KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed to be University Established Under Section 3 of UGC Act 1956)
Pollachi Main Road, Eachanari Post, Coimbatore - 641 021. INDIA
Phone : 0422-6471113-5, 6453777 Fax No : 0422 -2980022-3
Email : info@karpagam.com Web : www.kahedu.edu.in

DEPARTMENT OF BIOCHEMISTRY

SYLLABUS

SUBJECT NAME: MOLECULES OF LIFE **SUB.CODE: 19BCU101**

SEMESTER: I **CLASS: I B.Sc., BIOCHEMISTRY**

Course objectives

- To understand the properties and importance of water in biological system
- To know the various biomolecules present in biological system
- To introduce the importance of vitamins in human body

Course outcomes (CO's)

1. Recognize water as a universal solvent and elixir of life by knowing its importance
2. Identify the properties and classification of carbohydrates
3. Recall the role of various lipids in biomembrane including signal transduction
4. Categories the aminoacids and know their properties
5. Differentiate the structure, properties and functions of DNA and RNA
6. List the functions and deficiency disease of fat and water soluble vitamins

Unit I: The foundations of biochemistry and water

Cellular and chemical foundations of life. Unique properties, weak interactions in aqueous systems, ionization of water, buffers, water as a reactant and fitness of the aqueous environment.

Unit II: Carbohydrates and glycobiology

Monosaccharides - structure of aldoses and ketoses, ring structure of sugars, conformations of sugars, mutarotation, anomers, epimers and enantiomers, structure of biologically important sugar derivatives, oxidation of sugars. Formation of disaccharides, reducing and non-reducing disaccharides. Polysaccharides – homo- and heteropolysaccharides, structural and storage polysaccharides. Structure and role of proteoglycans, glycoproteins and glycolipids (gangliosides and lipopolysaccharides). Carbohydrates as informational molecules, working with carbohydrates

Unit III: Lipids

Building blocks of lipids - fatty acids, glycerol, ceramide. Storage lipids - triacyl glycerol and waxes. Structural lipids in membranes – glycerophospholipids, galactolipids and sulpholipids, sphingolipids and sterols, structure, distribution and role of membrane lipids.

Plant steroids. Lipids as signals, cofactors and pigments.

Unit IV: Amino acids and Nucleic acids

Structure and classification, physical, chemical and optical properties of amino acids.Nucleotides - structure and properties. Nucleic acid structure – Watson-Crick model of DNA. Structure of major species of RNA - mRNA, tRNA and rRNA. Nucleic acid chemistry - UV absorption, effect of acid and alkali on DNA. Other functions of nucleotides - source of energy, component of coenzymes, second messengers.

Unit V: Vitamins

Structure and active forms of water soluble and fat soluble vitamins, deficiency diseases and symptoms, hypervitaminosis

SUGGESTED READING

1. Ambika, S, (2004). Fundamentals of Biochemistry for Medical Students, CIT Chennai.

2. Deb, C., (2011). Fundamentals of Biochemistry, 9th edition New Central Book Agency, Calcutta.

3. Jain, J.L., Jain, S and Jain, N., (2005). Fundamentals of Biochemistry, S. Chand and Company Ltd, New Delhi.

4. Nelson, D., and Cox, M. W.H. (2012) Lehninger Principles of Biochemistry (4th Ed.) New York, Freeman and Company.

5. Stryer, L., (2009). Biochemistry, W.H. Freeman and Company, New York.

6. Murray, R.K., Bender, D.A., Botham, K.M., and Kennelly, P.J., (2012). Harper's illustrated Biochemistry, 29th Edition. McGraw-Hill Medical. London.

KARPAGAM ACADEMY OF HIGHER EDUCATION

(Deemed to be University Established Under Section 3 of UGC Act 1956)
Pollachi Main Road, Eachanari Post, Coimbatore - 641 021. INDIA
Phone : 0422-6471113-5, 6453777 Fax No : 0422 -2980022-3
Email : info@karpagam.com Web : www.kahedu.edu.in

DEPARTMENT OF BIOCHEMISTRY

LECTURE PLAN

SUBJECT NAME: MOLECULES OF LIFE

SUB.CODE: 19BCU101

SEMESTER: I **CLASS: I B.Sc., BIOCHEMISTRY**

S.No	Duration of Period	Topics to be Covered	Support materials with Page No.	Web page referred
UNIT I - The foundations of biochemistry and water				
1	1	Cellular foundations of life	S4: 3-11	
2	1	Chemical foundations of life	S4: 12-21	
3	1	Unique properties	S4: 12-21	
4	1	Weak interactions in aqueous systems	S2: 47-58	
5	1	Ionization of water	S2:13-15	
6	1	Buffers	S4:60-68	
7	1	Water as a reactant	S4: 690	
8	1	Fitness of the aqueous environment	S4: 90-91	
9	1	Revision and possible questions discussion		
Total No. of Hours planned for Unit I is 12 hours				
UNIT II- Carbohydrates and glycobiology				
1	1	Monosaccharides - structure of aldoses and ketoses, ring structure of sugars.	S4: 238-249	
2	1	Conformations of sugars, mutarotation,	S4: 238-249	
3	1	Anomers, epimers and enantiomers, structure of biologically important sugar derivatives,	S2: 39-47	
4	1	Oxidation of sugars. Formation of disaccharides,	S4: 245-246	
5	1	Reducing and non-reducing disaccharides.	S2: 48-49	
6	1	Polysaccharides – homo- and heteropolysaccharides, structural and storage polysaccharides.	S4: 247-254 S2: 49-52	
7	1	Structure and role of proteoglycans	S4: 255-258	
8	1	Glycoproteins and glycolipids (gangliosides and lipopolysaccharides).	S2: 56-59; 259-261	
9	1	Carbohydrates as informational molecules,	S4: 261-265, 267-268	

		working with carbohydrates	S2: 52-53	
Total No. of Hours planned for Unit II is 9 hours				
UNIT III - LIPIDS				
1	1	Building blocks of lipids - fatty acids, glycerol, ceramide. Storage lipids - triacyl glycerol and waxes.	S4: 342-348; S2: 56-57, 290-291	
2	1	Structural lipids in membranes – glycerophospholipids	S4: 348-350	
3	1	Galactolipids and sulpholipids,	S4: 351-355	
4	1	Sphingolipids and sterols	S4: 353-355	
5	1	Structure, distribution and role of membrane lipids.	S4: 353-355	
6	1	Plant steroids.	S4: 360-361	
7	1	Lipids as signals,	S2: 66-67	
8	1	Cofactors and pigments	S4: 357-359	
9	1	Revision and possible questions discussion		
Total No. of Hours planned for Unit III is 9 hours				
UNIT IV - Amino acids and Nucleic acids				
1	1	Structure and classification	S4: 75-84	
2	1	physical, chemical and optical properties of amino acids.	S4: 75-84	
3	1	Nucleotides - structure and properties.	S4: 273-278; S2: 89-94	
4	1	Nucleic acid structure –	S4: 279-280; S4: 95-96	
5	1	Watson-Crick model of DNA.	S4: 95-96	
6	1	Structure of major species of RNA - mRNA, tRNA and rRNA.	S4: 1008-1020; S2: 97-100	
7	1	Nucleic acid chemistry - UV absorption, effect of acid and alkali on DNA.	S4: 291-293	
8	1	Other functions of nucleotides - source of energy, component of coenzymes, second messengers.	S4: 300-302	
9	1	Revision and possible questions discussion		
Total No. of Hours planned for Unit IV is 9 hours				
UNIT - V - VITAMINS				
1	1	Introduction to Vitamins	S4:75-84	
2	1	Structure of water soluble vitamins	S4: 191-214	
3	1	Active forms of water soluble vitamins	S2: 191-214	
4	1	Structure of fat soluble vitamins	S4: 360-363	
5	1	Active forms of fat soluble vitamins	S2: 360-363; S2: 178-190	

6	1	Deficiency diseases	S2: 178-190	
7	1	Symptoms	S2: 178-190	
8	1	Hypervitaminosis		W1
9	1	Revision and possible questions discussion		
ESE Question paper discussi				
1	1	Previous End Semester Examinations question paper discussion		
2	1	Previous End Semester Examinations question paper discussion		
3	1	Previous End Semester Examinations question paper discussion		

SUGGESTED READING

1. Ambika, S, (2004). Fundamentals of Biochemistry for Medical Students, CIT Chennai.

2. Deb, C., (2011). Fundamentals of Biochemistry, 9th edition New Central Book Agency, Calcutta.

3. Jain, J.L., Jain, S and Jain, N., (2005). Fundamentals of Biochemistry, S. Chand and Company Ltd, New Delhi.

4. Nelson, D., and Cox, M. W.H. (2012) Lehninger Principles of Biochemistry (4th Ed.) New York, Freeman and Company.

5. Stryer, L., (2009). Biochemistry, W.H. Freeman and Company, New York.

6. Murray, R.K., Bender, D.A., Botham, K.M., and Kennelly, P.J., (2012). Harper's illustrated Biochemistry, 29th Edition. McGraw-Hill Medical. London.

WEBSITES

W1. http://www.en.wikipedia.org/wiki/hypervitaminosis.html

UNIT 1
SYLLABUS

The foundations of biochemistry and water: Cellular and chemical foundations of life. Unique properties, weak interactions in aqueous systems, ionization of water, buffers, water as a reactant and fitness of the aqueous environment.

The foundations of biochemistry and water

Fifteen to twenty billion years ago, the universe arose as a cataclysmic eruption of hot, energy-rich subatomic particles. Within seconds, the simplest elements (hydrogen and helium) were formed. As the universe expanded and cooled, material condensed under the influence of gravity to form stars. Some stars became enormous and then exploded as supernovae, releasing the energy needed to fuse simpler atomic nuclei into the more complex elements. Thus were produced, over billions of years, the Earth itself and the chemical elements found on the Earth today. About four billion years ago, life arose—simple microorganisms with the ability to extract energy from organic compounds or from sunlight, which they used to make a vast array of more complex biomolecules from the simple elements and compounds on the Earth’s surface.

Biochemistry asks how the remarkable properties of living organisms arise from the thousands of different lifeless biomolecules. When these molecules are isolated and examined individually, they conform to all the physical and chemical laws that describe the behavior of inanimate matter—as do all the processes occurring in living organisms. The study of biochemistry shows how the collections of inanimate molecules that constitute living organisms interact to maintain and perpetuate life animated solely by the physical and chemical laws that govern the nonliving universe.

Cellular Foundations

The unity and diversity of organisms become apparent even at the cellular level. The smallest organisms consist of single cells and are microscopic. Larger, multicellular organisms contain many different types of cells, which vary in size, shape, and specialized function. Despite these obvious differences, all cells of the simplest and most complex organisms share certain fundamental properties, which can be seen at the biochemical level. Cells Are the Structural and Functional Units of All Living Organisms Cells of all kinds share certain structural features. The plasma membrane defines the periphery of the cell, separating its contents from the surroundings. It is composed of lipid and protein molecules that form a thin, tough, pliable, hydrophobic barrier around the cell. The membrane is a barrier to the free passage of inorganic ions and most other charged or polar compounds. Transport proteins in the plasma membrane allow the passage of certain ions and molecules; receptor proteins transmit signals into the cell; and membrane enzymes participate in some reaction pathways. Because the individual lipids and proteins of the plasma membrane are not covalently linked, the entire structure is remarkably flexible, allowing changes in the shape and size of the cell. As a cell grows, newly made lipid and protein molecules are inserted into its plasma membrane; cell division produces two cells, each with its own membrane. This growth and cell division (fission) occurs without loss of membrane integrity.

- All organisms are assembled from simple atoms and molecules
- Atoms in soils are very similar to atoms in a tree
- How do some atoms form life, and others do not - answer lies in structure of the atoms and how they interact

Chemical Foundations of Life

- the atoms of all living things flow from one living thing to another
- not all chemicals sustain life, some damage it, such as pollutants
- mountain pines - ozone damage from pollution yellows the needles
- the pollution started around world war II
- matter is things that takes up space and has mass
- core of atom - nucleus, has protons and neutrons, protons have + charge
- around neutrons are electrons in motion, have a - charge
- neutral atoms have same number of protons as electrons
- atoms of a given element have same number of protons
- isotopes are atoms of the same element with a different mass because they have a different number of neutrons
- isotope compositions of water and air can allow scientists to see where pollution is coming from
- to measure pollutants - one can directly measure plant stems and needle growth
- compounds are made of two or more elements, chemically combined
- ozone is made of 3 atoms of oxygen per molecule
- electrons move in energy levels or shells around a nucleus, each shell can hold only specific numbers of atoms
- when sodium loses its lone electron in its outer shell to chlorine, it leaves the sodium with full shells and chlorine with full shells, but they have opposite charge so they stick together in an ionic bond
- many atoms share electrons to form covalent bonds - the electrons move around both atoms within combined shells
- when hydrogen bonds to water the electrons are not shared equally, causing oxygen to be slightly negative and hydrogen slightly positive - giving water molecules polarity
- the soil near the surface has more organic material, deeper soils have more inorganic material
- rain washes pollutants from the sky into the soil, damaging roots
- the newest young trees are more resistant to the pollution because they are produced from parents that survived the initial pulse of pollution before pollution controls went into effect

Water

Water is a essential for life, miracle of nature, and sustainer of life. Its important is known since there is no life without water. From water only the origin of life has started. All aspects of cell structure and function are adapted to the physical and chemical properties of water.

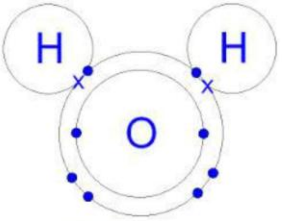
Structure and function of biomolecules

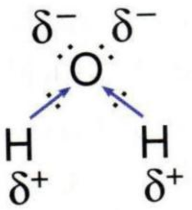
- Assemblage of cellular components
- Including enzymes and other proteins, nucleic acid and lipids
- Its used for biochemical reactions
- Transporting substances
- Maintaining body temperature
- Dissolving waste products for excretion and producing digestive fluids.
- water is the most important chemical on earth - makes up most of the body of all organisms

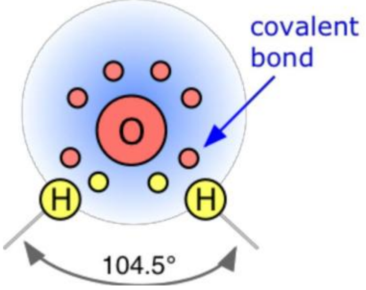
- everything needs water, near dry coasts people are trying to desalinate water to make fresh water from ocean water
- the large scale cost of heating water to evaporate and condense it to make it pure is too high to make it worthwhile
- water's polarity makes it difficult to boil
- as pressure is decreased (in a vacuum) the water boils at lower temperatures which are easier to attain
- as the water boils away, the brine that remains is very corrosive to the metal piping of the desalination plant
- an ion trap is used to screen the water before it goes into the desalination plant so that the water cannot corrode the aluminum piping in the plant
- the desalination plant will need a power plant nearby to run the facility, waste heat from the power plant would be used to heat the water to run the desalination plant
- No other substance on earth is as abundant as water (1/3)
- It is almost everywhere in air, clouds, oceans, lakes, rivers, springs or glaciers.
- Water is nearly 6 times as abundant as all other substances put together.
- None of other occurs in 3 states ie ., solid, liquid and gaseous- at the same time.
- It is water that had conditioned our climate. In hot weather, it absorbs heat and in cold, it gives up heat.
- Without water, our planet would be cooled to subzero temperatures long ago and all forms of life would have perished.
- In human, 70 % of weight is due to water (Intracellular fluids and extracellular fluids).
- 2.8 litres of water is excreted as urine so nearly 3 liters of water ahs to be taken every day. Metabolic water is also produced in our body.
- Water balance is very important. If the output of water significantly exceeds or decrease, dehydration and edema occurs respectively.
- By knowing the importance of water, NASA has launched a satellite named Aqua to study the effect of water in various forms on climate.

Structure of water

In water, each hydrogen nucleus is bound to the central oxygen atom by a pair of electrons that are shared between them The Molecular formula of water is H2O: One molecule of water has two hydrogen atoms covalently bonded to a single oxygen atom.
The structure of water molecule is depicted as follows







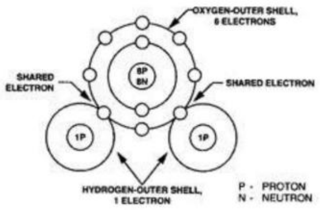
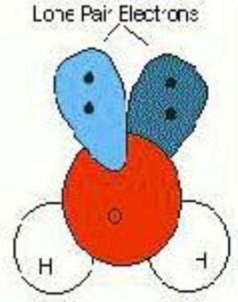


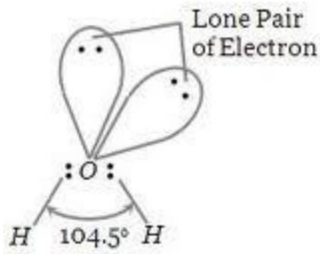
Figure 2-II. Illustration of a Molecule (H_2O)

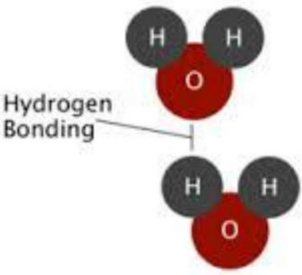
Tetra hedral arrangement of water:

The water molecule maintains a bent shape (bent at 107.5 degrees actually) because of two considerations. First the tetrahedral arrangement around the oxygen and Second the presence of lone pair electrons on the oxygen.

These are the electrons that are not involved in the covalent bonds. The pairs of electrons are left alone. In our picture they are represented by the double dots. These lone pairs are very negative - containing two negative electrons each - and want to stay away from each other as much as possible. These repulsive forces act to push the hydrogens closer together.







The bond angles for water are not 109.5. Because of the presence of the very negative lone pair electrons, the two hydrogens are squeezed together as the two lone pairs try to get away from each other as far as possible. The resulting angle gives water a 104.5 bond angle and the resulting tetrahedron "looks" BENT.

Properties of water

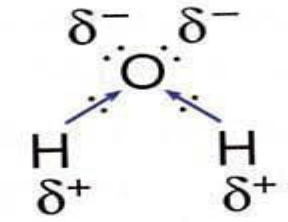
- Have high melting point- 0˚C
- Have high boiling point- 100˚C
- Heat of vaporization - 540
- Surface tension – 72.8
- Vapourization of ice is called sublimation, vapourization of liquid is called vaporation.Both occur more rapidly as the temperature increases. Evaporation occur when water is heated above its boiling point. Heat lost at the point of evaporation returns at the point of condensation. Such phenomena play an important role in meteorological cycle.

Some of the other properties of water are

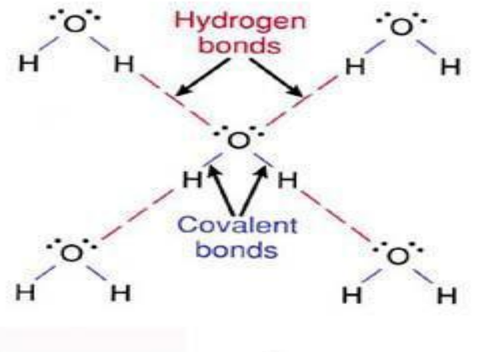
- Water is a liquid at standard temperature and pressure.
- Water is tasteless and odorless.
- Water is transparent in the visible electromagnetic spectrum.
- Water can act as either an acid or a base.
- Water is a universal solvent, dissolving many substances found in nature.

Electric dipole nature of Water:

The hydrogens are slightly positive. They get this way because of the "electronegativity" of oxygen. Electronegativity is a measure of how much one atom wants to have electrons, and oxygen wants to have electrons more than hydrogen does. Oxygen has a higher electronegativity. Because of this difference in electronegativity, the electrons in the covalent bonds between oxygen and hydrogen get pulled slightly toward the oxygen. This leaves the hydrogens a little bit electron-deficient and thus slightly positive. We can draw this polarization like this:

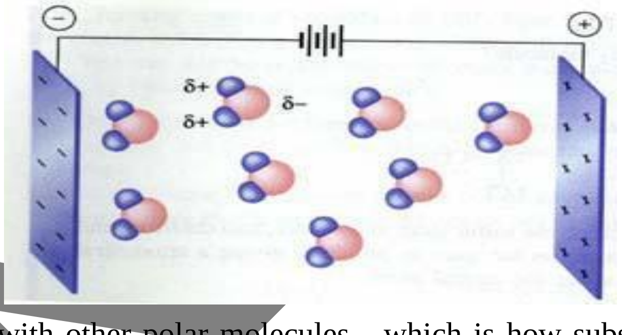


The polarization is responsible for all the properties of water. Because water has a slightly negative end and a slightly positive end, it can interact with itself and form a highly organized 'inter-molecular' network. The positive hydrogen end of one molecule can interact favorably with the negative lone pair of another water molecule. This interaction is call "Hydrogen Bonding". It is a type of weak electrostatic attraction (positive to negative).
Because each and every one of the water molecules can form four hydrogen Bonds, an elaborate network of molecules is formed.

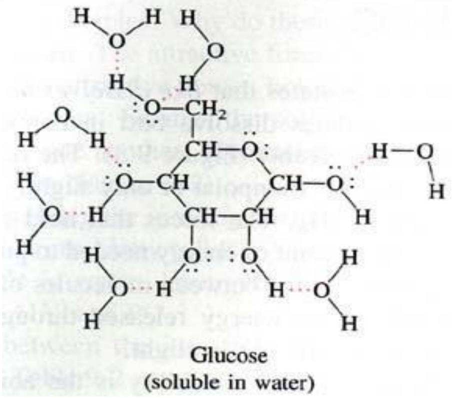


Hydrogen bonding in water.

The polarity also allows water interact with an electric field:



And to interact with other polar molecules - which is how substances become dissolved in water.



Glucose
(soluble in water)

Important properties of water that have physiological relevance:

- **Expansion of freezing:**

  Almost all substance contracts on water but water expands: If it contracts it become heavier and sink to bottom. So all water in earth would gradually become ice**.** When temperature of water is raised above 0˚C its volume decreases upto 4˚C and thereafter it increases. So water has a minimum volume at 4˚C. So 4˚C is a critical point above or below the volume change. (heating/cooling- it increases its volume). Almost all substances increases in volume when they melted but volume of ice decreases when melted.
- **Uniquely high surface tension**

  The surface of liquid tends to contact as much as possible- Water has highest surface tension of 72.8 of any known liquid. This is the reason why water rises to unusually high levels in narrow capillary tubes. This has great importance in physiology.
- **Uniquely high heat capacity**

  There occurs a smaller temperature rise in water as compared to most other substances, when a given amount of heat is applied. Thus, water acts as a temperature buffer. It maintains its temperature more successfully than most other substances. Thus, it has high heat capacity (1,000 cal/g).
- **High solvent power**

  Water has positive and negative charge and this polarity is responsible for its high solvent capacity. Universal solvent facilitates chemical reactions both outside and within biological system.

Weak Interactions in Aqueous Systems

- Hydrogen bonds between water molecules provide the cohesive forces that make water a liquid at room temperature and that favor the extreme ordering of molecules typical of crystalline water (ice). Polar biomolecules dissolve readily in water because they can replace energetically favorable water-water interactions with even more favorable water-solute interactions (hydrogen bonds and electrostatic interactions). In contrast, nonpolar biomolecules interfere with favorable water-water interactions and are poorly soluble in water. In aqueous solutions, these molecules tend to cluster together to minimize the energetically unfavorable effects of their presence.
- The attractions between adjacent water molecules gives liquid water great internal cohesion and leads to its unusual properties.
- The electrostatic interaction between the hydrogen atom of one water molecule and the oxygen atom of another yields the hydrogen bond.
- This bonds are relatively weak with bond dissociation energies of about 23 kJ/mol compared to 470 kJ/mol for the covalent hydroxyl bond. The tetrahedral arrangement of the water molecule gives each molecule the potential to form 4 hydrogen bonds (1 for each hydrogen and 2 for the oxygen)
- In the liquid state, the disorganization of the molecules yields an average of 3.4 bonds per molecule
- In the solid state, the fixed nature of the molecule in the crystal lattice yields the full hydrogen bonding compliment
- The number of hydrogen bonds possible in both states results in the high melting and boiling points for water
- This hydrogen bonding pattern gives water unique properties: – High boiling and melting points – High surface tension – A lower density in the solid state compared to the liquid state

Ionization of Water, Weak Acids, and Weak Bases

Although many of the solvent properties of water can be explained in terms of the uncharged H_20 molecule, the small degree of ionization of water to hydrogen ions (H+) and hydroxide ions (OH^+) must also be taken into account. Like all reversible reactions, the ionization of water can be described by an equilibrium constant. When weak acids or weak bases are dissolved in water, they can contribute H+ by ionizing (if acids) or consume H+ by being protonated (if bases); these processes are also governed by equilibrium constants. The total hydrogen ion concentration from all sources is experimentally measurable; it is expressed as the pH of the solution. To predict the state of ionization of solutes in water, we must take into account the relevant equilibrium constants for each ionization reaction. We therefore turn now to a brief discussion of the ionization of water and of weak acids and bases dissolved in water.

BUFFER

A buffer is an aqueous solution that has a highly stable pH. If you add acid or base to a buffered solution, its pH will not change significantly. Similarly, adding water to a buffer or allowing water to evaporate will not change the pH of a buffer.

MAKE A BUFFER

A buffer is made by mixing a large volume of a weak acid or weak base together with its conjugate. A weak acid and its conjugate base can remain in solution without neutralizing each other. The same is true for a weak base and its conjugate acid.

BUFFERS WORK

When hydrogen ions are added to a buffer, they will be neutralized by the base in the buffer. Hydroxide ions will be neutralized by the acid. These neutralization reactions will not have much effect on the overall pH of the buffer solution. When you select an acid for a buffer solution, try to choose an acid that has a pKa close to your desired pH. This will give your buffer nearly equivalent amounts of acid and conjugate base so it will be able to neutralize as much H+ and OH- as possible.

A buffer is a solution containing either a weak acid and its salt or a weak base and its salt, which is resistant to changes in pH. In other words, a buffer is an aqueous solution of either a weak acid and its conjugate base or a weak base and its conjugate acid.

Buffers are used to maintain a stable pH in a solution, as they can neutralize small quantities of additional acid of base. For a given buffer solution, there is a working pH range and a set amount of acid or base that can be neutralized before the pH will change. The amount of acid or base that can be added to a buffer before changing its pH is called its buffer capacity.

The Henderson-Hasselbalch equation may be used to gauge the approximate pH of a buffer. In order to use the equation, the initial concentration or stoichiometric concentration is entered instead of the equilibrium concentration. The general form of a buffer chemical reaction is:

$HA \rightleftharpoons H^+ + A^-$

Also Known As: Buffers are also called hydrogen ion buffers or pH buffers.

EXAMPLES OF BUFFERS

- blood - contains a bicarbonate buffer system
- TRIS buffer
- phosphate buffer
- As stated, buffers are useful over specific pH ranges. For example, here is the pH range of common buffering agents:

Buffer	pKa	pH range
citric acid	3.13., 4.76, 6.40	2.1 to 7.4
acetic acid	4.8	3.8 to 5.8
KH2PO4	7.2	6.2 to 8.2
borate	9.24	8.25 to 10.25
CHES	9.3	8.3 to 10.3

When a buffer solution is prepared, the pH of the solution is adjusted to get it within the correct effective range. Typically a strong acid, such as hydrochloric acid (HCl) is added to lower the pH of acidic buffers. A strong base, such as sodium hydroxide solution (NaOH), is added to raise the pH of alkaline buffers.

HOW BUFFERS WORK?

In order to understand how a buffer works, consider the example of a buffer solution made by dissolving sodium acetate into acetic acid. Acetic acid is (as you can tell from the name) an acid: CH_3COOH, while the sodium acetate dissociates in solution to yield the conjugate base, acetate ions of CH3COO-. The equation for the reaction is:
$CH_3COOH(aq) + OH^-(aq) \leftrightarrows CH_3COO^-(aq) + H_2O(aq)$
If a strong acid is added to this solution, the acetate ion neutralizes it:
$CH_3COO^-(aq) + H^+(aq) \leftrightarrows CH_3COOH(aq)$
This shifts the equilibrium of the initial buffer reaction, keeping the pH stable. A strong base, on the other hand, would react with the acetic acid.

UNIVERSAL BUFFERS

Most buffers work over a relative narrow pH range. An exception is citric acid because it has three pKa values. When a compound has multiple pKa values, a larger pH range becomes available for a buffer. It's also possible to combine buffers, providing their pKa values are close (differing by 2 or less), and adjusting the pH with strong base or acid to reach the required range. For example, McIvaine's buffer is prepared by combining mixtures of Na2PO4 and citric acid. Depending on the ratio between the compounds, the buffer may be effective from pH 3.0 to 8.0. A mixture of citric acid, boric acid, monopotassium phosphate, and diethyl barbituic acid can cover the pH range from 2.6 to 12

Water as a Reactant

Water is not just the solvent in which the chemical reactions of living cells occur; it is very often a direct participant in those reactions. The formation of ATP from ADP and inorganic phosphate is a condensation reaction in which the elements of water are eliminate. The compound formed by this condensation is called ; phosphate anhydride. Hydrolysis reactions are responsible for the enzymatic depolymerization of proteins, carbohydrates, and nucleic acids ingested in the diet. Hydrolytic enzymes (hydrolases) catalyzes the addition of the elements of water to the bonds that connect mono meric subunits in these macromolecules. Hydrolysis reactions are almost invariably exergonic, and the formation of cellular: polymers from their subunits by simple reversal of hydrolysis would be endergonic and as such does not occur. We shall see that cells circum vent this thermodynamic obstacle by coupling the endergonic condensation reactions to exergonic processes, such as breakage of the anhydride bond in ATP.

