrogen is atmosphere	All of these	The major reservoir of nitrogen is atmosphere
Majority of nitrogen fixation occurs by	Biological nitrogen fixing organisms	Lightning	Volcanic eruptions	Haber-Bosch process	Biological nitrogen fixing organisms
Nitrogen accounts nearly 79% of the air.Still nitrogen is the most limiting nutrient for plant growth	N2 cannot be directly utilized by plants	High energy is required to break triple bond	Nitrogen is almost an inert gas as N involved reaction requires extreme conditions such as high temperature	All the above	All the above
Biological nitrogen fixation is the conversion of	Conversion of N2 to NH3	Conversion of N2 to N	Conversion of N to urea	Conversion of N to nitrogen oxide	conversion of N2 to NH3
Which of the following is a symbiotic nitrogen fixing organism?	*Azospirillum*	*Rhizobium*	*Clostridium*	*Nitrococcus*	Rhizobium
The major enzymes involved in biological nitrogen fixation are?	Nitrogenase and hexokinase	Nitrogenase and hydrogenase	Nitrogenase and hydrolyase	Nitrogenase and peptidase	Nitrogenase and hydrogenase
Ammonification is the process of ?	Formation of ammonia from nitrogen by nitrogen fixers	Formation of ammonia from amino acids by decomposers	Formation of ammonia from nitrates by nitrogen fixers	Formation of ammonia from nitrates by decomposers	Formation of ammonia from amino acids by decomposers
The conversion of ammonia to nitrite and then to nitrates is called?	Nitrification	Ammonification	Assimilation	Denitrification	Nitrification
The process that convert nitrates back to nitrogen gas there by replenishing N2 in the atmosphere is called	Nitrification	Ammonification	Assimilation	Denitrification	Denitrification
Nitrogen fixation is the ?	Conversion of N2 to NH3	Conversion of N2 to N	Conversion of N to urea	Conversion of N2 to nitrates and ammonia	Conversion of N2 to nitrates and ammonia
In nitrogen cycle nitrite is converted to nitrate by	Azotobacter	Rhizobium	Nitrobacter	Clostridium	Nitrobacter
Nitrosomonas and Nitrobacter are	Ammonifying bacteria	Denitrifying bacteria	Nitrogen fixing bacteria	Nitrifying bacteria	Nitrifying bacteria
Non legume plant nodules contains nitrogen fixing	Ascomycetes	Basidiomycetes	Zygomycetes	Actinomycetes	Actinomycetes
Denitrification is also called ?	Putrefaction	Heterotrophic nitrification	Assimilatory nitrate reduction	Dissimilatory nitrate reduction	Dissimilatory nitrate reduction
Plants need nitrogen for ?	Growth	Food preparation	Strength	Support	Growth
Which of the followings fixed nitrogen in waterlogged soil?	Nostoc	Nitrobactor	Clostridium	Azotobacter	Nostoc

Which of the followings is non-aerobic bacterium?	Azotobacter	Nitrobactor	Clostridium	Nostoc	Azotobacter
Plants absorbs N2 in the form of?	Nitrites (NO2-)	Nitrates (NO3-)	Ammonium (NH4+)	All of the above	All of the above
Anabaena, a N2 fixer is present in the root pockets of	Marselia	Salvinia	Pistia	Azolla	Azolla
To fix one molecule of nitrogen	6 ATP molecules are required	12 ATP molecules are required	16ATP molecules are required	20 ATP molecules are required	16ATP molecules are required
The chief source of nitrogen for green plants is	Atmospheric nitrogen	Nitrates	Ammonium salts	Low molecular weight- organic nitrogenous compound	Nitrates
Plants absorb nitrates from soil and convert them into	Urea	Ammonia	Nitrogen	Nitrate	Ammonia
In the presence of carbon monoxide, nitrogen fixation	Increases	Decreases	Inhibits	Exhibits	Inhibits
Which crop helps in nitrogen fixation ?	Maize	Beans	Potatos	Rice	Beans
In the process of nitrogen fixation, which of the following microorganism is involved?	Non symbiotic microorganisms only	Symbiotic microorganisms only	Non symbiotic microorganisms and symbiotic microorganisms only	None of the above	Non symbiotic microorganisms and symbiotic microorganisms only
The conversion of molecular nitrogen into ammonia is known as	Nitrification	Denitrification	Nitrogen fixation	Ammonification	Nitrogen fixation
Asymbiotic N2 fixation is done by	Azatobacter	Azospirillum	Rhizobacter	Rhizobium	Rhizobium
Nitrification is an?	Aerobic process	Anaerobic process	Both aerobic and anaerobic process	Dissimilatory nitrate reduction	Aerobic process
Bacteria which is responsible for ammonification is called	Nitrogenous virus	Nitrogenous bacteria	Ammonifying virus	Ammonifying bacteria	Ammonifying bacteria
Nitrites are transformed with help of bacteria into	Nitrites	Nitrates	Ammonia nitrous	Ammonium nitrate	Nitrates
Process in which nitrites and nitrates are reduced into nitrogen gas by denitrification of bacteria is called	Ammonification	Assimilation	Nitrification	Denitrification	Denitrification
Nitrogen is a versatile element that exists in	Organic	Inorganic	Both organic and inorganic forms	Aerobic	
Nitrogen fixing bacteria such as *Rhizobium* form	Symbiotic relationships with host plants	Interrelationship with host plants	No relation with host plants	Intra-relation with host plants	symbiotic relationships with host plants
Which one of the following is an essential component of many organic molecules such as DNA, RNA and proteins, the building blocks of life	Sulphur	Nitrogen	Oxygen	Carbondioxide	Nitrogen
The nitrogen cycle is the	Geochemical cycle	Biochemical cycle	Biogeochemical cycle	Biological cycle	biogeochemical cycle
The conversion of nitrogen can be carried out through	Chemical process	Physical processes	Biological processes	Both biological and physical processes	both biological and physical processes
Symbiotic nitrogen-fixing bacteria such as *Rhizobium* usually live in the root nodules of	Legumes	Plants	Crops	Leaves	legumes
Ammonification is otherwise called as?	Mineralization	Nitrification	Nitrofication	Assimilation	Mineralization
The conversion of ammonium to nitrate is performed primarily by	Ammonifying bacteria	Soil-living bacteria	nitrifying bacteria	soil-living bacteria and other nitrifying bacteria	
ammonia gas is ?	Toxic to plants	Useful for plants	Strength to plants	Support for plants	toxic to plants

Denitrification is the reduction of nitrates back into	Nitrogen gas	Ammonia	Nitrate	Nitrite	nitrogen gas
Ammonia is produced by the breakdown of organic sources of	Nitrogen	Sulphur	Oxygen	Nitrite	nitrogen
Nitrification is the	Oxidation of ammonia	Biochemical oxidation of ammonia	Reduction of ammonia	biological oxidation of ammonia	biological oxidation of ammonia
Nitrification is a	Two step process	Three step process	One step process	Four step process	Two step process
The majority of nitrogen is fixed by	Bacteria	Virus	Fungi	Algae	bacteria
Denitrification means	Reduction of nitrates	Reduction of carbon	Reduction of oxygen	Reduction of ammonia	reduction of nitrates
Industrial nitrogen fixation is done by	Ames process	Acheson process	Alchemical process	Haber-Bosch process	Haber-Bosch process
Which one of the following is a free-living nitrogen-fixing bacterium	Azotobacter	Rhizobium	Clostridium	Nostoc	Azotobacter
Which one of the following cannot independently fix nitrogen	Azotobacter	Rhizobium	Clostridium	Nostoc	Rhizobium
Which one of the following is a genus comprising rod-shaped, gram-negative, and chemoautotrophic bacteria	Nitrobacter	Rhizobium	Clostridium	Nostoc	Nitrobacter
What is the first step in the nitrogen cycle?	Nitrogen fixation	Nitrification	Assimilation	Ammonification	Nitrogen fixation
Nitrogen is recycled in a process called the	Nitrogen cycle	Assimilation	Ammonification	Nitrification	Nitrogen cycle
Plants use nitrogen by absorbing either nitrate or ammonium ions through the	Roots	Flowers	Stem	Leaves	Roots
Plants absorb ammonium and nitrate during the	Assimilation process	Mineralization	Alchemical process	Haber-Bosch process	Assimilation process
Nitrogen is transported from the root to the shoot via the xylem in the form of	Nitrate	Sulphur	Oxygen	Nitrite	Nitrate
Which of the following cannot absorb nitrates directly	Animals	Fishes	Humans	Plants	Animals
Which of the following takes place under special conditions in both terrestrial and marine ecosystems	Denitrification	Mineralization	Ammonification	Nitrification	Denitrification
Bacteria or fungi convert the organic nitrogen within the remains back into ammonium (NH_4^+), a process called	Ammonification	Nitrofication	Assimilation	Nitrification	Ammonification
Plants absorb ammonium and nitrate during the	Assimilation process	Nitrofication process	Ammonification process	Nitrification process	Assimilation process
The transformation of ammonia to nitrite is usually the rate limiting step of	Nitrification	Nitrofication	Assimilation	Ammonification	Nitrification

UNIT-IV

Metal poisoning and drug action of Inorganic complexes compounds

Metal poisoning, treatment by using chelating agent, mercury, lead & cadmium poisoning

& treatment. Platinum complexes in treatment of cancer, Metal deficiency and use of metal chelates.

Metal toxicity

Definition

Metal toxicity or **metal poisoning** is the toxic effect of certain metals in certain forms and doses on life. Some metals are toxic when they form poisonous soluble compounds. Certain metals have no biological role, i.e. are not essential minerals, or are toxic when in a certain form. In the case of lead, any measurable amount may have negative health effects. Often heavy metals are thought as synonymous, but lighter metals may also be toxic in certain circumstances, such as beryllium and lithium. Not all heavy metals are particularly toxic, and some are essential, such as iron. The definition may also include trace elements when in abnormally high doses may be toxic. An option for treatment of metal poisoning may be chelation therapy, which is a technique which involves the administration of chelation agents to remove metals from the body.

Introduction

Toxic metals sometimes imitate the action of an essential element in the body, interfering with the metabolic process resulting in illness. Many metals, particularly heavy metals are toxic, but some heavy metals are essential, and some, such as bismuth, have a low toxicity. Most often the definition of toxic metals includes at least cadmium, manganese, lead, mercury and the radioactive metals. Metalloids (arsenic, polonium) may be included in the definition. Radioactive metals have both radiological toxicity and chemical toxicity. Metals in an oxidation state abnormal to the body may also become toxic: chromium(III) is an essential trace element, but chromium(VI) is a carcinogen.

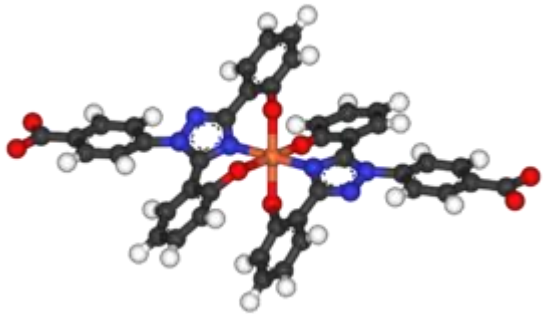
Toxicity is a function of solubility. Insoluble compounds as well as the metallic forms often exhibit negligible toxicity. The toxicity of any metal depends on its ligands. In some cases, organometallic forms, such as methylmercury and tetraethyl lead, can be extremely toxic. In other cases, organometallic derivatives are less toxic such as the cobaltocenium cation.

Decontamination for toxic metals is different from organic toxins: because toxic metals are elements, they cannot be destroyed. Toxic metals may be made insoluble or collected, possibly by the aid of chelating agents. Alternatively, they can be diluted into a sufficiently large reservoir, such as the sea, because immediate toxicity is a function of concentration rather than amount. However, bioaccumulation has the potential to reverse this.

Toxic metals can bioaccumulate in the body and in the food chain. Therefore, a common characteristic of toxic metals is the chronic nature of their toxicity. This is particularly notable with radioactive heavy metals such as radium, which imitates calcium to the point of being incorporated into human bone, although similar health implications are found in lead or mercury poisoning. The exceptions to this are barium and aluminium, which can be removed efficiently by the kidneys.

Chelation therapy

Chelation therapy



Two molecules of deferasirox, an orally administered chelator, binding iron. Deferasirox is used in the treatment of transfusional iron overloadin people with thalassemia.

Definition

Chelation therapy is a medical procedure that involves the administration of chelating agents to remove heavy metals from the body. Chelation therapy has a long history of use in clinical toxicology and remains in use for some very specific medical treatments, although it is administered under very careful medical supervision due to various inherent risks.

Chelation therapy must be administered with care as it has a number of possible side effects, including death. In response to increasing use of chelation therapy as alternative medicine and in circumstances in which the therapy should not be used in conventional medicine, various health organizations have confirmed that medical evidence does not support the effectiveness of chelation therapy for any purpose other than the treatment of heavy metal poisoning. Over-the-counter chelation products are not approved for sale in the United States.

Uses

Chelation therapy is the preferred medical treatment for metal poisoning, including acute mercury, iron (including in cases of thalassemia), arsenic, lead, uranium, plutoniumand other forms of toxic metal poisoning. The chelating agent may be administered intravenously, intramuscularly, or orally, depending on the agent and the type of poisoning.

Any urine testing for metals should be done before, and not after, the administration of any chelation therapy. Healthy individuals have normal amounts of metal in their bodies which would be removed by chelation therapy, and urine testing after chelation therapy cannot reliably diagnose metal poisoning.[10] Urine testing done after chelation therapy has been associated with harm, including further testing or treatment based on those unreliable results.

Chelating agents

There are a variety of common chelating agents with differing affinities for different metals, physical characteristics, and biological mechanism of action. For the most common forms of heavy metal intoxication – lead, arsenic, or mercury – a number of chelating agents are available. Dimercaptosuccinic acid (DMSA) has been recommended for the treatment of lead poisoning in children by poison control centers around the world. Other chelating agents, such as 2,3-dimercaptopropanesulfonic acid (DMPS) and alpha lipoic acid (ALA), are used in conventional and alternative medicine. Some common chelating agents are ethylenediaminetetraacetic acid (EDTA), 2,3-dimercaptopropanesulfonic acid (DMPS), and thiamine

tetrahydrofurfuryl disulfide (TTFD). Calcium-disodium EDTA and DMSA are only approved for the removal of lead by the Food and Drug Administration while DMPS and TTFD are not approved by the FDA. These drugs bind to heavy metals in the body and prevent them from binding to other agents. They are then excreted from the body. The chelating process also removes vital nutrients such as vitamins C and E, therefore these must be supplemented.

The German Environmental Agency (Umweltbundesamt) listed DMSA and DMPS as the two most useful and safe chelating agents available.

Chelator	Used in
Dimercaprol (British anti-Lewisite; BAL)	• acute arsenic poisoning • acute mercury poisoning • lead poisoning (in addition to EDTA) • Lewisite poisoning (for which it was developed as an antidote)
Dimercaptosuccinic acid (DMSA)	• lead poisoning • arsenic poisoning • mercury poisoning
Dimercapto-propane sulfonate (DMPS)	• severe acute arsenic poisoning • severe acute mercury poisoning
Penicillamine	*Mainly in:* copper toxicity *Occasionally adjunctive therapy in:* gold toxicity • arsenic poisoning • lead poisoning • rheumatoid arthritis
Ethylenediamine tetraacetic acid (calcium disodium versenate) ($CaNa_2$-EDTA)	• lead poisoning
Deferoxamine and Deferasirox	• acute iron poisoning • iron overload
maltol, thiomaltol	• lead(II) toxicity

Side effects

When used properly in response to a diagnosis of harm from metal toxicity, side effects of chelation therapy include dehydration, low blood calcium, harm to kidneys, increased enzymes as would be detected in liver function tests, allergic reactions, and lowered levels of dietary elements. When administered inappropriately, chelation therapy brings risk of cancer, neurodevelopmental disorder from toxicity, and death.

History

Chelation therapy can be traced back to the early 1930s, when Ferdinand Munz, a German chemist working for I.G. Farben, first synthesized ethylenediaminetetraacetic acid(EDTA). Munz was looking for a replacement for citric acid as a water softener. Chelation therapy itself began during World War II when chemists at the University of Oxfordsearched for an antidote for lewisite, an arsenic-based chemical weapon. The chemists learned that EDTA was particularly effective in treating lead poisoning.

Following World War II, chelation therapy was used to treat workers who had painted United States naval vessels with lead-based paints. In the 1950s, Norman Clarke, Sr. was treating workers at a battery factory for lead poisoning when he noticed that some of his patients had improved angina pectoris following chelation

therapy. Clarke subsequently administered chelation therapy to patients with angina pectoris and other occlusive vascular disease and published his findings in "*The American Journal of the Medical Sciences*" in December 1956. He hypothesized that **"EDTA could dissolve disease-causing plaques in the coronary systems of human beings."** In a series of 283 patients treated by Clarke et al. From 1956-1960, 87% showed improvement in their symptomatology. Other early medical investigators made similar observations of EDTA's role in the treatment of cardiovascular disease (Bechtel, 1956; Bessman, 1957; Perry, 1961; Szekely, 1963; Wenig, 1958: and Wilder, 1962).

In 1973, a group of practicing physicians created the Academy of Medical Preventics (now the American College for Advancement in Medicine). The academy trains and certifies physicians in the safe administration of chelation therapy. Members of the academy continued to use EDTA therapy for the treatment of vascular disease and developed safer administration protocols.

In the 1960s, BAL was modified into DMSA, a related dithiol with far fewer side effects. DMSA quickly replaced both BAL and EDTA as the primary treatment for lead, arsenic and mercury poisoning in the United States. Esters of DMSA have been developed which are reportedly more effective; for example, the monoisoamyl ester (MiADMSA) is reportedly more effective than DMSA at clearing mercury and cadmium.[22] Research in the former Soviet Union led to the introduction of DMPS, another dithiol, as a mercury-chelating agent. The Soviets also introduced ALA, which is transformed by the body into the dithiol dihydrolipoic acid, a mercury- and arsenic-chelating agent. DMPS has experimental status in the United States, while ALA is a common nutritional supplement.

Since the 1970s, iron chelation therapy has been used as an alternative to regular phlebotomy to treat excess iron stores in people with haemochromatosis. Other chelating agents have been discovered. They all function by making several chemical bonds with metal ions, thus rendering them much less chemically reactive. The resulting complex is water-soluble, allowing it to enter the bloodstream and be excreted harmlessly.

Calcium-disodium EDTA chelation has been studied by the U.S. National Center for Complementary and Alternative Medicine for treating coronary disease. In 1998, the U.S. Federal Trade Commission (FTC) pursued the American College for Advancement in Medicine (ACAM), an organization that promotes "complementary, alternative and integrative medicine" over the claims made regarding the treatment of atherosclerosis in advertisements for EDTA chelation therapy. The FTC concluded that there was a lack of scientific studies to support these claims and that the statements by the ACAM were false. In 1999, the ACAM agreed to stop presenting chelation therapy as effective in treating heart disease, avoiding legal proceedings. In 2010 the U.S. Food and Drug Administration (FDA) warned companies who sold over-the-counter (OTC) chelation products and stated that such "products are unapproved drugs and devices and that it is a violation of federal law to make unproven claims about these products. There are no FDA-a

Mercury poisoning

Elemental mercury

Mercury poisoning

Synonyms	Mercury toxicity, mercury overdose, mercury intoxication, hydrargyria, mercurialism
Elemental mercury	
Specialty	Toxicology
Symptoms	Muscle weakness, poor coordination, numbness in the hands and feet[1]
Complications	Kidney problems, decreased intelligence
Causes	Exposure to mercury
Diagnostic method	Difficult
Prevention	Decreasing use of mercury, low mercury diet
Medication	**Acute poisoning**: dimercaptosuccinic acid (DMSA), dimercaptopropane sulfonate (DMPS)

Introduction

Minamata disease

Mercury poisoning is a type of metal poisoning, due to mercury exposure. Symptoms depend upon the type, dose, method, and duration of exposure. They may include muscle weakness, poor coordination, numbness in the hands and feet, skin rashes, anxiety, memory problems, trouble speaking, trouble hearing, or trouble seeing. High level exposure to methylmercuryis known as Minamata disease. Methylmercury exposure in children may result in acrodynia (pink's disease) in which the skin becomes pink and peels. Long term complications may include kidney problems and decreased intelligence. The effects of long term low-dose exposure to methylmercury is unclear.

Mercury (chemical symbol Hg) exposure may occur in number of forms including: metal, vapor, salt, and organic compound. Most exposure is from eating fish, amalgam based dental fillings, or exposure at work. In fish, those higher up in the food chaingenerally have higher levels of mercury. Less commonly poisoning may occur as an attempt to end one's life. Human activities that release mercury into the environment include the burning of coal and mining of gold. Tests of the blood, urine, and hair for mercury are available but do not relate well to the amount in the body.

Prevention includes eating a diet low in mercury, removing mercury from medical and other devices, proper disposal of mercury, and not mining further mercury. In those with acute poisoning from inorganic mercury

salts, chelation with either dimercaptosuccinic acid (DMSA) or dimercaptopropane sulfonate (DMPS) appears to improve outcomes if given within a few hours of exposure. Chelation for those with long term exposure is of unclear benefit. In certain communities that survive on fishing, rates of mercury poisoning among children have been as high as 1.7 per 100.

Signs and symptoms

Common symptoms of mercury poisoning include peripheral neuropathy, presenting as paresthesia or itching, burning, pain, or even a sensation that resembles small insects crawling on or under the skin (formication); skin discoloration (pink cheeks, fingertips and toes); swelling; and desquamation (shedding or peeling of skin).

Mercury irreversibly inhibits selenium-dependent enzymes (see below) and may also inactivate *S*-adenosyl-methionine, which is necessary for catecholamine catabolism by catechol-*O*-methyl transferase. Due to the body's inability to degrade catecholamines (e.g. epinephrine), a person suffering from mercury poisoning may experience profuse sweating, tachycardia (persistently faster-than-normal heart beat), increased salivation, and hypertension (high blood pressure).

Affected children may show red cheeks, nose and lips, loss of hair, teeth, and nails, transient rashes, hypotonia (muscle weakness), and increased sensitivity to light. Other symptoms may include kidney dysfunction (e.g. Fanconi syndrome) or neuropsychiatric symptoms such as emotional lability, memory impairment, or insomnia.

Thus, the clinical presentation may resemble pheochromocytoma or Kawasaki disease. Desquamation (skin peeling) can occur with severe mercury poisoning acquired by handling elemental mercury.

Causes

The consumption of fish is by far the most significant source of ingestion-related mercury exposure in humans, although plants and livestock also contain mercury due to bioconcentration of mercury from seawater, freshwater, marine and lacustrine sediments, soils, and atmosphere, and due to biomagnification by ingesting other mercury-containing organisms. Exposure to mercury can occur from breathing contaminated air, from eating foods that have acquired mercury residues during processing, from exposure to mercury vapor in mercury amalgam dental restorations and from improper use or disposal of mercury and mercury-containing objects, for example, after spills of elemental mercury or improper disposal of fluorescent lamps.

All of these, except elemental liquid mercury produce toxicity or death with less than a gram. Mercury's zero oxidation state (Hg^0) exists as vapor or as liquid metal, its mercurous state (Hg^+) exists as inorganic salts, and its mercuric state (Hg^{2+}) may form either inorganic salts or organomercury compounds.

Consumption of whale and dolphin meat, as is the practice in Japan, is a source of high levels of mercury poisoning. Tetsuya Endo, a professor at the Health Sciences University of Hokkaido, has tested whale meat purchased in the whaling town of Taiji and found mercury levels more than 20 times the acceptable Japanese standard.

Human-generated sources, such as coal-burning power plants emit about half of atmospheric mercury, with natural sources such as volcanoes responsible for the remainder. An estimated two-thirds of human-generated mercury comes from stationary combustion, mostly of coal. Other important human-generated sources include gold production, nonferrous metal production, cement production, waste disposal, human crematoria, caustic soda production, pig iron and steel production, mercury production (mostly for batteries), and biomass burning.

Small independent gold-mining operation workers are at higher risk of mercury poisoning because of crude processing methods. Such is the danger for the galamsey in Ghana and similar workers known as *orpailleurs* in neighboring francophone countries. While no official government estimates of the labor force have been made,

observers believe 20,000-50,000 work as galamseys in Ghana, a figure including many women, who work as porters. Similar problems have been reported amongst the gold miners of Indonesia.

Mercury and many of its chemical compounds, especially organomercury compounds, can also be readily absorbed through direct contact with bare, or in some cases (such as methylmercury) insufficiently protected, skin. Mercury and its compounds are commonly used in chemical laboratories, hospitals, dental clinics, and facilities involved in the production of items such as fluorescent light bulbs, batteries, and explosives.

Many Ayurvedic medicine including Ayurvedic bhasmas contain mercury and other heavy metals.

No scientific data support the claim that mercury compounds in vaccine preservatives cause autism or its symptoms.

Sources

Compounds of mercury tend to be much more toxic than either the elemental or the salts. These compounds have been implicated in causing brain and liver damage. The most dangerous mercury compound, dimethylmercury, is so toxic that even a few microliters spilled on the skin, or even on a latex glove, can cause death, as in the case of Karen Wetterhahn.

Methylmercury and related organomercury compounds

i) ***Mercury in fish***

Methylmercury is the major source of organic mercury for all individuals. Due to bioaccumulation it works its way up through the food web and thus biomagnifies, resulting in high concentrations among populations of some species. Top predatory fish, such as tuna or swordfish, are usually of greater concern than smaller species. The US FDA and the EPAadvise women of child-bearing age, nursing mothers, and young children to completely avoid swordfish, shark, king mackerel and tilefish from the Gulf of Mexico, and to limit consumption of albacore ("white") tuna to no more than 6 oz (170 g) per week, and of all other fish and shellfish to no more than 12 oz (340 g) per week.[26] A 2006 review of the risks and benefits of fish consumption found, for adults, the benefits of one to two servings of fish per week outweigh the risks, even (except for a few fish species) for women of childbearing age, and that avoidance of fish consumption could result in significant excess coronary heart disease deaths and suboptimal neural development in children.

The period between exposure to methylmercury and the appearance of symptoms in adult poisoning cases is long. The longest recorded latent period is five months after a single exposure, in the Dartmouth case (see History); other latent periods in the range of weeks to months have also been reported. No explanation for this long latent period is known. When the first symptom appears, typically paresthesia (a tingling or numbness in the skin), it is followed rapidly by more severe effects, sometimes ending in coma and death. The toxic damage appears to be determined by the peak value of mercury, not the length of the exposure.

Methylmercury exposure during rodent gestation, a developmental period that approximately models human neural development during the first two trimesters of gestation, has long-lasting behavioral consequences that appear in adulthood and, in some cases, may not appear until aging. Prefrontal cortex or dopamine neurotransmission could be especially sensitive to even subtle gestational methylmercury exposure and suggests that public health assessments of methylmercury based on intellectual performance may underestimate the impact of methylmercury in public health.