Water and carbon dioxide are the end products of the oxidation of fuels such as glucose. The overall reaction of this process can be summarized by the equation:

$$\underset{\textbf{Glucose}}{\mathbf{C_6H_{12}O_6}} \mathbf{+ 6O_2 \dashrightarrow 6CO_2 + 6H_2O}$$

The "metabolic water" thus formed from stored fuels is actually enough to allow some animals in very dry habitats (gerbils, kangaroo rats, camels) to survive without drinking water for extended periods.

Green plants and algae use the energy of sunlight (represented by h v, the energy of light of frequency v; h is Planck's constant) to split water in the process of photosynthesis:

$$2\ H2O + 2A \xrightarrow{hv} O2 + 2AH2$$

In this reaction, A is an electron-accepting species, which varies with the type of photosynthetic organism.

The Fitness of the Aqueous Environment for Living Organisms

Organisms have effectively adapted to their aqueous environment and have even evolved means of exploiting the unusual properties of water. The high specific heat of water (the heat energy required to raise the temperature of 1 g of water by 1) is useful to cells and organisms because it allows water to act as a "heat buffer," permitting the temperature of an organism to remain relatively constant as the temperature of the air fluctuates and as heat is generated as a byproduct of metabolism. Furthermore, some vertebrates exploit the high heat of vaporization of water by using (thus losing) excess body heat to evaporate sweat. The high degree of internal cohesion of liquid water, due to hydrogen bonding, is exploited by plants as a means of transporting dissolved nutrients from the roots to the leaves during the process of transpiration. Even the lower density of ice than of liquid water has important biological consequences in the life cycles of aquatic organisms. Ponds freeze from the top down, and the layer of ice at the top insulates the water below from frigid air, preventing the pond (and the organisms in it) from freezing solid. Most fundamental to all living organisms is the fact that many physical and biological properties of cell macromolecules, particularly the proteins and nucleic acids, derive from their interactions with water molecules of the surrounding medium. The influence of water on the course of biological evolution has been profound and determinative. If life forms have evolved elsewhere in the universe, it is unlikely that they resemble those of earth, unless their extraterrestrial origin is also a place in which plentiful liquid water is available as solvent.

Possible Questions

2 marks

1. Define cell
2. List any two unique properties of water
3. What do you mean by buffer
4. Why water is so called reactant and fitness of the aqueous environment? Justify
5. List out the important features of ribosomes

8 marks

1. Explain the structure and properties of water
2. Explain about chemical foundation of life
3. Discuss about weak interactions in aqueous system
4. Explain any four organelles in plant cell and its functions
5. Explain in detail about water as a reactant molecule
6. Discuss about the chemical foundation of life
7. Discuss about cellular foundation of life
8. Give a detail account on buffer
9. Discuss in detail about ionization of water
10. Explain in detail about cellular foundation of life

KARPAGAM ACADEMY OF HIGHER EDUCATION
DEPARTMENT OF BIOCHEMISTRY
I-B.Sc., BIOCHEMISTRY
19BCU101 - MOLECULES OF LIFE
MULTIPLE CHOICE QUESTIONS

UNIT I

S.No	**Questions**	**Option A**	**Option B**	**Option C**	**Option D**	**Answer**
1	The atoms of metals form	anions	molecules	cation	none of above	**cation**
2	The interaction between highly electron deficient hydrogen and highly electronegative atom is called	Covalent bond	ionic bond	dipole-dipole interaction	hydrogen bond	**hydrogen bond**
3	Non-metals have	high ionization energies	low ionization energies	zero ionization energy	infinite ionization energy	**high ionization energies**

4	The two F-atoms share one electron in their outermost shell to gain electronic configuration of	Xe	Ar	Kr	Ne	**Ne**
5	The number of electrons lost by atoms of group IIIA equals	2	4	5	3	**3**
6	When partial positive end of one molecule is attracted weakly to partial negative end then force between them is	coulomb's force	electrostatic force	dipole-dipole interaction	ionic bond	**dipole-dipole interaction**
7	In NaCl crystal each Na+ ion is surrounded by	6 Cl- ions	6 Na+ ions	8 Cl- ions	12 Cl- ions	**6 Cl- ions**

8	Which of the following statements about the properties of life is false?	All organisms have the ability to take in energy and use it	All organisms have the ability to respond to stimuli from the environment	All organisms have the ability to reproduce	All organisms have the ability to maintain a constant internal temperature	**All organisms have the ability to maintain a constant internal temperature**
9	Which of the following is not one of the seven properties and processes that we associate with life?	Order	Balance	Regulation	Energy processing	**Balance**
10	If a solution has to be a buffer, its pH should be	At its pKa value	At is Ka value	At 7	At 14	**At its pKa value**
11	Buffers are mixtures of:	Strong acid and strong base	Strong acid and weak base	Weak acid and their conjugate base	Weak base and their conjugate acid	**Weak acid and their conjugate base**
12	As the pKa of an acid increases, the acid will be:	More weaker	More stronger	Converted to neutral solution	Converted to basic solution	**More weaker**

13	At room temperature most of ionic compounds are	amorphous solids	crystalline solids	liquids	gases	**crystalline solids**
14	The ratio of hydrogen (H) and oxygen (O) in water molecule by volume is	2: 1	1: 2	3: 1	4.1	**2: 1**
15	The density of water becomes maximum at	10°C	4°C	5°C	12°C	**4°C**
16	What percentage of fresh water is available to man?	20%	2%	0.20%	None of these	**0.20%**
17	What is the percentage of water from rivers and lakes?	0.001%	0.2%	0.6%	2.10%	**0.2%**
18	What is the percentage of ground water?	0.001%	0.2%	0.6%	2.10%	**0.6%**

19	Oxygen belongs to group VIA so number of electrons in its valence shell are	6	7	8	4	**6**
20	Electron pairs which are not shared by atoms are called	electron pairs	lone pairs	proton pairs	shell pairs	**lone pairs**
21	The strength of intermolecular forces from ionic or covalent bond is	weaker	stronger	equal	none of above	**weaker**
22	Ionic crystals have	low melting points	moderate melting points	high melting points	none of above	**high melting points**
23	The bond formed by mutual sharing of electron is	ionic bond	coordinate covalent bond	covalent bond	none of above	**covalent bond**

24	The covalent compound among the following is	NaCl	MgO	H2O	KF	**H2O**
25	The melting point of table salt is	800°C	801°C	901°C	1000°C	**801°C**
26	The bacterium E. coli requires simple organic molecules for growth and energy—it is therefore a:	chemoautotroph.	chemoheterotroph.	lithotroph..	photoautotroph	**chemoheterotroph.**

27	The three-dimensional structure of macromolecules is formed and maintained primarily through noncovalent interactions. Which one of the following is not considered a noncovalent	carbon-carbon bonds	hydrogen bonds	hydrophobic interactions	ionic interactions	carbon-carbon bonds
28	Which one of the following is not among the four most abundant elements in living organisms?	Carbon	Hydrogen	Oxygen	Phosphorus	**Phosphorus**

29	The macromolecules that serve in the storage and transmission of genetic information are:	carbohydrates.	lipids.	membranes.	nucleic acids.	**nucleic acids.**
30	Stereoisomers that are nonsuperimposable mirror images of each other are known as:	anomers.	cis-trans isomers.	diastereoisomers.	enantiomers	**enantiomers**
31	The major carrier of chemical energy in all cells is:	acetyl triphosphate.	adenosine monophosphate. .	adenosine triphosphate.	cytosine tetraphosphate	**adenosine triphosphate.**
32	Energy requiring metabolic pathways that yield complex molecules from simpler precursors are:	amphibolic.	anabolic.	autotrophic.	catabolic.	**anabolic.**

33	Which of these statements about hydrogen bonds is not true?	Hydrogen bonds account for the anomalously high boiling point of water.	In liquid water, the average water molecule forms hydrogen bonds with three to four other water molecules.	Individual hydrogen bonds are much weaker than covalent bonds.	Individual hydrogen bonds in liquid water exist for many seconds and sometimes for minutes.	**Individual hydrogen bonds in liquid water exist for many seconds and sometimes for minutes.**
34	What is the molecular weight of water?	10 g/mol	15 g/mol	18 g/mol	20 g/mol	**18 g/mol**
35	What is the H+ ion concentration in pure water?	1 X 10-7 m	1 X 107 m	1 X 10-14 m	1 X 1014 m	**1 X 10-7 m**
36	The equilibrium constant of ionization reaction of pure water is ____.	1.8 X 10-14 M	1.8 X 10-16 M	1.8 X 10-7 M	1.8 X 10-7 M	**1.8 X 10-16 M**

37	The pH of pure water is neutral, the best explanation for this is ______.	The pH of pure water is 7	In pure water the concentration of H+ and OH– are same	Water do not contain free H+ or OH– ions	What will never ionize	**In pure water the concentration of H+ and OH– are same**
38	The most important peculiarity of water when compared to other solvents is that water has	High boiling point, high melting point and high heat of vaporization	Low boiling point, high melting point and low heat of vaporization	High boiling point, low melting point and low heat of vaporization	Low boiling point, low melting point and low heat of vaporization	**High boiling point, high melting point and high heat of vaporization**
39	What is the approximate strength of hydrogen bonds in water (in kJ . mol-1)	0.2	2	20	100	**20**
40	A mixture that has uniform composition throughout is called	saturated solution	super saturated solution	solution	solvent	**solution**

41	The substance present in lesser amount in solution is	solute	solvent	aqueous solvent	none of above	**solute**
42	In air the nitrogen gas acts as	solute	solvent	gaseous solute	aqueous solute	**solvent**
43	Water is liquid at room temperature, the most important reason for this is the:	a. High boiling point of water	High melting point of water	High heat of vaporization of water	Cohesive forces due to hydrogen bonds in water	**Cohesive forces due to hydrogen bonds in water**
44	Water is a ___	a. Polar solvent	b. Non polar solvent	c. An amphipathic solvent	d. Non polar uncharged solvent	**Polar solvent**
45	Polar molecules can readily dissolve in water. This is because:	a. Polar molecules can form hydrogen bonds with water	b. Polar molecules can replace water-water interaction with more energetically favourable water-solute interactions	c. Polar charged water can interact with the charge of polar molecules	d. All polar molecules are amphipathic in nature	**Polar molecules can replace water-water interaction with more energetically favourable water-solute interactions**

46	Most important reason for the unusual properties of water is:	a. The covalent bonding pattern in water molecule	b. The bond angle between the two hydrogen atoms in water	Hydrogen bonding between water molecules	Water can be immediately ionized at room temperature	**Hydrogen bonding between water molecules**
47	The H – O – H bond angle in water molecule is:	a. 104.0o	b. 104.5o	c. 105.0o	d. 105.5o	**104.5o**
48	Which of the following statement is true regarding the electronegativity of atoms in water molecule ?	Hydrogen is more electronegative than oxygen	Hydrogen is less electronegative than oxygen c.	Electronegativity of hydrogen and oxygen is same	Oxygen and hydrogen do not have significant electronegativity in water	**Hydrogen is less electronegative than oxygen**
49	Which of the following represent the current melting point, boiling point and heat of vaporization of water?	a. 0oC ; 100oC ; 2260 J/g	100oC ; 0oC ; 2260 J/g	c. 0oC ; 100oC ; 1260 J/g	d. 100oC ; 0oC ; 1260 J/g	**0oC ; 100oC ; 2260 J/g**

50	The oxygen atom in the water molecule due to its high electronegativity bears ________	1 δ+ charge	2 δ+ charges	1 δ– charge	2 δ– charges	**2 δ– charges**
51	Hydrogen bond is best represented as the electrostatic attraction between:	A hydrogen covalently bounded to an electronegative atom and another hydrogen atom	A hydrogen covalently bounded to an electronegative atom and another electronegative atom	Two electronegative atoms and a hydrogen atom	Two hydrogen atoms	**A hydrogen covalently bounded to an electronegative atom and another electronegative atom**
52	A hydronium ion	is a hydrated hydrogen ion	is a hydrated proton	is the usual form of one of the dissociation products of water in solution	all the options	**all the options**
53	The pH of a solution of 1 M HCl is	0	0.1	1	0.01	**0**
54	The aqueous solution with the lowest pH is	0.01 M HCl.	0.1 M HCl	0.1 M acetic acid	10–12 M NaOH	**0.1 M HCl**

55	In which reaction below does water not participate as a reactant	Conversion of an acid anhydride to two acids	Conversion of ATP to ADP	Photosynthesis	Production of gaseous carbon dioxide from bicarbonate	**Production of gaseous carbon dioxide from bicarbonate**
56	Which of the following properties of water does not contribute to the fitness of the aqueous environment for living organisms?	Cohesion of liquid water due to hydrogen bonding	High heat of vaporization	High specific heat	The very low molecular weight of water	**The very low molecular weight of water**
57	The bond dissociation energy of hydrogen bonds in water molecule is	10 kJ / mol	23 kJ/mol	470 kJ/mol	348 kJ/mol	**23 kJ/mol**
58	Which of the following statement is correct regarding the hydrogen bonds in water?	Hydrogen bond is 10 % covalent and 90 % electrostatic	Hydrogen bond is 25% covalent and 75 % electrostatic	Hydrogen bond is 50% covalent and 50% electrostatic	Hydrogen bond is 100 % electrostatic	**Hydrogen bond is 10 % covalent and 90 % electrostatic**

59	A single water molecule can form how many hydrogen bonds at a time?	1	2	3	4	**4**
60	The life span of a hydrogen bond between two water molecule in liquid water is:	1 – 20 seconds	1 – 20 microseconds	1 – 20 nano-seconds	1 – 20 pico-seconds	**1 – 20 pico-seconds**
61	The bond dissociation energy of O – H bond in water is:	470 kJ/mol	348 kJ/mol	23 kJ/mol	10 kJ/mol	**470 kJ/mol**
62	What is the bond length of hydrogen bond between two water molecules in liquid water?	0.0177 nm	0.177 nm	1.177 nm	17.70 nm	**0.177 nm**
63	Water is composed of what two elements?	oxygen and nitrogren	oxygen and hydrogen	protons and neutrons	hydrogen and electrons	**oxygen and hydrogen**

6	The elements of a water molecule are held together by which type of bond?	ionic bond	hydrogen bond	double bond	covalent bond	**covalent bond**
65	Cohesion occurs due to which type of bonding?	ionic	covalent	Hydrogen bond is 50% covalent and 50% electrostatic	double	**Hydrogen bond is 50% covalent and 50% electrostatic**
66	Normal pH of blood is _____.	7	7.2	7.3	7.4	**7.4**
67	The heat of vaporization of water molecule at atmospheric temperature is ______.	2260 J/g	1260 J/g	2260 k.cal	1260 k.cal	**2260 J/g**
68	The water level in the human body is regulated by the hormone _____	ACTH	Oxytocin	FSH	Epinephrine	**Oxytocin**

69	The polarity of water molecule is due to _________.	Difference in electronegativity of oxygen and hydrogen atoms in water	The readily ionizing behavior of water	The positive charge of water molecule	The negative charge of water molecule	**Difference in electronegativity of oxygen and hydrogen atoms in water**
70	The vander Waals radius of hydrogen atom in water molecule is _________.	1.2 Å	1.4 Å	1.6 Å	1.8 Å	**1.2 Å**
71	What is the temperature at which water reaches maximum	32 degrees ferenheit	4 degrees celcius	100 degress celcius	0 degress celcius	**4 degrees celcius**
72	What how does water arrange around ions?	water froms a hydration shell	the more positve atoms attach to negative ions	the more negative atoms attach to positive ions	all of these answers are true	**all of these answers are true**

73	Why do the atoms of a water molecule have partial charges?	opposites attract	there is an unequal sharing of electrons between the atoms	oxygen donates an electron to hydrogen	hydrogen donates an electron to oxygen	**there is an unequal sharing of electrons between the atoms**
74	What is a polar molecule ?	a molecule with opposite charges at opposite ends	a molecule with no charge	a molecule with an unequal number of protons and electrons	a molecule with identical charges at opposite ends	**a molecule with opposite charges at opposite ends**
75	Which of the following is not one of water's special properties?	High Specific Heat Capacity	High Viscosity	High Surface Tension	Density Anomally	**High Viscosity**
76	Water falling from clouds forms a rain drop because of what?	viscosity	covalent bonding	adhesion	cohesion	**cohesion**
77	Water stuck to the windshield is an example of what?	cohesion	viscosity	adhesion	covalent bonding	**adhesion**

UNIT II
SYLLABUS

Carbohydrates and glycobiology: Monosaccharides - structure of aldoses and ketoses, ring structure of sugars, conformations of sugars, mutarotation, anomers, epimers and enantiomers, structure of biologically important sugar derivatives, oxidation of sugars. Formation of disaccharides, reducing and non-reducing disaccharides. Polysaccharides – homo- and heteropolysaccharides, structural and storage polysaccharides. Structure and role of proteoglycans, glycoproteins and glycolipids (gangliosides and lipopolysaccharides). Carbohydrates as informational molecules, working with carbohydrates.

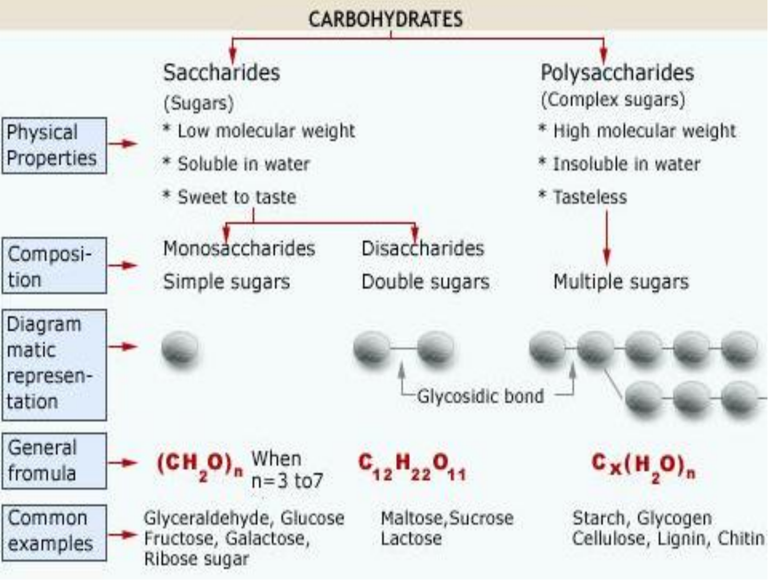
CARBOHYDRATES AND GLYCOBIOLOGY

Introduction:

A carbohydrate is an organic compound with the empirical formula $C_m(H_2O)_n$; that is, consists only of carbon, hydrogen, and oxygen, with hydrogen: oxygen atom ratio of 2:1 (as in water).
Carbohydrates participate in a wide range of functions

- They are the most abundant dietary source of energy (a Cal/S) for all organisms.
- Carbohydrates are precursors for many organic compounds (fats, amino acids).
- Carbohydrates (as glycoproteins and glycol-lipids) participate in the structure of cell membrane and cellular functions such as cell growth, adhesion and fertilization.
- They are structural components of many organisms. These include the fiber (cellulose) of plants, exoskeleton of some insects and the cell wall of microorganisms.
- Carbohydrates also serve as the storage form of energy (glycogen) to meet the immediate energy demands of the body.

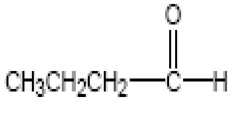
Classification:



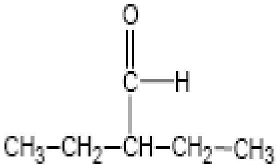
Characteristics of aldehyde and keto groups:

Aldehyde:

- Select the longest carbon chain containing the carbonyl carbon.
- The -e ending of the parent alkane name is replaced by the suffix -al.
- The carbonyl carbon is always numbered “1.” (It is not necessary to include the number in the name.)
- Name the substituents attached to the chain in the usual way.



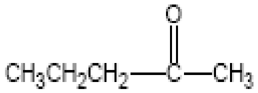
$CH_3CH_2CH_2-\overset{\overset{O}{\|}}{C}-H$



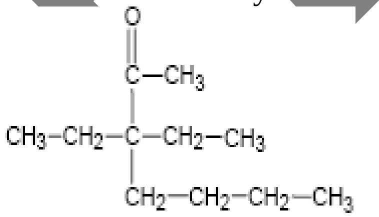
$CH_3-CH_2-\overset{\overset{\overset{O}{\|}}{C}-H}{\overset{|}{CH}}-CH_2-CH_3$

Ketones

- Select the longest carbon chain containing the carbonyl carbon.
- The -e ending of the parent alkane name is replaced by the suffix -one.
- Number the chain starting with the end closest to the ketone group (i.e., the carbonyl carbon should have the lowest possible number).
- Name the substituents attached to the chain in the usual way.



$CH_3CH_2CH_2-\overset{\overset{O}{\|}}{C}-CH_3$



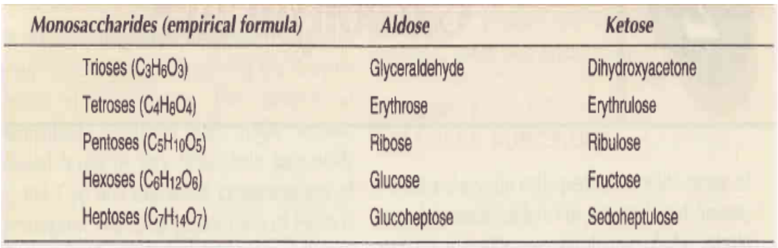
$CH_3-CH_2-\overset{\overset{\overset{O}{\|}}{C}-CH_3}{\overset{|}{C}}-CH_2-CH_3$ with $-CH_2-CH_2-CH_2-CH_3$ below the central C

ACTION OF ACIDS AND ALKALIES ON SUGARS:

- A sugar loses water on being heated with strong mineral acid, and forms furtural derivatives.
- These furfurals may from colored complexes with α-naphthol, thymol, resorcinol, orinol and phloroglucinol.
- On treatment with dilute aqucous alkali solutions, both aldose and ketose are changed to enediols which are good reducing agents.
- Only sugars with a free aldehyde or ketose group can form enediols because the reaction involves the free aldehyde or ketonyl C= O group.
- Glucose and fructose form a common 1,2 enediol in dilute alkaline solutions.

Monosaccharides:

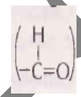
- Monosaccharides (G reek: mono-one) are the simplest group of carbohydrates and are often referred to as simple sugars.
- They have the general formula $Cn(H_2O)_n$, and they cannot be further hydrolysed.
- The monosaccharides are divided into different categories, based on the functional group and the number of carbon atoms.

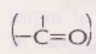


Monosaccharides (empirical formula)	Aldose	Ketose
Trioses ($C_3H_6O_3$)	Glyceraldehyde	Dihydroxyacetone
Tetroses ($C_4H_8O_4$)	Erythrose	Erythrulose
Pentoses ($C_5H_{10}O_5$)	Ribose	Ribulose
Hexoses ($C_6H_{12}O_6$)	Glucose	Fructose
Heptoses ($C_7H_{14}O_7$)	Glucoheptose	Sedoheptulose

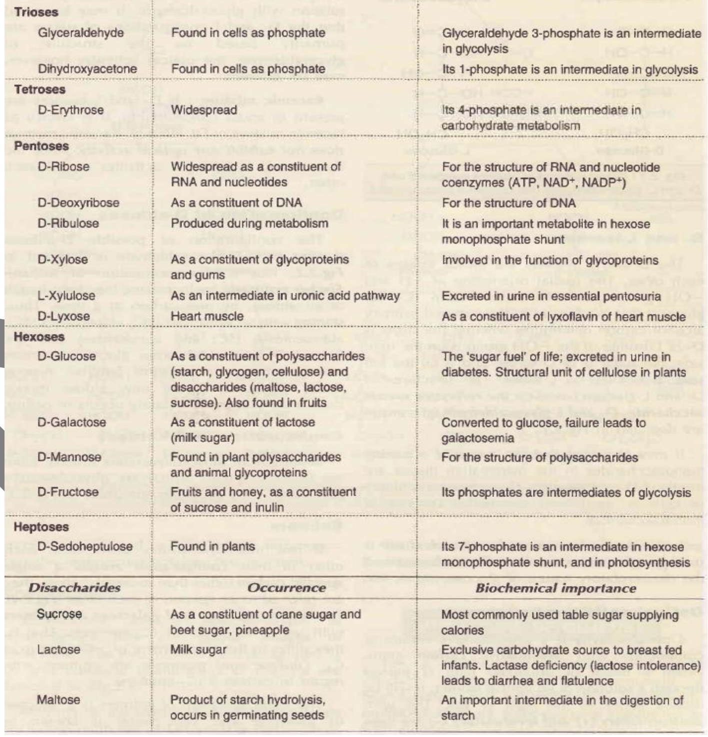
Classification of monosaccharide with selected examples

Structure of aldoses and ketoses

Aldoses: When the functional group in monosaccharides in aldehyde  $\left(\begin{array}{c}H\\|\\-C=O\end{array}\right)$ they are known as aldoses. Eg. glyceraldehyde, glucose.

Ketoses: When the functional group is a keto  $\left(\begin{array}{c}|\\-C=O\end{array}\right)$ group, they are referred to as ketoses Eg. dihydroxyacetone, fructose.

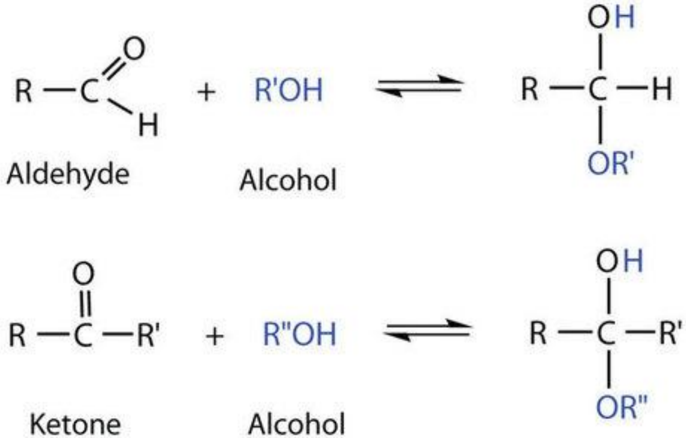
- Based on the number of carbon atoms, the monosaccharides are regarded as trioses (3C), tetroses (4C), pentoses (5C), hexoses (6C) and heptoses (7C).
- These terms along with functional groups are used while naming monosaccharides.
- For instance, glucose is an aldohexose while fructose is a ketohexose.
- The common monosaccharides and disaccharides of biological importance are given.



Monosaccharides	*Occurrence*	*Biochemical importance*
Trioses		
Glyceraldehyde	Found in cells as phosphate	Glyceraldehyde 3-phosphate is an intermediate in glycolysis
Dihydroxyacetone	Found in cells as phosphate	Its 1-phosphate is an intermediate in glycolysis
Tetroses		
D-Erythrose	Widespread	Its 4-phosphate is an intermediate in carbohydrate metabolism
Pentoses		
D-Ribose	Widespread as a constituent of RNA and nucleotides	For the structure of RNA and nucleotide coenzymes (ATP, NAD^+, $NADP^+$)
D-Deoxyribose	As a constituent of DNA	For the structure of DNA
D-Ribulose	Produced during metabolism	It is an important metabolite in hexose monophosphate shunt
D-Xylose	As a constituent of glycoproteins and gums	Involved in the function of glycoproteins
L-Xylulose	As an intermediate in uronic acid pathway	Excreted in urine in essential pentosuria
D-Lyxose	Heart muscle	As a constituent of lyxoflavin of heart muscle
Hexoses		
D-Glucose	As a constituent of polysaccharides (starch, glycogen, cellulose) and disaccharides (maltose, lactose, sucrose). Also found in fruits	The 'sugar fuel' of life; excreted in urine in diabetes. Structural unit of cellulose in plants
D-Galactose	As a constituent of lactose (milk sugar)	Converted to glucose, failure leads to galactosemia
D-Mannose	Found in plant polysaccharides and animal glycoproteins	For the structure of polysaccharides
D-Fructose	Fruits and honey, as a constituent of sucrose and inulin	Its phosphates are intermediates of glycolysis
Heptoses		
D-Sedoheptulose	Found in plants	Its 7-phosphate is an intermediate in hexose monophosphate shunt, and in photosynthesis
Disaccharides	*Occurrence*	*Biochemical importance*
Sucrose	As a constituent of cane sugar and beet sugar, pineapple	Most commonly used table sugar supplying calories
Lactose	Milk sugar	Exclusive carbohydrate source to breast fed infants. Lactase deficiency (lactose intolerance) leads to diarrhea and flatulence
Maltose	Product of starch hydrolysis, occurs in germinating seeds	An important intermediate in the digestion of starch

Ring structure of sugars

Monosaccharides as linear molecules, but many of them also adopt cyclic structures. This conversion occurs because of the ability of aldehydes and ketones to react with alcohols:



In some cases, OH and carbonyl groups on the same molecule are able to react with one another in an intramolecular reaction. Thus, monosaccharides larger than tetroses exist mainly as cyclic compounds (Figure 16.4.116.4.1). You might wonder why the aldehyde reacts with the OH group on the fifth carbon atom rather than the OH group on the second carbon atom next to it. Recall that cyclic alkanes containing five or six carbon atoms in the ring are the most stable. The same is true for monosaccharides that form cyclic structures: rings consisting of five or six carbon atoms are the most stable.

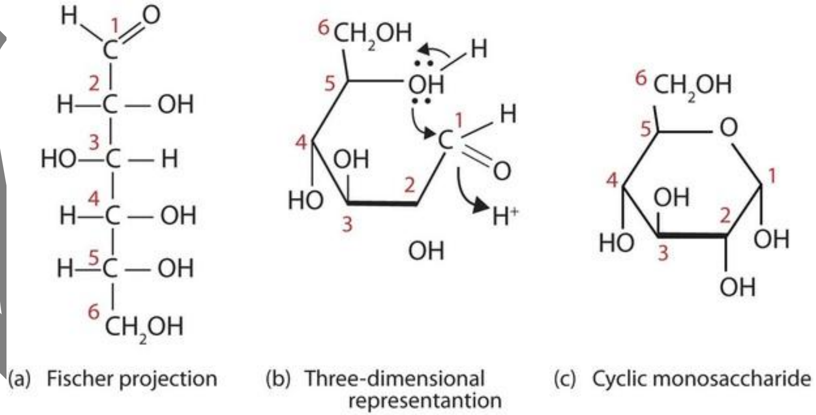


Figure 16.4.116.4.1*: Cyclization of D-Glucose. D-Glucose can be represented with a Fischer projection (a) or three dimensionally (b). By reacting the OH group on the fifth carbon atom with the aldehyde group, the cyclic monosaccharide (c) is produced.*

When a straight-chain monosaccharide, such as any of the structures shown in Figure 16.4.116.4.1, forms a cyclic structure, the carbonyl oxygen atom may be pushed either up or down, giving rise to two stereoisomers, as shown in Figure 16.4.216.4.2. The structure shown on the left side of Figure 16.4.216.4.2, with the OH group on the first carbon atom projected downward, represent what is called the *alpha (α) form*. The structures on the right side, with the

OH group on the first carbon atom pointed upward, is the *beta (β) form*. These two stereoisomers of a cyclic monosaccharide are known as anomers; they differ in structure around the anomeric carbon—that is, the carbon atom that was the carbonyl carbon atom in the straight-chain form.

It is possible to obtain a sample of crystalline glucose in which all the molecules have the α structure or all have the β structure. The α form melts at 146°C and has a specific rotation of +112°, while the β form melts at 150°C and has a specific rotation of +18.7°. When the sample is dissolved in water, however, a mixture is soon produced containing both anomers as well as the straight-chain form, in dynamic equilibrium (part (a) of Figure 16.4.216.4.2). You can start with a pure crystalline sample of glucose consisting entirely of either anomer, but as soon as the molecules dissolve in water, they open to form the carbonyl group and then reclose to form either the α or the β anomer. The opening and closing repeats continuously in an ongoing interconversion between anomeric forms and is referred to as mutarotation (Latin *mutare*, meaning "to change"). At equilibrium, the mixture consists of about 36% α-D-glucose, 64% β-D-glucose, and less than 0.02% of the open-chain aldehyde form. The observed rotation of this solution is +52.7°.

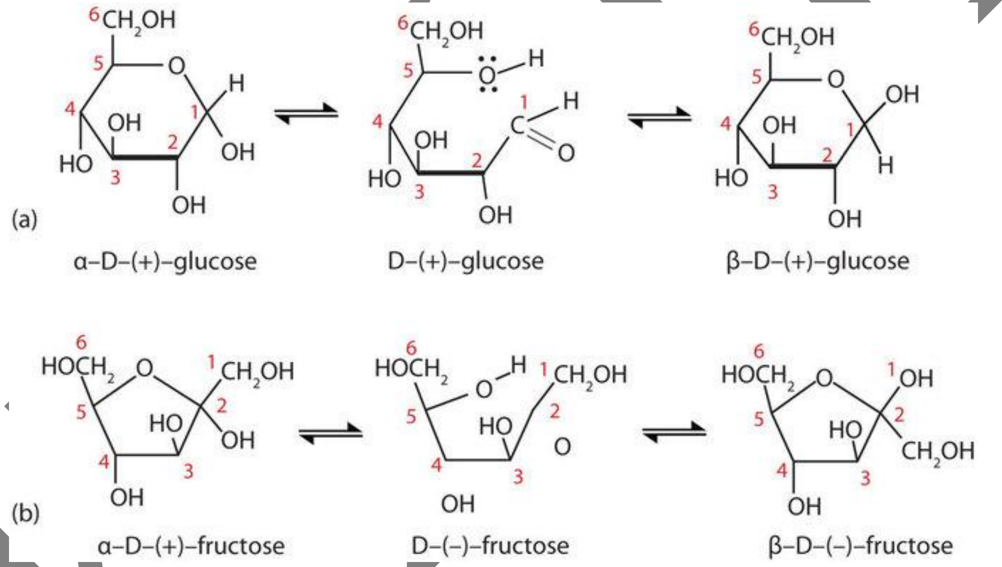


Figure 16.4.216.4.2*: Monosaccharides. In an aqueous solution, monosaccharides exist as an equilibrium mixture of three forms. The interconversion between the forms is known as mutarotation, which is shown for D-glucose (a) and D-fructose (b).*

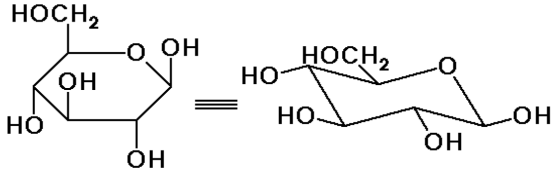
Even though only a small percentage of the molecules are in the open-chain aldehyde form at any time, the solution will nevertheless exhibit the characteristic reactions of an aldehyde. As the small amount of free aldehyde is used up in a reaction, there is a shift in the equilibrium to yield more aldehyde. Thus, *all* the molecules may eventually react, even though very little free aldehyde is present at a time.

Commonly, (e.g., in Figures 16.4.116.4.1 and 16.4.216.4.2) the cyclic forms of sugars are depicted using a convention first suggested by Walter N. Haworth, an English chemist. The molecules are drawn as planar hexagons with a darkened edge representing the side facing toward the viewer. The structure is simplified to show only the functional groups attached to the carbon atoms. Any group written to the right in a Fischer projection appears below the plane of the ring in a Haworth projection, and any group written to the left in a Fischer projection appears above the plane in a Haworth projection.

The difference between the α and the β forms of sugars may seem trivial, but such structural differences are often crucial in biochemical reactions. This explains why we can get energy from the starch in potatoes and other plants but not from cellulose, even though both starch and cellulose are polysaccharides composed of glucose molecules linked together.

Conformations of Sugars

- 5-membered rings are close to planar
  (Haworth projections are OK)
- 6-membered rings are chair conformations
  (Haworth projections are inaccurate)
- from a Haworth 6-membered ring,
  flex the right down and the left up



β-D-glucopyranose

- beta-D-glucose has every substituent equatorial (most stable)

Stereochemistry:

- Carbon 2 of glyceradehyde is a chiral center.
- There are thus 3 steroisomers of glyceraldehydes: D-glyceraldehyde and L-glyceraldehyde.
- By convention, sugars are written with the most oxidized carbon (i.e. aldehyde or ketone) at the top.
- The chiral center farthest from the most oxidized carbon determines if it is D or L.
- If the hydroxyl points to the left, then it is the L configuration if to the right then it is D.
- In general, only the D isomers are used biologically, but there are many exceptions to this generalization.
- Sugars can be conveniently written as Fischer projections to indicate stereochemistry.
- The most oxidized carbon is placed at the top and each carbon between it and the last carbon is a cross from which are appended the hydrogen and hydroxyl group.
- It makes a difference if the hydroxyl group is written to the or lift.
- It is important tp recognize that a Fischer projection indicates the stereochemistry of each chiral center.
- One must imagine that the groups to the left and right (-H and –OH) are coming out the plane towards the viewer, while the substituents above and below are out of the plane directed away from the viewer.

Mutarotation

Carbohydrates are polyhydroxy aldehydes and ketones which can be represented with different configuration. We know that an organic molecule will be optically active if there is no plane of symmetry in the molecule and there is at least one asymmetric carbon atom in the molecule. The asymmetric carbon atom is bonded with 4 different atoms or groups. The optical rotation plays a very important role in the determination of absolute configurations of sugar molecules because they have more than one asymmetric carbon atoms in the molecule.

According to stereoisomerism, an optically active molecule can exist in two isomeric forms which are known as dextro- and leavo- forms. The dextrorotatory form can rotate the plane polarised light in a clockwise manner whereas laevorotatory isomer can rotate the plane polarised light anticlockwise manner. Both of these isomers show same chemical and physical properties but have different optical properties.

Carbohydrates can also classify on the basis of optical rotation. Sugar molecules also show mutarotation which play an important role in the determination of structure of a carbohydrate. Carbohydrate is an important class of naturally occurring organic compounds such as glucose, fructose, maltose, sucrose, lactose starch, etc. The general formula of sugar molecules is Cm(H2O)nCm(H2O)n. Let's discuss about mutarotation in sugar molecules.

D and L Designations - Optical Isomers

Optical Isomers

An optically active compound is one which can rotate a plane polarized light to right or left. An optically active compound can exist in two isomeric forms which rotate the plane-polarized light in opposite directions. The isomer which rotates the light to right are called dextro rotatory or (+) form and the other one, is leavo or (-) form.

Glyceraldehyde contains a central asymmetric carbon atom. Therefore, it exists in two enantiomers, or mirror image isomers.

The enantiomer which rotates the plane of polarized light to right is written as (+) isomer and the other, which rotates plane polarized light to left is (-) isomer. The + and - sign indicates the direction of plane polarized light To left or right.

In 1906, Rosanoff decided arbitrarily that the enantiomer (1) with OH to the right may be designated as D- glyceraldehyde and the other enantiomer (2) (as L-glyceraldehyde.

This was similarly applied to the carbohydrates. The sugars are thus, divided into the D- family and the L-family. The sugars having same configuration as of D- glyceraldehyde at the asymmetric carbon most distant from the carbonyl group are designated as D- sugars. Those with opposite configuration are called as L- sugars. Thus, natural glucose is D(+) Glucose.

What is Mutarotation?

The change in the optical rotation of a solution of either form f glucose until a constant value is obtained is called Mutarotation.

Many sugars, like glucose, fructose, etc exist in α and β form and undergo mutarotation. Example: α -D fructose has a specific rotation of -21°, β - D fructose -133 ° and constant value 92°.

Mutarotation of Glucose

Glucose is the most common monosaccharide. It is known as Dextrose because it occurs in nature principally as the optically active dextroroatory isomer. It is a white crystalline solid, with a melting point of 146°.

Glucose is optically active and the ordinary naturally occurring form is (+) glucose. Two crystalline forms of D-glucose have been isolated.

1. α - D glucose which crystallizes from a concentrated aqueous solution at 30°C and it has a melting point of 146 degree Celsius and specific rotation of +112°.
2. β- D glucose which crystallizes from a hot, glacial acetic acid solution. It melts at 148 to 150 degree Celsius and has a specific rotation of +19 degrees.

When either of these forms of D- glucose is dissolved in water and allowed to stand, a gradual change in specific rotation occurs. The specific rotation of the alpha form falls and that of the beta form rises until a constant value of + 53° is obtained. Thus, two forms of glucose undergoes a phenomenon called as mutarotation. The form with the higher positive rotation is called α-D glucose and that with the lower rotation β-D glucose.

Explanation

Glucose forms a stable cyclic hemiacetal between the aldehyde group and the -OH group on the fifth carbon of glucose. In this process the first carbon becomes asymmetric, giving two isomers (I and II) which differ only in the configuration of the asymmetric carbon.

These are called as anomers and the new asymmetric carbon is referred to as Anomeric carbon. The anomer I with OH to the right is designated as the α - D glucose and the other with OH to the left is called as β-D glucose.

The mutarotation occurs because of the slow interconversion of α - D glucose via the open chain form until equilibrium is established giving a constant specific rotation of + 53°. The concentration of the open chain form and the cyclic forms I and II at equilibrium are 0.01% , 36% and 64% respectively.

Confirmation of Mutarotation

D- (+) Glucose forms two isomeric methyl D-glucosides. Aldehydes, react with alcohols in the presence of anhydrous HCl to form acetals. If the alcohol is, methanol, the acetal contains two methyl groups.

1. When D- (+) - glucose is treated with methanol and HCl, the product, methyl D-glucoside, contains only one -CH_3 group, yet it has properties resembling those of a full acetal. It does not spontaneously revert to aldehyde and alcohol on contact with water, but requires hydrolysis by aqueous acids.

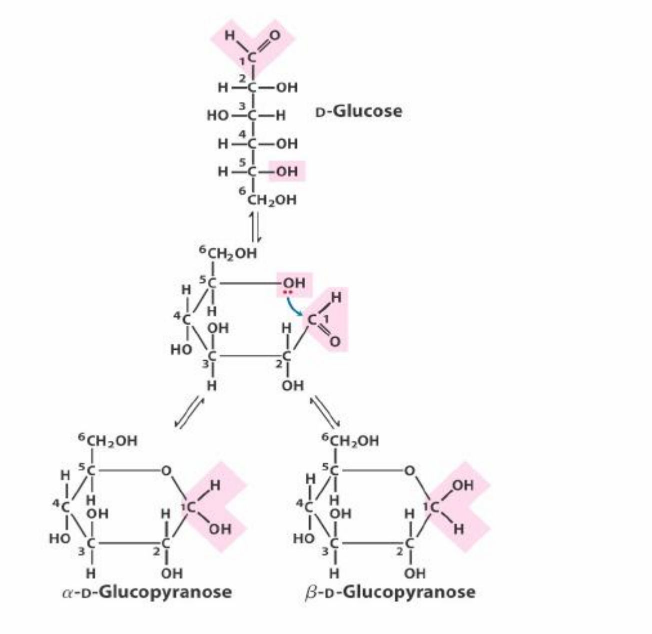
2. Furthermore, not just one but two of those mono methyl derivatives of D- (+) glucose are known, one with melting point of 165^o C and specific rotation +158^o and the other with melting point 107^{o}c and specific rotation -33^o.
3. The isomer of higher positive rotation is called methyl α - D glycoside and the other is called methyl β - D glycoside. These glycosides do not undergo mutarotation and do not reduce Tollen's reagent or Fehling's solution, as Glucose.
4. The two isomers, or anomers, α - D glucose and β- D glucose are diastereomers, differing in configuration about C-1 (first carbon). The mutarotation of these isomers or anomers results from the ready opening and closing of the hemiacetal ring.

Cyclic Structure of Glucose

1. The phenomenon of mutarotation was helpful in deciding the cyclic structure of d-glucose.
2. The french chemist, Tarnet established the existence of two crystalline forms of glucose, α - glucose and β - glucose.
3. Alpha- glucose had a specific rotation of +112^o and β - glucose, +19^o .
4. The optical rotation of each of these forms changed gradually with time till finally, a constant value of +53^o was established.
5. To explain this phenomenon of mutarotation, it was visualized that the α and β forms of glucose were in reality the cyclic hemiacetal forms of glucose which were inter convertible via the open chain form.
6. The constant value of +53^o represented the state of equilibrium between α and β forms of glucose.
7. This fact established why D-glucose can react both as an aldehyde and a cyclic hemiacetal in which CHO is absent.

Anomers

- Isomeric forms of monosaccharides that differ only in their configuration about the hemiacetal or hemiketal carbon atom are called **anomers**. The hemiacetal (or carbonyl) carbon atom is called the **anomeric carbon**. The _ and _ anomers of D-glucose interconvert in aqueous solution by a process called **mutarotation**
- The aldehyde or ketone carbon is referred to as the anomeric carbon, as this is the chiral center that differs between 2 Anomers.
- For D-sugars the anomer has the hydroxyl group down in the Haworth projection and on the same side as the ring oxygen in the Fisher projection.
- The different stereo isomers (α and β) are called Anomers.
- The aldehyde or ketone carbon is referred to as the anomeric carbon, as this is the chiral center that differs between 2 Anomers.
- For D-sugars the α anomer has the hydroxyl group down in the
- Haworth projection and on the same side as the ring oxygen in the Fisher projection.

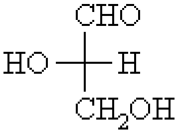


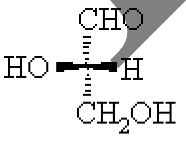
Haworth Projections:

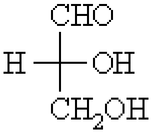
1. If the ring closes on a hydroxyl which points to the right (which it always does), then the hydroxymethyl (hydroxyalkyl) group point up. If the ring closes on a hydroxyl which points to the lift, then the hydroxymethyl (hydroxyalkyl) group points town.
2. The hydroxyls that point to the right in the Fischer projection, point down in the Haworth projection. The hydroxyls that point to the left in the Fischer projection point up in the Haworth projection.
3. For the D series: If the hydroxyl on the anomeric carbon points down, then it is α. It points up, and then the sugar is ß.

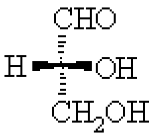
FISCHER PROJECTIONS

Fischer projections are very commonly used to represent sugars as the provide a quick way of representing multiple stereocenters *plus* they can be related to the cyclic sugar structures reasonably easily. Note that Fischer projections of carbohydrates are typically drawn with the longest chain oriented *vertically* and with the more highly oxidised C (the carbonyl group) at the top. Here we see the Fischer projections of the simplest carbohydrate, glyceraldehyde in its (S)-(-)- and (R)-(+)- forms:







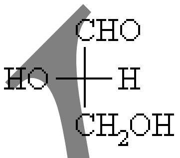


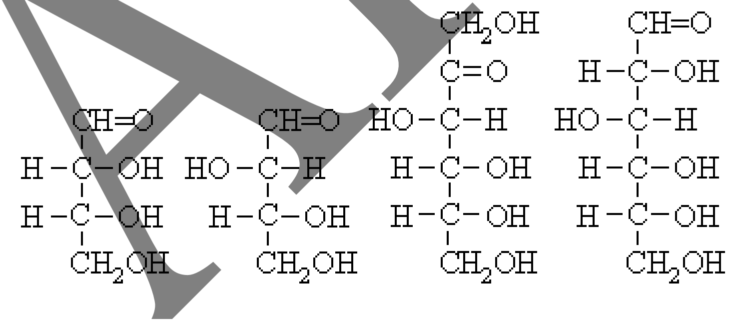
S-(-)-glyceraldehyde
or
L-glyceraldehyde

R-(+)-glyceraldehyde
or
D-glyceraldehyde

The **D-** and **L-** notation is based on these structures. (Note that D- and L- means something quite *different* to *d*-and *l*-).
By **definition** (R)-(+)-glyceraldehyde is D-glyceraldehyde and (S)-(-)-glyceraldehyde is L-glyceraldehyde.
Other carbohydrates are defined as either D- or L- by comparing the stereochemistry at the chirality center next to the -CH_2OH group (*i.e.* with the chirality center furthest from the carbonyl group or the highest numbered chirality center) with the chirality center in glyceraldehyde.

A series of carbohydrates are shown below, decide whether they are D- or L- by comparing them to glyceraldehyde



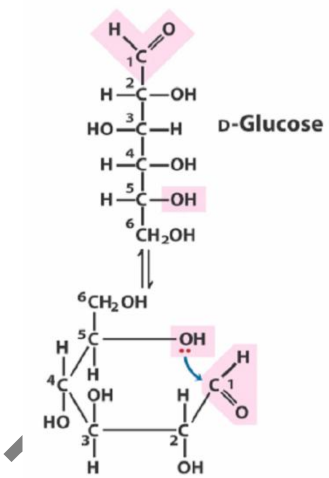


L-glyceraldehyde

Cyclic structure and anomeric forms:

- In aqueous solution, D-glucose exists in one of 2 forms: α-D-glucose and ß-D- glucose.
- This is because Aldehydes can react with alcohols to form a hemiacetal.
- In this case, the hydroxyl oxygen attacking the molecule it is an interamolecular reaction, which results in formation of a ring.
- Rings with 6 members are the most stable, but 5-membered rings are possible.
- The oxygen that attacked the carbonyl carbon will be a member of the ring.
- The carbonyl oxygen is converted to a hydroxyl group in the process.

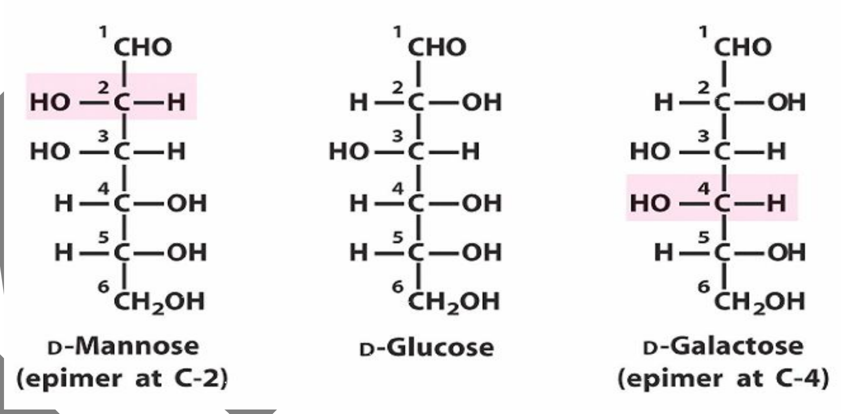
- The stereochemistry of this hydroxyl group is determined by the position of the carbonyl during the attack; it can be one of 2 possible configurations: α or ß.
- Six-member rings resemble pyran and are referred to as pyranosides.
- Five – member rings resemble furan and are referred to as furanosides.



Epimers

Carbohydrates that differ only in their stereochemistry at one position are called Epimers.

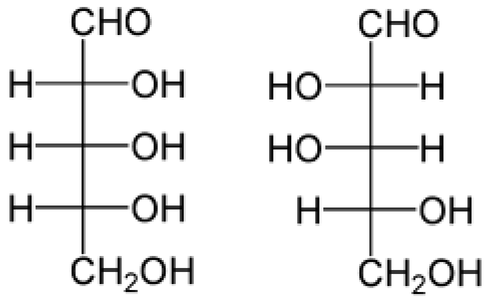
- Eg. Glucose and mannose (C-2)
- Glucose and galactose (C-4)



Enantiomer

- An enantiomer is one of the two molecules that are mirror images of each other and are non-superposable.
- Enantiomers have identical chemical and physical properties except for their ability to rotate plane-polarized light (+/-) by equal amounts but in opposite directions. Enantiomers interact differently with other chiral molecules i.e. biologically active molecules as aminoacids, sugars, steroids etc. This means that some molecules have, for example, different odours. Limonene is just such a case.

- Two chemical structures of mirror-image molecules, i.e. enantiomers, which cannot be superimposed. D-(+)-limonene (left) and L-(-)-limonene (right)
- Enantiomeric excess (ee) is a measure of composition of a mixture of enantiomers. It can be calculated using formula:
- ee = ((R-S)/(R+S)) with R and S, respectively amounts of enantiomer (R) and (S).
- It's an important characteristic since it's difficult to obtain specifically one enantiomer for the chemist. Indeed, contrary to reactions existing in the nature, this class of compounds is often obtained as a mixture of each form in a laboratory. So, an ee of 100% correspond to a perfectly pure enantiomer whereas ee = 0% describe a mixture with enantiomers of each configuration in an equal amount.
- Enantiomeric ratio (er) is a proportion of enantiomer in a mixture. For the historical reasons more often is used measure of Enantiomer excess.



Structure of biologically important sugar derivatives

Carbohydrates are organic compounds consisting of carbon, hydrogen and oxygen. They are present in all cellular organisms. The simple carbohydrates, known as monosaccharides, contain the three component elements C, H and O of which H and O are in the same ratio as that of water.

The number of carbon atoms in simple sugars may be 3, 4, 5, 6 or 7, and the monosaccharides are accordingly known as triose, tetrose, pentose, hexose and heptose, respectively. In biological organisms, these sugars exist generally as esters of phosphoric acid and they serve as intermediates of different metabolic pathways. Among the monosaccharides, pentose's like ribose and deoxyribose are of special importance as constituents of nucleic acids.

Similarly, glucose is the most important among hexose sugars. It serves almost universally as the respiratory substrate. Derivatives of glucose are often the major constituents of cell wall and cell membrane. Thus, amino sugars like glucosamine and their derivatives are the major constituents of the cell walls of bacteria and fungi.

Some of the monosaccharides and their derivatives are shown in Fig. 8.1:

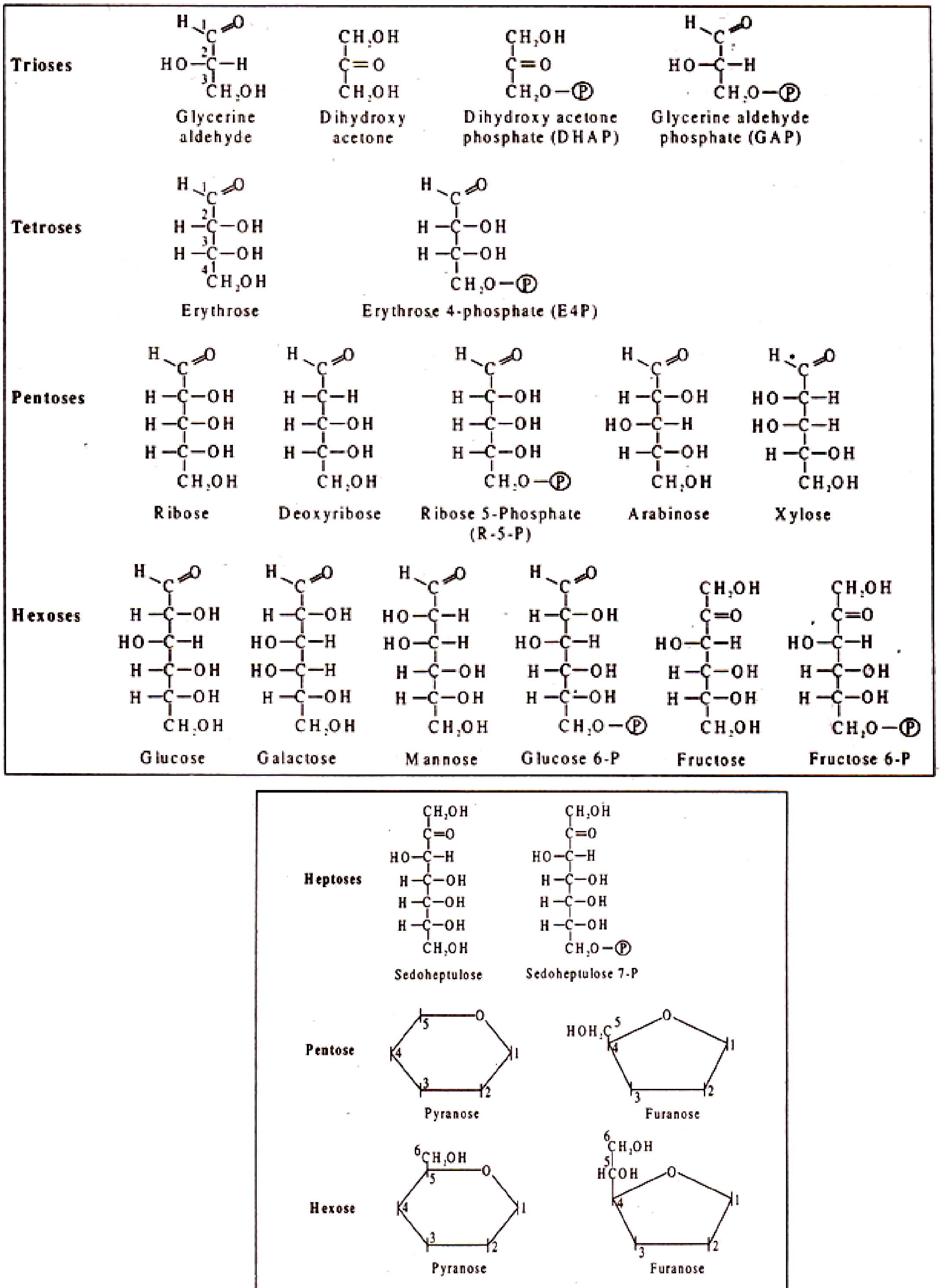
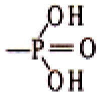


Fig.8.1 : Structures of some monosaccharides and their phosphoric acid esters

Ⓟ Represents



$-P(OH)(=O)OH$

Though for the sake of simplicity, the pentoses and hexoses are often represented in straight-chain form, the physico-chemical properties of sugars show that the $-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-$ bonds are at an angle of about 110° to each other. As a result C1 comes close to C5 and a ring structure is formed which may be five-membered (furanose) or six-membered (pyranose) as shown in the above figure. Monosaccharides are often present in the cells as phosphoesters, where a OH-group of orthophosphoric acid forms an ester bond with the primary alcoholic-OH group ($-CH_2OH$) of the sugar. Monosaccharides may be aldoses or ketoses. Thus, glucose is an aldose having an aldehyde group ($-\overset{O}{\overset{\|}{C}}-H$) at C1 position and fructose is a ketose having a keto ($-\overset{O}{\overset{\|}{C}}-$) group at C2 position. Similarly, aldose and ketose forms of pentoses are ribose and ribulose, xylose and xylulose, etc. All aldoses and ketoses are **reducing sugars** by virtue of their corresponding aldehyde or keto groups.

Another feature of monosaccharides is that, due to the presence of asymmetric C-atoms, they show optical rotation in solution and are present as D- or L- form. Thus, in the simplest monosaccharide, glycerine aldehyde, the C_2 is asymmetric because it has four different substituents — H, OH, CHO and CH_2OH — attached to it. In D-glycerein aldehyde, the asymmetric carbon atom has H on the left side and OH on the right and in the L-form they are opposite.