Ethylmercury is a breakdown product of the antibacteriological agent ethylmercurithiosalicylate, which has been used as a topical antiseptic and a vaccine preservative (further discussed under Thiomersal below). Its characteristics have not been studied as extensively as those of methylmercury. It is cleared from the blood much more rapidly, with a half-life of seven to 10 days, and it is metabolized much more quickly than methylmercury. It is presumed not to have methylmercury's ability to cross the blood–brain barrier via a transporter, but instead relies on simple diffusion to enter the brain.[25] Other exposure sources of organic mercury include

phenylmercuric acetate and phenylmercuric nitrate. These compounds were used in indoor latex paints for their antimildew properties, but were removed in 1990 because of cases of toxicity.

ii) Inorganic mercury compounds

Mercury occurs as salts such as mercuric chloride ($HgCl_2$) and mercurous chloride (Hg_2Cl_2), the latter also known as calomel. Because they are more soluble in water, mercuric salts are usually more acutely toxic than mercurous salts. Their higher solubility lets them be more readily absorbed from the gastrointestinal tract. Mercury salts affect primarily the gastrointestinal tract and the kidneys, and can cause severe kidney damage; however, as they cannot cross the blood–brain barrier easily, these salts inflict little neurological damage without continuous or heavy exposure. Mercuric cyanide ($Hg(CN)_2$) is a particularly toxic mercury compound that has been used in murders, as it contains not only mercury but also cyanide, leading to simultaneous cyanide poisoning. The drug n-acetyl penicillamine has been used to treat mercury poisoning with limited success.

iii) Elemental mercury

Quicksilver (liquid metallic mercury) is poorly absorbed by ingestion and skin contact. Its vapor is the most hazardous form. Animal data indicate less than 0.01% of ingested mercury is absorbed through the intact gastrointestinal tract, though it may not be true for individuals suffering from ileus. Cases of systemic toxicity from accidental swallowing are rare, and attempted suicide via intravenous injection does not appear to result in systemic toxicity, though it still causes damage by physically blocking blood vessels both at the site of injection and the lungs. Though not studied quantitatively, the physical properties of liquid elemental mercury limit its absorption through intact skin and in light of its very low absorption rate from the gastrointestinal tract, skin absorption would not be high. Some mercury vapor is absorbed dermally, but uptake by this route is only about 1% of that by inhalation.

In humans, approximately 80% of inhaled mercury vapor is absorbed via the respiratory tract, where it enters the circulatory system and is distributed throughout the body. Chronic exposure by inhalation, even at low concentrations in the range 0.7–42 $\mu g/m^3$, has been shown in case control studies to cause effects such as tremors, impaired cognitive skills, and sleep disturbance in workers.

Acute inhalation of high concentrations causes a wide variety of cognitive, personality, sensory, and motor disturbances. The most prominent symptoms include tremors (initially affecting the hands and sometimes spreading to other parts of the body), emotional lability (characterized by irritability, excessive shyness, confidence loss, and nervousness), insomnia, memory loss, neuromuscular changes (weakness, muscle atrophy, muscle twitching), headaches, polyneuropathy (paresthesia, stocking-glove sensory loss, hyperactive tendon reflexes, slowed sensory and motor nerve conduction velocities), and performance deficits in tests of cognitive function.

Mechanism

The toxicity of mercury sources can be expected to depend on its nature, i.e., salts vs. organomercury compounds vs. elemental mercury.

One mechanism of mercury toxicity involves its irreversible inhibition of selenoenzymes, such as thioredoxin reductase (IC50 = 9 nM). Although it has many functions, thioredoxin reductase restores vitamins C and E, as well as a number of other important antioxidant molecules, back into their reduced forms, enabling them to counteract oxidative damage. Since the rate of oxygen consumption is particularly high in brain tissues, production of reactive oxygen species (ROS) is accentuated in these vital cells, making them particularly vulnerable to oxidative damage and especially dependent upon the antioxidant protection provided by selenoenzymes. High mercury exposures deplete the amount of cellular selenium available for the biosynthesis of thioredoxin reductase and other selenoenzymes that prevent and reverse oxidative damage, which, if the depletion is severe and long lasting, results in brain cell dysfunctions that can ultimately cause death.

Mercury in its various forms is particularly harmful to fetuses as an environmental toxin in pregnancy, as well as to infants. Women who have been exposed to mercury in substantial excess of dietary selenium intakes during pregnancy are at risk of giving birth to children with serious birth defects. Mercury exposures in excess of dietary selenium intakes in young children can have severe neurological consequences, preventing nerve sheaths from forming properly. Mercury inhibits the formation of myelin.

Diagnosis

Diagnosis of elemental or inorganic mercury poisoning involves determining the history of exposure, physical findings, and an elevated body burden of mercury. Although whole-blood mercury concentrations are typically less than 6 μg/L, diets rich in fish can result in blood mercury concentrations higher than 200 μg/L; it is not that useful to measure these levels for suspected cases of elemental or inorganic poisoning because of mercury's short half-life in the blood. If the exposure is chronic, urine levels can be obtained; 24-hour collections are more reliable than spot collections. It is difficult or impossible to interpret urine samples of patients undergoing chelation therapy, as the therapy itself increases mercury levels in the samples.

Diagnosis of organic mercury poisoning differs in that whole-blood or hair analysis is more reliable than urinary mercury levels.

Prevention (case study)

Mercury poisoning can be prevented (or minimized) by eliminating or reducing exposure to mercury and mercury compounds. To that end, many governments and private groups have made efforts to regulate heavily the use of mercury, or to issue advisories about its use. For example, the export from the European Union of mercury and some mercury compounds has been prohibited since the 15th of March, 2010. The variability among regulations and advisories is at times confusing for the lay person as well as scientists.

Country	Regulating agency	Regulated activity	Medium	Type of mercury compound	Type of limit	Limit
US	Occupational Safety and Health Administration	occupational exposure	air	elemental mercury	Ceiling (not to exceed)	0.1 mg/m^3
US	Occupational Safety and Health Administration	occupational exposure	air	organic mercury	Ceiling (not to exceed)	0.05 mg/m^3
US	Food and Drug Administration	eating	sea food	methylmercury	Maximum allowable concentration	1 ppm (1 mg/L)
US	Environmental Protection Agency	drinking	water	inorganic mercury	Maximum contaminant level	2 ppb (0.002 mg/L)

The United States Environmental Protection Agency (EPA) issued recommendations in 2004 regarding exposure to mercury in fish and shellfish.[46] The EPA also developed the "Fish Kids" awareness campaign for children and young adults [47] on account of the greater impact of mercury exposure to that population.

Cleaning spilled mercury

Mercury thermometers and mercury light bulbs are not as common as they used to be, and the amount of mercury they contain is unlikely to be a health concern if handled carefully. However, broken items still require careful cleanup, as mercury can be hard to collect and it is easy to accidentally create a much larger exposure problem.

Treatment

Identifying and removing the source of the mercury is crucial. Decontamination requires removal of clothes, washing skin with soap and water, and flushing the eyes with saline solution as needed.

Chelation therapy

Chelation therapy for acute inorganic mercury poisoning can be done with DMSA, 2,3-dimercapto-1-propanesulfonic acid (DMPS), D-penicillamine (DPCN), or dimercaprol (BAL). Only DMSA is FDA-approved for use in children for treating mercury poisoning. However, several studies found no clear clinical benefit from DMSA treatment for poisoning due to mercury vapor. No chelator for methylmercury or ethylmercury is approved by the FDA; DMSA is the most frequently used for severe methylmercury poisoning, as it is given orally, has fewer side-effects, and has been found to be superior to BAL, DPCN, and DMPS. α-Lipoic acid (ALA) has been shown to be protective against acute mercury poisoning in several mammalian species when it is given soon after exposure; correct dosage is required, as inappropriate dosages increase toxicity. Although it has been hypothesized that frequent low dosages of ALA may have potential as a mercury chelator, studies in rats have been contradictory. Glutathione and *N*-acetylcysteine (NAC) are recommended by some physicians, but have been shown to increase mercury concentrations in the kidneys and the brain.

Chelation therapy can be hazardous if administered incorrectly. In August 2005, an incorrect form of EDTA (edetate disodium) used for chelation therapy resulted in hypocalcemia, causing cardiac arrest that killed a five-year-old autistic boy.

Other

Experimental findings have demonstrated an interaction between selenium and methylmercury, but epidemiological studies have found little evidence that selenium helps to protect against the adverse effects of methylmercury.

Prognosis

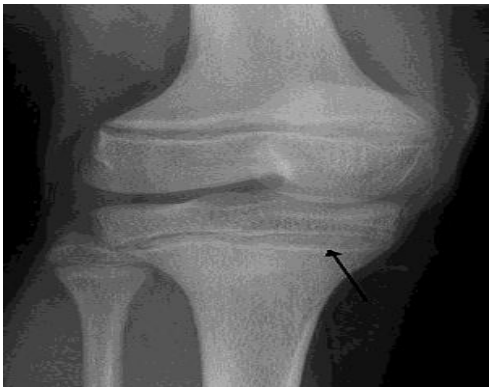
Some of the toxic effects of mercury are partially or wholly reversible, either through specific therapy or through natural elimination of the metal after exposure has been discontinued. Autopsy findings point to a half-life of inorganic mercury in human brains of 27.4 years. Heavy or prolonged exposure can do irreversible damage, in particular in fetuses, infants, and young children. Young's syndrome is believed to be a long-term consequence of early childhood mercury poisoning.

Mercuric chloride may cause cancer as it has caused increases in several types of tumors in rats and mice, while methyl mercury has caused kidney tumors in male rats. The EPA has classified mercuric chloride and methyl mercury as possible human carcinogens (ATSDR, EPA)

Detection in biological fluids

Mercury may be measured in blood or urine to confirm a diagnosis of poisoning in hospitalized people or to assist in the forensic investigation in a case of fatal overdosage. Some analytical techniques are capable of distinguishing organic from inorganic forms of the metal. The concentrations in both fluids tend to reach high levels early after exposure to inorganic forms, while lower but very persistent levels are observed following exposure to elemental or organic mercury. Chelation therapy can cause a transient elevation of urine mercury levels.

Lead poisoning



Lead poisoning is a type of metal poisoning caused by lead in the body. The brain is the most sensitive. Symptoms may include abdominal pain, constipation, headaches, irritability, memory problems, inability to have children, and tingling in the hands and feet. It causes almost 10% of intellectual disability of otherwise unknown cause and can result in behavioral problems. Some of the effects are permanent.[2] In severe cases anemia, seizures, coma, or death may occur.

Exposure to lead can occur by contaminated air, water, dust, food, or consumer products. Children are at greater risk as they are more likely to put objects in their mouth such as those that contain lead paint and absorb a greater proportion of the lead that they eat. Exposure at work is a common cause of lead poisoning in adults with certain occupations at particular risk. Diagnosis is typically by measurement of the blood lead level. The Centers for Disease Control (US) has set the upper limit for blood lead for adults at 10 µg/dl (10 µg/100 g) and for children at 5 µg/dl. Elevated lead may also be detected by changes in red blood cells or dense lines in the bones of children as seen on X-ray.

Lead poisoning is preventable. This includes by individual efforts such as removing lead-containing items from the home, workplace efforts such as improved ventilation and monitoring and nationwide policies such as laws that ban lead in products such as paint and gasoline, reduce allowable levels in water or soil, and provide for cleanup of contaminated soil. The major treatments are removal of the source of lead and the use of medications that bind lead so it can be eliminated from the body, known as chelation therapy. Chelation therapy in children is recommended when blood levels are greater than 40-45 µg/dl. Medications used include dimercaprol, edetate calcium disodium, and succimer.

In 2013 lead is believed to have resulted in 853,000 deaths. It occurs most commonly in the developing world. Those who are poor are at greater risk. Lead is believed to result in 0.6% of the world's disease burden. People have been mining and using lead for thousands of years. Descriptions of lead poisoning date to at least 2000 BC, while efforts to limit lead's use date back to at least the 1500s. Concerns for low levels of exposure begin in the 1970s with there being no safe threshold for lead exposure.

Classification

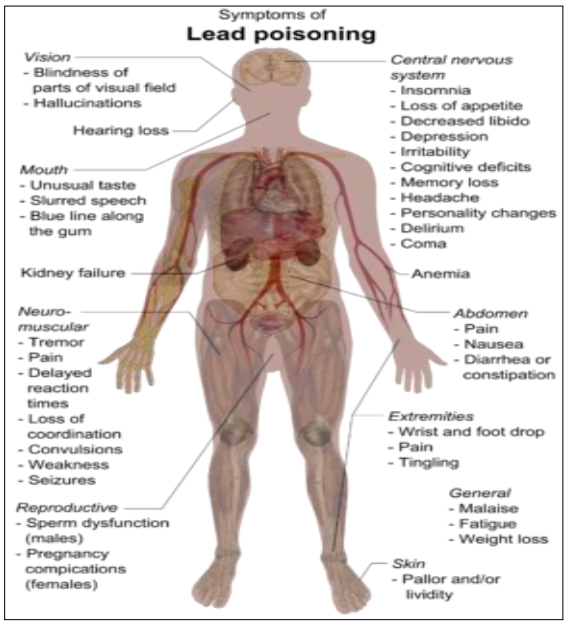
Classically, "lead poisoning" or "lead intoxication" has been defined as exposure to high levels of lead typically associated with severe health effects. Poisoning is a pattern of symptoms that occur with toxic effects from mid to high levels of exposure; toxicity is a wider spectrum of effects, including subclinical ones (those that do not cause symptoms). However, professionals often use "lead poisoning" and "lead toxicity" interchangeably, and official sources do not always restrict the use of "lead poisoning" to refer only to symptomatic effects of lead.

The amount of lead in the blood and tissues, as well as the time course of exposure, determine toxicity. Lead poisoning may be acute (from intense exposure of short duration) or chronic (from repeat low-level exposure over a prolonged period), but the latter is much more common. Diagnosis and treatment of lead exposure are based on blood lead level (the amount of lead in the blood), measured in micrograms of lead per deciliter of blood (μg/dL). Urine lead levels may be used as well, though less commonly. In cases of chronic exposure lead often sequesters in the highest concentrations first in the bones, then in the kidneys. If a provider is performing a provocative excretion test, or "chelation challenge", a measurement obtained from urine rather than blood is likely to provide a more accurate representation of total lead burden to a skilled interpreter.

The US Centers for Disease Control and Prevention and the World Health Organization state that a blood lead level of 10 μg/dL or above is a cause for concern; however, lead may impair development and have harmful health effects even at lower levels, and there is no known safe exposure level. Authorities such as the American Academy of Pediatrics define lead poisoning as blood lead levels higher than 10 μg/dL.

Lead forms a variety of compounds and exists in the environment in various forms. Features of poisoning differ depending on whether the agent is an organic compound (one that contains carbon), or an inorganic one. Organic lead poisoning is now very rare, because countries across the world have phased out the use of organic lead compounds as gasoline additives, but such compounds are still used in industrial settings. Organic lead compounds, which cross the skin and respiratory tract easily, affect the central nervous system predominantly.

Signs and symptoms



Lead poisoning can cause a variety of symptoms and signs which vary depending on the individual and the duration of lead exposure. Symptoms are nonspecific and may be subtle, and someone with elevated lead levels may have no symptoms. Symptoms usually develop over weeks to months as lead builds up in the body during a

chronic exposure, but acute symptoms from brief, intense exposures also occur. Symptoms from exposure to organic lead, which is probably more toxic than inorganic lead due to its lipid solubility, occur rapidly. Poisoning by organic lead compounds has symptoms predominantly in the central nervous system, such as insomnia, delirium, cognitive deficits, tremor, hallucinations, and convulsions.

Symptoms may be different in adults and children; the main symptoms in adults are headache, abdominal pain, memory loss, kidney failure, male reproductive problems, and weakness, pain, or tingling in the extremities.

Early symptoms of lead poisoning in adults are commonly nonspecific and include depression, loss of appetite, intermittent abdominal pain, nausea, diarrhea, constipation, and muscle pain. Other early signs in adults include malaise, fatigue, decreased libido, and problems with sleep. An unusual taste in the mouth and personality changes are also early signs.

In adults, symptoms can occur at levels above 40 μg/dL, but are more likely to occur only above 50–60 μg/dL. Symptoms begin to appear in children generally at around 60 μg/dL. However, the lead levels at which symptoms appear vary widely depending on unknown characteristics of each individual. At blood lead levels between 25 and 60 μg/dL, neuropsychiatriceffects such as delayed reaction times, irritability, and difficulty concentrating, as well as slowed motor nerve conduction and headache can occur. Anemia may appear at blood lead levels higher than 50 μg/dL. In adults, abdominal colic, involving paroxysms of pain, may appear at blood lead levels greater than 80 μg/dL. Signs that occur in adults at blood lead levels exceeding 100 μg/dL include wrist drop and foot drop, and signs of encephalopathy (a condition characterized by brain swelling), such as those that accompany increased pressure within the skull, delirium, coma, seizures, and headache. In children, signs of encephalopathy such as bizarre behavior, discoordination, and apathy occur at lead levels exceeding 70 μg/dL. For both adults and children, it is rare to be asymptomatic if blood lead levels exceed 100 μg/dL.

Acute poisoning

In acute poisoning, typical neurological signs are pain, muscle weakness, numbness and tingling, and, rarely, symptoms associated with inflammation of the brain. Abdominal pain, nausea, vomiting, diarrhea, and constipation are other acute symptoms. Lead's effects on the mouth include astringency and a metallic taste. Gastrointestinal problems, such as constipation, diarrhea, poor appetite, or weight loss, are common in acute poisoning. Absorption of large amounts of lead over a short time can cause shock (insufficient fluid in the circulatory system) due to loss of water from the gastrointestinal tract. Hemolysis (the rupture of red blood cells) due to acute poisoning can cause anemia and hemoglobin in the urine. Damage to kidneys can cause changes in urination such as decreased urine output. People who survive acute poisoning often go on to display symptoms of chronic poisoning.

Chronic poisoning

Chronic poisoning usually presents with symptoms affecting multiple systems, but is associated with three main types of symptoms: gastrointestinal, neuromuscular, and neurological. Central nervous system and neuromuscular symptoms usually result from intense exposure, while gastrointestinal symptoms usually result from exposure over longer periods. Signs of chronic exposure include loss of short-term memory or concentration, depression, nausea, abdominal pain, loss of coordination, and numbness and tingling in the extremities. Fatigue, problems with sleep, headaches, stupor, slurred speech, and anemia are also found in chronic lead poisoning. A "lead hue" of the skin with pallor and/or lividity is another feature. A blue line along the gum with bluish black edging to the teeth, known as a Burton line, is another indication of chronic lead poisoning. Children with chronic poisoning may refuse to play or may have hyperkinetic or aggressive behavior disorders. Visual disturbance may present with gradually progressing blurred vision as a result of central scotoma, caused by toxic optic neuritis.

Effects of children's

A fetus developing in the womb of a woman who has elevated blood lead level is susceptible to lead poisoning by intrauterine exposure, and is at greater risk of being born prematurely or with a low birth weight.

Children are more at risk for lead poisoning because their smaller bodies are in a continuous state of growth and development. Lead is absorbed at a faster rate compared to adults, which causes more physical harm than to older people. Furthermore, children, especially as they are learning to crawl and walk, are constantly on the floor and therefore more prone to ingesting and inhaling dust that is contaminated with lead.

The classic signs and symptoms in children are loss of appetite, abdominal pain, vomiting, weight loss, constipation, anemia, kidney failure, irritability, lethargy, learning disabilities, and behavioral problems. Slow development of normal childhood behaviors, such as talking and use of words, and permanent intellectual disability are both commonly seen. Although less common, it is possible for fingernails to develop leukonychia striata if exposed to abnormally high lead concentrations.

Complications

Lead affects every one of the body's organ systems, especially the nervous system, but also the bones and teeth, the kidneys, and the cardiovascular, immune, and reproductive systems. Hearing loss and tooth decay have been linked to lead exposure, as have cataracts. Intrauterine and neonatal lead exposure promote tooth decay. Aside from the developmental effects unique to young children, the health effects experienced by adults are similar to those in children, although the thresholds are generally higher.

Kidneys

Kidney damage occurs with exposure to high levels of lead, and evidence suggests that lower levels can damage kidneys as well. The toxic effect of lead causes nephropathy and may cause Fanconi syndrome, in which the proximal tubular function of the kidney is impaired. Long-term exposure at levels lower than those that cause lead nephropathy have also been reported as nephrotoxic in patients from developed countries that had chronic kidney disease or were at risk because of hypertension or diabetes mellitus. Lead poisoning inhibits excretion of the waste product urate and causes a predisposition for gout, in which urate builds up.This condition is known as *saturnine gout*.

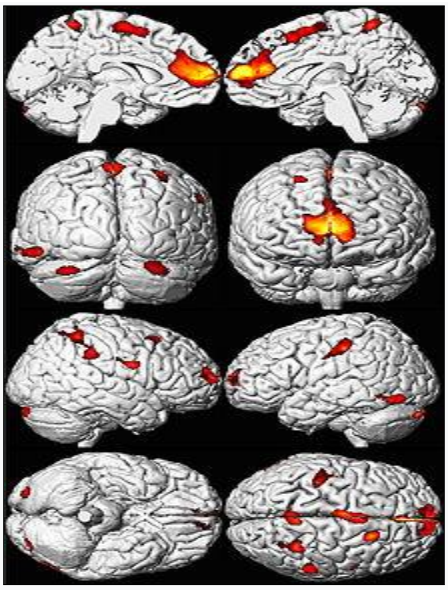
Cardiovascular system

Evidence suggests lead exposure is associated with high blood pressure, and studies have also found connections between lead exposure and coronary heart disease, heart rate variability, and death from stroke, but this evidence is more limited. People who have been exposed to higher concentrations of lead may be at a higher risk for cardiac autonomic dysfunction on days when ozone and fine particles are higher.

Reproductive system

Lead affects both the male and female reproductive systems. In men, when blood lead levels exceed 40 μg/dL, sperm count is reduced and changes occur in volume of sperm, their motility, and their morphology. A pregnant woman's elevated blood lead level can lead to miscarriage, prematurity, low birth weight, and problems with development during childhood. Lead is able to pass through the placenta and into breast milk, and blood lead levels in mothers and infants are usually similar. A fetus may be poisoned *in utero* if lead from the mother's bones is subsequently mobilized by the changes in metabolism due to pregnancy; increased calcium intake in pregnancy may help mitigate this phenomenon.

Nervous system



Lead affects the peripheral nervous system (especially motor nerves) and the central nervous system. Peripheral nervous system effects are more prominent in adults and central nervous system effects are more prominent in children. Lead causes the axons of nerve cells to degenerate and lose their myelin coats.

Lead exposure in young children has been linked to learning disabilities, and children with blood lead concentrations greater than 10 μg/dL are in danger of developmental disabilities. Increased blood lead level in children has been correlated with decreases in intelligence, nonverbal reasoning, short-term memory, attention, reading and arithmetic ability, fine motor skills, emotional regulation, and social engagement. The effect of lead on children's cognitive abilities takes place at very low levels. There is apparently no lower threshold to the dose-response relationship (unlike other heavy metals such as mercury). Reduced academic performance has been associated with lead exposure even at blood lead levels lower than 5 μg/dL. Blood lead levels below 10 μg/dL have been reported to be associated with lower IQ and behavior problems such as aggression, in proportion with blood lead levels. Between the blood lead levels of 5 and 35 μg/dL, an IQ decrease of 2–4 points for each μg/dL increase is reported in children. However, studies that show associations between low-level lead exposure and health effects in children may be affected by confounding and overestimate the effects of low-level lead exposure.

High blood lead levels in adults are also associated with decreases in cognitive performance and with psychiatric symptoms such as depression and anxiety. It was found in a large group of current and former inorganic lead workers in Korea that blood lead levels in the range of 20–50 μg/dL were correlated with neuro-cognitive defects. Increases in blood lead levels from about 50 to about 100 μg/dL in adults have been found to be associated with persistent, and possibly permanent, impairment of central nervous system function.

Lead exposure in children is also correlated with neuropsychiatric disorders such as attention deficit hyperactivity disorder and anti-social behaviour. Elevated lead levels in children are correlated with higher scores on aggression and delinquency measures. A correlation has also been found between prenatal and early childhood lead exposure and violent crime in adulthood. Countries with the highest air lead levels have also been found to have the highest murder rates, after adjusting for confounding factors. A May 2000 study by economic consultant Rick Nevin theorizes that lead exposure explains 65% to 90% of the variation in violent crime rates in the US. A 2007 paper by the same author claims to show a strong association between preschool blood lead and subsequent crime rate trends over several decades across nine countries. Lead exposure in childhood appears to increase school suspensions and juvenile detention among boys. It is believed that the U.S. ban on lead paint in

buildings in the late 1970s, as well as the phaseout of leaded gasoline in the 1970s and 1980s, partially helped contribute to the decline of violent crime in the United States since the early 1990s.

Diagnosis

Diagnosis includes determining the clinical signs and the medical history, with inquiry into possible routes of exposure. Clinical toxicologists, medical specialists in the area of poisoning, may be involved in diagnosis and treatment. The main tool in diagnosing and assessing the severity of lead poisoning is laboratory analysis of the blood lead level (BLL).

Basophilic stippling (arrows) of red blood cells in a 53-year-old who had elevated blood lead levels due to drinking repeatedly from glasses decorated with lead paint.

Blood film examination may reveal basophilic stippling of red blood cells (dots in red blood cells visible through a microscope), as well as the changes normally associated with iron-deficiency anemia (microcytosis and hypochromasia). However, basophilic stippling is also seen in unrelated conditions, such as megaloblastic anemia caused by vitamin B12 (colbalamin) and folatedeficiencies.

Exposure to lead also can be evaluated by measuring erythrocyte protoporphyrin (EP) in blood samples. EP is a part of red blood cells known to increase when the amount of lead in the blood is high, with a delay of a few weeks. Thus EP levels in conjunction with blood lead levels can suggest the time period of exposure; if blood lead levels are high but EP is still normal, this finding suggests exposure was recent. However, the EP level alone is not sensitive enough to identify elevated blood lead levels below about 35 μg/dL. Due to this higher threshold for detection and the fact that EP levels also increase in iron deficiency, use of this method for detecting lead exposure has decreased.

Blood lead levels are an indicator mainly of recent or current lead exposure, not of total body burden. Lead in bones can be measured noninvasively by X-ray fluorescence; this may be the best measure of cumulative exposure and total body burden. However this method is not widely available and is mainly used for research rather than routine diagnosis. Another radiographic sign of elevated lead levels is the presence of radiodense lines called lead lines at the metaphysis in the long bones of growing children, especially around the knees. These lead lines, caused by increased calcification due to disrupted metabolism in the growing bones, become wider as the duration of lead exposure increases. X-rays may also reveal lead-containing foreign materials such as paint chips in the gastrointestinal tract.

Fecal lead content that is measured over the course of a few days may also be an accurate way to estimate the overall amount of childhood lead intake. This form of measurement may serve as a useful way to see the extent of oral lead exposure from all the diet and environmental sources of lead.

Lead poisoning shares symptoms with other conditions and may be easily missed. Conditions that present similarly and must be ruled out in diagnosing lead poisoning include carpal tunnel syndrome, Guillain–Barré syndrome, renal colic, appendicitis, encephalitis in adults, and viral gastroenteritis in children. Other differential diagnoses in children include constipation, abdominal colic, iron deficiency, subdural hematoma, neoplasms of the central nervous system, emotional and behavior disorders, and intellectual disability.