The monosaccharides play many important roles in metabolism. The two trioses, glycerin aldehyde and dihydroxyacetone, in their phosphorylated form, are involved in the glycolytic pathways as also in the synthetic pathways like the Calvin cycle. The tetrose, erythrose, also as a phophoester, take part in the reductive and oxydative pentose phosphate cycles.

It also serves as an important intermediate in biosynthesis of aromatic compounds. The pentose's — ribose, deoxyribose, ribulose and xylulose — are important intermediates in the biosynthesis of nucleic acids as well as in other metabolic cycles. The hexoses — glucose and fructose — in their phosphorylated forms, are intermediates in glycolytic pathway. Sedoheptulose is an intermediate in the Calvin cycle and in the Pentose Phosphate cycle.

Some derivatives of sugars are of considerable biological importance. Among these are glucosamine and galactosamine, and the uronic acids. In the amino sugars, the -OH group of carbon atom2 is replaced by an amino ($-NH_2$) group. The amino group may be modified by addition of an acetyl ($-CO-CH_3$) group to produce an acetyl amino sugar (Fig. 8.2). Uronic acids are formed by oxidation of the primary alcoholic group at C6 position of hexose to a carboxyl group (-COOH).

Thus, glucose may be converted to glucuronic acid and mannose to mannuronic acid (Fig. 8.2):

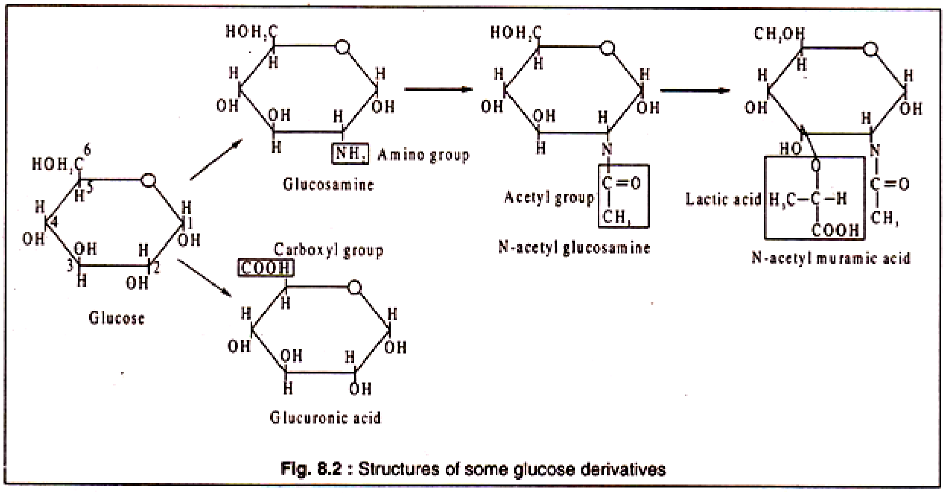


Fig. 8.2 : Structures of some glucose derivatives

N-acetyl glucosamine and N-acetyl muramic acid are constituents of the bacterial cell wall polymer, known as murein. A polymer of N-acetyl-glucosamine is chitin, the major cell wall material of higher fungi. N-acetyl glucosamine is also a constituent of hyaluronic acid present in the animal cells. Glucuronic acid is present in mucopolysaccharides.

Disaccharides are formed by joining two monosaccharide by a glycosidic bond with elimination of a molecule of water. The two monosaccharides may be identical or different. Thus, in maltose there are two glucose molecules, in lactose a glucose and a galactose, in sucrose a glucose and a fructose and so on.

The structures of maltose, lactose and sucrose are shown in Fig. 8.3:

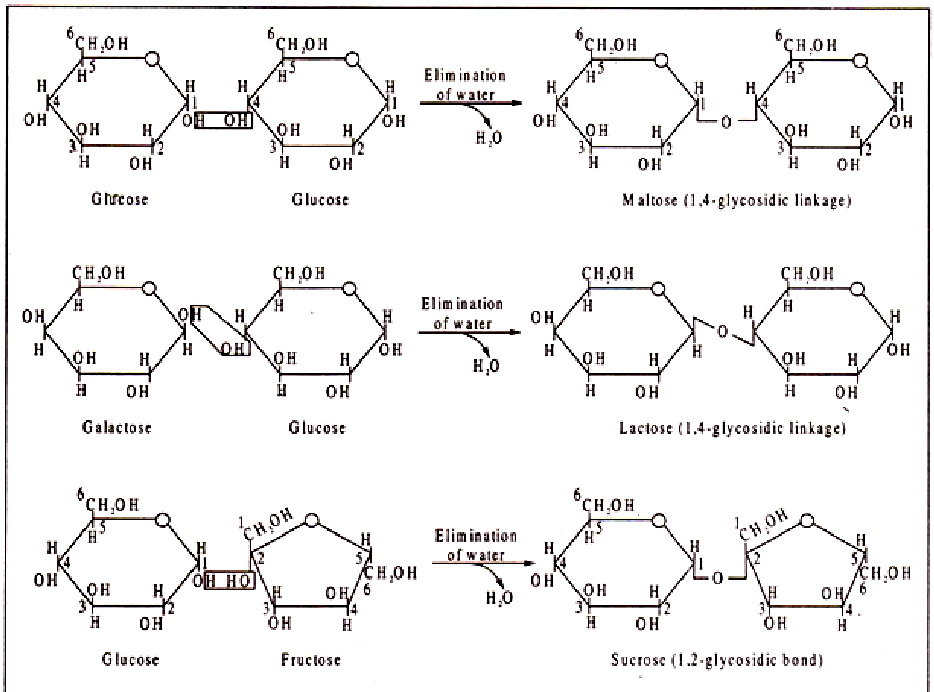


Fig. 8.3 : Formation and structures of three disaccharides — maltose, lactose and sucrose

While all monosaccharides possess reducing properties due to the presence of an aldehyde group in C1 position or a keto group in C2 position, disaccharides may be reducing or non-reducing. In the formation of the glycosidic linkage, C1 aldehyde group is involved resulting in the loss of a reducing group in one of the two monosaccharides.

If the reducing group of the other monosaccharide remains free, the resulting disaccharide still remains a reducing sugar. Thus, maltose and lactose possess reducing property. But, in case of sucrose, the aldehyde group (C1) of glucose and the keto group of fructose (C2) take part in glycosidic bond formation. Hence, sucrose is a non-reducing disaccharide.

Polysaccharides are composed of a large number of monosaccharides bound to each other by glycosidic bonds to form long chains which may be branched or linear. They may contain the same repeating units e.g. starch or glycogen contains only glucose, or may contain different monosaccharides or their derivatives.

The monosaccharides may be pentoses or hexoses. Depending on the nature of monosaccharides, polysaccharides are known as glucan, mannan, galactan, araban, xylan etc. The general formula of pentosans is $(C_5H_8O_4)_n$ and that of hexosans is $(C_6H_{10}O_5)_n$, where n denotes the number of monosaccharide units.

Starch, glycogen and cellulose are all polysaccharides containing glucose. Starch is characteristically formed in green plants as a photosynthetic reserve carbohydrate and serves as a source of carbon to humans. Similarly, cellulose is consumed by herbivorous animals. Glycogen is the main reserve carbohydrate in most animals and many fungi and some bacteria. Both starch and glycogen are branched polymers of glucose. While the straight chain portions of these molecules consist of glucose units linked by 1—>4 glycosidic bonds, the branching points have 1—>6 glycosidic bonds.

The long chains of these molecules are actually spirally coiled (Fig. 8.4):

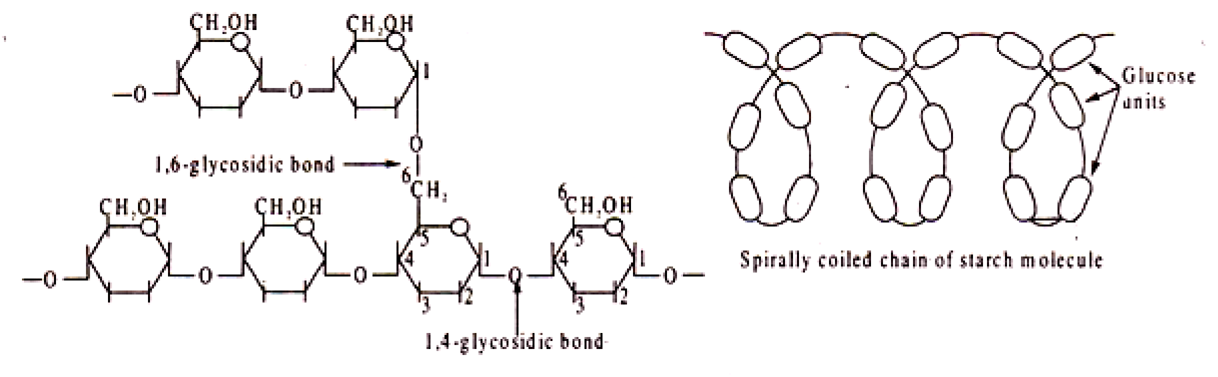


Fig. 8.4 : Branched molecule of starch and its spiral coiling

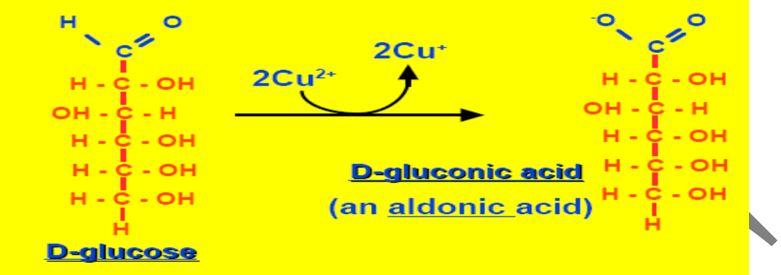
Mucopolysaccharides are composed of disaccharide units consisting of a uronic acid and an amino sugar. Hyaluronic acid is a mucopolysaccharide present in animal tissues. It is a polymer of glucuronic acid and N-acetyl glucosamine.

The capsules of many bacteria are made of complex polysaccharides e.g. capsule of pneumococci Type III is composed of glucuronic acid and glucose. The backbone of bacterial cell wall is a polymer of N-acetyl glucosamine and N-acetylmuramic acid, (see Fig. 8.2).

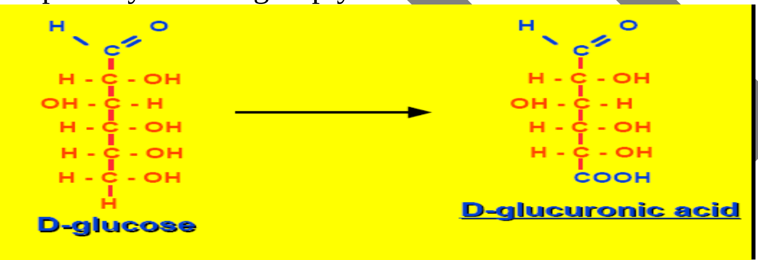
Oxidation of sugars

Reactions of monosaccharide:

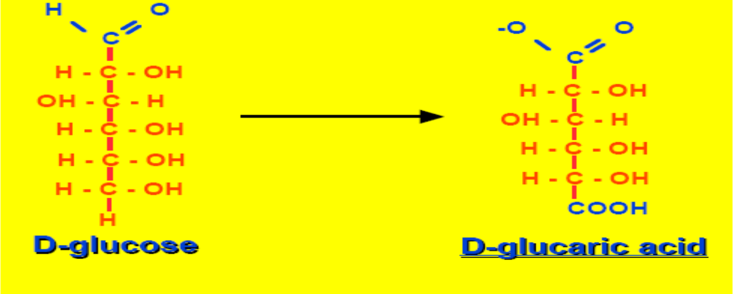
- Can be oxidized by mild oxidizing agents (i.e., ferric or cupric ions). Carbonyl goup is oxidized to a carboxylic acid.



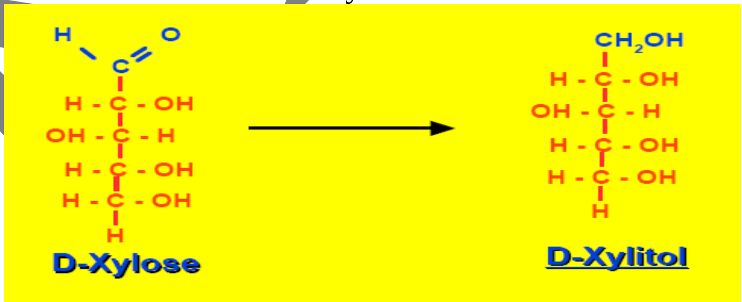
- Oxidation of the primary alcohol group yields a uronic acid:



- Aldoses can be oxidized at both c1 and c6 to yield aldaric acids.



- Aldoses and ketoses can be reduced to yield alditols.



- Sorbitol, mannitol (gum sweetener); glycerol (component of lipids)

Important Reactions of Sugars:

1) Oxidation of Aldehydes

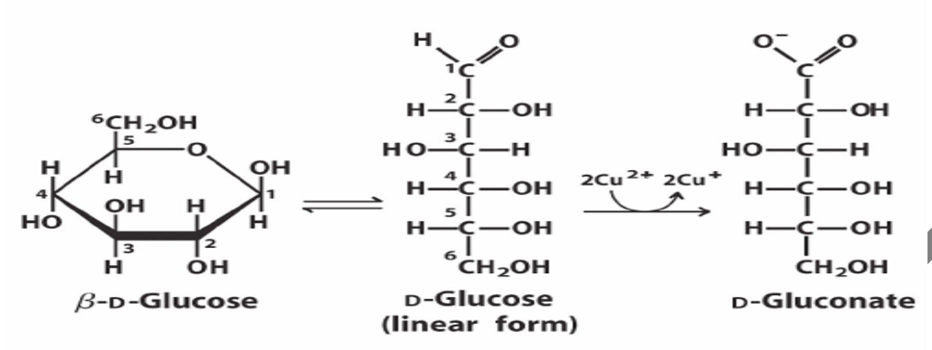
Aldehydes can be oxidized to carboxylic acids. Thus, aldoses are reducing agents. Any sugar that has (or potentially has) a free aldehyde is referred to as a reducing sugar. The name is made by changing the –ose ending to – onic acid (or onate).

Tests for reducing sugars:

a) Fehling's reaction [Cu (II)→ Cu (I)]:

$R\text{-}CHO + 2Cu^{2+} + 5\ OH^{-} \rightarrow R\text{-}CO_2^{-} + Cu_2O + 3\ H_2O$

Visualizad as deposition of Cu_2O (red).



b) **Tollen's reaction** [Ag(I) → Ag(o)]:

$R\text{-}CHO + 2\ Ag\ (NH_3)_2^{+} + 2\ OH^{-} \rightarrow R\text{-}Co_2^{-} + 2\ Ag + 3\ NH_3 + NH_4^{+} + H_2O$

(Visualized as deposition of metabolic silver).

c) Aldehyde can also be oxidized to carboxylic acid by Br_2.

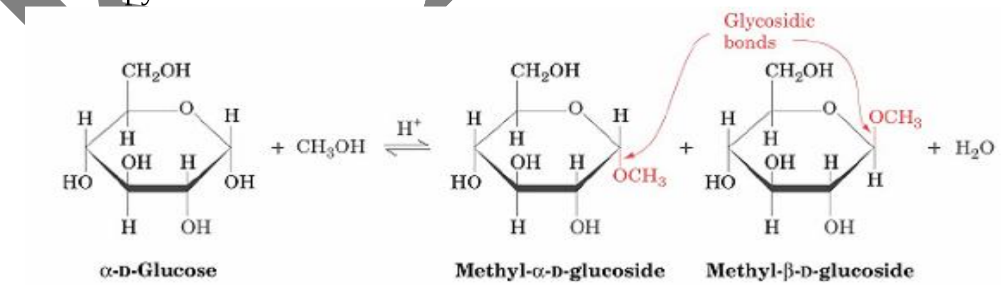
2) Oxidation of primary alcohol:

The CH_2OH group can be oxidized with dilute HNO_3 to a carboxylic acid. These are named with the root of the sugar plus – uronic acid or – aric acid.

(e.g. glucuronic acid is formed by oxidation of glucose).

3) Reaction with alcohols: formation of acetals:

This is one of the most important reactions of sugars, because this is the way they are linked together to form polymers. In its simplest form, one can consider the reaction of methanol with a pyranose:



L - Sugars:

- It is important to realize that the identity stereoisomer is determined by the relative orientations of its substituents (i.e. hydroxyls, etc). The L carbohydrate series represent mirror images to the D sugars.
- To get the configuration of L sugar, start with the D configuration and reverse it:

  - Fischer projection: Change the orientation of every chiral center – if the Hydroxyl points to the left, point it to the right and vice-versa.
  - Haworth projection: Move tham from up to down and vice versa. (The rules for α and β Anomers are reversed: the hydroxyl points up in α and down in β).
- Thus the relative orientation of the substituents is maintained, but you have a mirror image: the enantiomer.

Oligosaccharides:

- Oligosaccharides (Greek: oligo-few) contain 2-10 monosaccharide molecules which are liberated on hydrolysis.
- Based on the number of monosaccharide units present, the oligosaccharides are further subdivided to disaccharides, trisaccharides etc.

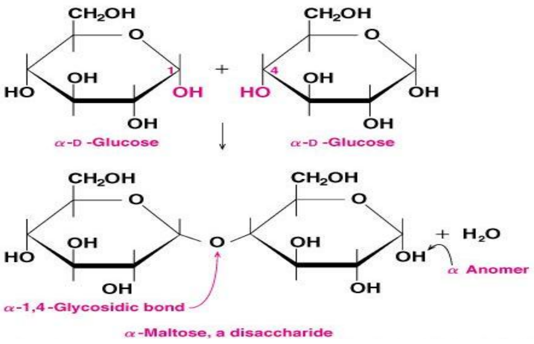
Formation of Disaccharides

- A disaccharide is formed when a hydroxyl group on one monosaccharide reacts with the anomeric carbon of another monosaccharide to form a glycosidic bond.
- Each disaccharide has a specific glycosidic linkage (depending on which hydroxyl reacts with which anomer).
- The three most common disaccharides are maltose, lactose and sucrose.
- When hydrolyzed using acid or an enzyme, the following monosaccharide are produced.
- The disaccharides are of two types
  1. Reducing disaccharides with free aldehyde or keto group e.g. maltose, lactose.
  2. Non-reducing disaccharides with no free aldehyde or keto group e.g. sucrose, Trehalose.

Reducing and non-reducing disaccharides

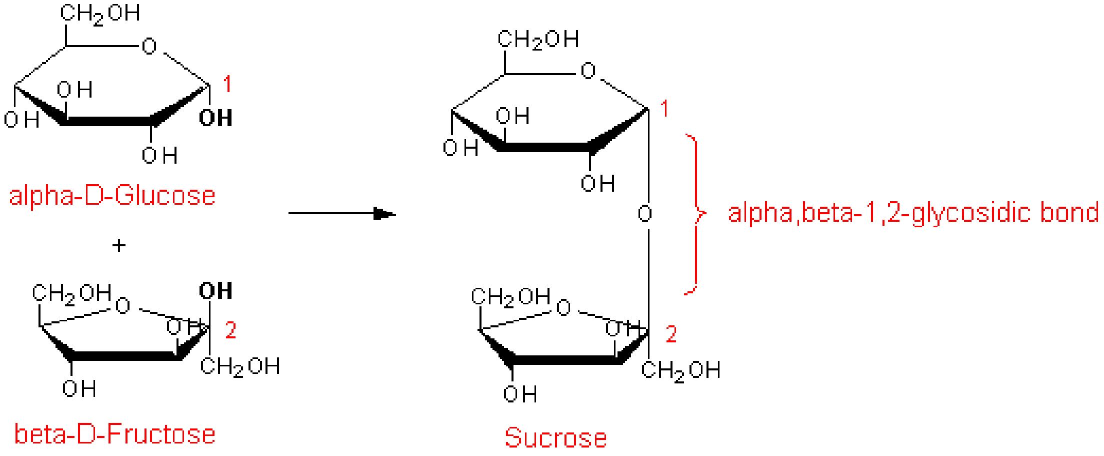
Maltose

- Maltose (malt sugar or corn sugar) consists of two glucose molecules linked by an α-1, 4-glycosidic bond.
- It comes from partial hydrolysis of starch by the enzyme amylase, which is in saliva and also in grains (like barley).
- Maltose can be fermented by yeast to produce ethanol.
- Maltose is also used in cereals, candies and malted milk.
- Because one of the glucose molecules is a hemiacetal, it can undergo mutorotation, and so maltose is a reducing sugar.



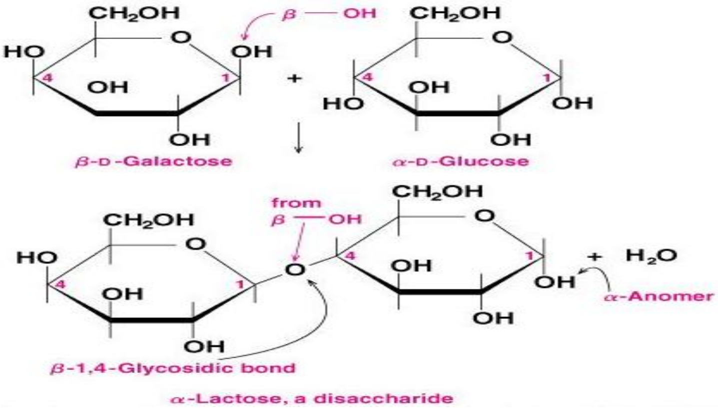
Sucrose

- Sucrose (table sugar) consists of one glucose molecule and one fructose molecule linked by an α,β-1,2-glycosidic bond.
- Sucrose is the most abundant disaccharide and is commercially produced from sugar cane and sugar beets.
- Because the glycosidic bond in sucrose involves both anomeric carbons, neither monosaccharide can undergo mutorotation, and so sucrose is not a reducing sugar.



Lactose

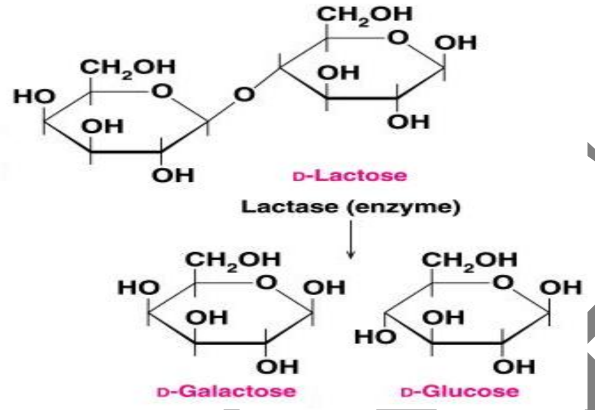
- Lactose (milk sugar) consists of one glucose molecule and one galactose molecule linked by a β-1,4 glycosidic bond.
- It comes from milk products (about 4-5% of cow's milk).
- Because the glucose is a hemiacetal, it can undergo mutorotation, and so lactose is a reducing sugar.



Hydrolysis of Lactose:

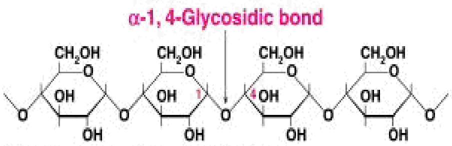
- Some people don't produce enough lactase, the enzyme that hydrolyzes lactose, and so can't digest lactose.

- Many adults become lactose intolerant, and develop abdominal cramps, nausea and diarrhea.
- Lactase can be added to milk products (or taken as a supplement) to combat this problem.

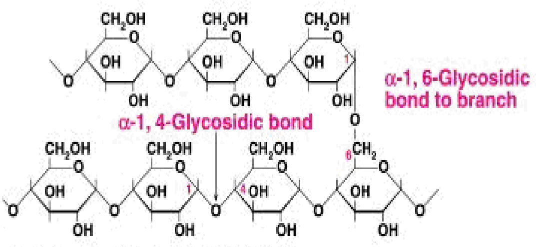


Polysaccharides

- A **polysaccharide** is a polymer consisting of hundreds to thousands of monosaccharide joined together by glycosidic linkages.
- Three biologically important polysaccharides are **starch, glycogen** and **cellulose**
  - all three are polymers of D-glucose, but they differ in the type of glycosidic bond and/or the amount of branching
- Starch and glycogen are used for storage of carbohydrates
  - Starch is found in plants and glycogen in animals
  - The polymers take up less room than would the individual glucose molecules, so are more efficient for storage
- Cellulose is a structural material used in formation of cell walls in plants Plant Starch (Amylose and Amylopectin)



(a) Unbranched chain of amylose



(b) Branched-chain of amylopectin

Homopolysaccharide

1.They are the complex carbohydrates formed by the polymerisation of one type of monosaccharide units.

e.g., Starch, glycogen and cellulose.

Heteropolysaccharide

1.They are the complex carbohydrates formed polymerisation of more than one type of monosaccharide units.
e.g., Chitin and agar.

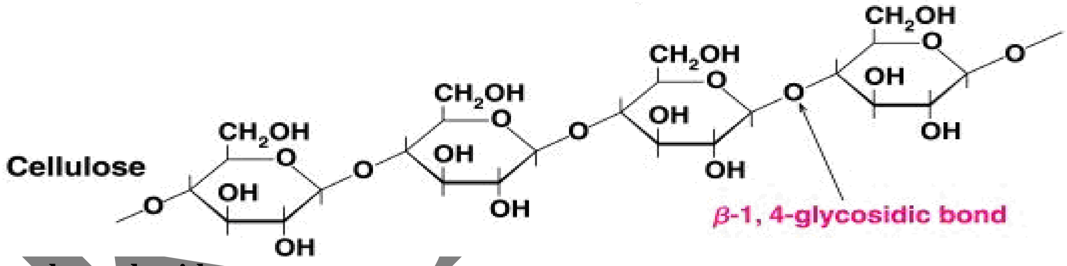
Structure and storage polysaccharides

Structural polysaccharides

- Structural polysaccharides are the polysaccharides that are found to form the structure of an organism.
  Eg. Cellulose - in plants
  Chitin - found in outer skeleton of insects and crabs
  Lignin - wood

Cellulose:

- The structural components of plants are formed primarily from cellulose.
- Wood is largely cellulose and lignin, while paper and cotton are nearly pure cellulose.
- Cellulose is a polymer made with repeated glucose units bonded together by *beta*-linkages.
- Humans and many other animals lack an enzyme to break the *beta*-linkages, so they do not digest cellulose.
- Certain animals such as termites can digest cellulose, because bacteria possessing the enzyme are present in their gut.
- Cellulose is insoluble in water. It does not change color when mixed with iodine. On hydrolysis, it yields glucose. It is the most abundant carbohydrate in nature.

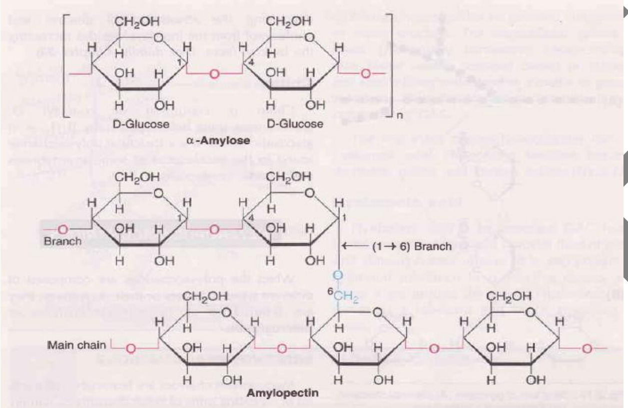


Storage polysaccharides

Starch

- Starch is the carbohydrate reserve of plants which is the most important dietary source for higher animals, including man.
- High content of starch is found in cereals, roots, tubers, vegetables etc.
- Starch is a homopolymer composed of D-glucose units held by a-glycosidic bonds.
- It is known as glucosan or glucan.
- Starch consists of two polysaccharide components-water soluble amylose (15-20%) and a water insoluble amylopectin (80-85%).
- Chemically, amylose is a long unbranched chain with 200-1,00O D-glucose units held by α (1 → 4) glycosidic linkages.

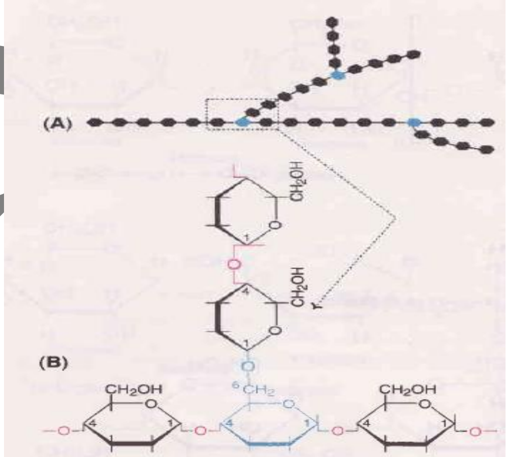
- Amylopectin on the other hand, is a branched chain with α (1 → 6) glycosidic bonds at the branching points and α (1 → 4) linkages everywhere else Amylopectin molecule containing a few thousand glucose units looks like a branched tree (20-30 glucose units per branch).
- Starches are hydrolysed by amylase (pancreatic or salivary) to liberate dextrins, and finally maltose and glucose units.
- Amylase acts specifically on a (1 → 4) glycosidic bonds.



Structure of starch (α-amylose and amylopectin)

Glycogen

- Glycogen is the carbohydrate reserve in animals, hence often referred to as animal starch.
- It is present in high concentration in liver, followed by muscle, brain etc. Glycogen is also found in plants that do not possess chlorophyll (e.g. yeast, fungi).
- The structure of glycogen is similar to that of amylopectin with more number of branches.
- Glucose is the repeating unit in glycogen joined together by α (1 → 4) glycosidic bonds, and α (1 → 6) glycosidic bonds at branching points.
- The molecular weight (up to 1 x 10^8) and the number of glucose units (up to 25,000) vary in glycogen depending on the source from which glycogen is obtained.



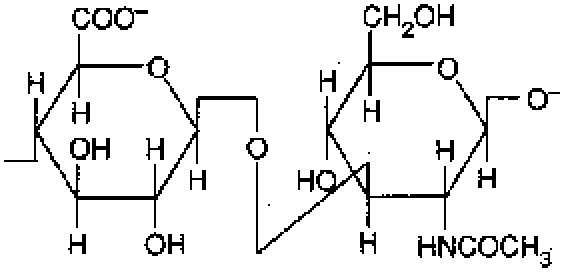
Structure of glycogen (A) General structure (B) Enlarged at a branch point

Structure and role of proteoglycans

- Proteoglycans (mucoproteins) are formed of glycosaminoglycans (GAGs) covalently attached to the core proteins.
- They are found in all connective tissues, extracellular matrix (ECM) and on the surfaces of many cell types. Proteoglycans are remarkable for their *diversity* (different cores, different numbers of GAGs with various lenghts and compositions).
- Glycosaminoglycans forming the proteoglycans are the most abundant heteropolisaccharides in the body. They are long unbranched molecules containing a *repeating disaccharide unit*. Usually one sugar is an uronic acid (either *D-glucuronic* or *L-iduronic*) and the other is either *GlcNAc* or *GalNAc*. One or both sugars contain sulfate groups (the only exception is hyaluronic acid).
- GAGs are highly negatively charged what is essential for their function.

THE SPECIFIC GAGs OF PHYSIOLOGICAL SIGNIFICANCE ARE :

Hyaluronic acid (D-glucuronate + GlcNAc)

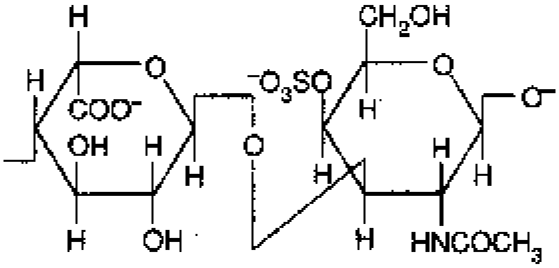


Occurence : synovial fluid, ECM of loose connective tissue

Hyaluronic acid is unique among the GAGs because it does not contain any sulfate and is not found covalently attached to proteins. It **forms non-covalently linked complexes with proteoglycans** in the ECM.

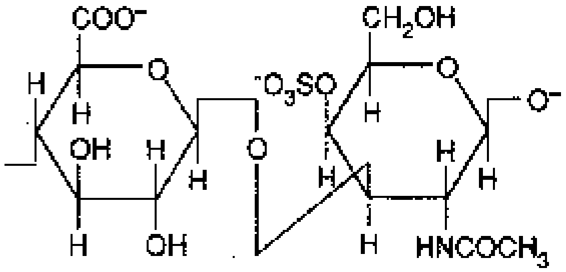
Hyaluronic acid polymers are very large (100 - 10,000 kD) and can displace a large volume of water.

Dermatan sulfate (L-iduronate + GlcNAc sulfate)



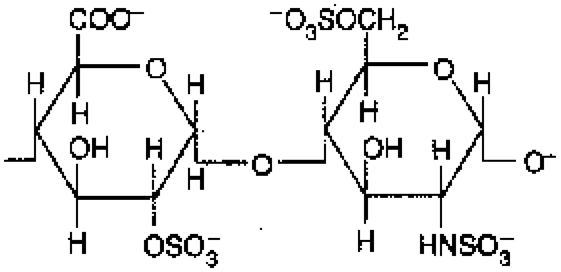
Occurence : skin, blood vessels, heart valves

Chondroitin sulfate (D-glucuronate + GalNAc sulfate)



Occurence : cartilage, bone, heart valves ; It is the most abundant GAG.

Heparin and heparan sulfate (D-glucuronate sulfate + N-sulfo-D-glucosamine)

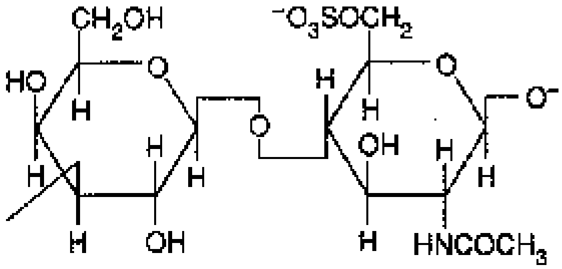


Heparans have less sulfate groups than heparins

Occurence :

- **Heparin** :component of intracellular granules of mast cells lining the arteries of the lungs, liver and skin
- **Heparan sulfate** : basement membranes, component of cell surfaces

Keratan sulfate (Gal + GlcNAc sulfate)



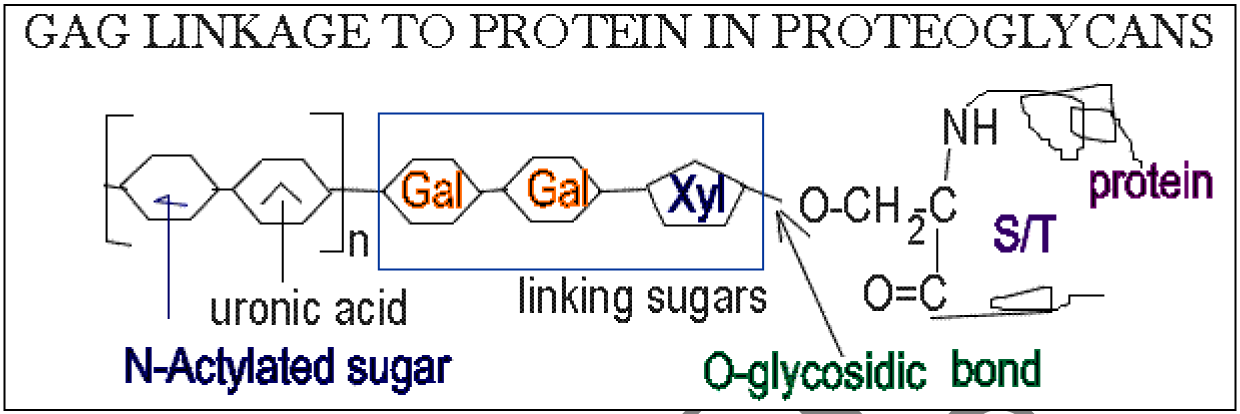
Occurence : cornea, bone, cartilage ;

Keratan sulfates are often aggregated with chondroitin sulfates.

Structure of proteoglycans

The GAGs extend perpendicular from the core protein in a bottlebrush- like structure.

The linkage of GAGs such as (*heparan sulfates and chondroitin sulfates*) to the protein core involves a specific **trisaccharide linker** :



Some forms of *keratan sulfates* are linked to the protein core through an **N-asparaginyl bond**. The protein cores of proteoglycans are rich in Ser and Thr residues which allows multiple GAG attachment.

Role of proteoglycans and glycosaminoglycans

They perform numerous vital functions within the body.

GAG dependent functions can be divided into two classes: the biophysical and the biochemical.

The biophysical functions depend on the unique properties of GAGs : the ability to fill the space, bind and organize water molecules and repel negatively charged molecules. Because of high viscosity and low compressibility they are ideal for a lubricating fluid in the joints. On the other hand their rigidity provides structural integrity to the cells and allows the cell migration due to providing the passageways between cells.

For example the large quantities of chondroitin sulfate and keratan sulfate found on *aggrecan* play an important role in the hydration of cartilage. They give the cartilage its gel-like properties and resistance to deformation.

Aggrecan is one of the most important extracellular proteoglycans. It forms very large aggregates (a single aggregate is one of the largest macromolecules known ; it can be more than *4 microns* long). Aggrecan molecules are non-covalently bound to the long molecule of hyaluronan (like bristles to the backbone in a bottlebrush). It is faciliated by the linking proteins. To each aggrecan core protein multiple chains of chondroitin sulfate and keratan sulfate are covalently attached through the trisaccharide linker .

The other, more biochemical functions of GAGs are mediated by specific binding of GAGs to other macromolecules, mostly proteins. Proteoglycans participate in cell and tissue development and physiology.

EXAMPLES OF GAG BINDING PROTEINS:

Secreted proteases and antiproteases

For example

antithrombin III (AT III) binds tightly to **heparin** and certain **heparan sulfates** (so do its substrates). Thus they control the blood coagulation. In the absence of GAGs **AT III** inactivates proteases (such as *thrombin*, factors *IXa* and *XIa*) very slowly. In the presence of appropriate GAGs these reactions are accelerated 2000-fold.

GAGs are sufficiently long that both protease and protease inhibitor can bind to the same chain (thus the likelyhood of the two proteins binding to each other is increased enormously). GAGs also affect the protein conformation that contributes to improving AT III binding kinetics.

Polypeptide growth factors

Members of the FGF family, as well as several other growth factors, bind to heparin or heparan sulfate. Binding to endogenous GAGs entraps these molecules in ECM from which they may be later released. GAGs can alter the conformation, proteolytic susceptibility and biological activity of some of these proteins. The bound growth factor is resistant to degradation by extracellular proteases. Active hormone is released by proteolysis of the heparan sulfate chains. It occurs during the tissue growth and remodeling after infection.

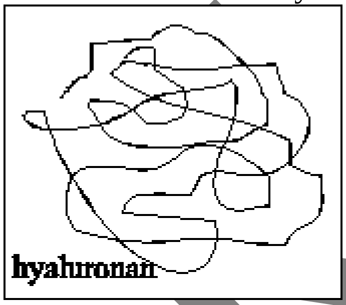
ECM proteins

Most of the large, multidomain ECM proteins contain at least one GAG binding site.

For example fibrous collagens (type I, III, V) and fibronectin bind to heparan sulfate chains which are attached to the integral membrane core proteins of cell surface proteoglycans such as *syndecan* and *fibroglycan*. Cell surface proteoglycans are thought to anchor cells to matrix fibers.

Cell - cell adhesion molecules

- For example NCAM interacts with cell surface heparan sulfate proteoglycans. This interaction is required for its function. NCAM has a distinct heparan binding domain.
- Hyaluronan is bound to the surface receptors (e.g. CD44) of many migrating cells. It is very important during differentiation (for example *myoblasts* which are undifferentiated muscle cell precursors bear hyaluronan- rich coat that prevents premature cell fusion). Because its loose, hydrated porous structure, the hyaluronan coat keeps cells apart from each other. They are free to move around and proliferate.



When the level of hyaluronan is lower (e.g. because of digesting by hyaluronidase), there is ceesation of cell movement and initiation of cell- cell attachment.

Glycoproteins and Glycolipids (gangliosides and lipopolysaccharides)

Many membrane proteins and certain classes of membrane lipids have more or less complex arrays of covalently attached oligosaccharides; these are glycoproteins and glycolipids. Most proteins that are secreted by eukaryotic cells are also glycoproteins. The biological advantage in the addition of oligosaccharides to proteins or lipids is not fully understood. The very hydrophilic clusters of carbohydrate alter the polarity and solubility of the proteins or lipids with which they are conjugated. Oligosaccharide chains attached to newly synthesized proteins in the Golgi complex may also influence the sequence of polypeptide-folding events that lead to the tertiary structure of the protein (see Fig. 7-22). Steric interactions between peptide and oligosaccharide may preclude one folding route and favor another. When numerous negatively charged oligosaccharide chains are clustered in a single region of a protein, the charge repulsion among them favors the formation of extended, rodlike structure in that region. The bulkiness and negative charge of oligosaccharide chains also protect some proteins from attack by proteolytic enzymes.

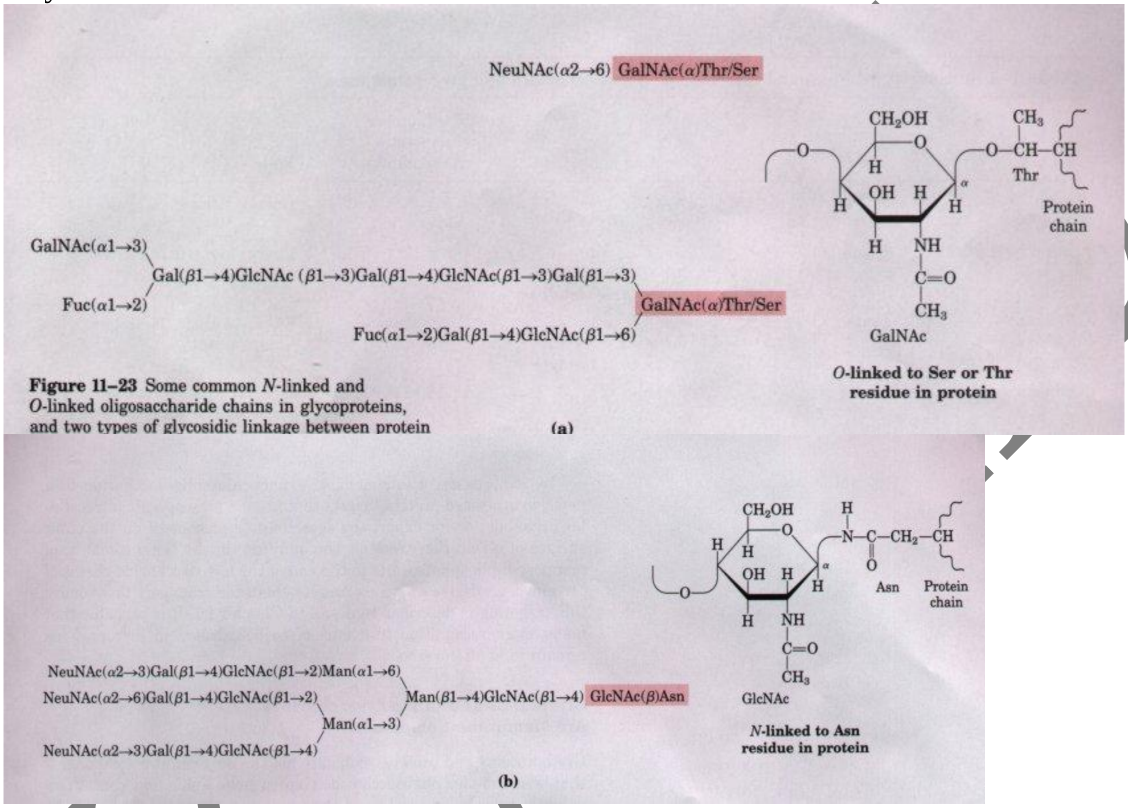


Figure 11-23 Some common N-linked and O-linked oligosaccharide chains in glycoproteins, and two types of glycosidic linkage between protein and oligosaccharide. (a) The O-glycosidic bond to the hydroxyl group of Ser or Thr side chains.(b) The N-glycosidic bond to the nitrogen of the Asn side chain. The protein-linked ends of the oligosaccharides (shaded in red) are shown in detail on the right.

Beyond these global physical effects on protein structure, there are more specific biological effects of oligosaccharide chains in glycoproteins and glycolipids. We have noted earlier the difference between the information-rich linear sequences of nucleic acids and proteins and the monotonous regularity of homopolysaccharides such as cellulose (see Fig. 3-15). The oligosaccharides attached to glycoproteins and glycolipids are generally not monotonous, but are enormously rich in structural information. Consider the oligosaccharide chains in Figure 11-23, typical of those found in many glycoproteins. The most complex of those shown contains 14 monosaccharide units, of four different kinds, variously linked (1→2), (1→3), (1→4), (1→6), (2→3), and (2→6), some with the α and some with the β configuration. The number of possible permutations and combinations of monosaccharide types and glycosidic linkages in an oligosaccharide this size is astronomical. Each of the oligosaccharides in Figure 11-23 therefore presents a unique face, recognizable by the enzymes and receptors that interact with it.

Because the analysis of oligosaccharide structure is much more difficult than the determination of the linear sequence of bases in nucleic acids, or of amino acid residues in proteins, the oligosaccharide structures of relatively few glycoproteins are known. From the few known structures, it is already clear that a given protein may have several different types of oligosaccharides attached at different positions, and that different glycoproteins have different oligosaccharides. Cells apparently use complex oligosaccharides to encode information about how a protein will fold, where in the cell it will be located, and whether it will be recognized by other proteins. We present here a few examples to illustrate this point.

The Oligosaccharides of Glycoproteins Have Biological Functions

The carbohydrate chains covalently attached to glycoproteins are generally oligosaccharides of much lower molecular weight than the glycosaminoglycans discussed above. The carbohydrate portion commonly constitutes from 1% to about 70% of a glycoprotein by weight, and never 99% as in the proteoglycans. Some glycoproteins have only one or a few carbohydrate groups; others have numerous oligosaccharide side chains, which may be linear or branched (Fig. 11-23). Many of the proteins of plasma membranes are glycoproteins, with their oligosaccharide moieties invariably located on the external surface of the membrane. One of the best-characterized membrane glycoproteins is glycophorin of the erythrocyte membrane (see Fig. 10-8), which contains 60% carbohydrate by weight in the form of 16 oligosaccharide chains (totaling 60 to 70 monosaccharide units) covalently attached to residues near the amino terminus of the polypeptide chain. Fifteen of the oligosaccharide units are O-linked to Ser or Thr side chains, and one is N-linked to an Asn residue, two basic types of linkages in glycoproteins (Fig. 11-23; see also Fig. 10-3). Many soluble glycoproteins are also known, including certain carrier proteins and immunoglobulins (antibodies) in the blood of vertebrates, and many of the proteins contained within lysosomes.

The sialic acid (NeuNAc) residues (see Fig. 11-9) found at the ends of the oligosaccharide chains of many soluble glycoproteins (Fig. 11-23) carry a message that determines whether a given protein will continue to circulate in the bloodstream or be removed by the liver. For example, ceruloplasmin is a copper-transporting glycoprotein in the blood of humans and other vertebrates. It has several oligosaccharide chains that end in sialic acid. When these terminal sialic acid units are lost, ceruloplasmin rapidly disappears from the blood. The plasma membrane of hepatocytes has specific binding sites for glycoproteins lacking sialic acid, known as asialoglycoprotein receptors. Glycoproteins bound by these receptors are taken up by the hepatocytes and degraded in lysosomes. Ceruloplasmin is only one of many sialoglycoproteins whose removal from the bloodstream is triggered by the loss of sialic acid units.

Removal of sialic acid is probably one of the ways in which the body marks "old" proteins for destruction and replacement. A similar mechanism is apparently responsible for removing old erythrocytes from the circulation of mammals. Newly synthesized erythrocytes have several membrane glycoproteins with oligosaccharide chains that end in sialic acid. When the sialic acid residues are removed experimentally (by withdrawing blood, treating it with sialidase in vitro, and reintroducing it into the bloodstream), the erythrocytes disappear from the bloodstream within a few hours, whereas cells with intact oligosaccharides continue to circulate for days.

In some cases, attachment of a particular oligosaccharide to a newly synthesized protein targets that protein for a specific intracellular organelle, or for export (by secretion) or placement on the outer surface of a cell. For example, the addition (in the Golgi complex) of mannose-6-phosphate units to the end of the oligosaccharide chains of certain degradative enzymes targets them for transport to lysomes; this targeting is described in detail in Chapter 26. It is probable that many more recognition functions of carbohydrates in glycoproteins remain to be discovered.

Glycolipids and Lipopolysaccharides Are Membrane Components

Glycoproteins and proteoglycans are not the only cellular components that bear complex oligosaccharide chains; some lipids, too, contain covalently bound oligosaccharide chains. In gangliosides (see Fig. 9-9), the polar head group is a complex oligosaccharide containing sialic acid and other monosaccharide units. Lipopolysaccharides are major components of the outer membrane of gram-negative bacteria such as E. coli and Salmonella typhimurium. The lipopolysaccharides of S. typhimurium contain six fatty acids bound to two glucosamine residues, one of which is the point of attachment for a complex oligosaccharide (Fig. 11-24). Lipopolysaccharides are the dominant surface feature of gram-negative bacteria; they are prime targets of the antibodies produced by the immune system in response to bacterial infection. The lipid A portion of the lipopolysaccharide of some bacteria is toxic to humans and other animals; for example, it is responsible for the dangerously lowered blood pressure that occurs with toxic shock syndrome in gram-negative bacterial infections of humans.

Carbohydrates as informational molecules, working with carbohydrates

Some oligosaccharides get bound to proteins called lectins that serve in a wide variety of cell to cell acknowledgment, signaling and sticking together procedure.The glycosaminoglycan GAG is the integral constitution of gel like extracellular matrix, i.e the ground substance that fills the extracellular space in animal tissues.Ribose is essential part of high energy phosphate compounds, i.e ATP, GTP, UTP, and CTP.A derivative of galactose is the component of H substance that gives rise to the ABO blood group system antigens.

Carbohydrate is also present in apoB part of certain lipoproteins.The role of carbohydrate containing proteins, i.e proteoglycans and glycoprotein in the transfer of information across the cell membrane has been discussed. The role of carbohydrate as informational molecules in association with specific proteins namely lectin is quite important.Lectins bind carbohydrate on the outer surface of cells where they initial interaction with other calls. Massages received by lectins from these oligosaccharides regulate the rate of degradation of certain peptide hormones, circulating proteinsand blood cells. Moreover the oligosaccharides present on cell surface bind the bacterial and viral pathogen thus causing infections. A certain type of lectin, namely selection, bound with oligosaccharides is present in the extracellour matrix and mediates the flow of information between cell and matrix and also from cell to cell. The unlimited variety of oligosaccharides showing different types and orientation of substitute groups and the number and types of branches enable the oligosaccharides to play as much greater role in receiving and transmitting information as compared to proteins and nucleic acids.

Possible Questions

2 marks

1. What do you mean by mutarotation
2. Mention the importance of storage polysaccharides
3. Write short notes on proteoglycans
4. List out the importance of carbohydrates
5. Differentiate between homopolysaccharides and heteropolysaccharides

8 marks

1. Explain about the classification of monosaccharides
2. Discuss in detail about storage polysaccharides
3. What are all the properties and functions of trisaccharides
4. Explain the structures of disaccharides
5. Write notes on Stereochemistry of Monosaccharide
6. Explain
   - i) Glycogen
   - ii) Dextrin
7. Describe the Properties and functions of polysaccharide
8. Briefly describe about classification and functions of disaccharides
9. Give detail account on
   - i) Cellulose
   - ii) Chitin

Karpagam Academy of Higher Education
Department of Biochemistry
I B.Sc., Biochemistry
19BCU101- Molecules of life
Prepared By Dr. A. RAMAKRISHNAN

Unit II

Question number	Question	Option I	Option II	Option III	Option IV	Answer
1	The general formula for polysaccharides	$(C_6H_{10}O_5)n$	$(C_6H_{12}O_6)n$	$(C_6H_{12}O_5)n$	$(C_6H_{10}O_6)n$	**$(C_6H_{10}O_5)n$**
2	The simplest of aldoses is	Glucose	Arabinose	Glyceraldehyde	Ribose	**Glyceraldehyde**
3	The number of isomers of glucose	4	8	12	16	**16**
4	The epimers of glucose	Fructose	galactose	ribose	deoxy ribose	**galactose**
5	The reducing property of glucose is due to	OH group	Hemiacetal group	Aldehyde group	Acid group	**Aldehyde group**

6	Oxidation of glucose with hydrogen peroxide gives	Glucuronic acid	Glucaric acid	Gluconic acid	Tartaric acid	**Glucuronic acid**
7	Human heart muscle contains	D-Arabinose	D-Ribose	D-Xylose	L-Xylose	**D-Xylose**
8	Lobry de Bruyn Alberda Van Ekenstein transformation is the reaction of	Glucose with mild alkali	Lactose with enzyme	sucrose with dil. Acids	starch with iodine	**Glucose with mild alkali**
9	Fucose is a	Glycoside	Hexose	Triose	methyl pentose	**Hexose**
10	Example for a fructosan is	Starch	inulin	cellulose	Chitin	**Starch**
11	Glucose reacts with phenyl hydrazine to give	osazone	glucocyanohydrin	gluconic acid	None	**osazone**
12	The dissacharide which does not show mutarotation	Sucrose	Lactose	Maltose	Cellobiose	**Sucrose**
13	Glycoside are found in many	Vitamins	drugs	Minerals	Nucleoproteins	**drugs**
14	Trehalose is a	Disaccharide	trisacharide	poly saccharide	Monosaccharide	**Disaccharide**

15	Galactose on oxidation with conc. HNO3 produces	Gluconic acid	saccharic acid	mucic acid	both a and b	**mucic acid**
16	Digitonin is a	Protein	Glycoside	lipid	Alkaloid	**Glycoside**
17	The following sugar exhibits inversion of optical rotation heating with dil. Acid	Sucrose	glucose	fructose	Lactose	**Lactose**
18	Hydrolysis of sucrose yields	Glucose	Glucose +Glucose	Maltose +glucose	Fructose + glucose	**Fructose + glucose**
19	Osazone formation is due to	Presence of aldehyde group	presence of keto group	presence of either aldehyde or keto group	presence of keto group	**presence of either aldehyde or keto group**
20	Raffinose is composed of	Glucose, ribose, galactose	glucose, galactose, mannose	glucose, galactose, fructose	glucose mannose fructose	**glucose, galactose, fructose**
21	A reducing disaccharide containing glucose is	maltose	lactose	trehalose	Furanose	**trehalose**

22	The reagent used for distinguishing a reducing monosaccharide from a reducing disacchride	Benedict's reagent	Barfoed's reagent	Fehling's reagent	all	**Benedict's reagent**
23	The arrangements of sugars into D&L configuration is based upon their resemblance toD&L	Glyceraldehydes	lactic acid	glucose		**Glyceraldehydes**
24	Starch is composed of repeating unit of	Maltose	Glucose	Cellobiose		**Maltose**
25	β (1-4) linkage is present in	Starch	Glycogen	cellulose		**cellulose**
26	Amylose contains glucose units	100-200	200-300	300-400		**300-400**
27	Each branch of amylopectin is an interval of glucose units	14-20	24-30	34-40		**24-30**

28	The end product of hydrolysis of strach by amylase is	Soluble starch	Glucose	dextrin		**Soluble starch**
29	The component present in starch that gives blue colour with iodine is	Amylase	amylopectin	amylose		**Amylase**
30	Amylopectins are present in	Hyaluronic acid	strach	sucrose		**Hyaluronic acid**
31	Erythrodextrin gives colour with iodine	blue	violet	red	all	**red**
32	Cellulose is made up of	α-glucose	β-glucose	fructose	all	**β-glucose**
33	Hyaluronidase is the enzyme, which acts on	homopolysaccharide	heteropolysaccharide	disaccharide	all	**heteropolysaccharide**
34	In place of glucuronic acid chondroitin sulphate B contains	gluconic acid	glucamic acid	iduronic acid	all	**iduronic acid**

35	Heparin has a molecular weight of about	14,000	15,000	16,000	all	**17,000**
36	Blood group subtances consists of	lactose	maltose	fucose		**fucose**
37	The component of cartilage & cornea is	Keratosulphate	chondroitin sulphate	cadmium sulphate		**Keratosulphate**
38	The compound which is an acid mucopolysacchride	dicoumarol	EDTA	Hyaluronic acid		**Hyaluronic acid**
39	A polymer of N-acetylated glucosamine is	dextran	heparin	chitin		**chitin**
40	Change in optical rotation is	specific rotation	mutarotation	epimerism	all	**mutarotation**
41	The polymer of fructose is	Strach	glycogen	cellulose	all	**insulin**
42	The glycosaminoglycan which acts as an anticoagulant is	Heparin	Hyaluronic acid	dextrin	all	**Heparin**

43	The glycosaminoglycan which is present in synovial fluid	Heparin	Hyaluronic acid	dextrin		**Hyaluronic acid**
44	2 carbon epimer of glucose	Fructose	galactose	Mannose	all	**Mannose**
45	The mirror images are	Enantiomers	Anomers	Epimers	all	**Epimers**
46	Chitin is composed of	fructofuranose	D-glucuronic	N-acetyl glucoseamine	Fructose + glucose	**N-acetyl glucoseamine**
47	the mucopolysaccharide which serve as lubricant and shock absorbent in joints is	heparin	chondroitin sulphate	hyaluronic acid	cellulose	**hyaluronic acid**
48	All carbohydrates contain carbon. This can be shown by heating with	sodium hydroxide solution	burning in air	heating with conc. Sulphuric acid	Hydrochloric acid	**heating with conc. Sulphuric acid**
49	The buffer acting in the osazone reaction is	phenyl hydrazine hydrochloride+ sodium acetate	acetic acid +phenyl hydrazine hydrochloride	sodium acetate +acetic acid	sodium acetate	**phenyl hydrazine hydrochloride+ sodium acetate**

50	The monosaccharide units of hyaluronic acid are	glucuronic acid & N-acetyl D-glucosamine	glucuronic acid & N-acetyl galactosemine	iduronic acid & N-Acetyl galactose amine		**glucuronic acid & N-acetyl D-glucosamine**
51	NASA has launched a satellite named ____ to study the effect of water in various forms on climate.	*Aqua*	*Hydro*	*Hi*	*Water*	***Aqua***
52	Water is	Tasteless	Odorless	both a and b	low boiling point	**both a and b**
53	The epimers of glucose	Fructose	galactose	ribose	deoxy ribose	**galactose**
54	The dissacharide which does not show mutarotation	sucrose	lactose	maltose	cellobiose	**sucrose**
55	Polysaccharides produce more than ___ monosaccharides on hydrolysis;	Eight	Ten	Six	five	**Ten**
56	Stereoisomer classified into	Two	Three	Four	Seven	**Two**

57	D isomer rotate the plane polarized light to	Left	Right	DL mixture	Interchange	**Right**
58	Isomers formed by the interchange of H and OH groups on Carbon atom2, 3 and 4 are known as	Monomer	Dimer	Epimers	Tetramer	**Epimers**
59	Sugars forming six member ring are known as	Furanose	racemixture	mannose	Pyranose	**Pyranose**
60	Maltose is composed of	two glucose molecules	three glucose molecules	four glucose molecules	six glucose molecules	**two glucose molecules**

UNIT III
SYLLABUS

Lipids : Building blocks of lipids - fatty acids, glycerol, ceramide. Storage lipids - triacyl glycerol and waxes. Structural lipids in membranes – glycerophospholipids, galactolipids and sulpholipids, sphingolipids and sterols, structure, distribution and role of membrane lipids. Plant steroids. Lipids as signals, cofactors and pigments

LIPIDS

Building blocks of lipids

Lipids are broadly classified (modified from Bloor) into simple, complex, derived and miscellaneous lipids, which are further subdivided.