Prevention

Testing kits are commercially available for detecting lead. These swabs, when wiped on a surface, turn red in the presence of lead.

In most cases, lead poisoning is preventable by avoiding exposure to lead. Prevention strategies can be divided into individual (measures taken by a family), preventive medicine (identifying and intervening with high-risk individuals), and public health (reducing risk on a population level).

Recommended steps by individuals to reduce the blood lead levels of children include increasing their frequency of hand washing and their intake of calcium and iron, discouraging them from putting their hands to their mouths, vacuuming frequently, and eliminating the presence of lead-containing objects such as blinds and jewellery in the house. In houses with lead pipes or plumbing solder, these can be replaced. Less permanent but cheaper methods include running water in the morning to flush out the most contaminated water, or adjusting the water's chemistry to prevent corrosion of pipes. Lead testing kits are commercially available for detecting the presence of lead in the household. As hot water is more likely than cold water to contain higher amounts of lead, use only cold water from the tap for drinking, cooking, and for making baby formula. Since most of the lead in household water usually comes from plumbing in the house and not from the local water supply, using cold water can avoid lead exposure. Measures such as dust control and household education do not appear to be effective in changing children's blood levels.

Screening is an important method in preventive medicine strategies. Screening programs exist to test the blood of children at high risk for lead exposure, such as those who live near lead-related industries.

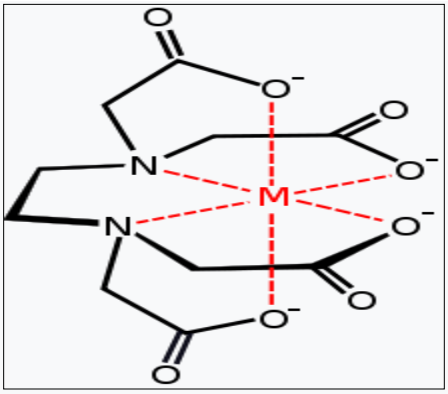
Prevention measures also exist on national and municipal levels. Recommendations by health professionals for lowering childhood exposures include banning the use of lead where it is not essential and strengthening regulations that limit the amount of lead in soil, water, air, household dust, and products. Regulations exist to limit the amount of lead in paint; for example, a 1978 law in the US restricted the lead in paint for residences, furniture, and toys to 0.06% or less. In October 2008, the US Environmental Protection Agencyreduced the allowable lead level by a factor of ten to 0.15 micrograms per cubic meter of air, giving states five years to comply with the standards. The European Union's Restriction of Hazardous Substances Directive limits amounts of lead and other toxic substances in electronics and electrical equipment. In some places, remediation programs exist to reduce the presence of lead when it is found to be high, for example in drinking water. As a more radical solution, entire towns located near former lead mines have been "closed" by the government, and the population resettled elsewhere, as was the case with Picher, Oklahoma in 2009.

Treatment

CDC management guidelines for children with elevated blood levels

Blood lead level (µg/dL)	Treatment
10–14	Education, repeat screening
15–19	Repeat screening, case management to abate sources
20–44	Medical evaluation, case management
45–69	Medical evaluation, chelation, case management
>69	Hospitalization, immediate chelation, case management

The mainstays of treatment are removal from the source of lead and, for people who have significantly high blood lead levels or who have symptoms of poisoning, chelation therapy. Treatment of iron, calcium, and zinc deficiencies, which are associated with increased lead absorption, is another part of treatment for lead poisoning. When lead-containing materials are present in the gastrointestinal tract (as evidenced by abdominal X-rays), whole bowel irrigation, cathartics, endoscopy, or even surgical removal may be used to eliminate it from the gut and prevent further exposure. Lead-containing bullets and shrapnel may also present a threat of further exposure and may need to be surgically removed if they are in or near fluid-filled or synovial spaces. If lead encephalopathy is present, anticonvulsants may be given to control seizures, and treatments to control swelling of the braininclude corticosteroids and mannitol. Treatment of organic lead poisoning involves removing the lead compound from the skin, preventing further exposure, treating seizures, and possibly chelation therapy for people with high blood lead concentrations.



EDTA, a chelating agent, binds a heavy metal, sequestering it.

A chelating agent is a molecule with at least two negatively charged groups that allow it to form complexes with metal ions with multiple positive charges, such as lead. The chelate that is thus formed is nontoxic and can be excreted in the urine, initially at up to 50 times the normal rate. The chelating agents used for treatment of lead poisoning are edetate disodium calcium ($CaNa_2EDTA$), dimercaprol (BAL), which are injected, and succimer and d-penicillamine, which are administered orally. Chelation therapy is used in cases of acute lead

poisoning, severe poisoning, and encephalopathy, and is considered for people with blood lead levels above 25 µg/dL. While the use of chelation for people with symptoms of lead poisoning is widely supported, use in asymptomatic people with high blood lead levels is more controversial. Chelation therapy is of limited value for cases of chronic exposure to low levels of lead. Chelation therapy is usually stopped when symptoms resolve or when blood lead levels return to premorbid levels. When lead exposure has taken place over a long period, blood lead levels may rise after chelation is stopped because lead is leached into blood from stores in the bone; thus repeated treatments are often necessary.

People receiving dimercaprol need to be assessed for peanut allergies since the commercial formulation contains peanut oil. Calcium EDTA is also effective if administered four hours after the administration of dimercaprol. Administering dimercaprol, DMSA (Succimer), or DMPS prior to calcium EDTA is necessary to prevent the redistribution of lead into the central nervous system. Dimercaprol used alone may also redistribute lead to the brain and testes. An adverse side effect of calcium EDTA is renal toxicity. Succimer (DMSA) is the preferred agent in mild to moderate lead poisoning cases. This may be the case in instances where children have a blood lead level >25µg/dL. The most reported adverse side effect for succimer is gastrointestinal disturbances. It is also important to note that chelation therapy only lowers blood lead levels and may not prevent the lead-induced cognitive problems associated with lower lead levels in tissue. This may be because of the inability of these agents to remove sufficient amounts of lead from tissue or inability to reverse preexisting damage. Chelating agents can have adverse effects; for example, chelation therapy can lower the body's levels of necessary nutrients like zinc. Chelating agents taken orally can increase the body's absorption of lead through the intestine.

Chelation challenge, also known as provocation testing, is used to indicate an elevated and mobilizable body burden of heavy metals including lead. This testing involves collecting urine before and after administering a one-off dose of chelating agent to mobilize heavy metals into the urine. Then urine is analyzed by a laboratory for levels of heavy metals; from this analysis overall body burden is inferred. Chelation challenge mainly measures the burden of lead in soft tissues, though whether it accurately reflects long-term exposure or the amount of lead stored in bone remains controversial. Although the technique has been used to determine whether chelation therapy is indicated and to diagnose heavy metal exposure, some evidence does not support these uses as blood levels after chelation are not comparable to the reference range typically used to diagnose heavy metal poisoning. The single chelation dose could also redistribute the heavy metals to more sensitive areas such as central nervous system tissue.

Cadmium poisoning

Cadmium poisoning	
Classification and external resources	
Specialty	emergency medicine
ICD-10	T56.3
ICD-9-CM	985.5

Cadmium is an extremely toxic metal commonly found in industrial workplaces. Due to its low permissible exposure limit, overexposures may occur even in situations where trace quantities of cadmium are found. Cadmium is used extensively in electroplating, although the nature of the operation does not generally lead to overexposures. Cadmium is also found in some industrial paints and may represent a hazard when sprayed. Operations involving removal of cadmium paints by scraping or blasting may pose a significant hazard. Cadmium is also present in the manufacturing of some types of batteries. Exposures to cadmium are addressed in

specific standards for the general industry, shipyard employment, construction industry, and the agricultural industry.

Sources of exposure

In the 1950s and 1960s industrial exposure to cadmium was high, but as the toxic effects of cadmium became apparent, industrial limits on cadmium exposure have been reduced in most industrialized nations and many policy makers agree on the need to reduce exposure further. While working with cadmium it is important to do so under a fume hood to protect against dangerous fumes. Brazing fillers which contain cadmium should be handled with care. Serious toxicity problems have resulted from long-term exposure to cadmium plating baths.

Buildup of cadmium levels in the water, air, and soil has been occurring particularly in industrial areas. Environmental exposure to cadmium has been particularly problematic in Japan where many people have consumed rice that was grown in cadmium-contaminated irrigation water. This phenomenon is known under the name itai-itai disease.

Food is another source of cadmium. Plants may only contain small or moderate amounts in non-industrial areas, but high levels may be found in the liver and kidneys of adult animals. The daily intake of cadmium through food varies by geographic region. Intake is reported to be approximately 8 to 30μg in Europe and the United States versus 59 to 113 μg in various areas of Japan.

Cigarettes are also a significant source of cadmium exposure. Although there is generally less cadmium in tobacco than in food, the lungs absorb cadmium more efficiently than the stomach.

Aside from tobacco smokers, people who live near hazardous waste sites or factories that release cadmium into the air have the potential for exposure to cadmium in air. However, numerous state and federal regulations in the United States control the amount of cadmium that can be released to the air from waste sites and incinerators so that properly regulated sites are not hazardous. The general population and people living near hazardous waste sites may be exposed to cadmium in contaminated food, dust, or water from unregulated or accidental releases. Numerous regulations and use of pollution controls are enforced to prevent such releases.

An experiment during the early 1960s involving the spraying of cadmium over Norwich was declassified in 2005 by the UK government, as documented in a BBC News article.

In February 2010, cadmium was found in an entire line of Wal-Mart exclusive Miley Cyrus jewelry. The charms were tested at the behest of the *Associated Press* and were found to contain high levels of cadmium. Wal-Mart did not stop selling the jewelry until May 12 because "it would be too difficult to test products already on its shelves". On June 4 cadmium was detected in the paint used on promotional drinking glasses for the movie *Shrek Forever After*, sold by McDonald's Restaurants, triggering a recall of 12 million glasses.

Mechanism of toxicity

Cadmium (Cd) is an extremely toxic industrial and environmental pollutant classified as a human carcinogen [Group 1 – according to International Agency for Research on Cancer; Group 2a – according to Environmental Protection Agency (EPA); and 1B carcinogen classified by European Chemical Agency.

Acute exposure to cadmium fumes may cause flu-like symptoms including chills, fever, and muscle ache sometimes referred to as "the cadmium blues." Symptoms may resolve after a week if there is no respiratory damage. More severe exposures can cause tracheo-bronchitis, pneumonitis, and pulmonary edema. Symptoms of inflammation may start hours after the exposure and include cough, dryness and irritation of the nose and throat, headache, dizziness, weakness, fever, chills, and chest pain.

Inhaling cadmium-laden dust quickly leads to respiratory tract and kidney problems which can be fatal (often from renal failure). Ingestion of any significant amount of cadmium causes immediate poisoning and damage to the liver and the kidneys. Compounds containing cadmium are also carcinogenic.

The bones become soft (*osteomalacia*), lose bone mineral density (*osteoporosis*) and become weaker. This causes the pain in the joints and the back, and also increases the risk of fractures. In extreme cases of cadmium poisoning, mere body weight causes a fracture.

The kidneys lose their function to remove acids from the blood in *proximal renal tubular dysfunction*. The kidney damage inflicted by cadmium poisoning is irreversible. The *proximal renal tubular dysfunction* creates low phosphate levels in the blood (*hypophosphatemia*), causing muscle weakness and sometimes coma. The dysfunction also causes gout, a form of arthritis due to the accumulation of uric acid crystals in the joints because of high acidity of the blood (*hyperuricemia*). Another side effect is increased levels of chloride in the blood (*hyperchloremia*). The kidneys can also shrink up to 30%. Cadmium exposure is also associated with the development of kidney stones.

Similar to zinc, long term exposure to cadmium fumes can cause irreversible total loss of smell.

Inside cells, cadmium ions act as a hydrogen peroxide generator. This sudden surge of cytosolic hydrogen peroxide causes increased lipid peroxidation and additionally depletes ascorbate and glutathione stores. Hydrogen peroxide can also convert thiol groups on proteins into nonfunctional sulfones and is also capable of directly attacking nuclear DNA. This oxidative stress causes the afflicted cell to manufacture large amounts of inflammatory cytokines.

Platinum complex in anticancer activity

Cisplatin is a chemotherapy medication used to treat a number of cancers. This includes testicular cancer, ovarian cancer, cervical cancer, breast cancer, bladder cancer, head and neck cancer, esophageal cancer, lung cancer, mesothelioma, brain tumors and neuroblastoma. It is used by injection into a vein.[1]

Common side effects include bone marrow suppression, hearing problems, kidney problems, and vomiting. Other serious side effects include numbness, trouble walking, allergic reactions, electrolyte problems, and heart disease. Use during pregnancy is known to harm the baby. Cisplatin is in the platinum-based antineoplastic family of medications. It works in part by binding to, and inhibiting DNA replication.

Cisplatin was discovered in 1845 and licensed for medical use in 1978/1979. It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. The wholesale cost in the developing worldis about US$5.56 to US$7.98 per 50-mg vial.

Medical use

Cisplatin is administered intravenously as short-term infusion in normal saline for treatment of solid malignancies. It is used to treat various types of cancers, including sarcomas, some carcinomas (e.g., small cell lung cancer, squamous cell carcinoma of the head and neck and ovarian cancer), lymphomas, bladder cancer, cervical cancer, and germ cell tumors.

Cisplatin is particularly effective against testicular cancer; the cure rate was improved from 10% to 85%.

In addition, cisplatin is used in Auger therapy.

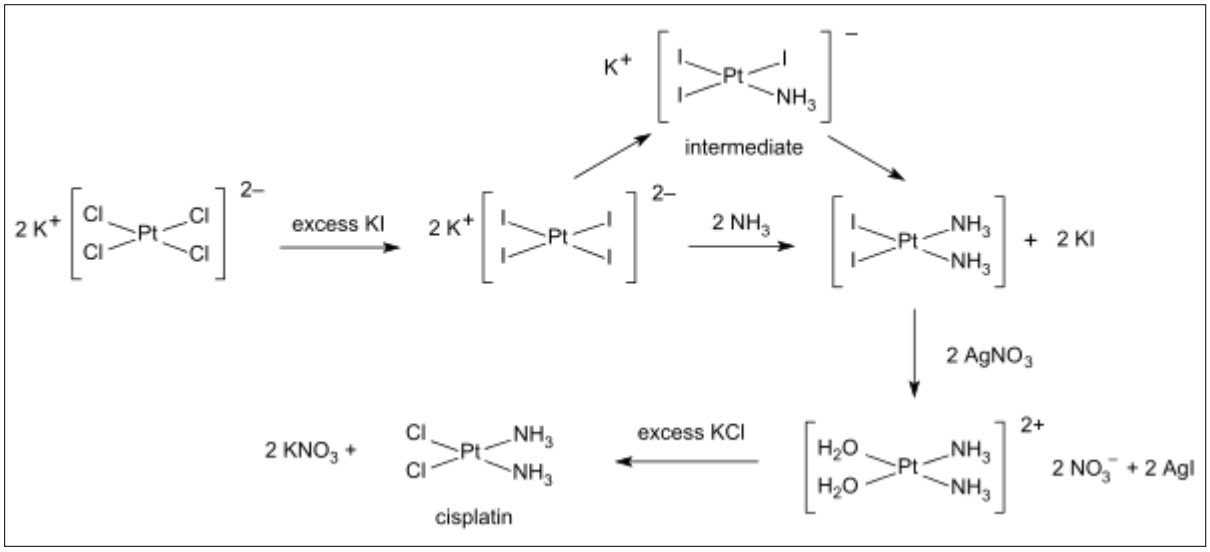
History

The compound *cis*-$[Pt(NH_3)_2(Cl)_2]$ was first described by Michele Peyrone in 1845, and known for a long time as Peyrone's salt. The structure was deduced by Alfred Werner in 1893. In 1965, Barnett Rosenberg, Van Camp et al. of Michigan State University discovered that electrolysis of platinum electrodes generated a soluble platinum complex which inhibited binary fission in *Escherichia coli* (*E. coli*) bacteria. Although bacterial cell growth continued, cell division was arrested, the bacteria growing as filaments up to 300 times their normal length. The octahedral Pt(IV) complex *cis*-$[PtCl_4(NH_3)_2]$, but not the *trans* isomer, was found to be effective at forcing

filamentous growth of *E. coli* cells. The square planar Pt(II) complex, *cis*-$[PtCl_2(NH_3)_2]$ turned out to be even more effective at forcing filamentous growth. This finding led to the observation that *cis*-$[PtCl_2(NH_3)_2]$ was indeed highly effective at regressing the mass of sarcomas in rats. Confirmation of this discovery, and extension of testing to other tumour cell lines launched the medicinal applications of cisplatin. Cisplatin was approved for use in testicular and ovarian cancers by the U.S. Food and Drug Administration on 19 December 1978., and in the UK (and in several other European countries) in 1979.

Synthesis

The synthesis of cisplatin starts from potassium tetrachloroplatinate. The tetraiodide is formed by reaction with an excess of potassium iodide. Reaction with ammonia forms $K_2[PtI_2(NH_3)_2]$ which is isolated as a yellow compound. When silver nitrate in water is added insoluble silver iodide precipitates and $K_2[Pt(OH_2)_2(NH_3)_2]$ remains in solution. Addition of potassium chloride will form the final product which precipitates In the triiodo intermediate the addition of the second ammonia ligand is governed by the trans effect.



For the synthesis of transplatin $K_2[PtCl_4]$ is first converted to $Cl_2[Pt(NH_3)_4]$ by reaction with ammonia. The trans product is then formed by reaction with hydrochloric acid.

Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

POSSIBLE QUESTIONS

MULTIPLE CHOICE QUESTIONS

1. Which one of the following is used as antiknock compounds in gasoline
   a. aryl leads b. free lead **c. alkyl lead** d. lead isotope
2. The word " encephalitis" refers the damage of
   a. brain cell disorder b. tissue disorder c. nerve cell disorder
   d. both nerve and brain cell
3. In the initial stage, the accumulation of lead ions bones are
   a. inert in nature b. explosive nature c. active nature d. catalytic nature
4. Which one of the following is recommended for detoxification of lead
   a. $CaNa_2$ b. Ca-C_2H_5 c. $Al(H_2O)_6$ d. $PuCa_2$
5. $Pb(C_2H_5)_4$ is also known as
   a. Catalyst **b. free radical sacavenger** c. by product d. co catalyst
6. he attachment of toxic Hg cause the
   a. inhibit the aminoacid synthesis b. inhibit the blood transport
   c. inhibit the enzyme production **d. inhibit the active transport of glucose**
7. 2,3-Dimercapto-1-propanesulfonic acid known as
   a. Uracil **b. Unithiol** c. Uranoporphyrinogen d. BAL
8. Cd and Zn are the
   a. co-catalyst b. core material **c. cogeners** d. same row elements
9. Which one of the following is attacks the cell division
   a. CH_3-Hg-CN b. C_2H_5-Hg-Cl c. CH_3-CO_2Hg-C_6H_5 **d.CH_3-Hg+**
10. NAPA is a
    a. **N-acetyl derivative** b. N-acyl derivative c..N-aryl derivative d. N-alkyl phenyl
11. Cigarette smoking increases the ---- burden

a. Al **b. Cd** c. Ca d. Cr

12. Which of the following colour is belongs to the CdS
    a. Orange colour b. Green colour **c. Brilliant yellow colour** d. bright blue colour
13. Isoniazid is an drug for
    a. inflammation b. cancer **c. tubercular** d. malaria
14. In which of the following have a property to cleave the DNA helix of the cancer cells
    a. belomycin b. streptomycin c. isonizid d. sanocrysin
15. The metal Cu(III) react with ---- to form the anticancer drugs
    a. halides b. alkalis c. semicarbazones **d. thiosemicarbazones**
16. The Salvarsan is the drug of
    a. mercury **b. Arsenic** c. Antimonial d. Cadmium
17. Solaganol is the drug of
    a. Ag **b. Au** c. Sb d. As
18. Which one of the following is used as the brain imaging agent
    a. **^{68}Ga** b. ^{131}I c. ^{60}Co d. ^{32}P
19. The isotope I131 is detect the tumor by the emission of
    a. α-ray b. β-ray c**. γ-ray** d. δ-ray
20. The trans platin is a
    a. **Toxic** b. non-toxic c. less toxic d. anticancer agent

8-MARKS

1. Explain in detail about source, toxicity and treatment of Pb?
2. Give a note on anticancer property of platinum complexes?
3. Name two platinum complexes approved clinically for the treatment of human cancer?
4. Give a note on treatment of Pb, Cd and Hg toxicity?
5. What are major sources of Hg toxicity? Explain how the CH_3Hg is more toxic than Hg^{2+}
6. Name the important 2nd generation anticancer drugs of platinum complex?
7. Graphically represent the effect of essential metal and toxic metal on biological growth?
8. Discuss the effect of deficiency of Pb, Cd, Hg on health and suggest treatment protocol?
9. Discuss the different sources of metal ion toxicity ?
10. Give the toxic symptoms in a) Pb b)Hg c)Cd- poisoning?

11. Give the uses of some metal chelating compounds?

12. What is metal deficiency? Give the table of metal deficiency effects of metal ions in our body?

UNIT 5

Trace Metals in Plant Life

Micronutrients in soil, role of micronutrients in plant life

Biogeochemistry : Biodegradation of minerals bacteria leaching and its applications.

Micronutrients

Micronutrients are nutrients required by organisms throughout life in small quantities to orchestrate a range of physiological functions. For people, they include dietary trace minerals in amounts generally less than 100 milligrams per day, as opposed to macro-minerals, which are required in larger quantities. The micro-minerals or trace elements include at least iron, cobalt, chromium, copper, iodine, manganese, selenium, zinc and molybdenum. Micronutrients also include vitamins, which are organic compounds required as nutrients in trace amounts.

Micronutrients in Soil

While it's common knowledge that plants need water and air to grow, sometimes the question of exactly what nutrients a plant needs in order to thrive can be challenging.

Nutrients in the soil are vital to the growth of plants, and proper allocation is critical to the plant's quality. Understanding fully what nutrients are and how they help a plant grow are the first steps in providing an enriching environment for your crops.

Essential nutrients are just that - nutrients that a plant needs for survival. They are divided into two categories: mineral and non-mineral. The non-mineral nutrients required by plants are carbon, hydrogen, and oxygen, found in the air and water. Mineral nutrients are classified as either macronutrients or micronutrients.

Plants need large amounts of macronutrients in order to thrive. Macronutrients are classified further into primary and secondary nutrients.

Proportionately, plants need the largest quantities of primary nutrients. Primary nutrients include:

- Nitrogen (N)
- Phosphorus (P)
- Potassium (K)

Secondary nutrients are as important to a plant's nutrition as the primary nutrients, but plants don’t require quite as much in terms of quantity. Secondary nutrients include:

- Calcium (Ca)
- Magnesium (Mg)
- Sulfur (S)

Proportionate to primary and secondary nutrients, plants need a much smaller quantity of micronutrients. However, their importance is still great. A shortage of micronutrients can limit plant growth and crop yields. Too great a shortage could even cause plant death, even with all other essential elements fully represented. Micronutrients include:

- Boron (B): Transports sugar to roots and tops
- Chloride (Cl): Aids in plant metabolism
- Copper (Cu): Activates enzymes, aides in chlorophyll production and is involved in protein synthesis
- Iron (Fe): Essential for formation of chlorophyll
- Manganese (Mn): Important for the production of chlorophyll
- Molybdenum (Mo): Reduces nitrates for protein synthesis
- Nickel (Ni): Essential for formation of chlorophyll
- Zinc (Zn): Activates enzymes

As plants develop, from seedling stage to harvest, their need for nutrition varies. During the seedling stage, the need for nutrients is low, but it gradually starts to increase. Nutrient demand quickly increases during the vegetative state. In the reproductive stage, demand lessens again: While plants still need nutrients, the demand is mostly met by a redistribution of elements held in the vegetative tissues.

Maximizing plant potential

The importance of micronutrients to a plant's health has gotten more attention recently as their incorporation into broad fertilizers has become more common.

One reason is increasing per-acre crop yields. This trend removes higher amounts of micronutrients from fields, and the soil is unable to naturally compensate for the loss. Growers are left with the burden of adding the nutrients back to the soil.

Also, advances in fertilizer technology have improved the removal of impurities in the manufacturing process. Adding micronutrients has become much easier and more effective.

In addition, before the common practice of adding primary nutrients to soil, farmers had fields lacking in these elements; the absence of micronutrients paled in comparison to the greater need for primary nutrients.

The Law of the Minimum places even more importance on micronutrients. The concept, developed by a German scientist in the mid-19th century, holds that "plants will use essential elements only in proportion to each other, and the element that is in shortest supply in proportion to the rest will determine how well the plant will use the other nutrient elements." Basically, a plant's growth will be limited by the specific nutrient it lacks most.

Smart growers strive to ensure that all the essential nutrients are provided for their crops. Farmers can analyze and improve nutrient programs through soil tests, plants analyses and local field demonstrations. For more information on proper nutrient management, please consult with your agronomist or local Extension resources.

Micronutrients in plant growth.

The early culture solutions were made with salts which were not pure, i.e., the salts contained a lot of traces of other elements as impurities. It was found that as better- purified salts were used for culture solutions, the growth of the plants instead of getting better, definitely got poorer.

This was followed up by direct evidence that other elements are needed for the normal growth of the plant but only in minute amounts. They are just as essential for the life and the growth of the plants as the macro elements and therefore no normal growth was possible in their complete absence. But in view of the fantastically small amounts needed, they are usually grouped separately from the macro- nutrients and called trace or micronutrient elements. Iron seems to occupy an intermediate position between the macro- and micronutrients.

It does not enter into the composition of plant food, or in the composition of the plant itself. The amount of iron necessary for normal growth of the plants is very small compared to the other six macronutrients, yet it is hardly as small as to rank as a micronutrient.

Bacterial leaching techniques

The two major techniques used in leaching are percolation and agitation leaching. Percolation leaching involves the percolation of a lixiviant through a static bed, whereas agitation leaching involves finer particle sizes agitated in a lixiviant. Due to the large scale operations involved in bacterial leaching, percolation leaching is preferred commercially. The principal commercial methods are in situ, dump, heap and vat leaching. In situ leaching involves pumping of solution and air under pressure into a mine or into ore bodies made permeable by explosive charging. The resulting metal-enriched solutions are recovered through wells drilled below the ore body.

Dump leaching involves uncrushed waste rock which is piled up. These dumps generally contain about 0.1-0.5% Cu, too low to recover profitably by conventional procedures. Some of these dumps are huge, containing in excess of 10 million tons of waste rock. Heap leaching requires the preparation of the ore, primarily size reduction, so as to maximize mineral- lixiviant interaction and the laying of an impermeable base to prevent lixiviant loss and pollution of water bodies. Essentially, both dump and heap leaching involve the application of lixiviant to the top of the dump or heap surface and the recovery of the metal laden solution that seeps to the bottom by gravity flow. The dilute sulphuric acid sprinkled on top percolates down through the dump, lowering the pH and promoting the growth of acidophilic microorganisms. The acid run-off is collected at the bottom of the dump, from where it is pumped to a recovery station. Copper is extracted from the acid run-off by cementation or solvent extraction or electro wining. All the above processes are essentially uncontrolled from a biological and engineering standpoint. Beside these processes are slow in nature and require long periods to recover a portion of the metal. Vat leaching as currently applied to oxide ores involves the dissolution of crushed materials in a confined tank. More controls can be brought in for enhanced recovery by the use of bioreactors, though necessarily these involve higher costs. However for ore concentrates and precious metals they are being considered actively.

Factors affecting bacterial leaching

The rate and efficiency of bacterial leaching of mineral ores depends upon a number of different factors. Brandl, (2001) has summarized these factors, which can be seen in table.

Table: Factors affecting bacterial leaching

Factor	Parameter	
Physicochemical parameters of a bioleaching environment	Temperature	nutrient availability
	pH	iron (II) concentration
	redox potential	light
	oxygen content and availability	pressure
	carbon dioxide content	surface tension
	mass transfer	presence of inhibitors
Microbiological parameters of a bioleaching environment	Microbial diversity	Metal tolerance
	Population diversity	Adaptation abilities of microorganisms
	Spatial distribution of microorganisms	
Properties of the minerals to be leached	mineral type	porosity
	mineral composition	hydrophobicity
	mineral dissemination	galvanic interactions
	grain size	formation of secondary minerals
	surface area	
Processing	Leaching mode (in situ, heap, dump, or tank leaching)	Stirring rate (in case of tank leaching operaions)
	Pulp density	Heap geometry (in case of heap leaching)

Physico-chemical as well as microbiological factors of the leaching environment affects bioleaching rates and efficiencies. Moreover, the properties of the mineral ores and the manner in which they are processed are also significant since they also affect bioleaching rates and efficiencies. The influence of different microbiological, mineralogical, physicochemical and process parameters on the oxidation of mineral ores has been reviewed by many researchers. Unfortunately whilst much has been published in this field, results are sometimes conflicting and often the conditions used are not described in much detail.

Trace elements can be conveniently divided into four groups:

(a) the essential—so far the following six have been conclusively proved to be essential for normal plant growth—B, Zn, Cu, Mn, Mo and Co; (b) the probably essential—-elements like selenium, barium, etc.; (c) the toxic—all essential macro- and micronutrients in high dosages and [d) physiologically inactive elements—arsenic, etc.

In 1914, Maze, a French scientist, using very highly purified chemicals in water culture solutions found that his very pure salt solutions did not support plant growth satisfactorily. Thus, although this observation was at the time given very little attention, it really laid the foundation of the importance of micronutrients.

Almost 50 years before that, however, Raulin (1869) when studying the role of zinc in the nutrition of Aspergillus niger concluded, with a remarkable insight for his day, that the microelements were required by plants in minute quantity and were present as impurities in the external medium.

The ratio between the amounts of micronutrients and the amounts of macro- nutrients will be roughly between, 1: 1000 and 1: 10,000. In soils, however, quantities are somewhat larger—rate of application in soil, when there is a known micronutrient deficiency, are usually at the rate of a few pounds per acre.

Actual amounts of the trace elements or micronutrients range from as little as 2-3 parts in 100 million parts up to 10-100 parts in 1.00 million. These amounts are so fantastically small that sceptics may be tempted to argue that the whole subject is an exaggeration of science.

Since such small amounts of trace elements are required for plant growth in the soil, it might seem unlikely that soils should ever be unable to provide enough for all crops, yet it is a fact that in the past 15-20 years, increasing number of serious micronutrient deficiencies have been recognised.

In many parts of the world, economic cropping would have probably ceased but for diagnosis of micro-elemental deficiency and subsequent remedial treatment.

Microelement shortage is not always induced by a real absence of the particular element in the top soil. A large supply may be present but it may be locked up as a result of soil condition and thus unable to enter the soil solution and become available to the roots.

Severe Zn deficiency effects on fruit trees were experienced in many countries though the soil contained enough Zn for the whole orchard's need for hundred years!

Even the addition of Zn salts in many cases to the soil could not correct the deficiency for the added Zn was also quickly made unavailable. The remedy was found in the spraying of a very dilute solution of $ZnSO_4$ on the foliage of the trees.

Another approach has been the injection of solid salt containing a trace element into the trunk of the tree. Like Zn, manganese deficiency is generally due to non-availability rather than to actual absence of the element from the soil.

On the other hand, boron deficiency is usually due to absence of boron in the soil for borates tend to be easily washed out of the soils, particularly in sandy soil. Here, the remedy of applying boron to the soil is reasonably effective.

Micronutrient elements, although they are as essential as the macronutrients in minute amounts, soon become toxic to the plants if the beneficial rate is exceeded.

Most artificial fertilisers always contain trace elements in any case; for instance, Chilean nitrate contains boron and basic slag contains manganese; superphosphates contain slight amounts of Cu and Zn, derived from the commercial H_2SO_4 used in the industrial manufacture of superphosphates.

Why are such minute quantities of some elements needed by plants? What indispensable roles do these elements play in the metabolism of the living cells?

We know that these elements are not direct plant foods. It was supposed also that they may act as catalysts or activators for certain chemical reactions in the plants and for that reason, it was understandable that their requirement will be much smaller, compared to the macronutrients, which directly enter into the composition of plant foods or living cells themselves.

Recent researches have given us the answers to the questions about the functions of the microelement which seemed so perplexing a few years before. There is no doubt whatsoever now, that the essentiality of heavy metals like Cu, Zn, Mn and Fe in minute traces for the normal growth of the plants is due to their forming constituents of the essential enzymes.

The enzyme, tyrosinase, which transfers hydrogen from the amino acid, tyrosine, is active only in the presence of a single atom of copper as a coenzyme (prosthetic group). Other copper-containing enzymes are also known such as Ascorbic acid oxidase which destroys vitamin C.

The non-protein prosthetic groups or coenzymes in these cases, consist only of a single metal atom of copper and nothing else. Terminal cytochrome oxidases (Cy a and Cy a_3) whose functions are to transfer electrons or hydrogen ions to molecular oxygen in the respiratory chain of oxidative phosphorylation Vitamin C, always contain either one or two atoms of copper per molecule of heme. Plastocyanin discovered by Katoh (1960) is a natural one-electron-transfer copper protein which occurs in chloroplastids in concentration of 1: 500 chlorophyll.

It may be a normal electron carrier between the two photochemical reactions. Thus it is only too true to suggest that copper serves a direct functional role in photosynthesis.

Atomic Zn is an activator component for a host of enzymes, e.g., carbonic anhydrase (catalyses the reaction $CO_2 + H_2O \rightarrow H^+ + HCO^-_3$), alcohol dehydrogenase, lactic dehydrogenase, glutamic dehydrogenase, triosephosphate dehydrogenase, aldolase (can be replaced by Co or Fe), etc.

It has been known for quite a long time that Zn is essential for the formation of the most important plant hormone, indole acetic acid. More recently it was shown that Zn in minute traces is indispensable for the formation of the amino acid, tryptophan, and the generally accepted precursor of indole acetic acid and is not directly concerned with the synthesis of the auxin.

The catabolic breakdown of tryptophan to, the indole nucleus of the auxin is accomplished by the enzyme tryptophanase. At the present moment, however, it is clear that the essentiality of Zn for the formation and breakdown of tryptophan is certainly due to its acting as an activator component of enzime tryptophanase.

Manganese forms activator components of several enzymes, such as some dehydrogenases, decarboxylases, kinases, oxidases and peroxidases, specifically and also non-specifically by other divalent cation-activated enzymes.

Manganese is also reportedly required by nitrite and hydroxylamine reductases in lower non-green plants but not in higher plants. One of the fundamental discoveries of the last few years is that a manganese enzyme is specifically required for photosynthetic evolution of oxygen.

Iron is an activator constituent of many enzymes such as peroxidase, catalase and of cytochromes. In the case of iron, however, the iron atom does not form the coenzyme by itself, but forms a more complex molecule with a porphyrin (tetrapyrrole structure).

And since the iron-porphyrin proteins are the primary catalysts in respiration of living cells, it is not surprising that minute traces of iron should be essential for the maintenance of life in animals as well as in plants.

Iron is also a constituent of non-heme iron proteins, such as, ferredoxin, which is involved in photosynthesis as the primary electron acceptor, as well as in nitrogen fixation and, also of respiratory-linked flavoprotein dehydrogenases.

It is now known definitely that molybdenum plays an important role in nitrate assimilation in plants and the fixation of atmospheric nitrogen by micro-organisms can occur only in the presence of minute traces of Mo. But in spite of great amount of work for almost 50 years on boron, its exact functions are as yet unknown.

Boron may be necessary in order that the plant can obtain calcium in an efficient way. According to the more recent prevalent idea, boron forms a complex with sugar in the plant cells that can penetrate through the living cell walls, more rapidly than free sugars and is, therefore, more readily translocated to the growing meristematic cells where the carbohydrates are most needed.

Cobalt and iodine are essential elements for animal nutrition, but all attempts to prove that these elements are essential micronutrients for plants have so far failed though iodine is accumulated in sea-weeds in large quantities.

Very recently, however, the importance of cobalt in promoting auxin formation in plants is being recognised— cobalt ion is known to depress the specific oxidase enzymes which destroy auxins. Likewise

boron has been found to be essential to plants but there has been no definite proof that it has any function in animal nutrition.

This might very well be our ignorance; just as the gaps in Mendeleef's periodic table were for a long time no more than evidences of our inability to isolate the missing elements.

So this strange anomaly in what seems to be an otherwise admirably planned natural arrangement (most of the element needed for plant nutrition as Ca, P, Fe, Mg, K and S are also essential for animal nutrition) will, it is hoped, in near future be satisfactorily explained.

Some investigators have produced evidence for the essentiality of a few other macroelements, not mentioned before, such as aluminium, silicon and selenium, at least for certain plants, but other workers have failed to confirm these results.

It is undoubtedly true for silicon (SiO_2) which occurs in large quantities in Equisetum and grasses, but silicon does not seem to be indispensable to such plants—Equisetum and grasses can get on quite as well without silicon.

As a matter of fact all soil-grown plants contain silicon and in many Gramineae (in rice it is about 10-15%) in addition to grasses and also other monocots, considerable silica is deposited in the form of opal, hydrated amorphous silica ($SiO_2.nH_2O$).

These silica deposits (natural crystalline silica SiO_2) have also been called opal phytoliths and their distribution in several species of Gramineae is known, without any indication, whatsoever, about the significance of their presence in these plants.

On the other hand, silicon seems to be essential for diatoms, the cell walls of which are almost entirely composed of silicon acid and which gives permanence and rigidity to the diatom cells.

Aluminium, while found in small quantities in almost all higher plants, is accumulated in any considerable amounts in only a few plants, such as Lycopodium. An interesting relation between large accumulation of aluminium in the cells and the development of blue-coloured flowers has been established recently in many blue-flowered or blue- fruited plants. Aluminium may also be more necessary to the water plants than to the land plants.

Elements such as aluminium and silicon have been called ballast elements by investigators who refuse to attribute any useful metabolic function to these elements because they are usually present in large amounts in plant tissues though the plant can be grown perfectly normally without them.

As ballast (heavy material) in a ship's hold gives stability to the ship and maintains its equilibrium, so can the large quantities of indium and silicon in the living cells be used for maintaining the stability of ionic potential and thus preventing the cell system from 'capsizing'.

Some plants are accumulate at ores, i.e., they concentrate in their cells large quantities of certain elements, as for example, iodine in sea-weeds, silicon in grasses, sodium in halophytes, selenium by some species of Astragals (about 5%), molybdenum by clover, etc.

Biodegradation

"A process by which microbial organisms transform or alter (through metabolic or enzymatic action) the structure of chemicals introduced into the environment."

Basically, organic (carbon-based) material is changed through chemical processes from complex molecules into simpler molecules, eventually returning the molecules into the environment. For example, a banana peel can be reduced from cellulose to water, carbon dioxide gas, and humus in a compost pile.

Biodegradation is the disintegration of materials by, fungi, or other biological means.

The term is often used in relation to: biomedicine, waste management, ecology, and the bioremediation of the natural environment. It is now cobacteriammonly associated with environmentally-friendly products, capable of decomposing back into natural elements.

Although often conflated, biodegradable is distinct in meaning from: compostable. While biodegradable simply means *can be consumed by* microorganisms, compostable makes the specific demand that the object break down under composting conditions.

Organic material can be degraded: aerobically (with oxygen) or anaerobically (without oxygen). Decomposition of biodegradable substances may include both biological and abiotic steps.

Biodegradable matter is generally organic material that provides a nutrient for microorganisms. These are so numerous and diverse that a huge range of compounds can be biodegraded, including: hydrocarbons (oils), polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs) and pharmaceutical substances. Microorganisms secrete biosurfactant, an extracellular surfactant, to enhance this process.

Factors affecting biodegradation rate

In practice, almost all chemical compounds and materials are subject to biodegradation processes. The significance, however, is in the relative rates of such processes, such as days, weeks, years or centuries. A number of factors determine the rate at which this degradation of organic compounds occurs. Salient factors include light, water and oxygen. Temperature is also important because chemical reactions

proceed more quickly at higher temperatures. The degradation rate of many organic compounds is limited by their bioavailability. Compounds must be released into solution before organisms can degrade them.

Biodegradability can be measured in a number of ways. Respirometry tests can be used for aerobic microbes. First one places a solid waste sample in a container with microorganisms and soil, and then aerate the mixture. Over the course of several days, microorganisms digest the sample bit by bit and produce carbon dioxide – the resulting amount of CO_2 serves as an indicator of degradation. Biodegradability can also be measured by anaerobic microbes and the amount of methane or alloy that they are able to produce. In formal scientific literature, the process is termed bio-remediation.

Biodegradable technology

In 1973 it was proven for the first time that polyester degrades when disposed in bioactive material such as soil. Polyesters are water resistant and can be melted and shaped into sheets, bottles, and other products, making certain plastics now available as a biodegradable product. Following, polyhydroxylalkanoates (PHAs) were produced directly from renewable resources by microbes. They are approximately 95% cellular bacteria and can be manipulated by genetic strategies. The composition and biodegradability of PHAs can be regulated by blending it with other natural polymers. In the 1980s the company ICI Zenecca commercialized PHAs under the name Biopol. It was used for the production of shampoo bottles and other cosmetic products. Consumer response was unusual. Consumers were willing to pay more for this product because it was natural and biodegradable, which had not occurred before.

Now biodegradable technology is a highly developed market with applications in product packaging, production and medicine. Biodegradable technology is concerned with the manufacturing science of biodegradable materials. It imposes science-based mechanisms of plant genetics into the processes of today. Scientists and manufacturing corporations can help impact climate change by developing a use of plant genetics that would mimic some technologies. By looking to plants, such as biodegradable material harvested through photosynthesis, waste and toxins can be minimized.

Oxo-biodegradable technology, which has further developed biodegradable plastics, has also emerged. Oxo-biodegradation is defined by CEN (the European Standards Organisation) as "degradation resulting from oxidative and cell-mediated phenomena, either simultaneously or successively." Whilst sometimes described as "oxo-fragmentable," and "oxo-degradable" this describes only the first or oxidative phase. These descriptions should not be used for material which degrades by the process of oxo-biodegradation defined by CEN, and the correct description is "oxo-biodegradable."

By combining plastic products with very large polymer molecules, which contain only carbon and hydrogen, with oxygen in the air, the product is rendered capable of decomposing in anywhere from a

week to one to two years. This reaction occurs even without prodegradant additives but at a very slow rate. That is why conventional plastics, when discarded, persist for a long time in the environment. Oxo-biodegradable formulations catalyze and accelerate the biodegradation process but it takes considerable skill and experience to balance the ingredients within the formulations so as to provide the product with a useful life for a set period, followed by degradation and biodegradation.

Biodegradable technology is especially utilized by the bio-medical community. Biodegradable polymers are classified into three groups: medical, ecological, and dual application, while in terms of origin they are divided into two groups: natural and synthetic. The Clean Technology Group is exploiting the use of supercritical carbon dioxide, which under high pressure at room temperature is a solvent that can use biodegradable plastics to make polymer drug coatings. The polymer (meaning a material composed of molecules with repeating structural units that form a long chain) is used to encapsulate a drug prior to injection in the body and is based on lactic acid, a compound normally produced in the body, and is thus able to be excreted naturally. The coating is designed for controlled release over a period of time, reducing the number of injections required and maximizing the therapeutic benefit. Professor Steve Howdle states that biodegradable polymers are particularly attractive for use in drug delivery, as once introduced into the body they require no retrieval or further manipulation and are degraded into soluble, non-toxic by-products. Different polymers degrade at different rates within the body and therefore polymer selection can be tailored to achieve desired release rates.

Other biomedical applications include the use of biodegradable, elastic shape-memory polymers. Biodegradable implant materials can now be used for minimally invasive surgical procedures through degradable thermoplastic polymers. These polymers are now able to change their shape with increase of temperature, causing shape memory capabilities as well as easily degradable sutures. As a result, implants can now fit through small incisions, doctors can easily perform complex deformations, and sutures and other material aides can naturally biodegrade after a completed surgery.

Applications of minerals bio-degradation by bacteria

The type of enzyme to be used, and quantification of degradation, will depend on the polymer being screened. For example, the effects of draw ratio of polycaprolactone fibers on enzymatic hydrolysis by lipase. Degrad- ability of PCL fibers was monitored by dissolved organic carbon (DOC) formation and weight loss. Similar systems with lipases have been used for studying the hydrolysis of broad ranges of aliphatic polyesters, copolyesters with aro- matic segments, and copolyester amides. Other enzymes such as α-chymotrypsin and α-trypsin have also been applied for these polymers. Biodegradability of poly (vinyl alcohol) segments with respect to block length and stereo chemical configuration has been studied using isolated poly (vinyl alcohol)-dehydrogenase .Cellulolytic enzymes have been used to study the

biodegradability of cellulose ester derivatives as a function of degree of substitution and the substituent size. Similar work has been performed with starch esters using amylolytic enzymes such as α-amylases, β-amylases, glucoamylases, and amyloglucosidases. Enzymatic methods have also been used to study the biodegradability of starch plastics or packaging materials containing cellulose.

Text book:

T1: Dr. Asim K. Das, " Bioinorganic Chemistry", 2015, Arunabha Sen Books & Allied, Kolkata**.**

T2: Asim K. Das, " Environmental Chemistry with Green Chemistry", 2010, Arunabha Sen Books & Allied, Kolkata.

POSSIBLE QUESTIONS

MULTIPLE CHOICE QUESTIONS 20x1 =20

1. Which is the essential element of grasses
   a. Silicon b. Titanium c. Ts d. Aluminium
2. Calcium is essential for the production of
   a. Cell wall **b. middle lamella** c. phloem d. xylem
3. In the C4 plants are essentialy have --- for its photosynthesis
   a. Na b. Ca c. B d. Cd
4. The Boron is essential for
   a. Translocation of elements b. photo synthesis c. cell synthesis d. water uptaken
5. Which of the following metal is helpful in O_2 evolution
   a. Mn b. Mg c. Fe d. Ni
6. The role of Mn is to evoluated the
   a. H_2O b. energy c. (CH_2O) **d. O_2**
7. Grey speck of oats occur due to the deficiency of
   a. Mn b. Mg c. Fe d. Ni
8. The nutrients are released from the plants during the process of
   a. **Mineralization** b. volatization c. Immobalization d. Nitrification
9. Which one of the following is an amino acid
   a. **Taurine** b. Glycogen c. catalase d. Globular
10. Which is the essential elements of grasses
    a. **Silicon** b. Titanium c. Ts d. Aluminium
11. Which of the following is used for denitrification in plants
    a. Nitrobactor b. Rhizobium c. **Pseduomonase** d. Azotobactor
12. Ion can accumalate against concentration gradient due to
    a. Mass flow **b. Active uptake** c. Passive uptake d. Donnan equilibrium
13. Specific ions are acquired by root hairs by the process of
    a. simple diffusion b. osmosis **c. active transport** d. reverse osmosis
14. Apparently ------ is the source of energy for keeping stomata open
    a. photosynthesis b. transpiration c. ion transfer d. sodium pump
15. Loss of turgor pressure in guard cells cause an uptake of
    a. K^+ b. H^+ c. Na^+ d. CO_2
16. About --- % of the water taken in by roots is lost by transpiration
    a. 100 **b. 90** c. 80 d. 60
17. Guttation is
    a. movement of soluble organic material b. movement of water
    c. evidence of root pressure d. negative pressure created by transpiration
18. Stomata close when the guard cells
    a. become turgid b. gain Cl ion c. gain K ion **d. lose water**

19. Which of the following macronutrient in the operation of stomata
    a. **K** b. Mn c. Mg d. Fe
20. In which one is essential for chlorophyll synthesis
    a. P b. Mg **c. Fe** d. I

8-MARKS

1. What are the micro-nutrients and explain its role in plant life?
2. What is biodegradation and explain it briefly?
3. List out the micronutrients in soil?
4. What is the major role of micronutrients in soil composition?
5. What are the micro-nutrients and explain its role in plant life?
6. Discuss the biodegradation of bio mass present in soil?
7. Explain the application of bio-degradation?
8. What are important micronutrients? Explain its role in photo synthesis?
9. How the micronutrients stabilize the soil matter?
10. What is the role of bacteria leaching in bio-degradation?

15CHU505C
Karpagam Academy of Higher Education
Coimbatore-21
(For the candidate admitted on 2015 onwards)
Department of Chemistry
V- semester
Bio-Inorganic Chemistry

UNIT V- Objective Questions for online examination
(Each carry 1 Marks)

Questions	Option A	Option B	Option C	Option D	Answer
Which one of the following is not an energy source of the body	Protien	Mineral	glucose	fructose	Mineral
Mineral is an ---- source of the body	enegy source	essential source	enzyme synthesis	blood cell synthesis	essential source
Which one of the following is an carbohydrates	Glucose	Globular	catalase	Arginase	Glucose
Fatty acids are a break down molecules of	fats	protiens	minerals	enzymes	fats
The Lipids are break down and give a	amino acids	fatty acids	glucose	energy molecules	fatty acids
Amino acids are produced from	fats	protiens	minerals	enzymes	protiens
The Protiens are breaked down to produce	amino acids	fatty acids	glucose	energy molecules	amino acids
Glycogen is a break down molecule of	Protien	Mineral	fat	carbohydrates	carbohydrates
Taurine is an essential aminoacid for	rat	humen	cat	elephant	cat
Which one of the following is an amino acid	Taurine	Glycogen	catalase	Globular	Taurine
Which is the essential elements of grasses	Silicon	Titanium	Ts	Aluminium	Silicon
Calcium is essential for the production of	Cell wall	middle lamella	pholem	xylem	middle lamella
In the C4 plants are essentialy have --- for its photosynthesis	Na	Ca	B	Cd	Na
The Boron is essential for	Translocation of elements	photo synthesis	cell synthesis	water uptaken	Translocation of elements
Which of the following metal is helpful in O_2 evolution	Mn	Mg	Fe	Ni	Mn
The role of Mn is to evoluated the	H_2O	enegy	(CH_2O)	O_2	O_2
Grey speck of oats occur due to the deficiency of	Mn	Mg	Fe	Ni	Mn
The nutrients are released from the plants during the process of	Mineralization	volatization	Immobalization	Nitrification	Mineralization
Nitrogens are uptake in the form of	NH_4	NH_3	NO	NO_2	NO_2
Which of the following groups are the micro nutrients	Nitrogen, Phospours, Potassium	phospours, calcium, Iron	Calcium, Hydrogen, Oxygen	calcium, megnesium, Phospours	Calcium, Hydrogen, Oxygen
Molybdenum is essential for the	Nitrogen fixation	photo synthesis	energy transport	water uptaken	Nitrogen fixation
Which one of the following is important in the synthesis of auxin	Zn	S	K	P	Zn
The dieases die back of shoots is caused due to deficiency of	Cu	Cl	Mn	Mb	Cu
Little leaf disease is occurred due to deficiency of	N	Zn	Mn	Mb	Zn

Hydroponics is	growing of aquatic plants	Growing off floating aquatic plants	soilless cultivation of plants	Growing of plants inside the water	soilless cultivation of plants
Molybdenum involved in the plant metabolism of	Translocation of solutes	Tryphtophan synthesis	ABA synthesis	Nitarte reduction	Nitarte reduction
Plant required Fe and Mg for	Synthesis of chlorophyll	Opening and closing of stomata	Translocation of carbohydrates	Nitrification	Synthesis of chlorophyll
Bacteroid is the	dead bacteria	living bacteria	bacteria like substance	living bacteria but cannot divide	living bacteria but cannot divide
Which of the following is used for denitrification	Nitrobactor	Rhizobium	Pseduomonase	Azotobactor	Pseduomonase
Ion can accumalate against concentration gradient due to	Mass flow	Active uptake	Passive uptake	Donnan equilibrium	Active uptake
Which of the following is essential in the nitrogen fixation by leguminous plants	Chlorophyll	Leghaemoglobin	Anthocyanin	Phycocyanin	Leghaemoglobin
First experiments related to the method of hydroponics were done by	Knop	Sachs	Arnon	Hill	Sachs
The most widely accepted theoryto explain the translocation of carbohydrates in higher plants is	Root pressure theory	Osmotic theory	Imbibition theory	Mass flow theory	Mass flow theory
Which elements is required for Nodulation in Legumes	Mn	Mo	Fe	**B**	Mo
Which of the following is acorrect list of the organic material in soil	humus,roots, decomposed materials	roots, small animals	minerals, small animals,roots	small animals,humus	roots, small animals
Turgor pressure also referred as	solute potential	water potential	pressure potential	osmotic potential	pressure potential
The opening of the stomata is effected by all of the following except	Oxygen concentration	temperature	light	Carbondioxide concentration	Oxygen concentration
Capillary forces will lift water --- in a glass tube equal to the diameter of a xylem element	10.4 meters	8.3m	5.6m	less than 1m	less than 1m
In plants, water rises beyond the points supported by the atmospheric pressure mostly because of	gravity	capillarity	evaporation	active transport	evaporation
The combination of pressure potential and solute potential is	waterpotential	transpiration potential	field potential	stem potential	waterpotential
Scientists take advantage of --- in studying translocationby phloem	ants	aphids	bees	butterflies	aphids
Water potential begins to become less negative	in the darkof the night	just before dawn	at sunrise	just after sunset	just after sunset
The smallest amount of pressure needed to stop fluid from moving by osmosis is referred to as the	turgor pressure	water potential	solute potential	energy potential	solute potential
In the absence of transpiration water moves into and up xylem because of	root pressure	turgor pressure	evaporation	guttation	root pressure
Air is transported in xylem in the form of bubbles by	the proton pump	active transport	chemiosmosis	none of these	none of these
High root pressure can cause water to be lost by leaves through the process of	respiration	transpiration	guttation	translocation	guttation
When a plant is flooded it often increases its	cytokines	ethylene	gibberellins	cytochrome	ethylene
A common adaptation of plants to an aquatic existence is the formation of	chlorenchyma	aerenchyma	sclerenchyma	hydrenchyma	sclerenchyma

The plant hormone, -----, plays a role in closing of stomata	auxin	abscissic acid	cytochrome	ethylene	abscissic acid
Water potential is the	Combination of turgor pressure and pressure potential	difference between pressure potential and osmotic potential	combination of pressure potential and solute potential	product of pressure potential and osmotic potential	combination of pressure potential and solute potential
Specific ions are acquired by root hairs by the process of	simple diffusion	osmosis	active transport	reverse osmosis	active transport
Apparently ------ is the source of energy for keeping stomata open	photosynthesis	transpiration	ion transfer	sodium pump	photosynthesis
Loss of turgor pressure in guard cells cause an uptake of	K^+	H^+	Na^+	CO_2	K^+
About --- % of the water taken in by roots is lost by transpiration	100	90	80	60	90
Guttation is	movement of soluble organic material	movement of water	evidence of root pressure	negative pressure created by transpiration	evidence of root pressure
Stomata close when the guard cells	become turgid	gain Cl ion	gain K ion	lose water	lose water
Which of the following macronutrient in the operation of stomata	K	Mn	Mg	Fe	K
In which one is essential for chlorophyll synthesis	P	Mg	Fe	I	Fe
The macroelement which is needed for the formation of coenzyme A	S	P	N	C	S
Which one of the following is important in osmosis and ionic balance	Cl	Cu	Zn	Fe	Cl

[15CHU505C] Reg. No.....