1. Simple lipids:

Esters of fatty acids with alcohols.

These are mainly of two types:

(a) Fats and oils (triacylglycerol's):

These are esters of fatty acids with glycerol. The difference between fat and oil is only physical. Thus, oil is a liquid while fat is a solid at room temperature.

(b) Waxes:

Esters of fatty acids (usually long chain) with alcohols other than glycerol. Cetyl alcohol is most commonly found in waxes.

2. Complex (or compound) lipids:

Esters of fatty acids with alcohols containing additional groups such as phosphate, nitrogenous base, carbohydrate, protein etc.

They are further divided:

(a) Phospholipids:

Lipids containing phosphoric acid and frequently a nitrogenous base. This is in addition to alcohol and fatty acids.

(b) Glycolipids:

These lipids contain a fatty acid, carbohydrate and nitrogenous base. The alcohol is sphingosine, hence they are also called as glycosphingolipids. Glycerol and phosphate are absent e.g., cerebrosides, gangliosides.

(c) Lipoproteins:

Macromolecular complexes of lipids with proteins.

(d) Other complex lipids:

Sulfolipids, amino- lipids and lipopolysaccharides are among the other complex lipids.

3. Derived lipids:

These are the derivatives obtained on the hydrolysis of group I and group 2 lipids which possess the characteristics of lipids. These include glycerol and other alcohols, fatty acids, mono- and diacylglycerols, lipid soluble vitamins, steroid hormones, hydrocarbons and ketone bodies.

4. Miscellaneous lipids:

These include a large number of compounds possessing the characteristics of lipids e.g., carotenoids, squalene, hydrocarbons such as pentacosane (in bees wax), terpenes etc.

5. Neutral lipids:
The lipids which are uncharged are referred to as neutral lipids. These are mono-, di-, and triacylglycerol's, cholesterol and cholesteryl esters.

Functions of Lipids:

Lipids perform several important functions:

1. They are the concentrated fuel reserve of the body (triacylglycerol's).
2. Lipids are the constituents of membrane structure and regulate the membrane permeability (phospholipids and cholesterol).
3. They serve as a source of fat soluble vitamins (A, D, E and K).
4. Lipids are important as cellular metabolic regulators (steroid hormones and prostaglandins).

Fatty Acids

Fatty acids are carboxylic acids with hydrocarbon side chain. They are the simplest form of lipids.

Even and odd carbon fatty acids:
Most of the fatty acids that occur in natural lipids are of even carbons (usually 14C-20C). This is due to the fact that biosynthesis of fatty acids mainly occurs with the sequential addition of 2 carbon units. Palmitic acid (16C) and stearic acid (18C) are the most common. Among the odd chain fatty acids, propionic acid (3C) and valeric acid (5C) are well known.

Saturated and unsaturated fatty acids:
Saturated fatty acids do not contain double bonds, while unsaturated fatty acids contain one or more double bonds. Both saturated and unsaturated fatty acids almost equally occur in the natural lipids. Fatty acids with one double bond are known as monounsaturated and those with 2 or more double bonds are collectively known as polyunsaturated fatty acids (PUFA).

Shorthand representation of fatty acids:
Instead of writing the full structures, biochemists employ shorthand notations (by numbers) to represent fatty acids. The general rule is that the total number of carbon atoms is written first, followed by the number of double bonds and finally the (first carbon) position of double bonds, starting from the carboxyl end. Thus, saturated fatty acid, palmitic acid is written as 16 : 0, oleic acid as 18 : 1; 9, arachidonic acid as 20 : 4; 5, 8, 11, 14.

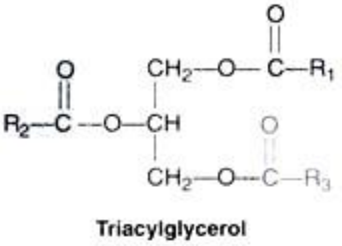


Fig. 65.2 : General structure of triacylglycerol.

Essential fatty acids:
The fatty acids that cannot be synthesized by the body and, therefore, should be supplied in the diet are known as essential fatty acids (EFA). Chemically, they are polyunsaturated fatty acids, namely linoleic acid (18 : 2; 9, 12) and linolenic acid (18 : 3; 9, 12, 15). Arachidonic acid (20 : 4;

5, 8, 11, 14) becomes essential, if its precursor linoleic acid is not provided in the diet in sufficient amounts.

Glycerol

Glycerol is a colorless, odorless liquid with a sweet taste. It is viscous at room temperature and non-toxic in low concentrations. Glycerol was discovered in 1779. It is also called glycyl alcohol, glycerin or glycerine in some literature.

Glycerol is seen in biological systems as an intermediate in carbohydrate and lipid metabolism because surplus carbohydrate can be converted into long chain fatty acids and esterified with the three hydroxyl groups. Glycerol can influence immune reactions in the body through histamines, increased antibody production and by enhancing immune cell activity and is therefore classified as an allergen. In the blood, glycerol can increase blood pressure by preferentially attracting the water from tissues into plasma and lymph. In nephrons, glycerol can increase urine volume by preventing water resorption.

Properties of Glycerol

Pure glycerol has a melting point of 17.8°C. Its boiling point is 290°C but it also decomposes at that temperature. The presence of three hydroxyl groups makes the compound hygroscopic, with a tendency to absorb moisture from the air. This also makes it useful as a humectant in cosmetics and food, retaining water and preventing the substance from drying out.

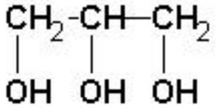
Glycerol is easily soluble in water, due to the ability of the polyol groups to form hydrogen bonds with water molecules. Glycerol is slightly denser than water with a specific gravity of 1.26. This means that when glycerol is poured into a container of water, it will sink to the bottom. However, due to its solubility, over time and with mild agitation, glycerol will form an aqueous solution.

Glycerol can cause mild irritation to the eyes, nose, lungs and skin, particularly due to its hygroscopic nature. Skin and other internal organs can get dried out when pure glycerol comes into contact with these moist tissues. Since the molecule can bind to water, the same property that makes glycerol a good humectant also desiccates internal tissues. On the other hand, if a cosmetic preparation with high water content is applied on the skin, especially in arid environments, the presence of glycerol can prevent the lotion, cream or gel from drying out quickly.

The three hydroxyl groups of glycerol allow reactions with many organic acids to form esters. When all three reactive groups are esterified with long chain organic fatty acids, a triglyceride is formed. Triglycerides are among the most common lipids in the human body.

Structure

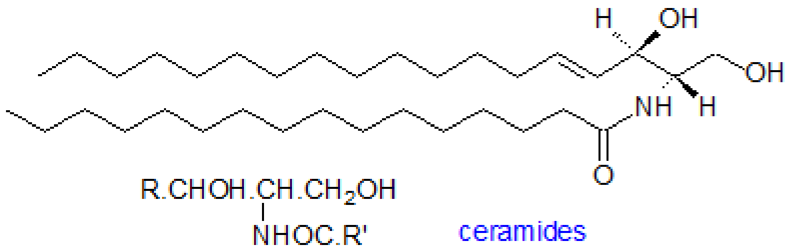
Glycerol is a trihydroxy sugar alcohol with three carbon atoms and three hydroxyl groups. The presence of multiple hydroxyl groups and carbon atoms makes it an organic polyol compound with the IUPAC name of 1, 2, 3 – Propanetriol.



$$\underset{OH}{\underset{|}{CH_2}}-\underset{OH}{\underset{|}{CH}}-\underset{OH}{\underset{|}{CH_2}}$$

Ceramide

Ceramides consist of a long-chain or sphingoid base linked to a fatty acid via an amide bond. They are the key intermediates in the biosynthesis of all the complex sphingolipids in which the terminal primary hydroxyl group is linked to carbohydrate, phosphate, and so forth. While ceramides are rarely found as such at greater than trace amounts in tissues other than skin, they can exert important biological effects at these low levels. They are present in membranes where they participate in the formation of raft domains.



$$\underset{\displaystyle \text{NHOC.R}'}{\text{R.CHOH.}\underset{|}{\text{CH}}\text{.CH}_2\text{OH}}$$

ceramides

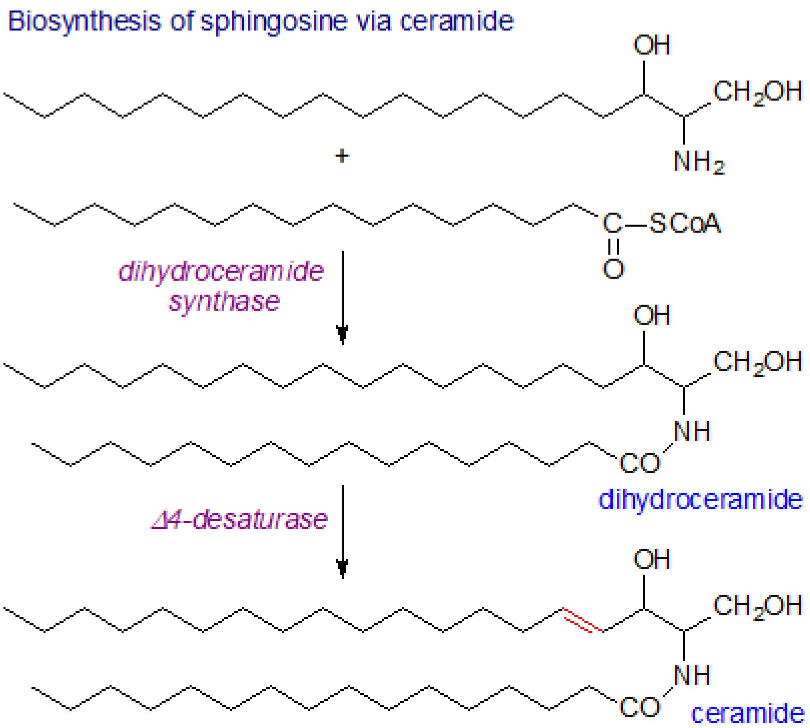
Each organism and indeed each tissue may synthesise ceramides in which there are a variety of di- and trihydroxy long-chain bases linked to fatty acids, the latter consisting mainly of longer-chain (to C_{24} or greater) saturated and monoenoic (mainly (*n*-9)) components, sometimes with a hydroxyl group in position 2; more than 200 structurally distinct molecular species of ceramides have been characterized from mammalian cells. Other than in certain testicular cells, polyunsaturated fatty acids do not occur. In plants, 2-hydroxy acids predominate sometimes accompanied by small amounts of 2,3-dihydroxy acids. Although small amounts of free ceramides are produced in all tissues as required for the specific biological functions described below, most is converted rapidly to more complex sphingolipids, including sphingomyelin and the various glycosylceramides (see theseparate web pages). The ceramides in skin are a remarkable exception to this rule, and as such they are discussed separately below.

A shorthand nomenclature simply combines those used conventionally for fatty acids and long-chain bases to denote molecular species of ceramides, including those as components of more complex lipids, e.g. *N*-palmitoyl-sphingosine is d18:1-16:0. Ceramides containing sphinganine are sometimes termed 'dihydroceramides'.

Biosynthesis

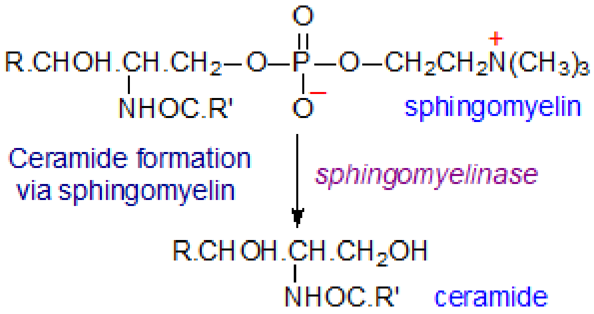
Ceramide biosynthesis is complex and involves at least three pathways. Biosynthesis *de novo* takes place in the endoplasmic reticulum with palmitoyl-CoA and serine as the precursors for the long-chain base component, while the sphingomyelinase pathway for the conversion of sphingomyelin into ceramides (and *vice versa*) occurs in the plasma membrane, Golgi and mitochondria. Finally, the salvage pathway converts complex sphingolipids into ceramides in both lysosomes and endosomes as part of a re-cycling/catabolic process. As these biosynthetic pathways are located in different organelles, specific pools of ceramide and sphingolipids result with differing biological properties and functions.

These pathways are described in mechanistic terms in our web pages dealing with sphingoid bases, as important structural features of the latter (double bonds, etc.) are introduced only when they are incorporated into ceramides. In brief in animals, sphinganine is coupled to a long-chain fatty acid to form dihydroceramide by means of one of six ceramide synthases in the endoplasmic reticulum mainly, before the double bond is introduced into position 4 of the sphingoid base. Of these, ceramide synthase 2 is most abundant and is specific for CoA esters of very-long-chain fatty acids (C_{20} to C_{26}) synthesised by elongases in the endoplasmic reticulum; it is most active in the central nervous system. Ceramide synthase 1 is specific for 18:0 and is located exclusively in brain and skeletal muscle, ceramide synthase 3 is responsible for the unusual ceramides of skin and testes, and ceramide synthases 5 and 6 generate 16:0-containing ceramides.



Each synthase has six membrane-spanning domains and contains a characteristic motif with the specific structures required for catalysis and substrate binding that are essential for its activity, and they have been shown to differ primarily in an 11-residue sequence in a loop between the last two putative transmembrane domains. In addition to separate transcriptional regulation of each of these enzymes, ceramide synthase activity is modulated by many different factors including reversible dimerization, while ceramide synthase 2 has a sphingosine-1-phosphate binding motif and this lipid may inhibits its activity. Acyl-coenzyme A-binding protein (ACBP) facilitates the synthesis of ceramides containing very-long fatty acids and stimulates ceramide synthases 2 and 3 especially.

Three ceramide synthase isoforms have been identified in Arabidopsis, designated LOH1, LOH2 and LOH3, and again the specificities of these are discussed in more detail in relation to the biosynthesis of long-chain bases.



Ceramides are also produced during the catabolism of other complex sphingolipids, for example by the action of one or other of the sphingomyelinases or of phospholipase C on sphingomyelin in animal tissues as part of the 'sphingomyelin cycle' (see the web page on this lipid for a more detailed discussion). Many agonists including chemotherapeutic agents, tumor necrosis factor-alpha, 1,25-dihydroxy-vitamin D_3, endotoxin, gamma-interferon, interleukins, nerve growth factor, ionizing radiation and heat stimulate hydrolysis of sphingomyelin to produce ceramide. In addition, reversal of the sphingomyelin synthesis reaction may generate ceramide, and some may be generated by operation of the enzyme ceramidase in reverse (see next section). Such reactions are much more rapid than synthesis *de novo*, so they are of special relevance in relation to the signalling functions of ceramides, especially when they occur at the plasma membrane. In this context, the acid sphingomyelinase may be especially important.

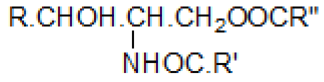
Glycosphingolipids also can be hydrolysed by glycosidases to ceramides in tissues, but the process tends to be less important in quantitative terms (other than in skin). The key enzymes of sphingolipid metabolism were first characterized from the yeast *Saccharomyces cerevisiae*, and these were found to be sufficiently similar to the corresponding enzymes in mammals to facilitate their study in the latter.

Biosynthesis of the very specific fatty acids in ceramides involving various chain elongases (ELOVL) requires consideration also, but this is discussed in our web page dealing with saturated fatty acids, although much remains to be learned of how the distinctive fatty acid compositions of ceramides and thence of complex sphingolipids are attained (see the introductory web page). As discussed in our web page on long-chain bases, there are specific ceramide synthases that utilize specific fatty acids for ceramide biosynthesis, and knowledge is slowly being acquired of how these are compartmentalized and regulated within cells. Thus, the synthesis and subsequent catabolism of ceramides involves a complex web of at least 28 distinct enzymes, including six ceramide synthases and five sphingomyelinases, which are all products of different genes. Each of these enzymes may produce distinctive molecular species of ceramides with their own characteristic biological properties.

Most of the ceramide required for the production of complex lipids is synthesised on the cytoplasmic leaflet of the endoplasmic reticulum, with subsequent formation of complex sphingolipids occurring in the Golgi apparatus. A key cytoplasmic protein, ceramide transporter or 'CERT', mediates the transport of ceramide between these organelles in a non-vesicular manner. It has a number of distinct functional domains including a phosphatidylinositol-4-monophosphate-binding domain (the multiple factors that control the biosynthesis of this lipid must also influence sphingolipid metabolism), which targets the Golgi apparatus, and a ‘START’ domain capable of catalysing inter-membrane transfer of ceramide; there is also a short peptide motif that recognizes a specific protein in the endoplasmic reticulum. The CERT protein extracts ceramides only from membrane bilayers with some specificity for those containing C_{14} to C_{20} fatty acids, but not those of longer chain length, and delivers them for the synthesis of sphingomyelin by an ATP-dependent pathway. As a neutral lipid, ceramide can flip readily across membrane leaflets, and this is also necessary for the synthesis of sphingomyelin, which occurs on the lumen of the Golgi. The pool of ceramide utilized for synthesis of glycosylceramide is delivered to the Golgi by a separate transport mechanism that also does not require ATP.

In addition, some ceramide synthesis occurs in mitochondria although this has the potential to lead to cell death. Regulation of ceramide and subsequent sphingolipid biosynthesis is crucial as an excess of sphingolipids can be toxic, while reduced synthesis can inhibit cell proliferation.

In yeasts, ceramide synthase activity is regulated by the Torc2 kinase complex, which controls the steady-state levels of long-chain bases and ceramides, but by mechanisms that are poorly understood.



$$R.CHOH.\underset{\substack{| \\ NHOC.R'}}{CH}.CH_2OOCR''$$

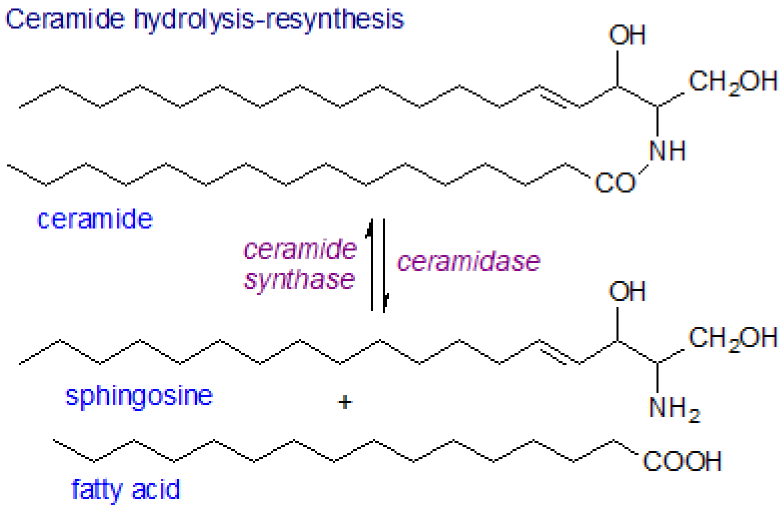
1-O-Acylceramides

1-*O*-Acylceramides in which a fatty acid is *O*-esterified to position 1 of the sphingoid base are essential if minor components of lipid droplets. They are formed by the reaction of fatty acyl-CoA esters, produced by the long-chain acyl-CoA synthase ACSL5, with ceramide generated *de novo* and catalysed by diacylglycerol acyltransferase 2 (DGAT2 - a key enzyme in triacylglycerol biosynthesis) on the surface of lipid droplets. It is believed that formation of acylceramides diverts ceramide from a bioactive pool into a storage pool, so limiting ceramide-mediated apoptosis in lipid droplets. Similar lipids are present in skin (see below).

Ceramide Catabolism

In animals, ceramide metabolism and function is controlled in part by the action of ceramidases, which effect hydrolysis to sphingoid bases and free fatty acids. Five such enzymes are known in humans, classified according to their pH optima, i.e. acid (‘ASAH1’), neutral (‘ASAH2’) and alkaline (three enzymes - ‘ACER1 to ACER3’), with differing cellular locations and fatty acid specificities and with the potential to affect distinct signalling and metabolic events. The acid ceramidase is of particular importance, and aberrations in its synthesis or activity is involved in several human disease states, including Farber’s disease where there is a deficiency in the enzyme so ceramide accumulates; ceramide containing 26:0 in blood is considered to be a biomarker for diagnosis of the disease. ASAH1 is located in the lysosomes and hydrolyses ceramides with medium chain fatty acid components most efficiently. The neutral ceramidase is located in the plasma membrane, especially of intestinal epithelial cells, and prefers long-chain to very-long-chain components (C_{16} to $>C_{24}$); it also catalyses the reverse reaction, and this may be a means of ceramide synthesis in mitochondria. ACER1 and ACER2 are found in the endoplasmic reticulum and Golgi, respectively, and they prefer very-long-chain acyl groups also. ACER3 is present in both the endoplasmic reticulum and Golgi; it has a marked specificity for ceramides, dihydroceramides and phytoceramides linked to unsaturated long-chain fatty acids

(18:1, 20:1 or 20:4) *in vitro* at least. Neutral/alkaline ceramidase activity has also been found in mitochondria and nuclei.



An enzyme broadly similar to the neutral ceramidase has been isolated from plants such as rice, but its specificity is odd in that it does not hydrolyse ceramides containing phytosphingosine. There does not appear to be an equivalent to the acid ceramidase in plants. Ceramidases are also present in lower organisms such as *Pseudomonas aeruginosa* and slime moulds, where they are secreted proteins rather than integral membrane enzymes. A neutral ceramidase only is found in prokaryotes, including some pathogenic bacteria.

Sphingoid bases released by the action of acid ceramidase can escape from the lysosomes and be re-utilized for ceramide biosynthesis through the action of a ceramide synthase. This has been termed the 'salvage' pathway and is important in both quantitative and biological terms. For example, it has been estimated that it contributes from 50 to 90% of sphingolipid biosynthesis. The biological functions of ceramides are discussed below, but there are reasons to believe that ceramides derived from the salvage pathway are spacially and thence functionally distinct from those synthesised *de novo*. In addition, sphingoid bases released in this way have their own biological functions, and indeed this is the only route to the formation of free sphingosine, which can in turn be utilized for the synthesis of the biologically important metabolite sphingosine-1-phosphate. Therefore, regulation of ceramidase action is central to innumerable biological processes in animals.

Storage lipids

Triacylglycerol

Triacylglycerol's (formerly triglycerides) are the esters of glycerol with fatty acids. The fats and oils that are widely distributed in both plants and animals are chemically triacylglycerol's. They are insoluble in water and non-polar in character and commonly known as neutral fats.

Fats as stored fuel:

Triacylglycerol's are the most abundant group of lipids that primarily function as fuel reserves of animals. The fat reserve of normal humans (men 20%, women 25% by weight) is sufficient to meet the body caloric requirements for 2-3 months.

Structures of acylglycerols:
Monoacylglycerols, diacylglycerojs and triacylglycerol’s, respectively consisting of one, two and three molecules of fatty acids esterified to a molecule of glycerol, are known. Among these, triacylglycerol’s are the most important biochemically. Triacylglycerol’s of plants have higher content of unsaturated fatty acids compared to that of animals.

Waxes

Waxes are esters of long chain fatty acids with monohydric alcohols. The fatty acids and alcohols in the waxes vary from 24 to 36 carbons. Waxes form water-proof coating on the surface of plants and animals.
The well known waxes are as follows:
i. Bee-Wax:
Secreted from the abdominal glands of worker bees to build honeycombs. It is the ester of palmitic acid and hexacosonol.
ii. Carnauba wax:
It occurs as a coating on the leaves of Carnauba palm tree of Brazil (Copernicia prunifera). It is used in automobile polishes.
iii. Spermaceti (Sperm oil):
It is the hardest known wax obtained from the head of sperm whale. It is used as lubricating wax.
iv. Lanolin (wool fat):
Secreted from the cutaneous glands of fur bearing animals. It is closing similar to sebum.
v. Wax-D:
It is secreted by tuberculosis and leprosy causing bacteria. It is a measure cause of the diseases.
vi. Cerumen (ear wax):
Secreted from the ceruminous glands of external auditory canal.
vii. Paraffin wax:
It is obtained from petroleum. Candles are prepared from paraffin wax and stearic acid.

Structural Lipids in Membranes

The central architectural feature of biological membranes is a double layer of lipids, which constitutes a barrier to the passage of polar molecules and ions. Membrane lipids are amphipathic; the orientation of their hydrophobic and hydrophilic regions directs their packing into membrane bilayers. Three general types of membrane lipids will be described:glycerophospholipids, in which the hydrophobic regions are composed of two fatty acids joined to glycerol; sphingolipids, in which a single fatty acid is joined to a fatty amine, sphingosine; and sterols, compounds characterized by a rigid system of four fused hydrocarbon rings. The hydrophilic moieties in these amphipathic compounds may be as simple as a single -OH group at one end of the sterol ring system, or they may be more complex. Glycerophospholipids and sphingolipids contain polar or charged alcohols at their polar ends; some also contain phosphate groups (Fig. 9-6). Within these three classes of membrane lipids, enormous diversity results from various combinations of fatty acid "tails" and polar "heads." We describe here a representative sample of the types of membrane lipids found in living organisms.

The arrangement of these lipids in membranes, and their structural and functional roles therein, are considered in the next chapter.