KARPAGAM UNIVERSITY
KARPAGAM ACADEMY OF HIGHER EDUCATION
(Under Section 3 of UGC Act 1956)
COIMBATORE-641 021
(For the candidates admitted from 2015 & onwards)

III B.Sc. Chemistry
INTERNAL EXAM I
MAJOR ELECTIVE-I
(Bio-inorganic chemistry)

Time: 2 hours Maximum: 50 Marks

PART A (20 x 1 = 20 Marks)
Answer all the questions

1. Movement of water through a cell membrane with the use of a transport protein is called
a) osmosis b) simple diffusion c) solvent diffusion d) solute diffusion

2. Ion chennals in a cell membrane permit the selective passage of
a) amino acids b) respiratory gases c) sodium and potassium ion d) small organic wastes

3. If transport through a cell membrane requires the expenditure of energy, it is called
a) osmosis b) simple diffusion c) active transport d) solute diffusion

4. Osmotic pressure is a type of
a) force b) friction c) work d) none of above

5. If difference in tonicity across membrane is greater than osmotic pressure will be
a) greater b) less c) zero d) infinite

6. Which of the following is not true regarding osmotic pressure/osmosis
a) solute molecules move into the solvent phase b) requires a semipermeable membrane c) is independent of temperature d) requires two phases

7. The contractility of a muscle fiber is its
a) contraction strength at any length b) contraction strength at a particular fiber length. c) Concentration frequency, which determines heart rate. d) ability to contract, which is restored after the refractory period

8. The colloid osmotic pressure of blood plasma is due to its high concentration of
a) albumin b) hemoglobin c) sodium d) glucose

9. Which of the following are the *parts* of neurons?
a) brain, spinal cord, and vertebral column b) dendrite, axon, and cell body c) sensory and motor d) cortex, medulla and sheath

10. A dendrite conducts nerve impulses _____ the cell body.
a) away from b) toward c) both toward and away from d) only inside

11. An axon conducts nerve impulses _____ the cell body.
a. Away from b. Towards c. Both toward and away from d. Only inside

12. Axoplasm is the _____
a) cytoplasm of the axon b) cytoplasm of the dendrite c) fluid external to the axon but inside the myelin sheath d) blood plasma that nourishes a nerve

13. The resting potential indicates that the inside of the neuron is _____ compared to the outside.
a) under ionic pressure b) positive c) negative d) inactive

14. The "sodium-potassium pump" pumps _____
a) sodium ions out and potassium ion in b) sodium ions in and potassium ions out c) sodium ions and potassium ion in d) sodium ions and potassium ion out

15. In humans, transmission of nerve impulses across a synaptic cleft is carried out by _____
a) sodium ion b) potassium ions c) neurotransmitter molecule d) the nodes of ranvier

16. Major constituent of hemoglobin receives iron from
a) liver b) bolus c) chyme d) lungs

17. Porphyrin ring in hemoglobin molecules have in center an atom of
a) magnesium b) iron c) hydrogen d) nickel

18. Oxygen combine with hemoglobin in blood and form
a) oxyhemoglobin b) deoxyhemoglobin c) hemoglobin d) carbohemoglobin

19. A special kind of protein containing iron is called as
a) hormones b) hemoglobin c) red blood cell d) white blood cell

20. Myoglobin binding of oxygen depends on:
a) the oxygen concentration b) the hemoglobin concentration c) the affinity of hemoglobin for the oxygen d) the carbon dioxide concentration

PART- B (3 x 10= 30 Marks)

21. Discuss the properties of the Na+-K+ channels involved in nerve impulse transmission. how do they function? how doyou explain their ion selectivity?

OR

What is nerve impulse transmission? How is it created?

22. What is Ca2+? how does it function

OR

Discuss the Biochemical function of Zn, Fe, Mn, CO

23. Discuss the structural features of hemoglobin and myoglobin.

OR

Name some important synthetic oxygen carriersnand give their structural features

Reg.No: ---------- **[15CHU505C]**

KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed University Established Under Section 3 of UGC Act 1956)

COIMBATORE-21

DEPARTMENT OF CHEMISTRY

III B.Sc Chemistry
Internal-I
Major Elective-I (Bio-Inorganic Chemistry)

Key answer

Part-A **20 X1 = 20**

1. (a) Osmosis
2. © sodium and potassium ion
3. © active transport
4. (a) force
5. (a) greater
6. (b) requires a semipermeable membrane
7. © Concentration frequency, which determines heart rate
8. (b) hemoglobin
9. (b) dendrite, axon and cell body
10. (b) toward
11. (b) towards
12. (a) cytoplasm of the axon
13. (b) positive
14. (a) sodium ions and potassium ions
15. (a) neurotransmitter molecule
16. (a) liver
17. (b) Iron
18. (a) oxyhemoglobin
19. (b) hemoglobin
20. (a) the oxygen concentration

Part-B **3 X 10 = 30**

21. a) Nerve impulse transmission

The transmission of a nerve impulse along a neuron from one end to the other occurs as a result of electrical changes across the membrane of the neuron. The membrane of an unstimulated neuron is polarized—that is, there is a difference in electrical charge between the outside and inside of the membrane. The inside is negative with respect to the outside.

Na^+-K^+ channels

Polarization is established by maintaining an excess of sodium ions (Na^+) on the outside and an excess of potassium ions (K^+) on the inside. A certain amount of Na^+ and K^+ is always leaking

across the membrane through leakage channels, but Na^+/K^+ pumps in the membrane actively restore the ions to the appropriate side.

The main contribution to the resting membrane potential (a polarized nerve) is the difference in permeability of the resting membrane to potassium ions versus sodium ions. The resting membrane is much more permeable to potassium ions than to sodium ions resulting in slightly more net potassium ion diffusion (from the inside of the neuron to the outside) than sodium ion diffusion (from the outside of the neuron to the inside) causing the slight difference in polarity right along the membrane of the axon.

Other ions, such as large, negatively charged proteins and nucleic acids, reside within the cell. It is these large, negatively charged ions that contribute to the overall negative charge on the inside of the cell membrane as compared to the outside.

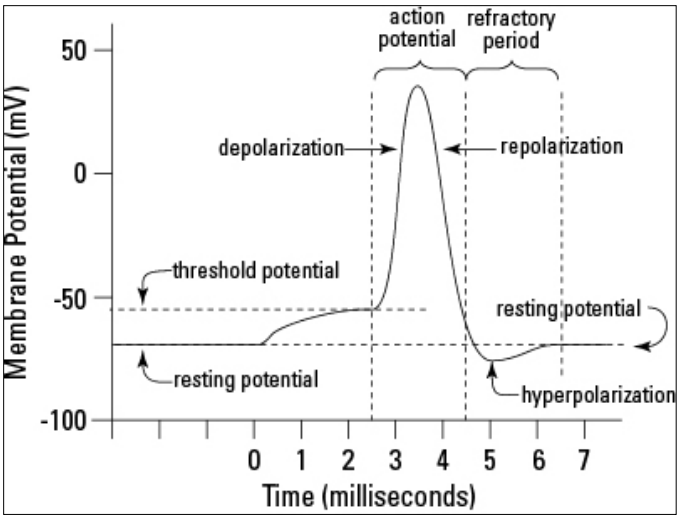
In addition to crossing the membrane through leakage channels, ions may cross through **gated channels.** Gated channels open in response to neurotransmitters, changes in membrane potential, or other stimuli.

The following events characterize the transmission of a nerve impulse (see Figure 1):

- **Resting potential.** The resting potential describes the unstimulated, polarized state of a neuron (at about –70 millivolts).

- **Graded potential.** A graded potential is a change in the resting potential of the plasma membrane in the response to a stimulus. A graded potential occurs when the stimulus causes Na^+ or K^+ gated channels to open. If Na^+ channels open, positive sodium ions enter, and the membrane depolarizes (becomes more positive). If the stimulus opens K^+ channels, then positive potassium ions exit across the membrane and the membrane**hyperpolarizes** (becomes more negative). A graded potential is a local event that does not travel far from its origin. Graded potentials occur in cell bodies and dendrites. Light, heat, mechanical pressure, and chemicals, such as neurotransmitters, are examples of stimuli that may generate a graded potential (depending upon the neuron).

Figure 1.Events that characterize the transmission of a nerve impulse.



The following four steps describe the initiation of an impulse to the "resetting" of a neuron to prepare for a second stimulation:

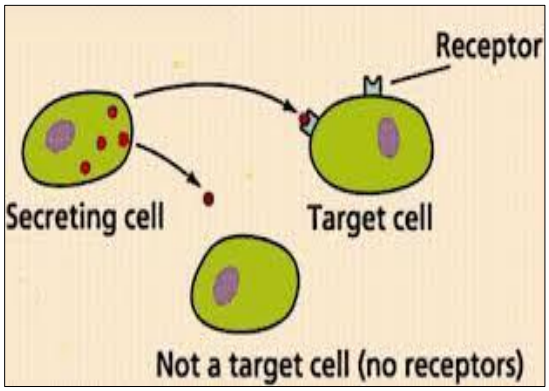
1. **Action potential.** Unlike a graded potential, an action potential is capable of traveling long distances. If a depolarizing graded potential is sufficiently large, Na^+ channels in the trigger zone open. In response, Na^+ on the outside of the membrane becomes depolarized (as in a graded potential). If the stimulus is strong enough—that is, if it is above a certain threshold level—additional Na^+ gates open, increasing the flow of Na^+ even more, causing an action potential, or complete depolarization (from –70 to about +30 millivolts). This in turn stimulates neighboring Na^+ gates, farther down the axon, to open. In this manner, the action potential travels down the length of the axon as opened Na^+ gates stimulate neighboring Na^+ gates to open. The action potential is an all-or-nothing event: When the stimulus fails to produce depolarization that exceeds the threshold value, no action potential results, but when threshold potential is exceeded, complete depolarization occurs.
2. Repolarization. In response to the inflow of Na^+, K^+ channels open, this time allowing K^+ on the inside to rush out of the cell. The movement of K^+ out of the cell causes repolarization by restoring the original membrane polarization. Unlike the resting potential, however, in repolarization the K^+ are on the outside and the Na^+ are on the inside. Soon after the K^+ gates open, the Na^+ gates close.
3. **Hyperpolarization.** By the time the K^+ channels close, more K^+ have moved out of the cell than is actually necessary to establish the original polarized potential. Thus, the membrane becomes hyperpolarized (about –80 millivolts).
4. Refractory period. With the passage of the action potential, the cell membrane is in an unusual state of affairs. The membrane is polarized, but the Na^+ and K^+ are on the wrong sides of the membrane. During this refractory period, the axon will not respond to a new stimulus. To reestablish the original distribution of these ions, the Na^+ and K^+ are returned to their resting potential location by Na^+/K^+ pumps in the cell membrane. Once these ions are completely returned to their resting potential location, the neuron is ready for another stimulus.

b) Nerve impulse transmission and its creation

The transmission of a nerve impulse along a neuron from one end to the other occurs as a result of electrical changes across the membrane of the neuron. The membrane of an unstimulated neuron is polarized—that is, there is a difference in electrical charge between the outside and inside of the membrane. The inside is negative with respect to the outside.

Trigger reaction

A **trigger** is an experience that causes someone to recall a previous traumatic memory, although the trigger itself need not be frightening or traumatic and can be indirectly or superficially reminiscent of an earlier traumatic incident. Trauma triggers are related to posttraumatic stress disorder (PTSD), a condition in which people often cannot control the recurrence of emotional or physical symptoms, or of repressed memory. Triggers can be subtle and difficult to anticipate, and can sometimes exacerbate PTSD. A trauma trigger may also be referred to as a trauma stimulus or a trauma stressor.



Calcium and Muscle Contractions

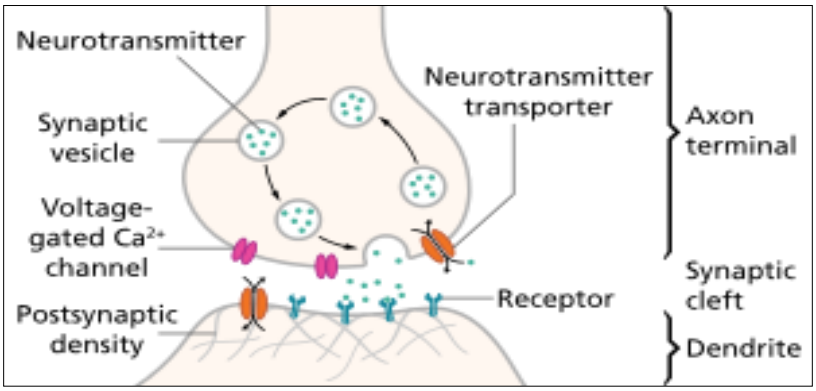
When a nerve impulse reaches a muscle cell, movement of the muscle requires calcium as well. Your muscle cells store calcium and upon nerve impulse, the cell is flooded with calcium. In order for a skeletal muscle to move, two myofilaments, actin and myosin, inside a muscle fiber must bind to one another to create a pulling action which shortens the muscle. However, a molecule known as tropomyosin blocks the binding site and must be moved to create a contraction. Calcium binds to troponin which is attached to tropomyosin. Upon binding with calcium, troponin moves tropomyosin, exposing the binding site and creating movement.

Dynamics

Action potentials are most commonly initiated by excitatory postsynaptic potentials from a presynaptic neuron. Typically, neurotransmitter molecules are released by the presynaptic neuron. These neurotransmitters then bind to receptors on the postsynaptic cell. This binding opens various types of ion channels. This opening has the further effect of changing the local permeability of the cell membrane and, thus, the membrane potential. If the binding increases the voltage (depolarizes the membrane), the synapse is excitatory. If, however, the binding decreases the voltage (hyperpolarizes the membrane), it is inhibitory. Whether the voltage is increased or decreased, the change propagates passively to nearby regions of the membrane (as described by the cable equation and its refinements). Typically, the voltage stimulus decays exponentially with the distance from the synapse and with time from the binding of the neurotransmitter. Some fraction of an excitatory voltage may reach the axon hillock and may (in rare cases) depolarize the membrane enough to provoke a new action potential. More typically, the excitatory potentials from several synapses must work together at nearly the same time to provoke a new action

potential. Their joint efforts can be thwarted, however, by the counteracting inhibitory postsynaptic potentials.

Neurotransmission can also occur through electrical synapses. Due to the direct connection between excitable cells in the form of gap junctions, an action potential can be transmitted directly from one cell to the next in either direction. The free flow of ions between cells enables rapid non-chemical-mediated transmission. Rectifying channels ensure that action potentials move only in one direction through an electrical synapse. Electrical synapses are found in all nervous systems, including the human brain, although they are a distinct minority.



22. <u>A) Ca^{2+} and its function</u>

<u>Nerve Impulse and Calcium</u>

It is well-known that calcium is another positive molecule useful for the conduction of a nerve impulse to a muscle fiber. However, Clay Armstrong, a neurobiologist, believes that calcium may play a larger role. Armstrong suspects that calcium is in charge of the gated channels that release potassium and sodium to facilitate a nerve impulse. Armstrong's theory proposes that calcium ions are like a door to these gated channels. Calcium must move to release the ions and calcium must return before the impulse will stop and homeostasis is returned.

<u>Calcium and Muscle Contractions</u>

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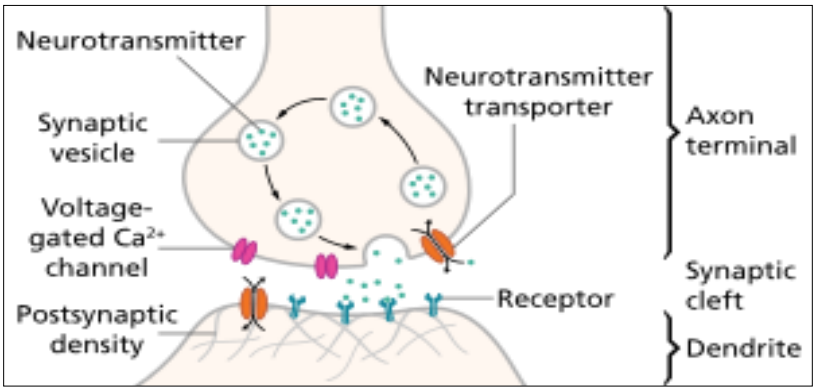


Ion Channels

In contrast to carrier proteins, channel proteins simply form open pores in the membrane, allowing small molecules of the appropriate size and charge to pass freely through the lipid bilayer. One group of channel proteins, discussed earlier, is the porins, which permit the free passage of ions and small polar molecules through the outer membranes of bacteria. Channel proteins also permit the passage of molecules between cells connected at gap junctions, which are discussed later in the chapter. The plasma membranes of many cells also contain water channel proteins (aquaporins), through which water molecules are able to cross the membrane much more rapidly than they can diffuse through the phospholipid bilayer. The best-characterized channel proteins, however, are the ion channels, which mediate the passage of ions across plasma membranes. Although ion channels are present in the membranes of all cells, they have been especially well studied in nerve and muscle, where their regulated opening and closing is responsible for the transmission of electric signals.

Three properties of ion channels are central to their function (Figure). First, transport through channels is extremely rapid. More than a million ions per second flow through open channels—a flow rate approximately a thousand times greater than the rate of transport by carrier proteins. Second, ion channels are highly selective because narrow pores in the channel restrict passage to ions of the appropriate size and charge. Thus, specific channel proteins allow the passage of Na^+, K^+, Ca^{2+}, and Cl^- across the membrane. Third, most ion channels are not permanently open. Instead, the opening of ion channels is regulated by "gates" that transiently open in response to specific stimuli. Some channels (called **ligand-gated channels**) open in response to the binding

of neurotransmitters or other signaling molecules; others (**voltage-gated channels**) open in response to changes in electric potential across the plasma membrane.

b) ***Biochemical function of Zn,Fe, Mn and Co***

Zinc

Zinc (Zn) was incorporated into living cells in two waves. Four to three Ga, anaerobic prokaryotes arose, and the atmosphere was full of $H_2S$and highly reductive. Thus most zinc was in the form of insoluble ZnS. However, because seawater at the time was slightly acidic, some Zn(II) was available in its ionic form and became part of early anaerobic prokaryotes' external proteases, external nucleases, internal synthetases and dehydrogenases.

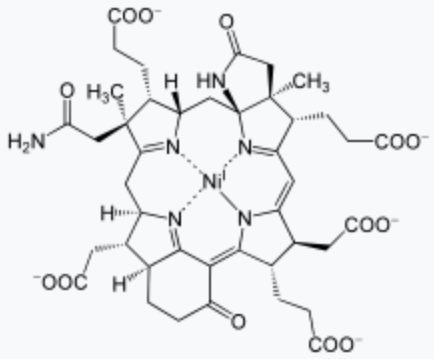
During the second wave, once the Great Oxygenation Event occurred, more Zn(II) ions were available in the seawater. This allowed its incorporation in the single-cell eukaryotes as they arose at this time. It is believed that the later addition of ions such as zinc and copper allowed them to displace iron and manganese from the enzyme superoxide dismutase (SOD). Fe and Mn complexes dissociate readily (Irving-Williams series) while Zn and Cu do not. This is why eukaryotic SOD contains Cu or Zn and its prokaryotic counterpart contains Fe or Mn.

Zn (II) doesn't pose an oxidation threat to the cytoplasm. This allowed it to become a major cytoplasmic element in the eukaryotes. It became associated with a new group of transcription proteins, zinc fingers. This could only have occurred due to the long life of eukaryotes, which allowed time for zinc to exchange and hence become an internal messenger coordinating the action of other transcription factors during growth.

Iron

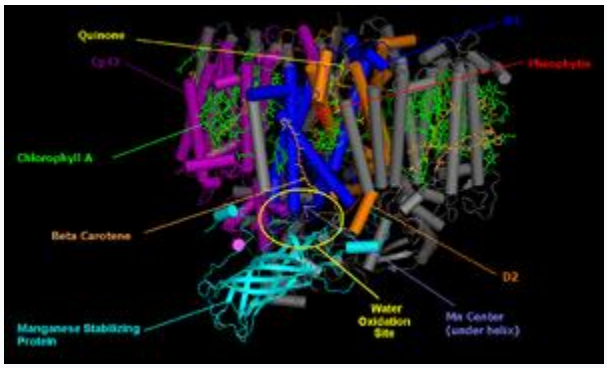
Iron (Fe) is the most abundant element in the Earth and the fourth most abundant element in the crust, approximately 5 percent by mass. Due to the abundance of iron and its role in biological systems, the transition and mineralogical stages of iron have played a key role in Earth surface systems. It played a larger role in the geological past in marine geochemistry, as evidenced by the deposits of Precambrian iron-rich sediments. The redox transformation of Fe(II) to Fe(III), or vice versa, is vital to a number of biological and element cycling processes. The reduction of Fe(III) is seen to oxidize sulfur (from H_2S to SO_4^{-2}), which is a central process in marine sediments. Many of the first metalloproteinsconsisted of iron-sulphur complexes formed during photosynthesis. Iron is the main redox metal in biological systems. In proteins, it is found in a variety of sites and cofactors, including, for instance, haem groups, Fe–O–Fe sites, and iron–sulfur clusters.

The prevalence of iron is apparently due to the large availability of Fe(II) in the initial evolution of living organisms, before the rise of photosynthesis and an increase in atmospheric oxygen levels which resulted in the precipitation of iron in the environment as $Fe(OH)_3$. It has flexible redox properties because such properties are sensitive to ligand coordination, including geometry. Iron can be also used in enzymes due to its Lewis acid properties, for example in nitrile hydratase. Iron is frequently found in mononuclear sites in the reduced Fe(II) form, and functions in dioxygen activation; this function is used as a major mechanism adopted by living organisms to avoid the kinetic barrier hindering the transformation of organic compounds by O_2. Iron can be taken up selectively as ferredoxins, Fe-O-Fe (hemerythrin and ribonucleotide reductase), Fe (many oxidases), apart from iron porphyrin. Variation in the related proteins with any one of these chemical forms of iron has produced a wide range of enzymes. All of these arrangements are modified to function both in the sense of reactivity and the positioning of the protein in the cell. Iron can have various redox and spin states, and it can be held in many stereochemistries.



Coenzyme F430- Theorized as the first occurrence of nickel in biological systems

Manganese



Magnesium Center in Cyanobacterial photosystem II. Incorporation of manganese sparked evolution of complex plant life.

Evidence suggests that manganese (Mn) was first incorporated into biological systems roughly 3.2 - 2.8 billion years ago, during the Archean Period. Together with calcium, it formed the manganese-calcium oxide complex (determined by X-ray diffraction) which consisted of a manganese cluster, essentially an inorganic cubane (cubical) structure. The incorporation of a manganese center in photosystem II was highly significant, as it allowed for photosynthetic oxygen evolution of plants. The oxygen-evolving complex (OEC) is a critical component of photosystem II contained in the thylakoid membranes of chloroplasts; it is responsible for terminal photooxidation of water during light reactions.

The incorporation of Mn in proteins allowed the complexes the ability to reduce reactive oxygen species in Mn-superoxide dismutatse (MnSOD) and catalase, in electron transfer-dependent catalysis (for instance in certain class I ribonucleotide reductases) and in the oxidation of water by photosystem II (PSII), where the production of thiobarbituric acid-reactive substances is decreased. This is due to manganese's ability to reduce superoxide anion and hydroxyl radicals as well as its chain-breaking capacity.

Copper

Before the Great Oxygenation Event, copper was not readily available for living organisms. Most early copper was Cu^{+} and Cu. This oxidation state of copper is not very soluble in water. One billion years ago, after the great oxidation event the oxygen pressure rose sufficiently to oxidise Cu^{+} to Cu^{2+}, increasing its solubility in water. As a result, the copper became much more available for living organisms.

Most copper-containing proteins and enzymes can be found in eukaryotes. Only a handful of prokaryotes such as aerobic bacteria and cyanobacteria contain copper enzymes or proteins. Copper can be found in both prokaryotes and eukaryotes superoxide dismutase (SOD)enzyme. There are three distinct types of SOD, containing Mn, Fe and Cu respectively. Mn-SOD and Fe-SOD are found in most

prokaryotes and mitochondria of the eukaryotic cell. Cu-SOD can be found in the cytoplasmic fraction of the eukaryotic cells. The three elements, copper, iron and manganese, can all catalyze superoxide to ordinary molecular oxygen or hydrogen peroxide. However, Cu-SOD is more efficient than Fe-SOD and Mn-SOD. Most prokaryotes only utilize Fe-SOD or Mn-SOD due to the lack of copper in the environment. Some organisms did not develop Cu-SOD due to the lack of a gene pool for the Cu-SOD adoption.

23. A) Structural features of Hemoglobin and myoglobin

Hemoglobin (American) or **haemoglobin** (British); abbreviated **Hb** or **Hgb**, is the iron-containing oxygen-transport metalloprotein in the red blood cells of all vertebrates (with the exception of the fish family Channichthyidae) as well as the tissues of some invertebrates. It has the formula $C_{2952}H_{4664}O_{832}N_{812}S_8Fe_4$. Hemoglobin in the blood carries oxygen from the respiratory organs (lungs or gills) to the rest of the body (i.e. the tissues). There it releases the oxygen to permit aerobic respiration to provide energy to power the functions of the organism in the process called metabolism.

In mammals, the protein makes up about 96% of the red blood cells' dry content (by weight), and around 35% of the total content (including water). Hemoglobin has an oxygen-binding capacity of 1.34 mL O_2 per gram, which increases the total blood oxygen capacity seventy-fold compared to dissolved oxygen in blood. The mammalian hemoglobin molecule can bind (carry) up to four oxygen molecules.

Hemoglobin is involved in the transport of other gases: It carries some of the body's respiratory carbon dioxide (about 20–25% of the total) as carbaminohemoglobin, in which CO_2 is bound to the globin protein. The molecule also carries the important regulatory molecule nitric oxide bound to a globin protein thiol group, releasing it at the same time as oxygen.

Hemoglobin is also found outside red blood cells and their progenitor lines. Other cells that contain hemoglobin include the A9 dopaminergic neurons in the substantia nigra, macrophages, alveolar cells, and mesangial cells in the kidney. In these tissues, hemoglobin has a non-oxygen-carrying function as an antioxidant and a regulator of iron metabolism.

Hemoglobin and hemoglobin-like molecules are also found in many invertebrates, fungi, and plants. In these organisms, hemoglobins may carry oxygen, or they may act to transport and regulate other small molecules and ions such as carbon dioxide, nitric oxide, hydrogen sulfide and sulfide. A variant of the molecule, called leghemoglobin, is used to scavenge oxygen away from anaerobic systems, such as the nitrogen-fixing nodules of leguminous plants, before the oxygen can poison (deactivate) the system.

Discovery

In 1825 J. F. Engelhard discovered that the ratio of Fe to protein is identical in the hemoglobins of several species. From the known atomic mass of iron he calculated the molecular mass of hemoglobin to $n \times 16000$ (n = number of iron atoms per hemoglobin, now known to be 4), the first determination of a protein's molecular mass. This "hasty conclusion" drew a lot of ridicule at the time from scientists who could not believe that any molecule could be that big. Gilbert Smithson Adair confirmed Engelhard's results in 1925 by measuring the osmotic pressure of hemoglobin solutions.

The oxygen-carrying protein hemoglobin was discovered by Hünefeld in 1840 and 1851 German physiologist Otto Funke published a series of articles in which he described growing hemoglobin crystals by successively diluting red blood cells with a solvent such as pure water, alcohol or

ether, followed by slow evaporation of the solvent from the resulting protein solution. Hemoglobin's reversible oxygenation was described a few years later by Felix Hoppe-Seyler.

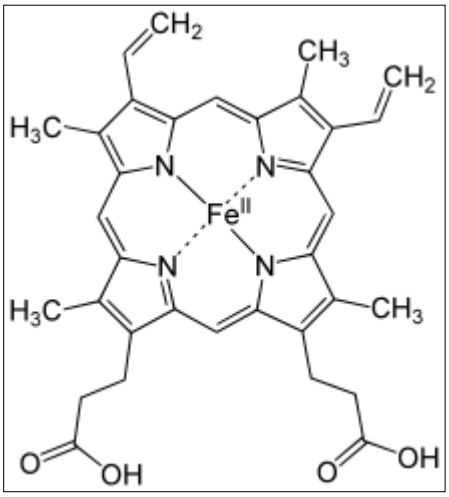
In 1959, Max Perutz determined the molecular structure of hemoglobin by X-ray crystallography. This work resulted in his sharing with John Kendrew the 1962 Nobel Prize in Chemistry for their studies of the structures of globular proteins.

The role of hemoglobin in the blood was elucidated by French physiologist Claude Bernard. The name *hemoglobin* is derived from the words *heme*and *globin*, reflecting the fact that each subunit of hemoglobin is a globular protein with an embedded heme group. Each heme group contains one iron atom, that can bind one oxygen molecule through ion-induced dipole forces. The most common type of hemoglobin in mammals contains four such subunits.

Synthesis

Hemoglobin (Hb) is synthesized in a complex series of steps. The heme part is synthesized in a series of steps in the mitochondria and the cytosol of immature red blood cells, while the globin protein parts are synthesized by ribosomes in the cytosol.[30] Production of Hb continues in the cell throughout its early development from the proerythroblast to the reticulocyte in the bone marrow. At this point, the nucleus is lost in mammalian red blood cells, but not in birds and many other species. Even after the loss of the nucleus in mammals, residual ribosomal RNA allows further synthesis of Hb until the reticulocyte loses its RNA soon after entering the vasculature (this hemoglobin-synthetic RNA in fact gives the reticulocyte its reticulated appearance and name).

Structure



Heme b group

Hemoglobin has a quaternary structure characteristic of many multi-subunit globular proteins. Most of the amino acids in hemoglobin form alpha helices, and these helices are connected by short non-helical segments. Hydrogen bonds stabilize the helical sections inside this protein, causing attractions within the molecule, which then causes each polypeptide chain to fold into a specific shape. Hemoglobin's quaternary structure comes from its four subunits in roughly a tetrahedral arrangement.

In most vertebrates, the hemoglobin molecule is an assembly of four globular protein subunits. Each subunit is composed of a protein chain tightly associated with a non-protein prosthetic heme group. Each protein chain arranges into a set of alpha-helix structural

segments connected together in a globin fold arrangement. Such a name is given because this arrangement is the same folding motif used in other heme/globin proteins such as myoglobin. This folding pattern contains a pocket that strongly binds the heme group.
A heme group consists of an iron (Fe) ion (charged atom) held in a heterocyclic ring, known as a porphyrin. This porphyrin ring consists of four pyrrole molecules cyclically linked together (by methine bridges) with the iron ion bound in the center. The iron ion, which is the site of oxygen binding, coordinates with the four nitrogen atoms in the center of the ring, which all lie in one plane. The iron is bound strongly (covalently) to the globular protein via the N atoms of the imidazole ring of F8 histidine residue (also known as the proximal histidine) below the porphyrin ring. A sixth position can reversibly bind oxygen by a coordinate covalent bond, completing the octahedral group of six ligands. Oxygen binds in an "end-on bent" geometry where one oxygen atom binds to Fe and the other protrudes at an angle. When oxygen is not bound, a very weakly bonded water molecule fills the site, forming a distorted octahedron.
Even though carbon dioxide is carried by hemoglobin, it does not compete with oxygen for the iron-binding positions but is bound to the protein chains of the structure.
The iron ion may be either in the Fe^{2+} or in the Fe^{3+} state, but ferrihemoglobin (methemoglobin) (Fe^{3+}) cannot bind oxygen.[38] In binding, oxygen temporarily and reversibly oxidizes (Fe^{2+}) to (Fe^{3+}) while oxygen temporarily turns into the superoxide ion, thus iron must exist in the +2 oxidation state to bind oxygen. If superoxide ion associated to Fe^{3+} is protonated, the hemoglobin iron will remain oxidized and incapable of binding oxygen. In such cases, the enzyme methemoglobin reductase will be able to eventually reactivate methemoglobin by reducing the iron center.
In adult humans, the most common hemoglobin type is a tetramer (which contains four subunit proteins) called *hemoglobin A*, consisting of two α and two β subunits non-covalently bound, each made of 141 and 146 amino acid residues, respectively. This is denoted as $\alpha_2\beta_2$. The subunits are structurally similar and about the same size. Each subunit has a molecular weight of about 16,000 daltons, for a total molecular weight of the tetramer of about 64,000 daltons (64,458 g/mol).[40] Thus, 1 g/dL = 0.1551 mmol/L. Hemoglobin A is the most intensively studied of the hemoglobin molecules.
In human infants, the hemoglobin molecule is made up of 2 α chains and 2 γ chains. The gamma chains are gradually replaced by β chains as the infant grows.
The four polypeptide chains are bound to each other by salt bridges, hydrogen bonds, and the hydrophobic effect.

b) Important synthetic oxygen carriers

Oxygen carrier systems

The interaction of molecular dioxygen (O_2) with metalloporphyrin species has intrigued scientists of all disciplines ever since such species were recognized as being important centers in some naturally occurring oxygen- storage and transport systems. The iron porphyrin moiety (the heme unit) is the prosthetic group present in myoglobin and hemoglobin (oxygen carriers) and various oxygenases (Which are a class of enzymes that incorporate one or two O_2 to a substrate).

Heme unit are also components of cytochrome c oxidase, the terminal enzyme in the respiratory redox chain that reduces O_2 to water. Oxidases are enzymes that convert both atoms of O_2 to water of hydrogen peroxide.
Heavy medical interventions in severely injured patients and complex transplantation surgery are currently performed with success, but they have increased the need of human blood. At the same

time, the risk of transmission of viral diseases, the risk of errors in blood transfusion and the insufficiency of palliative treatments (blood predonation, pre- and perioperative hemodilution, perioperative blood sparing, lowering of transfusion trigger) accelerated the development of blood substitutes as alternatives to human blood.

- Together with the property of carrying O2 , a blood substitute must have at least the following properties: Free of toxicity and side effects
- Adequate O_2 uptake in the lungs and adequate delivery to tissues
- Sufficient half
- Life time in the circulation to avoid repeated administrations
- Harmful and rapid excretion
- Stable at room temperature, easy to store and easy to use
- Easy to sterilize (to assure the absence of pathogens and viruses transmission)
- Cheap to manufacture.

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[15CHU505C]

KARPAGAM UNIVERSITY

(KARPAGAM ACADEMY OF HIGHER EDUCATION)

COIMBATORE-641021

DEPARTMENT OF CHEMISTRY

II[nd] Internal Test

BIO-INORGANIC CHEMISTRY

Time : 2 Hours

Maximum: 50 marks

Date: 11.8.2017 AN

Section-A **20X1=20**

1. Redox reactions involves exchange of
   a. Electrons between atoms b. Protons between atoms
   c. Neutrons between atoms d. Neurons between molecules
2. Which one of the following has smaller monomer of polypeptide structure
   a. Hemoglobin b. Myoglobin c. Oxyhemoglobin d. Coenzyme
3. Which particles are gained and lost during a redox reaction?
   a. Electrons b. Neutron c. Positron d. Duetron
4. In an oxidation-reduction reduction, reduction is defined as
   a. Loss of protons b. Loss of electrons c. Loss of positron d. Gain of electrons
5. Reducing agent
   a. Donor of electrons b. Acceptor of electrons c. Loss of electrons d. Gain of electrons
6. The primary process of reducing ore at high temperature to produce metals is known as
   a. Smelting b. Galvanization c. Electroplating d. Electrorefining
7. Which of the following ETC components accepts only electrons?
   a. Coenzyme Q b. Cytochrome b c. FAD d. FMN
8. Oxidizing which of the following substances yields the most energy?
   a. Proteins b. Glucose c. Fatty acids d. Water
9. Nitrosomonas and Nitrobacter are
   a. Ammonifying bacteria b. Denitrifying bacteria c. Nitrogen fixing bacteria
   d. Nitrifying bacteria
10. Non legume plant nodules contains nitrogen fixing
    a. Ascomycetes b. Basidiomycetes c. Zygomycetes d. Actinomycetes
11. Denitrification is also called ?
    a. Putrefaction b. Heterotrophic nitrification c. Assimilatory nitrate reduction
    d. Dissimilatory nitrate reduction
12. Plants need nitrogen for ?
    a. Growth b. Food preparation c. Strength d. Support
13. Which of the followings fixed nitrogen in waterlogged soil?
    a. Nostoc b. Nitrobactor c. Clostridium d. Azotobacter
14. Which of the followings is non-aerobic bacterium?
    a. Azotobacter b. Nitrobactor c. Clostridium d. Nostoc
15. Plant absorbs N_2 in the form of?
    a. Nitrites (NO_2-) b. Nitrates (NO_3-) c. Ammonium (NH_4+) d. NH_3
16. Anabaena, a N2 fixer is present in the root pockets of
    a. Marselia b. Salvinia c. Pistia d. Azolla
17. To fix one molecule of nitrogen
    a. 6 ATP molecules are required b. 12 ATP molecules are required
    c. 16ATP molecules are required d. 20 ATP molecules are required
18. The chief source of nitrogen for green plants is
    a. Atmospheric nitrogen b. Nitrates c. Ammonium salts
    d. Low molecular weight- organic nitrogenous compound
19. Ammonia gas is ?
    a. Toxic to plants b. Useful for plants c. Strength to plants
    d. Support for plants
20. Denitrification is the reduction of nitrates back into
    a. Nitrogen gas b. Ammonia c. Nitrate d. Nitrite

Section – B **3 × 10 = 30**

21. (a) Name some synthetic oxygen carriers and explain its structure and uses?

    (Or)

    (b) Write a note on mechanism occurs at photosynthesis?

22. (a) Explain the role of bacteria in nitrogen fixation?

    (Or)

    (b) What is nitrogen cycle? Explain it with suitable diagram?

23. (a) Write a note on different oxidaized state of "Co" in vitamin B_{12}?

    (Or)

    (b) Discuss the structural importance of vitamin B_{12} ?

Reg. No. : ---------- **[15CHU505C]**

KARPAGAM ACADEMY OF HIGHER EDUCATION

COIMBATORE-641021

DEPARTMENT OF CHEMISTRY

IInd Internal Test

BIOINORGANIC CHEMISTRY

ANSWER KEY

Time: 2 Hours **Maximum: 50 marks**

Section-A (answer all the questions)

1. (a) Electron between atoms
2. (b) Myoglobin
3. (a) Electrons
4. (d) Gain of electrons
5. (a) donor of electrons
6. (a) smelting
7. (b) Cytochrome
8. © Fatty acids
9. (d) Nitrifying bacteria
10. (d) action mycycetes
11. (d) Dissmilarity nitrate reduction
12. (a) Growth
13. (a) Nostoc
14. (a) Acetobactor
15. (a) NO_2^-
16. (d) Azolla
17. © 16ATP molecules are required
18. (b) nitrates
19. (a) Toxic to plants
20. (a) Nitrogen gas

Section – B **3 × 10 = 30**

21. (a) **Name some synthetic oxygen carriers and explain its structure and uses**?

The interaction of molecular dioxygen (O_2) with metalloporphyrin species has intrigued scientists of all disciplines ever since such species were recognized as being important centers in some naturally occurring oxygen- storage and transport systems. The iron porphyrin moiety (the heme unit) is the prosthetic group present in myoglobin and hemoglobin (oxygen carriers) and various oxygenases (Which are a class of enzymes that incorporate one or two O_2 to a substrate).

Heme unit are also components of cytochrome c oxidase, the terminal enzyme in the respiratory redox chain that reduces O_2 to water. Oxidases are enzymes that convert both atoms of O_2 to water of hydrogen peroxide.

Heavy medical interventions in severely injured patients and complex transplantation surgery are currently performed with success, but they have increased the need of human blood. At the same time, the risk of transmission of viral diseases, the risk of errors in blood transfusion and the insufficiency of palliative treatments (blood predonation, pre- and perioperative hemodilution, perioperative blood sparing, lowering of transfusion trigger) accelerated the development of blood substitutes as alternatives to human blood.

- Together with the property of carrying O2 , a blood substitute must have at least the following properties: Free of toxicity and side effects
- Adequate O_2 uptake in the lungs and adequate delivery to tissues
- Sufficient half
- Life time in the circulation to avoid repeated administrations
- Harmful and rapid excretion
- Stable at room temperature, easy to store and easy to use
- Easy to sterilize (to assure the absence of pathogens and viruses transmission)
- Cheap to manufacture.

(b) **Write a note on mechanism occurs at photosynthesis**?

Photo synthesis in porphyrin ring complexes

The two components were separated by shaking a light petroleum solution of chlorophyll with aqueous methanol: chlorophyll-*a* remains in the light petroleum but chlorophyll-*b* is transferred into the aqueous methanol. Cholorophyll-*a* is a bluish-black solid and cholorophyll-*b* is a dark green solid, both giving a green solution in organic solutions. In natural chlorophyll there is a ratio of 3 to 1 (of *a* to *b*) of the two components.

Chlorophyll's most important use, however, is in nature, in photosynthesis. It is capable of channelling the energy of sunlight into chemical energy through the process of photosynthesis. In this process the energy absorbed by chlorophyll transforms carbon dioxide and water into carbohydrates and oxygen:

$$CO_2 + H_2O \longrightarrow (CH_2O) + O_2$$

The chemical energy stored by photosynthesis in carbohydrates drives biochemical reactions in nearly all living organisms.

In the photosynthetic reaction electrons are transferred from water to carbon dioxide that is carbon dioxide is reduced by water. Chlorophyll assists this transfer as when chlorophyll absorbs light energy, an electron in chlorophyll is excited from a lower energy state to a higher energy state. In this higher energy state, this electron is more readily transferred to another molecule. This starts a chain of electron-transfer

steps, which ends with an electron being transferred to carbon dioxide. Meanwhile, the chlorophyll which gave up an electron can accept an electron from another molecule. This is the end of a process which starts with the removal of an electron from water. Thus, chlorophyll is at the centre of the photosynthetic oxidation-reduction reaction between carbon dioxide and water.

22. (a) Explain the role of bacteria in nitrogen fixation?

Nitrogen fixation

A relatively small amount of ammonia is produced by lightning. Some ammonia also is produced industrially by the Haber-Bosch process, using an iron-based catalyst, very high pressures and fairly high temperature. But the major conversion of N_2 into ammonia, and thence into proteins, is achieved by microorganisms in the process called nitrogen fixation (or dinitrogen fixation).
The table below shows some estimates of the amount of nitrogen fixed on a global scale. The total biological nitrogen fixation is estimated to be twice as much as the total nitrogen fixation by non-biological processes.

To illustrate the importance of biological nitrogen fixation, the image below shows part of the Lower Sonoran desert in Arizona. Every plant that we see in this scene depends ultimately on biological nitrogen fixation. Both free-living cyanobacteria and the cyanobacterial associates of lichens initially contributed nitrogen to the soil by forming a cryptobiotic crust. Now numerous leguminous plants occur in this desert, with nitrogen-fixing *Rhizobium* in their root nodules.

Mechanism of biological nitrogen fixation

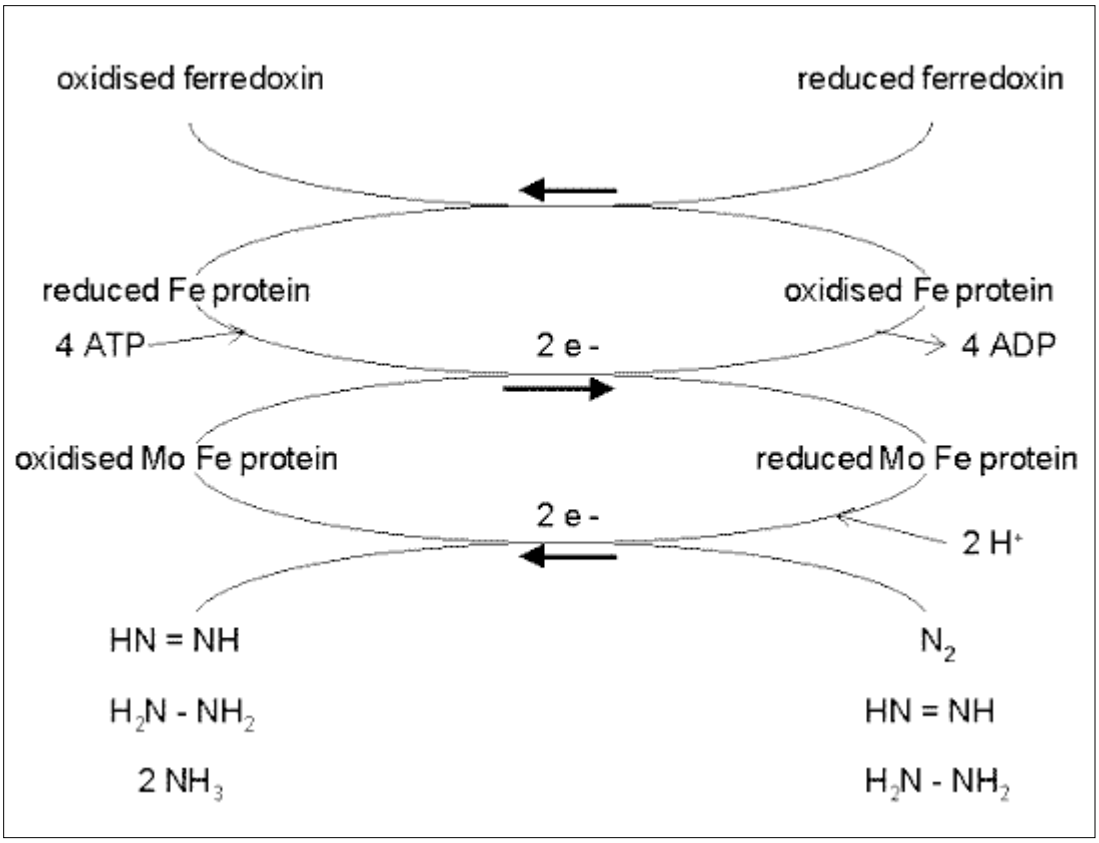
Biological nitrogen fixation can be represented by the following equation, in which two moles of ammonia are produced from one mole of nitrogen gas, at the expense of 16 moles of ATP and a supply of electrons and protons (hydrogen ions):

$$\mathbf{N_2 + 8H^+ + 8e^- + 16\ ATP = 2NH_3 + H_2 + 16ADP + 16\ Pi}$$

This reaction is performed exclusively by prokaryotes (the bacteria and related organisms), using an enzyme complex termed **nitrogenase**. This enzyme consists of two proteins - an iron protein and a molybdenum-iron protein, as shown below.

The reactions occur while N_2 is bound to the nitrogenase enzyme complex. The Fe protein is first reduced by electrons donated by ferredoxin. Then the reduced Fe protein binds ATP and reduces the molybdenum-iron protein, which donates electrons to N_2, producing HN=NH. In two further cycles of this process (each requiring electrons donated by ferredoxin) HN=NH is reduced to $H_2N\text{-}NH_2$, and this in turn is reduced to $2NH_3$.

Depending on the type of microorganism, the reduced ferredoxin which supplies electrons for this process is generated by photosynthesis, respiration or fermentation.



There is a remarkable degree of functional conservation between the nitrogenase proteins of all nitrogen-fixing bacteria. The Fe protein and the Mo-Fe protein have been isolated from many of these bacteria, and nitrogen fixation can be shown to occur in cell-free systems in a laboratory when the Fe protein of one species is mixed with the Mo-Fe protein of another bacterium, even if the species are very distantly related.

Abiological Nitrogen Fixation

In abiological nitrogen fixation the nitrogen is reduced to ammonia without involving any living cell. Abiological fixation can be of two types: **industrial and natural**.

For example, in the Haber's process, synthetic ammonia is produced by passing a mixture of nitrogen and hydrogen through a bed of catalyst (iron oxides) at a very high temperature and pressure.

$$N_2 + 3H_2 \rightarrow 2NH_3$$

This is industrial fixation wherein nitrogen gets reduced to ammonia.

In natural process nitrogen can be fixed especially during electrical discharges in the atmosphere. It may occur during lightning storms when nitrogen in the atmosphere can combine with oxygen to form oxides of nitrogen.

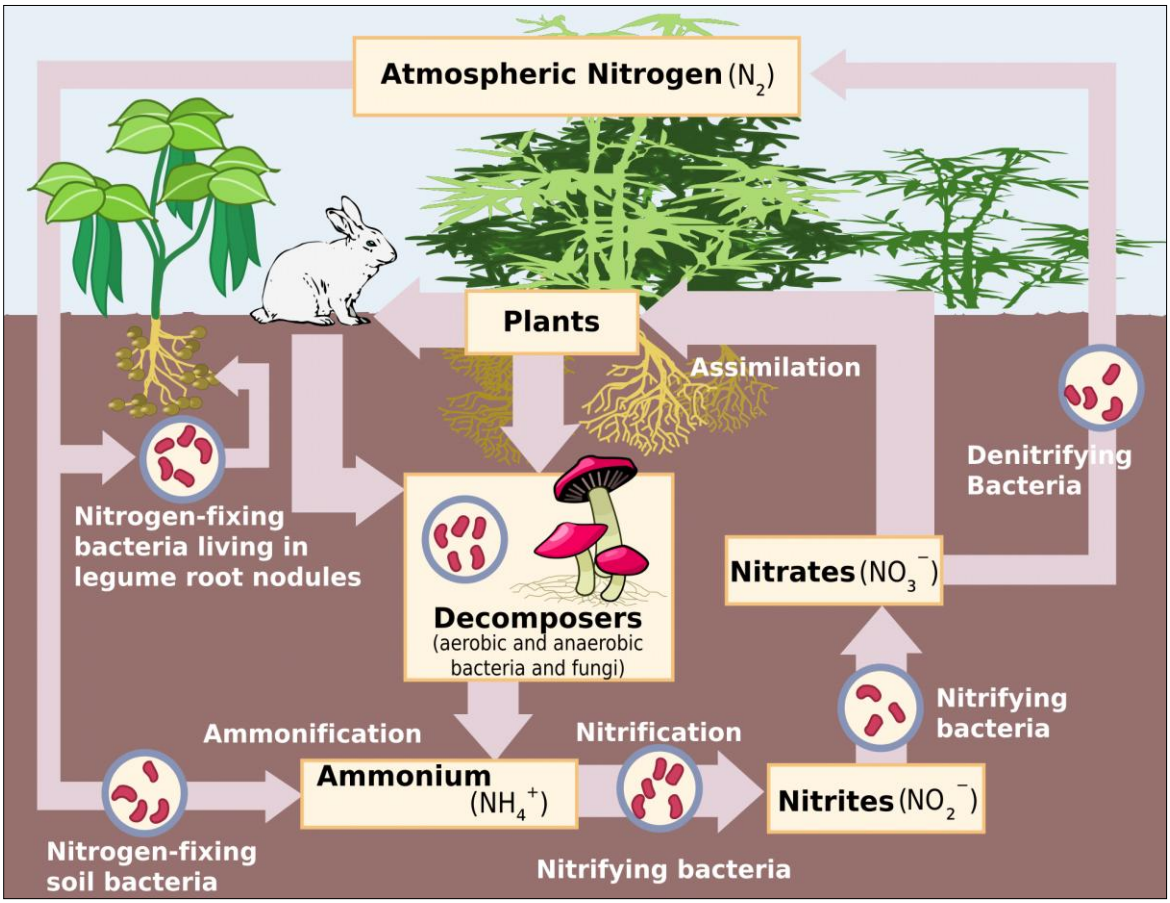
$$N_2 + O_2 \rightarrow 2NO_2$$

These oxides of nitrogen may be hydrated and trickle down to earth as combined nitrite and nitrate

(b) **What is nitrogen cycle? Explain it with suitable diagram**?

Nitrogen cycle

The nitrogen cycle is the biogeochemical cycle by which nitrogen is converted into various chemical forms as it circulates among the atmosphere, terrestrial, and marine ecosystems. The conversion of nitrogen can be carried out through both biological and physical processes. Important processes in the nitrogen cycle include fixation, ammonification, nitrification, and denitrification. The majority of Earth's atmosphere (78%) is nitrogen, making it the largest source of nitrogen. However, atmospheric nitrogen has limited availability for biological use, leading to a scarcity of usable nitrogen in many types of ecosystems. The nitrogen cycle is of particular interest to ecologists because nitrogen availability can affect the rate of key ecosystem processes, including primary production and decomposition. Human activities such as fossil fuel combustion, use of artificial nitrogen fertilizers, and release of nitrogen in wastewater have dramatically altered the global nitrogen cycle.



Schematic representation of the flow of nitrogen through the land environment. The importance

of bacteria in the cycle is immediately recognized as being a key element in the cycle, providing different forms of nitrogen compounds assimilable by higher organisms.