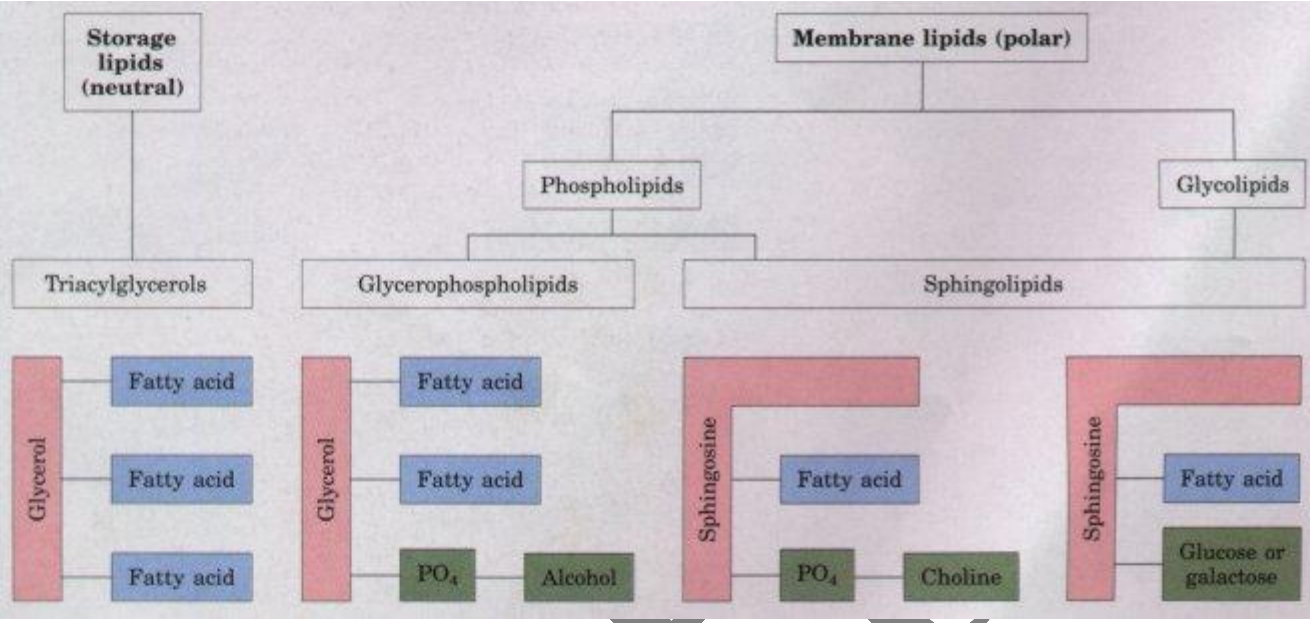
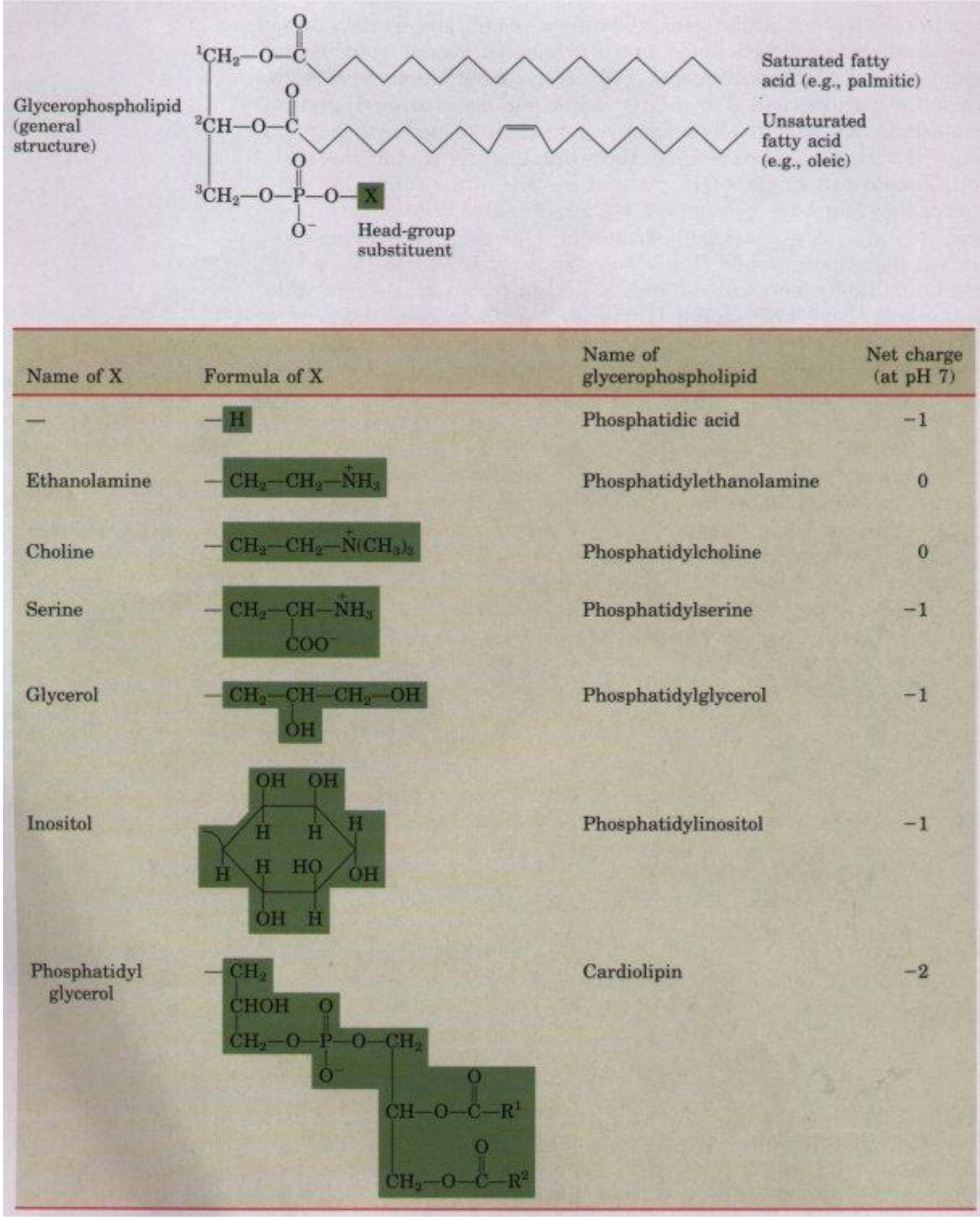


Figure 9-6 The principal classes of storage and membrane lipids. All of the classes shown here have either glycerol or sphingosine as the backbone. A third class of membrane lipids, the sterols, is described later (see Fig. 9-13).

Glycerophospholipids

Membranes contain several classes of lipids in which two fatty acids are ester-linked to glycerol at C-1 and C-2, and a highly polar or charged (and therefore hydrophilic) head group is attached to C-3 (Fig. 9-6). The most abundant of these polar lipids in most membranes are the glycerophospholipids, sometimes called phosphoglycerides (Fig. 9-7). In glycerophospholipids, a polar alcohol is joined to C-3 of glycerol through a phosphodiester bond. All glycerophospholipids are derivatives of phosphatidic acid (Fig. 9-7) and are named for their polar head groups (phosphatidylcholine and phosphatidylethanolamine, for example). All have a negative charge on the phosphate group at pH 7.0. The head-group alcohol may also contribute one or more charges at pH near 7.

The fatty acids in glycerophospholipids can be any of a wide variety. They are different in different species, in different tissues of the same species, and in different types of glycerophospholipids in the same cell or tissue. In general, glycerophospholipids contain a saturated fatty acid at C-1 and an unsaturated fatty acid at C-2, and the fatty acyl groups are commonly 16 or 18 carbons long-but there are many exceptions.



Name of X	Formula of X	Name of glycerophospholipid	Net charge (at pH 7)
—	—H	Phosphatidic acid	−1
Ethanolamine	$—CH_2—CH_2—\overset{+}{N}H_3$	Phosphatidylethanolamine	0
Choline	$—CH_2—CH_2—\overset{+}{N}(CH_3)_3$	Phosphatidylcholine	0
Serine	$—CH_2—\underset{COO^-}{CH}—\overset{+}{N}H_3$	Phosphatidylserine	−1
Glycerol	$—CH_2—\underset{OH}{CH}—CH_2—OH$	Phosphatidylglycerol	−1
Inositol	OH OH H H H H H HO OH OH H	Phosphatidylinositol	−1
Phosphatidyl glycerol	$—CH_2$ $CHOH \quad O$ $CH_2—O—P—O—CH_2$ O^- $CH—O—\overset{O}{C}—R^1$ $CH_2—O—\overset{O}{C}—R^2$	Cardiolipin	−2

Phospholipids Have Ether-Linked Fatty Acids

Some animal tissues and some unicellular organisms are rich in ether lipids, in which one of the two acyl chains is attached to glycerol in ether, rather than ester, linkage. The ether-linked chain may be saturated, as in the alkyl ether lipids, or may contain a double bond between C-1 and C-

2, as in plasmalogens (Fig. 9-8). Vertebrate heart tissue is uniquely enriched in ether lipids; about half of the heart phospholipids are plasmalogens. The membranes of halophilic bacteria, of ciliated protists, and of certain invertebrates also contain high proportions of ether lipids. Their functional significance in these membranes is unknown; perhaps they confer resistance to phospholipases that cleave ester-linked fatty acids from membrane lipids. At least one ether lipid, platelet-activating factor (Fig. 9-8), is an important hormone. It is released from white blood cells called basophils and stimulates platelet aggregation and the release of serotonin from platelets. It exerts a variety of effects on liver, smooth muscle, heart, uterine, and lung tissues, and plays an important role in inflammation and the allergic response.

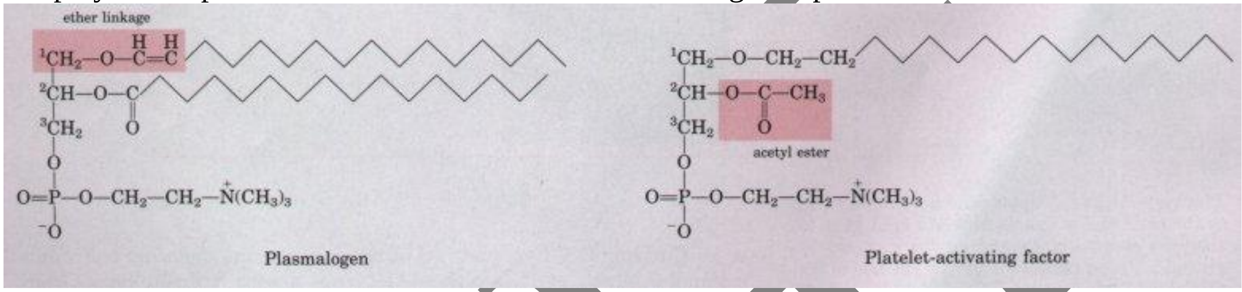


Figure 9-8 Plasmalogens and platelet-activating factor. Plasmalogens have one ether-linked alkenyl chain where most glycerophospholipids have an ester-linked fatty acid (compare Fig. 9-7). Plateletactivating factor has a long ether-linked alkyl chain at C-1 of glycerol, but C-2 is ester-linked to a very short fatty acid (acetic acid), which makes the compound much more water-soluble than most glycerophospholipids and plasmalogens. The head group alcohol is choline in plasmalogens and plateletactivating factor.

Galactolipids

Galactolipids are a type of glycolipid whose sugar group is galactose. They differ from glycosphingolipids in that they do not have nitrogen in their composition. They are the main part of plant membrane lipids where they substitute phospholipids to conserve phosphate for other essential processes. These chloroplast membranes contain a high quantity of monogalactosyldiacylglycerol (MGDG) and digalactosyldiacylglycerol (DGDG). They probably also assume a direct role in photosynthesis, as they have been found in the X-ray structures of photosynthetic complexes.

Galactolipids are more bioavailable than free fatty acids, and have been shown to exhibit COX mediated anti-inflammatory activity. Bio-guided fractionation of spinach leaves (*Spinacia oleracea*) revealed alpha-linolenic acid galactolipids (18:3, n-3) were responsible for inhibitory effects on tumor promoter-induced Epstein-Barr virus (EBV) activation. Recently, it has been demonstrated that this same galactolipid, 1,2-di-O-α-linolenoyl-3-O-α-D-galactopyranosyl-*sn*-glycerol, may be important for the anti-inflammatory activity of Dog Rose (*Rosa canina*), a medicinal plant with documented effect on inflammatory diseases such as arthritis.

The galactosphingolipid galactocerebroside (GalC) and its sulfated derivative sulfatide is also in abundance present (together with a small group of proteins) in myelin, the membrane around the axons in the nervous system of vertebrates. It is galactolipids, rather than phlorotannins, that act as herbivore deterrents in *Fucus vesiculosus* against the sea urchin *Arbacia punctulata*

Sphingolipids

Sphingolipids, the second large class of membrane lipids, also have a polar head and two nonpolar tails, but unlike glycerophospholipids they contain no glycerol. Sphingolipids are composed of one molecule of the long-chain amino alcohol sphingosine (4-sphingenine) or one of its derivatives, one molecule of a long-chain fatty acid, a polar head alcohol, and sometimes phosphoric acid in diester linkage at the polar head group (Fig. 9-9).

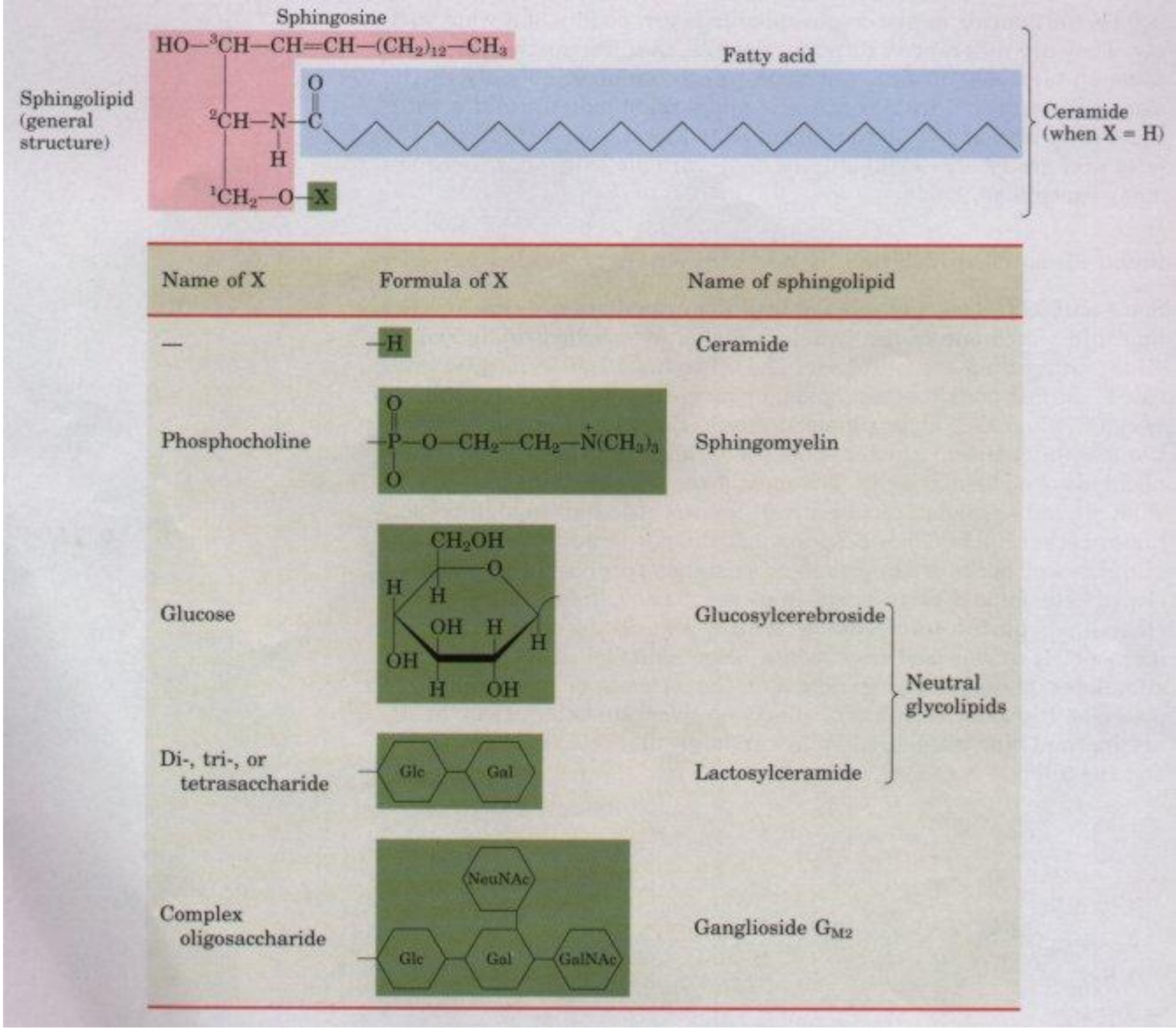


Figure 9-9 Sphingolipids. The first three carbons at the polar end of sphingosine are analogous to the three carbons of glycerol in glycerophospholipids. In ceramide, the parent compound for this group, the amino group at C-2 bears a fatty acid in amide linkage. Individual sphingolipids differ in the polar head group (X); attached at C-l. The fatty acid components of sphingolipids are usually saturated or monounsaturated, and contain 16, 18, 22, or 24 carbon atoms.

Gangliosides have very complex oligosaccharide head groups. These compounds are given identifying symbols (e.g., G_{M1}, G_{M2},) that indicate the structure of the head group. At least 15 different classes of gangliosides have been found in higher animals. Standard symbols for sugars are used in this figure: Glc, D-glucose; Gal, D-galactose; GalNAc, N-acetyl-n-galactosamine; NeuNAc, N-acetylneuraminic acid (sialic acid).

Carbons C-l, C-2, and C-3 of the sphingosine molecule bear functional groups (-OH, $-NH_2$, -OH) that are structurally homologous with the three hydroxyl groups of glycerol in glycerophospholipids. When a fatty acid is attached in amide linkage to the $-NH_2$, the resulting compound is a eeramide (Fig. 9-9), which is structurally similar to a diacylglycerol. Ceramide is the fundamental structural unit common to all sphingolipids.

There are three subclasses of sphingolipids, all derivatives of ceramide, but differing in their head groups: sphingomyelins, neutral (uncharged) glycolipids, and gangliosides (Fig. 9-9). Sphingomyelins contain phosphocholine or phosphoethanolamine as their polar head group, and are therefore classified as phospholipids, together with glycerophospholipids. Indeed, sphingomyelins resemble phosphatidylcholines in their general properties and three-dimensional structure, and in having no net charge on their head groups (Fig. 9-10). Sphingomyelins are present in plasma membranes of animal cells; the myelin sheath which surrounds and insulates the axons of myelinated neurons is a good source of sphingomyelins, and gives them their name.

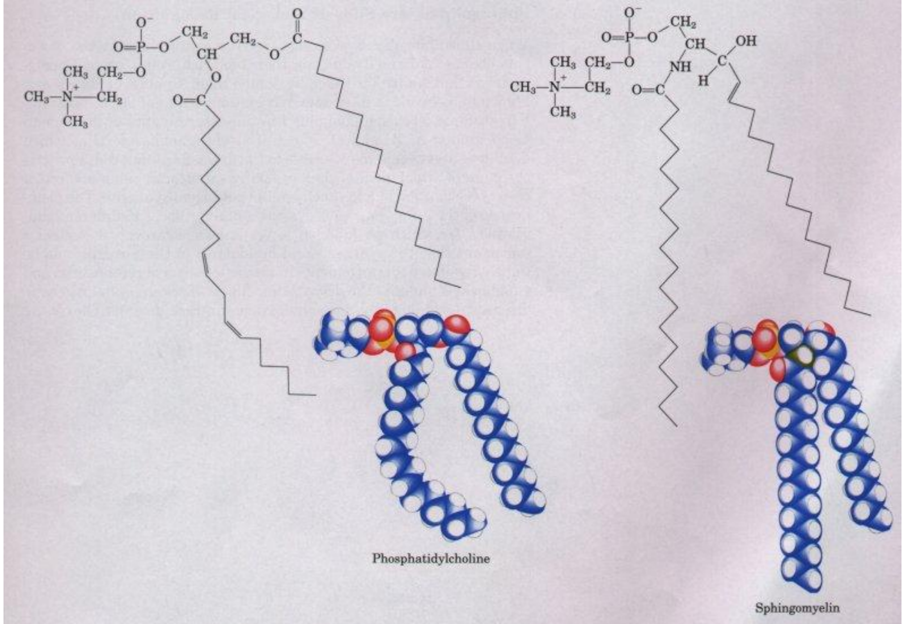
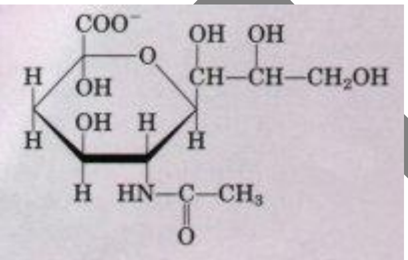


Figure 9–10 The similarities in shape and in molecular structure of phosphatidylcholine (a glycerophospholipid) and sphingomyelin (a sphingolipid) are clear when their space-filling and structural formulas are drawn as here.

Neutral glycolipids and gangliosides have one or more sugars in their head group, connected directly to the -OH at C-1 of the ceramide moiety; they do not contain phosphate. These sugar-containing sphingolipids are sometimes called glycosphingolipids. Neutral glycolipids contain one to six (sometimes more) sugar units, which may be n-glucose, n-galactose, or N-acetyl-n-galactosamine (Fig. 9-9). These glycosphingolipids occur largely in the outer face of the plasma membrane. Cerebrosides have a single sugar linked to ceramide (Fig. 9-9); those with galactose are characteristically found in the plasma membranes of cells in neural tissue, and those with glucose, in the plasma membranes of cells in nonneural tissues.

Gangliosides, the most complex sphingolipids (Fig. 9-9), contain very large polar heads made up of several sugar units. One or more of the terminal sugar units of gangliosides is N-acetylneuraminic acid, also called sialic acid, which has a negative charge at pH 7. Gangliosides make up about 6% of the membrane lipids in the gray matter of the human brain, and they are present in lesser amounts in the membranes of most nonneural animal tissues.



N-Acetylneuraminic acid
(sialic acid)

Sphingolipids

Sphingolipids Are Sites of Biological Recognition

When the sphingolipids were discovered a century ago by the physician-chemist Johann Thudicum, their biological role seemed as enigmatic as the Sphinx, for which he named them. Sphingolipids are now known to be involved in various recognition events at the cell surface. For example, glycosphingolipids are the determinants of the human blood groups A, B, and O (Fig. 9-11). The ganglioside G_{M1}, which doubtless plays some role of value to the animal cell that contains it, is the point of attachment of cholera toxin as it attacks an animal cell, a case of coevolution of a host cell and its pathogenic parasite. The membranes of the human nervous system contain at least 15 different gangliosides for which no function is yet known. However, it is clearly important that the synthesis and breakdown of these compounds be tightly regulated; derangements in the metabolism of cerebrosides and gangliosides underlie the devastating effects of several human genetic diseases, including Tay-Sachs and Niemann-Pick diseases (Box 9-2)

.

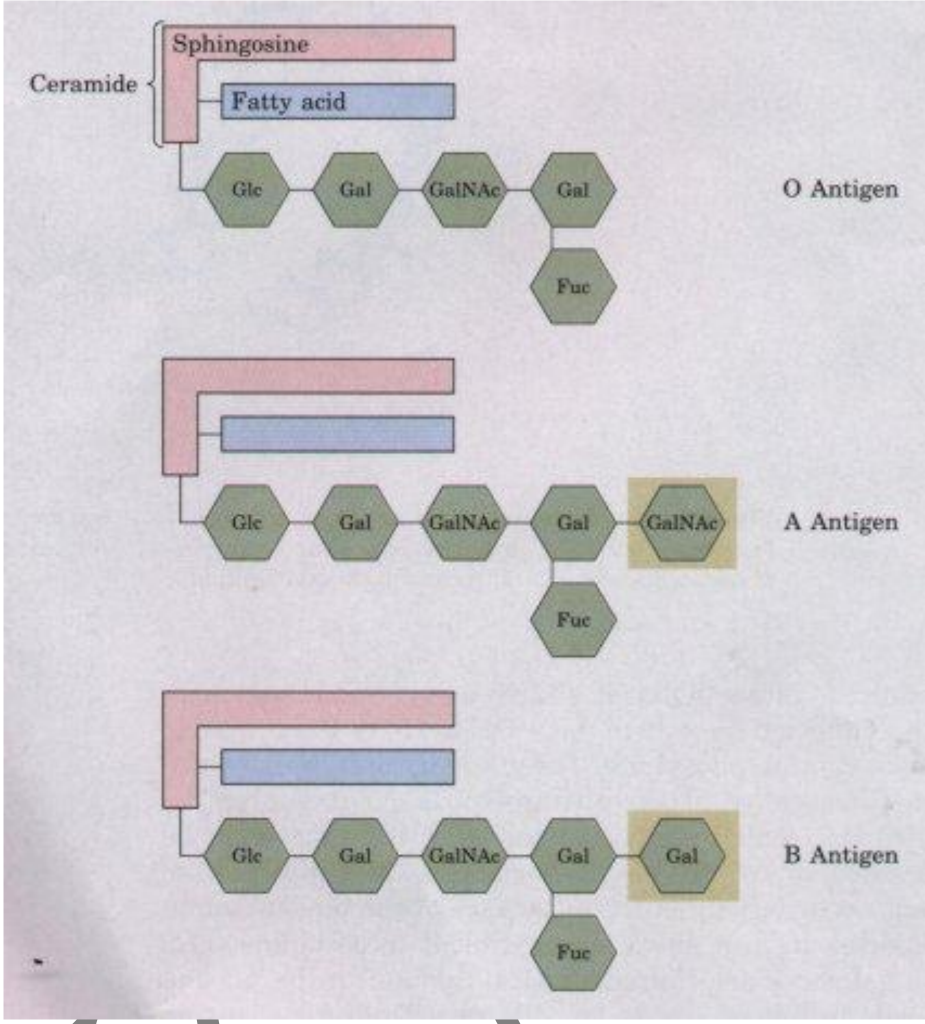


Figure 9-11 The human blood groups (O, A, B) are determined in part by the sugar head groups in these glycosphingolipids. The same three types of complex sugar groups are also found attached to certain blood proteins of individuals of blood types O, A, and B, respectively. The symbol Fuc represents the sugar fucose.

Specific Phospholipases Degrade Membrane Phospholipids

Most cells continually degrade and replace their membrane lipids. For each of the bonds in a glycerophospholipid, there is a specific hydrolytic enzyme (Fig. 9-12). Phospholipases of the A type remove one of the two fatty acids, producing a lysophospholipid; these esterases do not attack the ether link in plasmalogens. Lysophospholipases remove the remaining fatty acid.

Phospholipid breakdown is part of at least two signaling processes in animal cells. Extracellular signals (certain hormones, for example) activate a phospholipase C that specifically cleaves phosphatidylinositols, releasing diacylglycerol and inositol phosphates, which serve as intracellular signals. Other extracellular stimuli activate a phospholipase A that releases arachidonic acid from membrane lipids; arachidonate serves as a precursor in the synthesis of one of the eicosanoids that act as intracellular messengers.

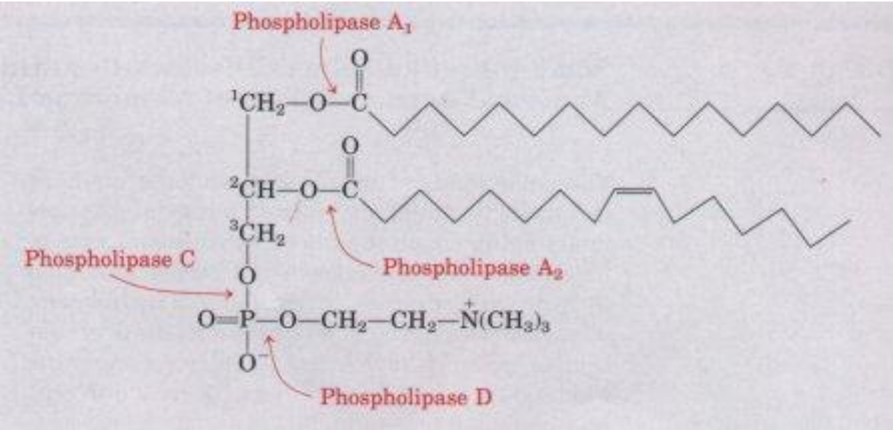


Figure 9-12 The specificities of phospholipases. Phospholipases A_1, and A_2hydrolyze the ester bonds of intact glycerophospholipids at C-1 and C-2 of glycerol, respectively. Phospholipases C and D each split one of the phosphodiester bonds in the head group, as indicated. Some phospholipases act only on one type of glycerophospholipid, such as phosphatidylinositol or phosphatidylcholine; others are less specific. When one of the fatty acids has been removed by a type-A phospholipase, the second fatty acid is cleaved from the molecule by a lysophospholipase

Sterols

Sterols are structural lipids present in the membranes of most eukaryotic cells.

Their characteristic structure is the steroid nucleus consisting of four fused rings, three with six carbons and one with five (Fig. 9-13). The steroid nucleus is almost planar, and relatively rigid; the fused rings do not allow rotation about C-C bonds. Cholesterol, the major sterol in animal tissues, is amphipathic, with a polar head group (the hydroxyl group at C-3) and a nonpolar hydrocarbon body (the steroid nucleus and the hydrocarbon side chain at C-17) about as long as a 16-carbon fatty acid in its extended form. Similar sterols are found in other eukaryotes: stigmasterol in plants and ergosterol in fungi, for example. With rare exceptions, bacteria lack sterols. The sterols of all species are synthesized from

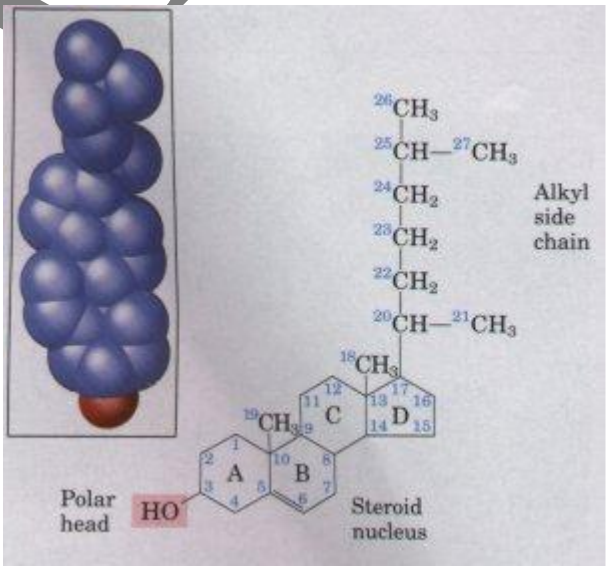
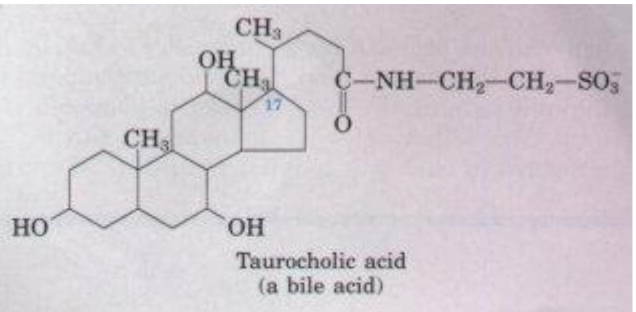


Figure 9-13 Cholesterol. To simplify reference to derivatives of the steroid nucleus, the rings are labeled A through D and the carbon atoms are

simple five-carbon isoprene subunits.

In addition to their roles as membrane constituents, the sterols serve as precursors for a variety of products with specific biological activities. Bile acids, in which the side chain at C-17 is hydrophilic, act as detergents in the intestine, emulsifying dietary fats to make them more readily accessible to digestive lipases. A variety of steroid hormones (described below) are also produced from cholesterol by oxidation of the side chain at C-17.

numbered (in blue) as shown. The hydroxyl group on C-3 represents the polar head group. For storage and transport of the sterol, this hydroxyl group condenses with a fatty acid to form a sterol ester.