Nitrogen is present in the environment in a wide variety of chemical forms including organic nitrogen, Ammonium (NH_4^+), nitrite (NO_2^-), nitrate (NO_3^-), nitrous oxide (N_2O), Nitric oxide (NO) or inorganic nitrogen gas (N_2). Organic nitrogen may be in the form of a living organism, humus or in the intermediate products of organic matter decomposition. The processes of the nitrogen cycle transform nitrogen from one form to another. Many of those processes are carried out by microbes, either in their effort to harvest energy or to accumulate nitrogen in a form needed for their growth. For example, the nitrogenous wastes in animal urine are broken down by nitrifying bacteria in the soil to be used as new. The diagram besides shows how these processes fit together to form the nitrogen cycle.

Nitrogen fixation

Conversion of nitrogen into nitrates and nitrites through atmospheric, industrial and biological processes is called as nitrogen fixation. Atmospheric nitrogen must be processed, or "fixed", in a usable form to be taken up by plants. Between $5x10^{12}$ and $10x10^{12}$ g per year are fixed by lightning strikes, but most fixation is done by free-living or symbiotic bacteria known as diazotrophs. These bacteria have the nitrogenase enzyme that combines gaseous nitrogen with hydrogen to produce ammonia, which is converted by the bacteria into other organic compounds. Most biological nitrogen fixation occurs by the activity of Mo-nitrogenase, found in a wide variety of bacteria and some Archaea. Mo-nitrogenase is a complex two-component enzyme that has multiple metal-containing prosthetic groups. An example of the free-living bacteria is *Azotobacter*. Symbiotic nitrogen-fixing bacteria such as *Rhizobium* usually live in the root nodules of legumes (such as peas, alfalfa, and locust trees). Here they form a mutualistic relationship with the plant, producing ammonia in exchange for carbohydrates. Because of this relationship, legumes will often increase the nitrogen content of nitrogen-poor soils. A few non-legumes can also form such symbioses. Today, about 30% of the total fixed nitrogen is produced industrially using the Haber-Bosch process, which uses high temperatures and pressures to convert nitrogen gas and a hydrogen source (natural gas or petroleum) into ammonia.

Assimilation

Plants take nitrogen from the soil by absorption through their roots as amino acids, nitrate ions, nitrite ions, or ammonium ions. Most nitrogen obtained by terrestrial animals can be traced back to the eating of plants at some stage of the food chain.

Plants can absorb nitrate or ammonium from the soil via their root hairs. If nitrate is absorbed, it is first reduced to nitrite ions and then ammonium ions for incorporation into amino acids, nucleic acids, and chlorophyll. In plants that have a symbiotic relationship with rhizobia, some nitrogen is assimilated in the form of ammonium ions directly from the nodules. It is now known that there is a more complex cycling of amino acids between *Rhizobia* bacteroids and plants. The plant provides amino acids to the bacteroids so ammonia assimilation is not required and the bacteroids pass amino acids (with the newly fixed nitrogen) back to the plant, thus forming an interdependent relationship. While many animals, fungi, and other heterotrophic organisms obtain nitrogen by ingestion of amino acids, nucleotides, and other small organic molecules, other heterotrophs (including many bacteria) are able to utilize inorganic compounds, such as ammonium as sole N sources. Utilization of various N sources is carefully regulated in all

organisms.

Ammonification

When a plant or animal dies or an animal expels waste, the initial form of nitrogen is organic. Bacteria or fungi convert the organic nitrogen within the remains back into ammonium (NH_4^+), a process called ammonification or mineralization.

Nitrification

The conversion of ammonium to nitrate is performed primarily by soil-living bacteria and other nitrifying bacteria. In the primary stage of nitrification, the oxidation of ammonium (NH_4^+) is performed by bacteria such as the *Nitrosomonas* species, which converts ammonia to nitrites (NO_2^-). Other bacterial species such as *Nitrobacter*, are responsible for the oxidation of the nitrites (NO_2^-) into nitrates (NO_3^-). It is important for the ammonia (NH_3) to be converted to nitrates or nitrites because ammonia gas is toxic to plants.

Due to their very high solubility and because soils are highly unable to retain anions, nitrates can enter groundwater. Elevated nitrate in groundwater is a concern for drinking water use because nitrate can interfere with blood-oxygen levels in infants and cause methemoglobinemia or blue-baby syndrome. Where groundwater recharges stream flow, nitrate-enriched groundwater can contribute to eutrophication, a process that leads to high algal population and growth, especially blue-green algal populations. While not directly toxic to fish life, like ammonia, nitrate can have indirect effects on fish if it contributes to this eutrophication.

Denitrification

Denitrification is the reduction of nitrates back into nitrogen gas (N_2), completing the nitrogen cycle. This process is performed by bacterial species such as *Pseudomonas* and *Clostridium* in anaerobic conditions. They use the nitrate as an electron acceptor in the place of oxygen during respiration. These facultatively anaerobic bacteria can also live in aerobic conditions. Denitrification happens in anaerobic conditions e.g. waterlogged soils. The denitrifying bacteria use nitrates in the soil to carry out respiration and consequently produce nitrogen gas, which is inert and unavailable to plants.

23. (a) **Write a note on different oxidaized state of "Co" in vitamin B_{12}?**

B_{12} is the most chemically complex of all the vitamins. The structure of B_{12} is based on a corrin ring, which is similar to the porphyrin ring found in heme, chlorophyll, and cytochrome. The central metal ion is cobalt. Four of the six coordination sites are provided by the corrin ring, and a fifth by a dimethylbenzimidazole group. The sixth coordination site, the center of reactivity, is variable, being a cyano group (–CN), a hydroxyl group (–OH), a methyl group ($–CH_3$) or a 5′-deoxyadenosyl group (here the C5′ atom of the deoxyribose forms the covalent bond with cobalt), respectively, to yield the four B_{12} forms mentioned below. Historically, the covalent C-Co bond is one of the first examples of carbon-metal bonds to be discovered in biology. The hydrogenases and, by necessity, enzymes associated with cobalt utilization, involve metal-carbon bonds.

Vitamin B_{12} is a generic descriptor name referring to a collection of cobalt and corrin ring molecules which are defined by their particular vitamin function in the body. All of the substrate cobalt-corrin molecules from which B_{12} is made must be synthesized by bacteria. After this synthesis is complete, the

human body has the ability (except in rare cases) to convert any form of B_{12} to an active form, by means of enzymatically removing certain prosthetic chemical groups from the cobalt atom and replacing them with others.

The four forms (vitamers) of B_{12} are all deeply red colored crystals and water solutions, due to the color of the cobalt-corrin complex.

- **Cyanocobalamin** is one such form, i.e. "vitamer", of B_{12} because it can be metabolized in the body to an active coenzymeform. The cyanocobalamin form of B_{12} does not occur in nature normally, but is a byproduct of the fact that other forms of $B_{12}$are avid binders of cyanide (–CN) which they pick up in the process of activated charcoal purification of the vitamin after it is made by bacteria in the commercial process. Since the cyanocobalamin form of B_{12} is easy to crystallize and is not sensitive to air-oxidation, it is typically used as a form of B_{12} for food additives and in many common multivitamins. Pure cyanocobalamin possesses the deep pink color associated with most octahedral cobalt(II) complexes and the crystals are well formed and easily grown up to millimeter size.

- **Hydroxocobalamin** is another form of B_{12} commonly encountered in pharmacology, but which is not normally present in the human body. Hydroxocobalamin is sometimes denoted B_{12a}. This form of B_{12} is the form produced by bacteria, and is what is converted to cyanocobalmin in the commercial charcoal filtration step of production. Hydroxocobalamin has an avid affinity for cyanide ions and has been used as an antidote to cyanide poisoning. It is supplied typically in water solution for injection. Hydroxocobalamin is thought to be converted to the active enzymic forms of B_{12} more easily than cyanocobalamin, and since it is little more expensive than cyanocobalamin, and has longer retention times in the body, has been used for vitamin replacement in situations where added reassurance of activity is desired. Intramuscular administration of hydroxocobalamin is also the preferred treatment for pediatric patients with intrinsic cobalamin metabolic diseases, for vitamin B_{12} deficient patients with tobacco amblyopia (which is thought to perhaps have a component of cyanide poisoning from cyanide in cigarette smoke); and for treatment of patients with pernicious anemia who have optic neuropathy.

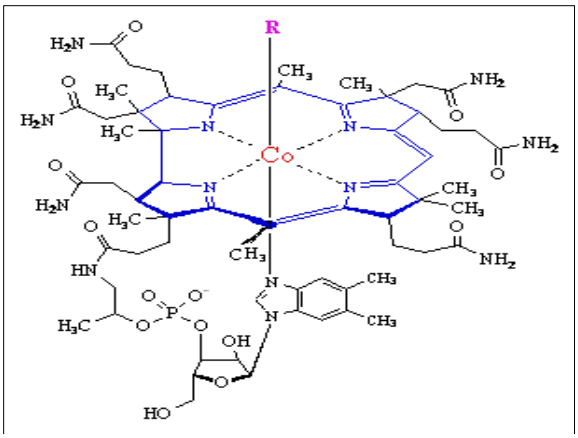
- **Adenosylcobalamin** (adoB_{12}) and **methylcobalamin** (MeB_{12}) are the two enzymatically active cofactor forms of B_{12} that naturally occur in the body. Most of the body's reserves are stored as adoB_{12} in the liver. These are converted to the other methylcobalamin form as needed.

(b) **Discuss the structural importance of vitamin B_{12}**?

Vitamin B-12

Vitamin B_{12} is the only known essential biomolecule with a stable metal-carbon bond, that is, it is an organometallic compound. The cobalt can link to:

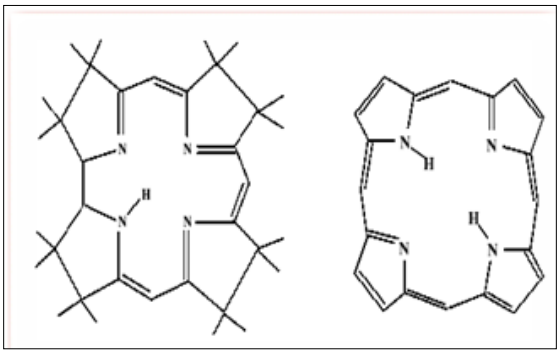
1. a methyl group - as in methylcobalamin
2. a 5'-deoxyadenosine at the the 5' positon - as in adenosylcobalamin (coenzyme B_{12}
3. a cyanide group - as in Vitamin B_{12} - as supplied from drug companies.

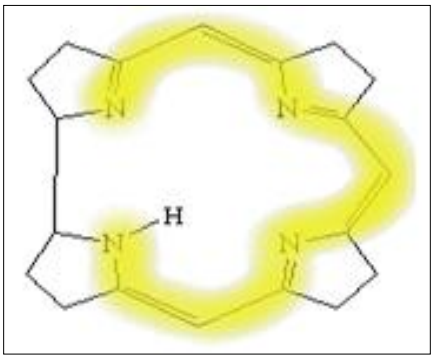


The particular link in the cobalamin has a profound effect upon the mechanism of the enzyme reaction.

A methyl-nickel intermediate on acetyl-CoA synthase is also known, but only as an intermediate rather than a stable, isolable compound as the three cobalamins. Other organometals such as the methylmercury ion are highly toxic, it is interesting that there is an unfortunate connection between CH_3Hg^+ and methylcobalamin.

The core of the molecule is a corrin ring with various attached sidegroups. The ring consists of 4 pyrrole subunits, joined on opposite sides by a C-CH_3 methylene link, on one side by a C-H methylene link, and with the two of the pyrroles joined directly. It is thus like a porphyrin, with one of the bridging methylene groups removed. The nitrogen of each pyrolle is coordinated to the central cobalt atom.





Links are to Chime pbd files to enable comparisons of the structures

The sixth ligand below the ring is a nitrogen of a 5,6-dimethylbenzimidazole. The other nitrogen of the 5,6-dimethylbenzimidazole is linked to a five-carbon sugar, which in turn connects to a phosphate group, and thence back onto the corrin ring via one of the seven amide groups attached to the periphery of the corrin ring. The base ligand thus forms a 'strap' back onto the corrin ring. An important aspect of the corrin ring, when compared to the porphyrin, is the relative flexibility of the corrin system, the corrin ring is also less flat when viewed from the side

than is a porphyrin ring. This adds up to some considerable differences between the chemistry of a cobalt porphyrin and a cobalt corrin. In addition, the corrin only has a conjugated chain around part of the ring system, whereas a porphyrin is delocalised around the whole four pyrolle rings. The center-piece in the structure is of course the cobalt(III), the octahedral coordination to five nitrogens and a carbon is common to all three cobalamins, and can be found in a number of simple coordination complexes. The simple complexes have attracted wide interest as models for cobalamins.

Chemistry

B_{12} is the most chemically complex of all the vitamins. The structure of B_{12} is based on a corrin ring, which is similar to the porphyrin ring found in heme, chlorophyll, and cytochrome. The central metal ion is cobalt. Four of the six coordination sites are provided by the corrin ring, and a fifth by a dimethylbenzimidazole group. The sixth coordination site, the center of reactivity, is variable, being a cyano group (–CN), a hydroxyl group (–OH), a methyl group ($–CH_3$) or a 5′-deoxyadenosyl group (here the C5′ atom of the deoxyribose forms the covalent bond with cobalt), respectively, to yield the four B_{12} forms mentioned below. Historically, the covalent C-Co bond is one of the first examples of carbon-metal bonds to be discovered in biology. The hydrogenases and, by necessity, enzymes associated with cobalt utilization, involve metal-carbon bonds.

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The four forms (vitamers) of B_{12} are all deeply red colored crystals and water solutions, due to the color of the cobalt-corrin complex.

[15CHU505C]

Reg. No. : ----------

KARPAGAM UNIVERSITY

COIMBATORE-21

(For the candidates admitted from 2015 & onwards)

III B. Sc CHEMISTRY

MODEL EXAM

BIO-INORGANIC CHEMISTRY

Time: 3 Hours
Date:

Maximum: 60 marks

PART- A (20 x 1= 20 Marks)

Answer ALL the Questions

1. The actions of an enzyme can be affected by all of the following except
   a. p/PH b. allosteric inhibitors c. temperature d. availability ATP
2. Which of the following are mismatched
   a. anabolic reactions-expend energy b. reduction-gain of an electron
   c. activation energy-entropy d. exergonic reaction-catabolism
3. The activation energy of a chemical reaction is the energy that
   a. initiates the reaction b. activates the catalyst
   c. must be removed from the mixture d. must be released from the mixture
4. In a catalyzed chemical reaction, one function of a catalyst is to
   a. increase the number of successful reactant collisions.
   b. decrease the concentration of reactants.
   c. change the equilibrium concentrations of the products and reactants
   d. increase the energy given off during the reaction
5. The oxidation state of an individual atom is
   a. Zero b. One c. Two d. Three
6. Low counts of hemoglobin leads to
   a. Anemia b. Pellagra c. Sterility d. Scurvey
7. Which one of the following has 153 amino acids residues?
   a. Hemoglobin b. Myoglobin c. Oxyhemoglobin d. Coenzyme
8. Muscle injury is commonly associated with the release of
   a. Hemoglobin b. Myoglobin c. Oxyhemoglobin d. Coenzyme
9. Which one of the following takes place under special conditions in both terrestrial and marine ecosystems
   a. Denitrification b. Mineralization c. Ammonification d. Nitrification
10. Bacteria or fungi convert the organic nitrogen within the remains back into ammonium (NH_4^+), a process called
    a. Ammonification b. Nitrofication c. Assimilation d. Nitrification
11. Plants absorb ammonium and nitrate during the
    a. Assimilation process b. Nitrofication process
    c. Ammonification process d. Nitrification process
12. The transformation of ammonia to nitrite is usually the rate limiting step of
    a. Nitrification b. Nitrofication c. Assimilation d. Ammonification
13. Solaganol is the drug of
    a. Ag b. Au c. Sb d. As
14. Which one of the following is used as the brain imaging agent
    a. ^{68}Ga b. ^{131}I c. ^{60}Co d. ^{32}P
15. The isotope I131 is detect the tumor by the emission of
    a. α-ray b. β-ray c. γ-ray d. δ-ray
16. The trans platin is a
    a. Toxic b. non-toxic c. less toxic d. anticancer agent
17. Guttation is
    a. movement of soluble organic material b. movement of water
    c. evidence of root pressure d. negative pressure created by transpiration
18. Stomata close when the guard cells
    a. become turgid b. gain Cl ion c. gain K ion d. lose water
19. Which of the following macronutrient in the operation of stomata
    a. K b. Mn c. Mg d. Fe
20. In which one is essential for chlorophyll synthesis
    a. P b. Mg c. Fe d. I

PART – B $5 \times 8 = 40$

21. (a) What is Na^+-K^+ ATP ase? Explain it function?
    (Or)
    (b) What are the biochemical importance of Co and Zn?
22. (a) Give an account of biological oxygen carriers?
    (Or)
    (b) Discuss the structural features of Vitamin B12?
23. (a) What are the importance of nitrogen cycle in atmosphere?
    (Or)
    (b) Differentiate biological and abiological nitrogen fixation?
24. (a) Discuss the different sources of metal ion toxicity ?
    (Or)
    (b) Give the toxic symptoms in a) Pb b)Hg c)Cd- poisoning?
25. (a) How the micronutrients stabilizes the soil matter?
    (Or)
    (b) What is the role of bacteria leaching in bio-degradation?

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KARPAGAM ACADEMY OF HIGHER EDUCATION
COIMBATORE-641021
DEPARTMENT OF CHEMISTRY
Model Exam
BIOINORGANIC CHEMISTRY
ANSWER KEY

Time: 3 Hours Maximum: 60 marks

Section-A (Answer all the questions.) **20X1=20**

1. d. availability ATP
2. c. activation energy-entropy
3. a. initiates the reaction
4. d. increase the energy given off during the reaction
5. a. Zero
6. a. Anemia
7. b. Myoglobin
8. b. Myoglobin
9. a. Denitrification
10. a. Ammonification
11. a. Assimilation process
12. a. Nitrification
13. b. Au
14. a. ^{68}Ga
15. c. γ-ray
16. A. Toxic
17. c. evidence of root pressure
18. d. lose water
19. a. K
20. c. Fe

Section – B **5 × 8 = 40**

21. (a) **<u>What is Na^+-K^+ ATP ase? Explain it function</u>**?

<u>Na+/K+-ATPase</u>

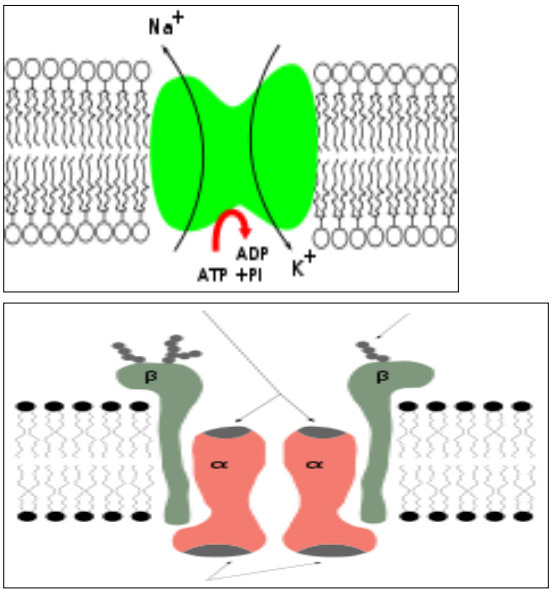
(sodium-potassium adenosine triphosphatase, also known as the **Na+/K+ pump** or **sodium-potassium pump**) is an enzyme (an electrogenic transmembrane ATPase) found in the plasma membrane of all animal cells.

The Na+/K+-ATPase enzyme is a solute pump that pumps sodium out of cells while pumping potassium into cells, both against their concentration gradients. This pumping is active (i.e. it uses energy from ATP) and is important for cell physiology. An example application is nerve conduction.

It has antiporter-like activity, but since it moves both molecules against their concentration gradients it is not a true antiporter, which would require one solute to move with its gradient.

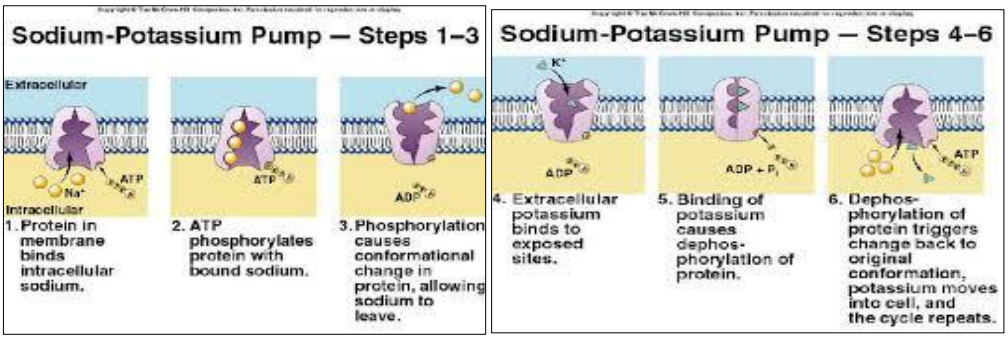
Sodium-potassium pumps

Active transport is responsible for the fact that cells contain a relatively high concentration of potassium ions but low concentrations of sodium ions. The mechanism responsible for this is the sodium-potassium pump, which moves these two ions in opposite directions across the plasma membrane. This was investigated by following the passage of radioactively labeled ions across the plasma membrane of certain cells. It was found that the concentrations of sodium and potassium ions on the two sides of the membrane are interdependent, suggesting that the same carrier transports both ions. It is now known that the carrier is an ATP-ase and that it pumps three sodium ions out of the cell for every two potassium ions pumped in.



Function

The Na+/K+-ATPase helps maintain resting potential, effect transport, and regulate cellular volume. It also functions as a signal transducer/integrator to regulate MAPK pathway, ROS, as well as intracellular calcium. In most animal cells, the Na+/K+ -ATPase is responsible for about 1/5 of the cell's energy expenditure. For neurons, the Na+/K+-ATPase can be responsible for up to 2/3 of the cell's energy expenditure.



Resting potential

The Na+/K+-ATPase, as well as effects of diffusion of the involved ions maintain the resting potential across the membranes.

In order to maintain the cell membrane potential, cells keep a low concentration of sodium ions and high levels of potassium ions within the cell (intracellular). The sodium-potassium pump mechanism moves 3 sodium ions out and moves 2 potassium ions in, thus, in total, removing one positive charge carrier from the intracellular space. It contributes -6mV to resting potential but does not in fact generate it.

Transport

Export of sodium from the cell provides the driving force for several secondary active transporters membrane transport proteins, which import glucose, amino acids, and other nutrients into the cell by use of the sodium gradient.

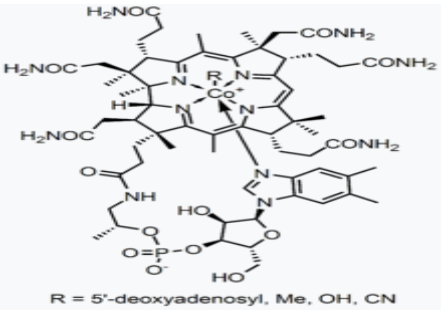
Another important task of the Na^+-K^+ pump is to provide a Na^+ gradient that is used by certain carrier processes. In the gut, for example, sodium is transported out of the reabsorbing cell on the blood (interstitial fluid) side via the Na^+-K^+ pump, whereas, on the reabsorbing (lumenal) side, the Na^+

-glucose symporter uses the created Na^+ gradient as a source of energy to import both Na^+

and glucose, which is far more efficient than simple diffusion. Similar processes are located in the renal tubular system.

(b) **What are the biochemical importance of Co and Zn**?

Cobalt



Theorized as the first occurrence of cobalt in a biological system

Around 4-3 Ga, anaerobic prokaryotes began developing metal and organic cofactors for light absorption. They ultimately ended up making chlorophyll from Mg(II), as is found in cyanobacteria and plants, leading to modern photosynthesis. However, chlorophyll synthesis requires numerous steps. The process starts with uroporphyrin, a primitive precursor to the porphyrin ring which may be biotic or abiotic in origin, which is then modified in cells differently to make Mg, Fe, nickel (Ni), and cobalt (Co) complexes. The centers of these rings are not selective, thus allowing the variety of metal ions to be incorporated. Mg porphyrin gives rise to chlorophyll, Fe porphyrin to heme proteins, Ni porphyrin yields factor F-430, and Co porphyrin Coenzyme B12.

Zinc

Zinc (Zn) was incorporated into living cells in two waves. Four to three Ga, anaerobic prokaryotes arose, and the atmosphere was full of $H_2S$and highly reductive. Thus most zinc was in the form of insoluble ZnS. However, because seawater at the time was slightly acidic, some Zn(II) was available in its ionic form and became part of early anaerobic prokaryotes' external proteases, external nucleases, internal synthetases and dehydrogenases.

During the second wave, once the Great Oxygenation Event occurred, more Zn(II) ions were available in the seawater. This allowed its incorporation in the single-cell eukaryotes as they arose at this time. It is believed that the later addition of ions such as zinc and copper allowed them to displace iron and manganese from the enzyme superoxide dismutase (SOD). Fe and Mn complexes dissociate readily (Irving-Williams series) while Zn and Cu do not. This is why eukaryotic SOD contains Cu or Zn and its prokaryotic counterpart contains Fe or Mn.

Zn (II) doesn't pose an oxidation threat to the cytoplasm. This allowed it to become a major cytoplasmic element in the eukaryotes. It became associated with a new group of transcription proteins, zinc fingers. This could only have occurred due to the long life of eukaryotes, which allowed time for zinc to exchange and hence become an internal messenger coordinating the action of other transcription factors during growth.

22. (a) **Give an account of biological oxygen carriers**?

Oxygen carrier systems

The interaction of molecular dioxygen (O_2) with metalloporphyrin species has intrigued scientists of all disciplines ever since such species were recognized as being important centers in some naturally occurring oxygen- storage and transport systems. The iron porphyrin moiety (the heme unit) is the prosthetic group present in myoglobin and hemoglobin (oxygen carriers) and various oxygenases (Which are a class of enzymes that incorporate one or two O_2 to a substrate).

Heme unit are also components of cytochrome c oxidase, the terminal enzyme in the respiratory redox chain that reduces O_2 to water. Oxidases are enzymes that convert both atoms of O_2 to water of hydrogen peroxide.

Heavy medical interventions in severely injured patients and complex transplantation surgery are currently performed with success, but they have increased the need of human blood. At the same time, the risk of transmission of viral diseases, the risk of errors in blood transfusion and the insufficiency of palliative treatments (blood predonation, pre- and perioperative

hemodilution, perioperative blood sparing, lowering of transfusion trigger) accelerated the development of blood substitutes as alternatives to human blood.

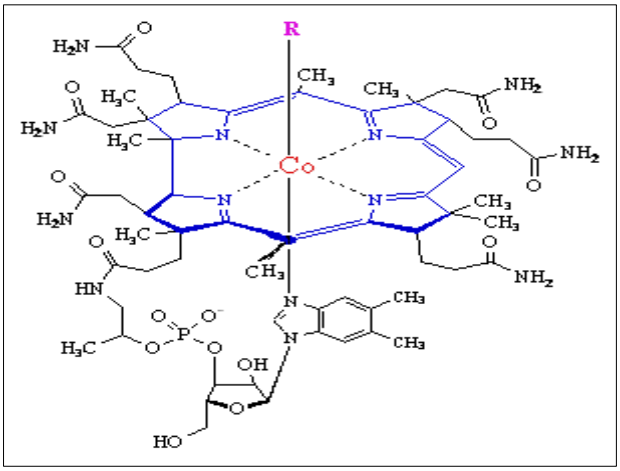
- Together with the property of carrying O2, a blood substitute must have at least the following properties: Free of toxicity and side effects
- Adequate O_2 uptake in the lungs and adequate delivery to tissues
- Sufficient half
- Life time in the circulation to avoid repeated administrations
- Harmful and rapid excretion
- Stable at room temperature, easy to store and easy to use
- Easy to sterilize (to assure the absence of pathogens and viruses transmission)
- Cheap to manufacture.

(b) **Discuss the structural features of Vitamin B12**?

Vitamin B-12

Vitamin B_{12} is the only known essential biomolecule with a stable metal-carbon bond, that is, it is an organometallic compound. The cobalt can link to:

1. a methyl group - as in methylcobalamin
2. a 5'-deoxyadenosine at the the 5' positon - as in adenosylcobalamin (coenzyme B_{12}
3. a cyanide group - as in Vitamin B_{12} - as supplied from drug companies.



The particular link in the cobalamin has a profound effect upon the mechanism of the enzyme reaction.

A methyl-nickel intermediate on acetyl-CoA synthase is also known, but only as an intermediate rather than a stable, isolable compound as the three cobalamins. Other organometals such as the methylmercury ion are highly toxic, it is interesting that there is an unfortunate connection between CH_3Hg^+ and methylcobalamin.

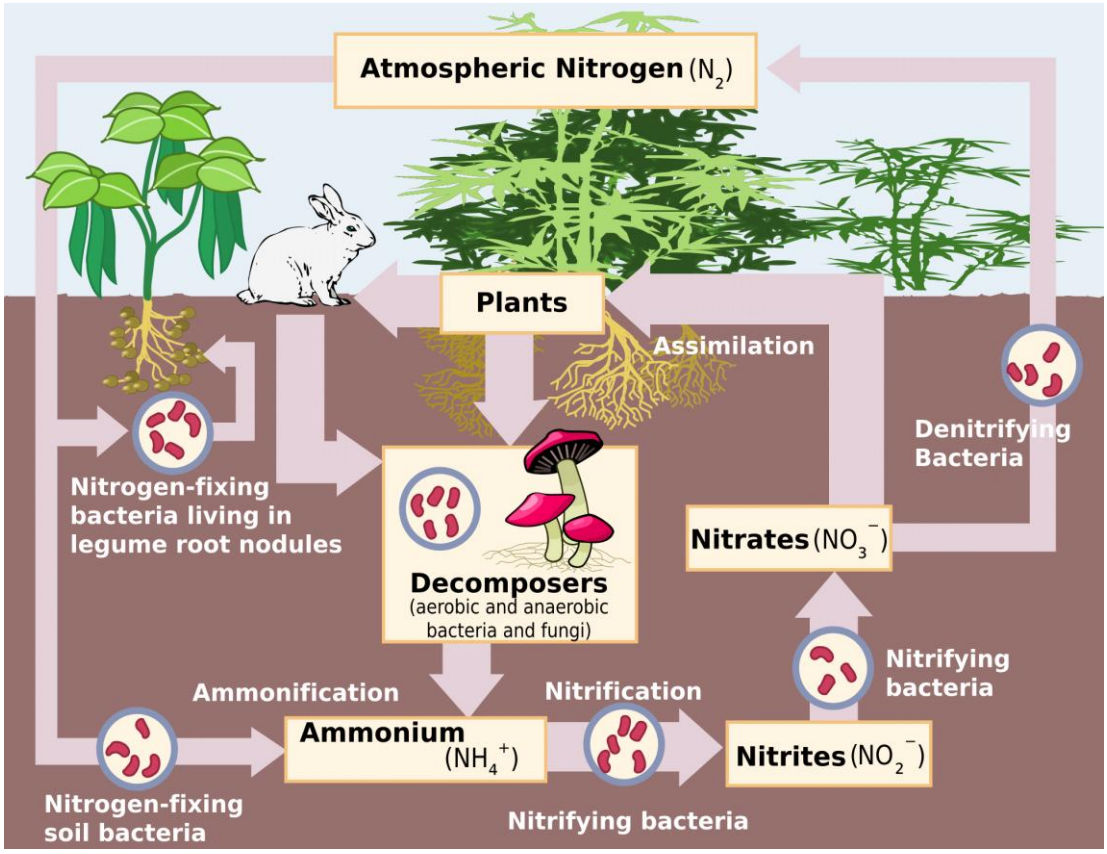
Chime enhanced structures

The core of the molecule is a corrin ring with various attached sidegroups. The ring consists of 4 pyrrole subunits, joined on opposite sides by a C-CH_3 methylene link, on one side by a C-H methylene link, and with the two of the pyrroles joined directly. It is thus like a porphyrin, but with one of the bridging methylene groups removed. The nitrogen of each pyrolle is coordinated to the central cobalt atom

23. (a) **<u>What are the importance of nitrogen cycle in atmosphere</u>**?

<u>Nitrogen cycle</u>

The nitrogen cycle is the biogeochemical cycle by which nitrogen is converted into various chemical forms as it circulates among the atmosphere, terrestrial, and marine ecosystems. The conversion of nitrogen can be carried out through both biological and physical processes. Important processes in the nitrogen cycle include fixation, ammonification, nitrification, and denitrification. The majority of Earth's atmosphere (78%) is nitrogen, making it the largest source of nitrogen. However, atmospheric nitrogen has limited availability for biological use, leading to a scarcity of usable nitrogen in many types of ecosystems. The nitrogen cycle is of particular interest to ecologists because nitrogen availability can affect the rate of key ecosystem processes, including primary production and decomposition. Human activities such as fossil fuel combustion, use of artificial nitrogen fertilizers, and release of nitrogen in wastewater have dramatically altered the global nitrogen cycle.



Schematic representation of the flow of nitrogen through the land environment. The importance of bacteria in the cycle is immediately recognized as being a key element in the cycle, providing different forms of nitrogen compounds assimilable by higher organisms.

Nitrogen is present in the environment in a wide variety of chemical forms including organic nitrogen, Ammonium (NH_4+), nitrite (NO_2-), nitrate (NO_3-), nitrous oxide (N_2O), Nitric oxide (NO) or inorganic nitrogen gas (N_2). Organic nitrogen may be in the form of a living organism, humus or in the intermediate products of organic matter decomposition. The processes of the nitrogen cycle transform nitrogen from one form to another. Many of those processes are carried out by microbes, either in their effort to harvest energy or to accumulate nitrogen in a form needed for their growth. For example, the nitrogenous wastes in animal urine are broken down by nitrifying bacteria in the soil to be used as new. The diagram besides shows how these processes fit together to form the nitrogen cycle.

(b) **Differentiate biological and abiological nitrogen fixation?**

Nitrogen fixation

A relatively small amount of ammonia is produced by lightning. Some ammonia also is produced industrially by the Haber-Bosch process, using an iron-based catalyst, very high pressures and fairly high temperature. But the major conversion of N_2 into ammonia, and thence into proteins, is achieved by microorganisms in the process called nitrogen fixation (or dinitrogen fixation).

The table below shows some estimates of the amount of nitrogen fixed on a global scale. The total biological nitrogen fixation is estimated to be twice as much as the total nitrogen fixation by non-biological processes.

To illustrate the importance of biological nitrogen fixation, the image below shows part of the Lower Sonoran desert in Arizona. Every plant that we see in this scene depends ultimately on biological nitrogen fixation. Both free-living cyanobacteria and the cyanobacterial associates of lichens initially contributed nitrogen to the soil by forming a cryptobiotic crust. Now numerous leguminous plants occur in this desert, with nitrogen-fixing *Rhizobium* in their root nodules.

Mechanism of biological nitrogen fixation

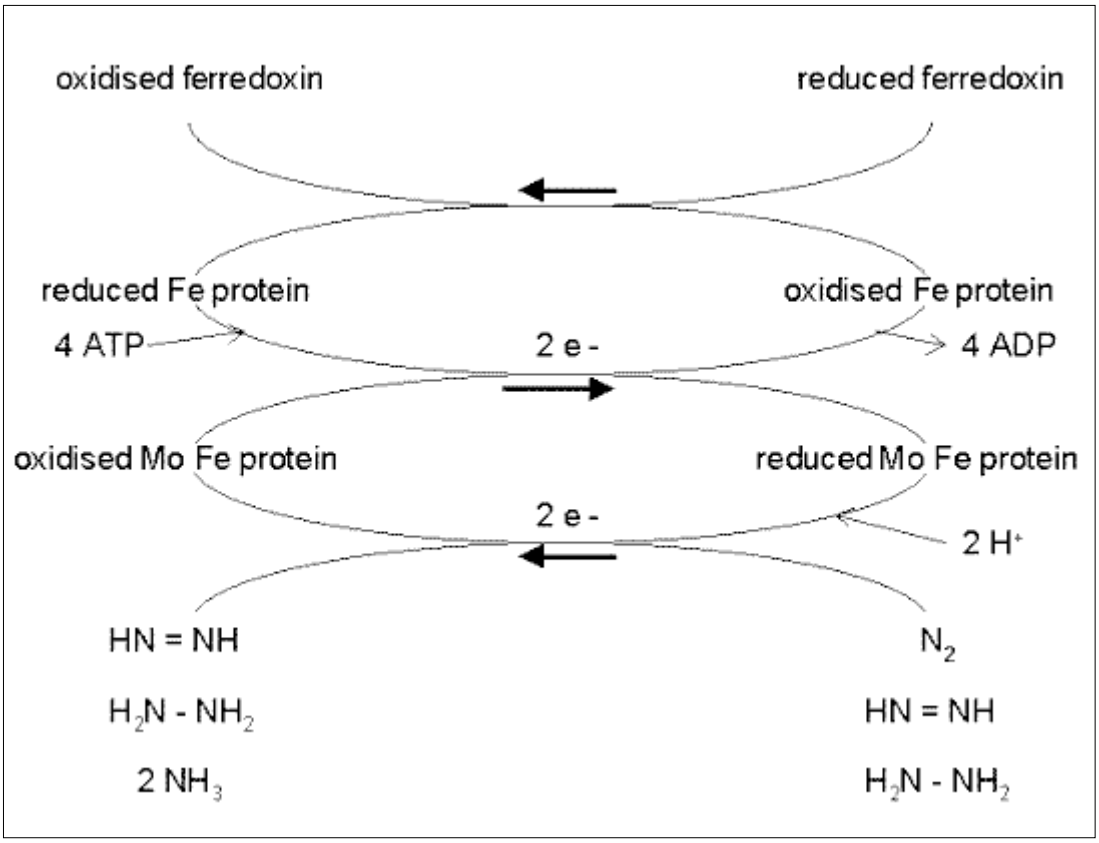
Biological nitrogen fixation can be represented by the following equation, in which two moles of ammonia are produced from one mole of nitrogen gas, at the expense of 16 moles of ATP and a supply of electrons and protons (hydrogen ions):

$$\mathbf{N_2 + 8H+ + 8e^- + 16\ ATP = 2NH_3 + H_2 + 16ADP + 16\ Pi}$$

This reaction is performed exclusively by prokaryotes (the bacteria and related organisms), using an enzyme complex termed nitrogenase. This enzyme consists of two proteins - an iron protein and a molybdenum-iron protein, as shown below.

The reactions occur while N_2 is bound to the nitrogenase enzyme complex. The Fe protein is first reduced by electrons donated by ferredoxin. Then the reduced Fe protein binds ATP and reduces the molybdenum-iron protein, which donates electrons to N_2, producing HN=NH. In two further cycles of this process (each requiring electrons donated by ferredoxin) HN=NH is reduced to $H_2N\text{-}NH_2$, and this in turn is reduced to $2NH_3$.

Depending on the type of microorganism, the reduced ferredoxin which supplies electrons for this process is generated by photosynthesis, respiration or fermentation.



There is a remarkable degree of functional conservation between the nitrogenase proteins of all nitrogen-fixing bacteria. The Fe protein and the Mo-Fe protein have been isolated from many of these bacteria, and nitrogen fixation can be shown to occur in cell-free systems in a laboratory when the Fe protein of one species is mixed with the Mo-Fe protein of another bacterium, even if the species are very distantly related.

Abiological Nitrogen Fixation

In abiological nitrogen fixation the nitrogen is reduced to ammonia without involving any living cell. Abiological fixation can be of two types: **industrial and natural**.

For example, in the Haber's process, synthetic ammonia is produced by passing a mixture of nitrogen and hydrogen through a bed of catalyst (iron oxides) at a very high temperature and pressure.

$$N_2 + 3H_2 \rightarrow 2NH_3$$

This is industrial fixation wherein nitrogen gets reduced to ammonia.

In natural process nitrogen can be fixed especially during electrical discharges in the atmosphere. It may occur during lightning storms when nitrogen in the atmosphere can combine with oxygen to form oxides of nitrogen.

$$N_2 + O_2 \rightarrow 2NO_2$$

These oxides of nitrogen may be hydrated and trickle down to earth as combined nitrite and nitrate.

24. (a) **Discuss the different sources of metal ion toxicity**?

Metal toxicity

Metal toxicity or **metal poisoning** is the toxic effect of certain metals in certain forms and doses on life. Some metals are toxic when they form poisonous soluble compounds. Certain metals have no biological role, i.e. are not essential minerals, or are toxic when in a certain form. In the case of lead, any measurable amount may have negative health effects. Often heavy metals are thought as synonymous, but lighter metals may also be toxic in certain circumstances, such as beryllium and lithium. Not all heavy metals are particularly toxic, and some are essential, such as iron. The definition may also include trace elements when in abnormally high doses may be toxic. An option for treatment of metal poisoning may be chelation therapy, which is a technique which involves the administration of chelation agents to remove metals from the body.

Mechanism of toxicity

Cadmium (Cd) is an extremely toxic industrial and environmental pollutant classified as a human carcinogen [Group 1 – according to International Agency for Research on Cancer; Group 2a – according to Environmental Protection Agency (EPA); and 1B carcinogen classified by European Chemical Agency.

Acute exposure to cadmium fumes may cause flu-like symptoms including chills, fever, and muscle ache sometimes referred to as "the cadmium blues." Symptoms may resolve after a week if there is no respiratory damage. More severe exposures can cause tracheo-bronchitis, pneumonitis, and pulmonary edema. Symptoms of inflammation may start hours after the exposure and include cough, dryness and irritation of the nose and throat, headache, dizziness, weakness, fever, chills, and chest pain.

Inhaling cadmium-laden dust quickly leads to respiratory tract and kidney problems which can be fatal (often from renal failure). Ingestion of any significant amount of cadmium causes immediate poisoning and damage to the liver and the kidneys. Compounds containing cadmium are also carcinogenic.

The bones become soft (*osteomalacia*), lose bone mineral density (*osteoporosis*) and become weaker. This causes the pain in the joints and the back, and also increases the risk of fractures. In extreme cases of cadmium poisoning, mere body weight causes a fracture.

The kidneys lose their function to remove acids from the blood in *proximal renal tubular dysfunction*. The kidney damage inflicted by cadmium poisoning is irreversible. The *proximal renal tubular dysfunction* creates low phosphate levels in the blood (*hypophosphatemia*), causing muscle weakness and sometimes coma. The dysfunction also causes gout, a form of arthritis due to the accumulation of uric acid crystals in the joints because of high acidity of the blood (*hyperuricemia*). Another side effect is increased levels

of chloride in the blood (*hyperchloremia*). The kidneys can also shrink up to 30%. Cadmium exposure is also associated with the development of kidney stones.

Similar to zinc, long term exposure to cadmium fumes can cause irreversible total loss of smell.

Inside cells, cadmium ions act as a hydrogen peroxide generator. This sudden surge of cytosolic hydrogen peroxide causes increased lipid peroxidation and additionally depletes ascorbate and glutathione stores. Hydrogen peroxide can also convert thiol groups on proteins into nonfunctional sulfones and is also capable of directly attacking nuclear DNA. This oxidative stress causes the afflicted cell to manufacture large amounts of inflammatory cytokines.

(b) **Give the toxic symptoms in a) Pb b) Hg c) Cd- poisoning**?

Mercury poisioning (Hg)

Mercury poisoning	
Specialty	Toxicology
Symptoms	Muscle weakness, poor coordination, numbness in the hands and feet[1]
Complications	Kidney problems, decreased intelligence
Medication	**Acute poisoning**: dimercaptosuccinic acid (DMSA), dimercaptopropane sulfonate (DMPS)

symptoms

Common symptoms of mercury poisoning include peripheral neuropathy, presenting as paresthesia or itching, burning, pain, or even a sensation that resembles small insects crawling on or under the skin (formication); skin discoloration (pink cheeks, fingertips and toes); swelling; and desquamation (shedding or peeling of skin).

Mercury irreversibly inhibits selenium-dependent enzymes (see below) and may also inactivate *S*-adenosyl-methionine, which is necessary for catecholamine catabolism by catechol-*O*-methyl transferase. Due to the body's inability to degrade catecholamines (e.g. epinephrine), a person suffering from mercury poisoning may experience profuse sweating, tachycardia (persistently faster-than-normal heart beat), increased salivation, and hypertension (high blood pressure).

Affected children may show red cheeks, nose and lips, loss of hair, teeth, and nails, transient rashes, hypotonia (muscle weakness), and increased sensitivity to light. Other symptoms may include kidney dysfunction (e.g. Fanconi syndrome) or neuropsychiatric symptoms such as emotional lability, memory impairment, or insomnia.

Thus, the clinical presentation may resemble pheochromocytoma or Kawasaki disease. Desquamation (skin peeling) can occur with severe mercury poisoning acquired by handling elemental mercury.

Lead poisoning

Lead poisoning can cause a variety of symptoms and signs which vary depending on the individual and the duration of lead exposure. Symptoms are nonspecific and may be subtle, and someone with elevated lead levels may have no symptoms. Symptoms usually develop over weeks to months as lead builds up in the body during a chronic exposure, but acute symptoms from brief, intense exposures also occur. Symptoms from exposure to organic lead, which is probably more toxic than inorganic lead due to its lipid solubility, occur rapidly. Poisoning by organic lead compounds has symptoms predominantly in the central nervous system, such as insomnia, delirium, cognitive deficits, tremor, hallucinations, and convulsions.

Symptoms may be different in adults and children; the main symptoms in adults are headache, abdominal pain, memory loss, kidney failure, male reproductive problems, and weakness, pain, or tingling in the extremities.

Cadmium poisoning

Cadmium poisoning	
Classification and external resources	
Specialty	emergency medicine
ICD-10	T56.3
ICD-9-CM	985.5

Cadmium is an extremely toxic metal commonly found in industrial workplaces. Due to its low permissible exposure limit, overexposures may occur even in situations where trace quantities of cadmium are found. Cadmium is used extensively in electroplating, although the nature of the operation does not generally lead to overexposures. Cadmium is also found in some industrial paints and may represent a hazard when sprayed. Operations involving removal of cadmium paints by scraping or blasting may pose a significant hazard. Cadmium is also present in the manufacturing of some types of batteries. Exposures to cadmium are addressed in specific standards for the general industry, shipyard employment, construction industry, and the agricultural industry.

25. (a) **How the micronutrients stabilize the soil matter**?

Micronutrients in Soil

While it's common knowledge that plants need water and air to grow, sometimes the question of exactly what nutrients a plant needs in order to thrive can be challenging.

Nutrients in the soil are vital to the growth of plants, and proper allocation is critical to the plant's quality. Understanding fully what nutrients are and how they help a plant grow are the first steps in providing an enriching environment for your crops.

Essential nutrients are just that - nutrients that a plant needs for survival. They are divided into two categories: mineral and non-mineral. The non-mineral nutrients required by plants are carbon, hydrogen, and oxygen, found in the air and water. Mineral nutrients are classified as either macronutrients or micronutrients.

Plants need large amounts of macronutrients in order to thrive. Macronutrients are classified further into primary and secondary nutrients.

Proportionately, plants need the largest quantities of primary nutrients. Primary nutrients include:

- Nitrogen (N)
- Phosphorus (P)
- Potassium (K)

Secondary nutrients are as important to a plant's nutrition as the primary nutrients, but plants don’t require quite as much in terms of quantity. Secondary nutrients include:

- Calcium (Ca)
- Magnesium (Mg)
- Sulfur (S)

Proportionate to primary and secondary nutrients, plants need a much smaller quantity of micronutrients. However, their importance is still great. A shortage of micronutrients can limit plant growth and crop yields. Too great a shortage could even cause plant death, even with all other essential elements fully represented. Micronutrients include:

- Boron (B): Transports sugar to roots and tops
- Chloride (Cl): Aids in plant metabolism
- Copper (Cu): Activates enzymes, aides in chlorophyll production and is involved in protein synthesis
- Iron (Fe): Essential for formation of chlorophyll
- Manganese (Mn): Important for the production of chlorophyll
- Molybdenum (Mo): Reduces nitrates for protein synthesis
- Nickel (Ni): Essential for formation of chlorophyll
- Zinc (Zn): Activates enzymes

As plants develop, from seedling stage to harvest, their need for nutrition varies. During the seedling stage, the need for nutrients is low, but it gradually starts to increase. Nutrient demand quickly increases during the vegetative state. In the reproductive stage, demand lessens again: While plants still need nutrients, the demand is mostly met by a redistribution of elements held in the vegetative tissues.

(b) **What is the role of bacteria leaching in bio-degradation**?

Bacterial leaching techniques

The two major techniques used in leaching are percolation and agitation leaching. Percolation leaching involves the percolation of a lixiviant through a static bed, whereas agitation leaching involves finer particle sizes agitated in a lixiviant. Due to the large scale operations involved in bacterial leaching, percolation leaching is preferred commercially. The principal commercial methods are in situ, dump, heap and vat leaching. In situ leaching involves pumping of solution and air under pressure into a mine or into ore bodies made permeable by explosive charging. The resulting metal-enriched solutions are recovered through wells drilled below the ore body.

Dump leaching involves uncrushed waste rock which is piled up. These dumps generally contain about 0.1-0.5% Cu, too low to recover profitably by conventional procedures. Some of these dumps are huge, containing in excess of 10 million tons of waste rock. Heap leaching requires the preparation of the ore, primarily size reduction, so as to maximize mineral-lixiviant interaction and the laying of an impermeable base to prevent lixiviant loss and pollution of water bodies. Essentially, both dump and heap leaching involve the application of lixiviant to the top of the dump or heap surface and the recovery of the metal laden solution that seeps to the bottom by gravity flow. The dilute sulphuric acid sprinkled on top percolates down through the dump, lowering the pH and promoting the growth of acidophilic microorganisms. The acid run-off is collected at the bottom of the dump, from where it is pumped to a recovery station. Copper is extracted from the acid run-off by cementation or solvent extraction or electro wining. All the above processes are essentially uncontrolled from a biological and engineering standpoint. Beside these processes are slow in nature and require long periods to recover a portion of the metal. Vat leaching as currently applied to oxide ores involves the dissolution of crushed materials in a confined tank. More controls can be brought in for enhanced recovery by the use of bioreactors, though necessarily these involve higher costs. However, for ore concentrates and precious metals they are being considered actively.

Applications of minerals bio-degradation by bacteria

The type of enzyme to be used, and quantification of degradation, will depend on the polymer being screened. For example, the effects of draw ratio of polycaprolactone fibers on enzymatic hydrolysis by lipase. Degrad- ability of PCL fibers was monitored by dissolved organic carbon (DOC) formation and weight loss. Similar systems with lipases have been used for studying the hydrolysis of broad ranges of aliphatic polyesters, copolyesters with aro- matic segments, and copolyester amides. Other enzymes such as α-chymotrypsin and α-trypsin have also been applied for these polymers. Biodegradability of poly (vinyl alcohol) segments with respect to block length and stereo chemical configuration has been studied using isolated poly (vinyl alcohol)-dehydrogenase .Cellulolytic enzymes have been used to study the biodegradability of cellulose ester derivatives as a function of degree of substitution and the substituent size. Similar work has been performed with starch esters using amylolytic enzymes such as α-amylases, β-amylases, glucoamylases, and amyloglucosidases. Enzymatic

methods have also been used to study the biodegradability of starch plastics or packaging materials containing

Factors affecting bacterial leaching

The rate and efficiency of bacterial leaching of mineral ores depends upon a number of different factors. Brandl, (2001) has summarized these factors, which can be seen in table.

Table: Factors affecting bacterial leaching

Factor	Parameter	
Physicochemical parameters of a bioleaching environment	Temperature	nutrient availability
	pH	iron (II) concentration
	redox potential	light
	oxygen content and availability	pressure
	carbon dioxide content	surface tension
	mass transfer	presence of inhibitors
Microbiological parameters of a bioleaching environment	Microbial diversity	Metal tolerance
	Population diversity	Adaptation abilities of microorganisms
	Spatial distribution of microorganisms	
Properties of the minerals to be leached	mineral type	porosity
	mineral composition	hydrophobicity
	mineral dissemination	galvanic interactions
	grain size	formation of secondary minerals
	surface area	
Processing	Leaching mode (in situ, heap, dump, or tank leaching)	Stirring rate (in case of tank leaching operaions)
	Pulp density	Heap geometry (in case of heap leaching)

Physico-chemical as well as microbiological factors of the leaching environment affects bioleaching rates and efficiencies. Moreover, the properties of the mineral ores and the manner in which they are processed are also significant since they also affect bioleaching rates and efficiencies. The influence of different microbiological, mineralogical, physicochemical and process parameters on the oxidation of mineral ores has been reviewed by many researchers. Unfortunately, whilst much has been published in this field, results are sometimes conflicting and often the conditions used are not described in much detail.

Reg. No.....

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KARPAGAM UNIVERSITY
Karpagam Academy of Higher Education
(Established Under Section 3 of UGC Act 1956)
COIMBATORE – 641 021
(For the candidates admitted from 2015 onwards)

B.Sc., DEGREE EXAMINATION, NOVEMBER 2017
Fifth Semester

CHEMISTRY

BIOINORGANIC CHEMISTRY

Time: 3 hours Maximum : 60 marks

PART – A (20 x 1 = 20 Marks) (30 Minutes)
(Question Nos. 1 to 20 Online Examinations)

PART B (5 x 8 = 40 Marks) (2 ½ Hours)
Answer ALL the Questions

21. a. Explain the ion channel of Ca^{+}-Mg^{+} charge carriers in muscle contraction of bones?

Or

b. What is Zn-acid catalyst? And discuss it role in biological system

22. a. What is Vitamin B-12? Name the important biological reactions

Or

b. What is porphyrin ring ? Mention it occurrence in biological system?

23. a. Write a note on Nitrogen cycle?

Or

b. What is nitrogenase ? What is its biological function?

24. a. Name two platinum complexes approved clinically for the treatment of human cancer?

Or

b. Give a note on treatment of Pb, Cd and Hg toxicity?

25. a. List out the micronutrients in soil?

Or

b. What is the major role of micronutrients in soil composition?