Taurocholic acid
(a bile acid)

On receiving the Nobel Prize in 1985 for their work on cholesterol metabolism, Michael Brown and Joseph Goldstein recounted in their lecture the extraordinary history of cholesterol:

Cholesterol is the most highly decorated small molecule in biology. Thirteen Nobel Prizes have been awarded to scientists who devoted major parts of their careers to cholesterol. Ever since it was isolated from gallstones in 1784, cholesterol has exerted an almost hypnotic fascination for scientists from the most diverse areas of science and medicine.

We shall return to cholesterol later, to consider its role in biological membranes, its remarkable biosynthetic pathway, and its role as precursor to the steroid hormones.

Amphipathic Lipids Aggregate

We have noted that glycerophospholipids, sphingolipids, and sterols are virtually insoluble in water. When mixed with water, these amphipathic compounds form microscopic lipid aggregates in a phase separate from their aqueous surroundings. Lipid molecules cluster together with their hydrophobic moieties in contact with each other and their hydrophilic groups interacting with the surrounding water. Recall that lipid clustering reduces the amount of hydrophobic surface exposed to water and thus minimizes the number of molecules in the shell of ordered water at the lipid-water interface (see Fig. 4-7), resulting in an increase in entropy. Hydrophobic interactions among lipid molecules provide the thermodynamic driving force for the formation and maintenance of these structures.

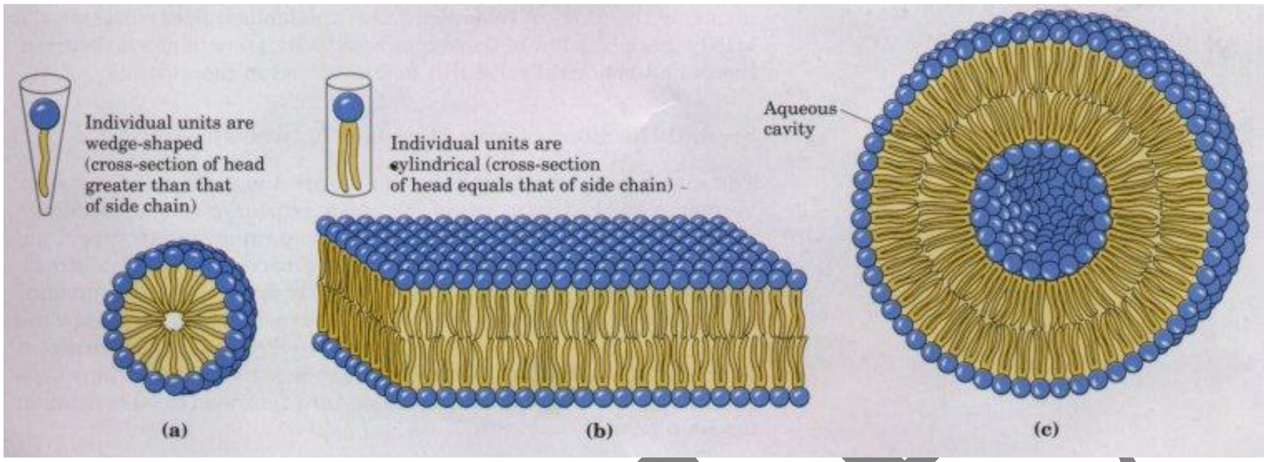


Figure 9-14 Amphipathic lipid aggregates that form in water. (a) In spherical micelles, the hydrophobic chains of the fatty acids are sequestered at the core of the sphere. There is virtually no water in the hydrophobic interior of the micelle. (b) In a bilayer, all acyl side chains except those at the edges of the sheet are protected from interaction with water. (c) When an extensive two-dimensional bilayer folds on itself, it forms a liposome, a threedimensional hollow vesicle enclosing an aqueous cavity.

Depending on the precise conditions and the nature of the lipids used, three types of lipid aggregates can form when amphipathic lipids are mixed with water (Fig. 9-14). Micelles are relatively small, spherical structures involving a few dozen to a few thousand molecules arranged so that their hydrophobic regions aggregate in the interior, excluding water, and their hydrophilic head groups are at the surface, in contact with water. Micelle formation is favored when the crosssectional area of the head group is greater than that of the acyl side chain(s) (Fig. 9-14a), as it is in free fatty acids, lysophospholipids (which lack one fatty acid), and the detergent SDS.

A second type of lipid aggregate in water is the bilayer, in which two lipid monolayers combine to form a two-dimensional sheet. Bilayer formation occurs most readily when the cross-sectional areas of the head group and side chain(s) are similar (Fig. 9-14b), as in glycerophospholipids and sphingolipids. The hydrophobic portions in each monolayer interact, excluding water. The hydrophilic head groups interact with water at the two surfaces of the bilayer.

The third type of lipid aggregate is formed when a lipid bilayer folds back on itself to form a hollow sphere called a liposome or vesicle (Fig. 9-14c). By forming vesicles, bilayer sheets lose their hydrophobic edge regions, achieving maximal stability in their aqueous environment. These bilayer vesicles enclose water, creating a separate aqueous compartment. It is likely that the first living cells resembled liposomes, their aqueous contents segregated from the rest of the world by a hydrophobic shell. We shall see in the next chapter that lipid bilayers are fundamental to the structure of all biological membranes.

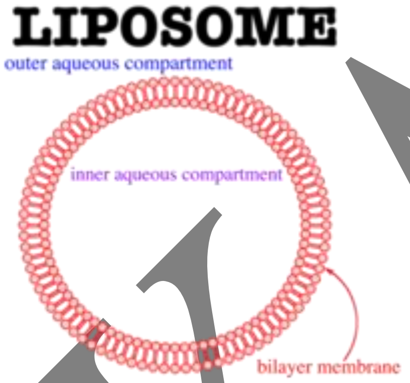
Structure, distribution and role of membrane lipids

Lipid Vesicles

Lipid vesicles, also known as **liposomes**, are vesicles that are essentially aqueous vesicles that are surrounded by a circular phospholipid bilayer. Like the other phospholipid structures, they have the hydrocarbon/hydrophobic tails facing inward, away from the aqueous solution, and the hydrophilic heads facing towards the aqueous solution. These vesicles are structures that form enclosed compartments of ions and solutes, and can be utilized to study the permeability of certain membranes, or to transfer these ions or solutes to certain cells found elsewhere.

Liposomes, with a diameter of roughly 500 A, are formed by dispelling a suitable lipid in an aqueous environment, and then sonicating the solution with high-frequency sound waves, for example, which aid these molecules to form a dispersed set of closed vesicles that are all nearly identical in size. Larger vesicles can be formed by placing a phospholipid in a solution containing both organic and aqueous solvents and then slowly evaporate the organic solvent. When this occurs with ions and solutes in the solution as well, that is when these compartments can entrap these ions and solutes in their lipid vesicles. The vesicles that contain the ions or solutes can then be separated by gel-filtration chromatography or dialysis. The permeability of a molecule can be obtained using this idea and then measuring the rate at which the molecule moves from the inner compartment of the vesicle to the outer solution.

The formation of liposomes is extremely useful in drug transport and delivery. Since drugs cannot readily diffuse through cell membranes, by creating liposomes in a solution containing a specific drug, the drug can enter into the cell by fusion of the liposome bilayer with the cell bilayer, delivering the liposome's contents. This technique can also be used to deliver DNA.



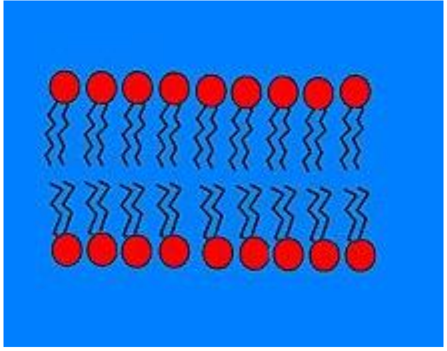
Liposomes as vesicles can serve various clinical uses. Injecting liposomes containing medicine or DNA (for gene therapy) into patients is a possible method of drug delivery. The liposomes fuse with other cells' membranes and therefore combine their contents with that of the patient's cell. This method of drug delivery is less toxic than direct exposure because the liposomes carry the drug directly to cells without any unnecessary intermediate steps. Long-circulating liposomes are more concentrated in regions of high blood circulation(like tumors and inflamed areas), and the selective fusion exhibited by liposomes allows them to be able to target specific types of cells. This is a very useful tool in designing carefully-controlled drug delivery techniques.

Lipid Bilayer

Because of the hydrophobic interactions among several phospholipids and glycolipids, a certain structure called the lipid bilayer or bimolecular sheet is favored. As mentioned earlier, phospholipids and glycolipids have both hydrophilic and hydrophobic moieties; thus, when several phospholipids or glycolipids come together in an aqueous solution, the hydrophobic tails interact with each other to form a hydrophobic center, while the hydrophilic heads interact with each other forming a hydrophilic coating on each side of the bilayer.

The cellular bilayer is not a rigid and clearly defined structure separating the intracellular and extracellular environments. Realistically, there is significant fluid motion of individual lipid headgroups and their aliphatic chains within the plane of the bilayer. This is due to the low torsional angle barriers within the structures of the lipids and to the steric hindrances that result from the cis-double bounds of some aliphatic chains.

Due to the large variety lipids that can exist in a single cell, regions of cellular membranes will comprise of heterogeneous mixtures of lipids and membrane proteins. The unique interactions within these heterogeneous regions are the bases of the function of the cellular membrane.



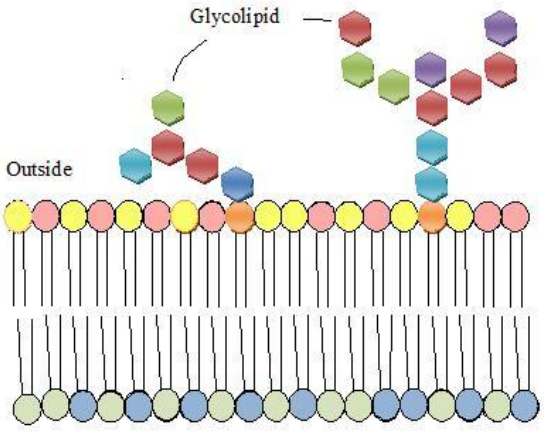
membrane bilayer

This lipid bilayer formation is spontaneous because of the hydrophobic interactions and energetically favorably structure. Other intermolecular forces such as Van der Waals, which hold the hydrophobic tails together, and hydrogen bonding, which bind the hydrophilic heads with water, help stabilize the lipid bilayer structure. Because of these interactions, the lipid bilayer inherits unique properties. The lipid bilayer have "extensive" properties, and can enclose and form compartments. Lastly, they can also recover quickly if there is a hole in the lipid bilayer, due to energetic reasons. However, phospholipids and glycolipids do not form micelles like fatty acids do because phospholipids and glycolipids have two fatty acids chains and are too big to form the interior of the micelle.

In aqueous solution, amphipathic molecules will orientate themselves in such a way as to prevent the hydrophobic region coming into contact with water molecules. In the case of those fatty acid salts which contain only one fatty acid chain (such as sodium palmitate, a constituent of soap), the molecules form a spherical micellar structure (diameter usually <20 nm) in which the hydrophobic fatty acid chains are hidden inside the micelle and the hydrophilic headgroups interact with the surrounding water molecules. Because the two fatty acid chains of phospholipids are too bulky to fit into the interior of a micelle, the favored structure for most phospholipids in aqueous solution is a two-dimensional bimolecular sheet or lipid bilayer.

Asymmetry of Lipid Bilayer

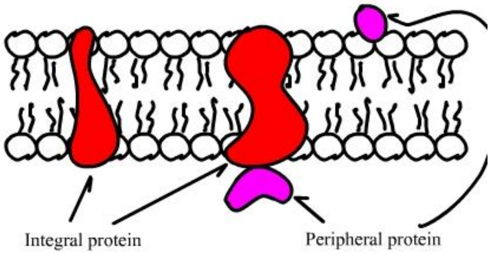
Plasma membranes are structurally and functionally asymmetric. There are different compositions and ratios of phospholipids inside and outside of lipid bilayer. In the plasma membrane, phosphatidylcholine and sphingomyelin are found in the outer monolayer (outer leaflet) but phosphatidylserine, phosphatidylethanolamine and the phosphatidylinositols are found in the inner monolayer (inner leaflet). Cholesterols are found in both leaflets.

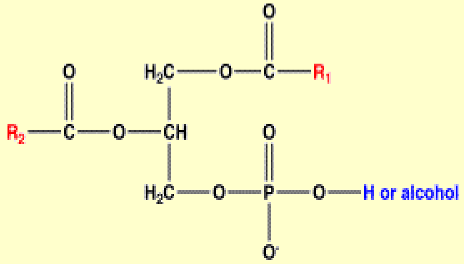
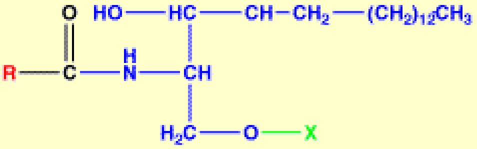
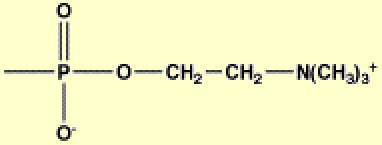
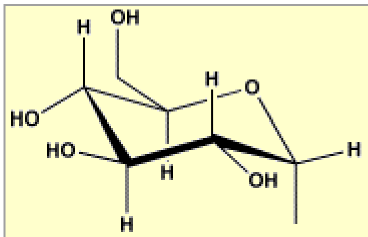
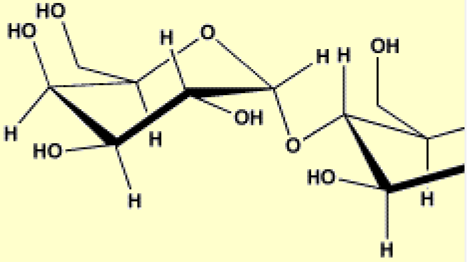
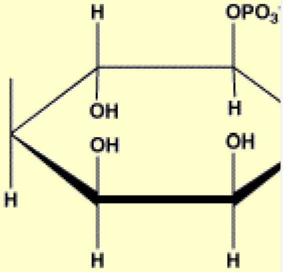
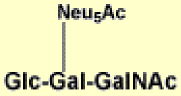


Asymmetry of Lipid Bilayer

The distribution of lipids between the lipid bilayer often changes to induce biological effect. A good example is that platelet moves phosphatidylserine to the outer leaflet to enable the ability of blood clotting. Phosphatidylserine is also an important signal for programmed cell death. In some cells, the presence of phosphatidylserine on the outer surface of cell membrane signals the immune system to destroy the marked cell. The asymmetry property of cell membrane enables cell to have multiple biological functions.

Membrane proteins are also inserted into the membrane in an asymmetric way. In a lipid membrane, there are proteins embedded in them. The mass ratio of the lipid molecules and the proteins that are embedded in them ranges from 1:4 to 4:1. There are two types of proteins in lipid bilayer: integral and peripheral membrane proteins. Integral membrane proteins traverse the lipid bilayer meaning they interact extensively with the hydrophobic region (hydrocarbon region) of the lipid bilayer. Peripheral membrane proteins are usually attached to surfaces of integral proteins; therefore, they are on both faces of lipid bilayer. Peripheral membrane proteins interact with the hydrophilic polar head groups of the lipid molecule. Some peripheral membrane proteins can only be found outside the membrane or inside the membrane. This contributes the asymmetric property of membrane.

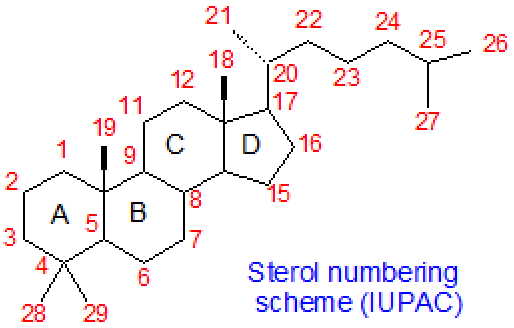


<table>
<tr><td colspan="2">
glycerophospholipids</td><td colspan="2">
glycolipids</td></tr>
<tr><td>Name</td><td>Alcohol</td><td>Name</td><td>X</td></tr>
<tr><td>phosphatidic acid</td><td>H</td><td>ceramide</td><td>H</td></tr>
<tr><td>phosphatidylethanolamine</td><td>$—CH_2—CH_2—NH_3^+$
ethanolamine</td><td>sphingomyelin</td><td>$—\overset{O}{\overset{\|}{\underset{O^-}{\underset{|}{P}}}}—O—CH_2—CH_2—N(CH_3)_3^+$
phosphocholine</td></tr>
<tr><td>phosphatidylcholine</td><td>$—CH_2—CH_2—N(CH_3)_3^+$
choline</td><td>glucosylcerebroside</td><td>
glucose</td></tr>
<tr><td>phosphatidylserine</td><td>serine</td><td>lactosylceramide (globoside)</td><td>
glucose-galactose</td></tr>
<tr><td>phosphatidylinositol-4,5-bisphosphate</td><td>
myo-inositol-4,5-bisphosphate</td><td>ganglioside</td><td>
complex oligosaccharide</td></tr>
</table>

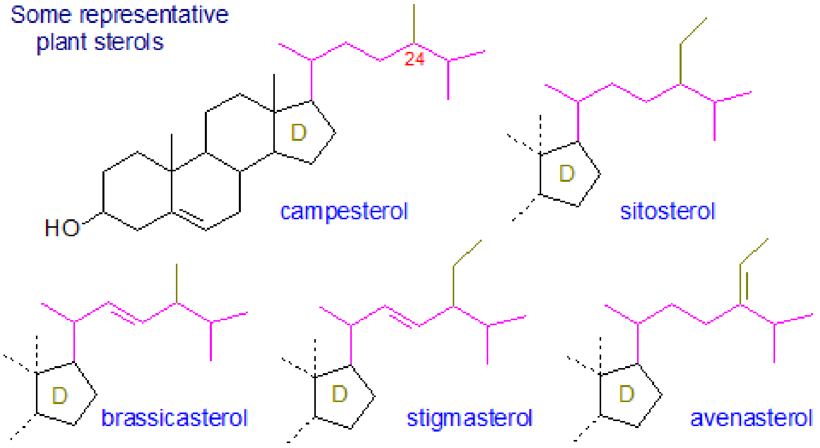
Membrane lipids are a broad group consisting of phospholipids (glycerophospholipids, sphingoplipids with phosphate) and glycolipids (sphingolipids lacking phosphate). Sphingolipids are based upon sphingosine. As you can observe, sphingolipids may include or lack a phosphate group. The X group in glycolipids (sphingolipids) is a mono-, di, tri, tetra, or oligosaccharide.

Plant steroids

Plants, algae and fungi contain a rather different range of sterols from those in animals. Like cholesterol, to which they are related structurally and biosynthetically, plant sterols form a group of triterpenes with a tetracyclic cyclopenta[*a*]phenanthrene structure and a side chain at carbon 17. The four rings (A, B, C, D) have *trans* ring junctions, and the side chain and two methyl groups (C-18 and C-19) are at an angle to the rings above the plane with β stereochemistry (as for a hydroxyl group commonly located on C-3 also). The basic sterol from which other sterol structures are defined is 5α-cholestan-3β-ol with the numbering scheme recommended by IUPAC.



The phytosterols (as opposed to zoosterols) include campesterol, β-sitosterol, stigmasterol and Δ5-avenasterol, some of which are illustrated. These more common plant sterols have a double bond in position 5, and a definitive feature – a one- or two-carbon substituent with variable stereochemistry in the side chain at C-24, which is preserved during subsequent metabolism. For example, campesterol is a 24-methylsterol, while β-sitosterol and stigmasterol are 24-ethylsterols. Occasionally, there is a double bond in this chain that can be of the *cis* or *trans* configuration.



Phytosterols can be further classified on a structural or biosynthetic basis as 4-desmethyl sterols (i.e. with no substituent on carbon-4), 4α-monomethyl sterols and 4,4-dimethyl sterols. The most abundant group are the 4-desmethyl sterols, which may be subdivided into Δ5-sterols, Δ7-sterols and Δ5,7-sterols depending on the position of the double bonds in the B ring. As the name suggests, brassicasterols (24-methyl-cholesta-5,22-dien-3β-ol) and related sterols are best known from the brassica family of plants, but they are also common constituents of marine algae (phytoplankton). Phytostanols (fully saturated) are normally present at trace levels only in plants, but they are relatively abundant in cereal grains.

Many different sterols may be present in photosynthetic organisms, and the amounts and relative proportions are dependent on the species. Over 250 different phytosterols have been recorded with 60 in corn (maize) alone, for example. As a rough generality, a typical plant sterol mixture would be 70% sitosterol, 20% stigmasterol and 5% campesterol (or >70% 24-ethyl-sterols and <30% 24-methyl-sterols).

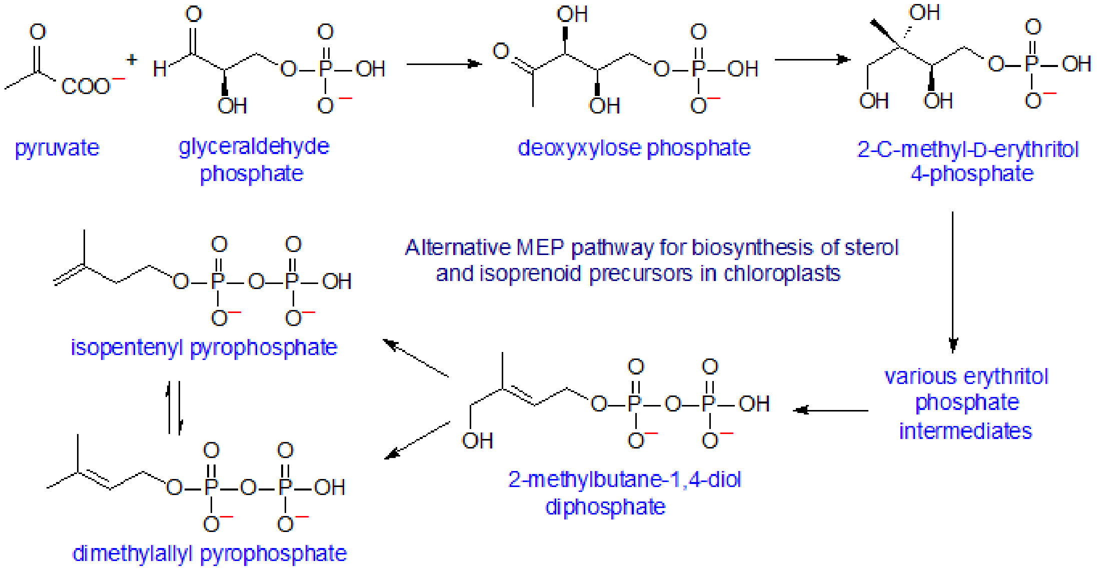
Cholesterol is usually a minor component only of plant sterols (<1%), but it is unwise to generalize too much as it can be the main sterol component of red algae and of some families of higher plants such as in the Solanaceae, Liliaceae and Scrophylariaceae. It can also be a significant constituent sterol of chloroplasts, shoots, pollen and leaf surface lipids in other plant families; wheat roots contain 10% and Arabidopsis cells 19% of the sterols as cholesterol. Yeasts and fungi tend to contain ergosterol as their main sterol.

Ecdysteroids (phytoecdysteroids) are polyhydroxylated plant sterols that can occur in appreciable amounts in some species.

Sterols can occur in plants in the 'free' state, i.e. in which the sterol hydroxyl group is not linked to any other moiety, but they are usually present also as conjugates with the hydroxyl group covalently bound via an ester bond to a fatty acid, for example, i.e. as sterol esters, or via a glycosidic linkage to glucose (and occasionally other sugars), i.e. as steryl glycosides.

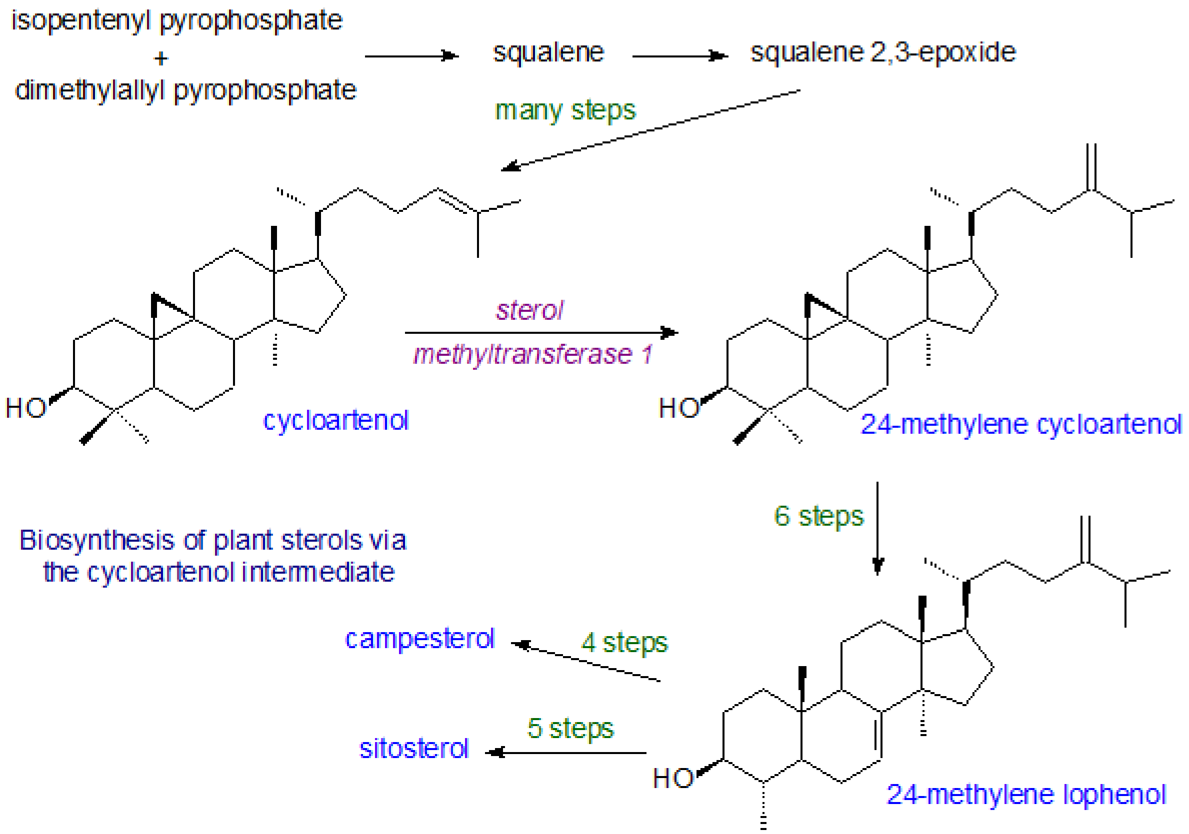
Biosynthesis: The biosynthetic route to plant sterols resembles that to cholesterol in many aspects in that it follows an isoprenoid biosynthetic pathway with isopentenyl pyrophosphate, derived primarily from mevalonate, as the key building block in the cytoplasm (but not plastids) at least. The main pathway for the biosynthesis of isopentenyl pyrophosphate and dimethylallyl pyrophosphate, the isoprene units, is described in our web page on cholesterol and so need not be repeated here. It is known as the 'mevalonic acid (MVA) pathway' and functions in the cytosol, endoplasmic reticulum and mitochondria.

However, an alternative pathway that does not use mevalonic acid as a precursor was established first for bacterial hopanoids, but has since been found in plant chloroplasts, algae, cyanobacteria, eubacteria and some parasites (but not in animals). This route is variously termed the ‘non-mevalonate’, ‘1-deoxy-D-xylulose-5-phosphate’ (DOXP) or better the '2*C*-methyl-D-erythritol 4-phosphate (MEP)' pathway as the last compound is presumed to be the first committed intermediate in sterol biosynthesis by this route. In the first step, pyruvate and glyceraldehyde phosphate are combined to form deoxyxylose phosphate, which is in turn converted to 2C-methyl-D-erythritol 4-phosphate. The pathway then proceeds via various erythritol intermediates until isopentenyl pyrophosphate and dimethylallyl pyrophosphate are formed, when sterol biosynthesis thereafter continues via squalene and cycloartenol. There is evidence that some of the isoprene units are exchanged between the cytoplasm and plastids. In much of the plant kingdom, both the MVA and MEP pathways operate in parallel, but green algae use the MEP pathway only.



Alternative MEP pathway for biosynthesis of sterol and isoprenoid precursors in chloroplasts

In photosynthetic organisms (as opposed to yeast and fungi), the subsequent steps in the biosynthesis of plant sterols differ from that for cholesterol in that the important intermediate in the route from squalene via 2,3-oxidosqualene is cycloartenol, rather than lanosterol, and this is produced by the action of a 2,3(*S*)-oxidosqualene-cycloartenol cyclase (cycloartenol synthase). Then, the enzyme sterol methyltransferase 1 is of special importance in that it converts cycloartenol to 24-methylene cycloartenol, as the first step in introducing the methyl group onto C-24, while the enzyme cyclopropyl sterol isomerase is required to open the cyclopropane ring. Animals lack the sterol C24-methyltransferase gene. While this pathway is in essence linear up to the synthesis of 24-methylene lophenol, a bifurcation then occurs that results in two alternative pathways, one of which leads to the synthesis of sitosterol and stigmasterol and the other to that of campesterol. In fact, there are more than thirty enzyme-catalysed steps in the overall process of plant sterol biosynthesis, each associated with membranes, and detailed descriptions are available from the reading list below. The 4,4-dimethyl- and 4α-methylsterols are part of the biosynthetic pathway, but are only minor if ubiquitous sterol components of plants.

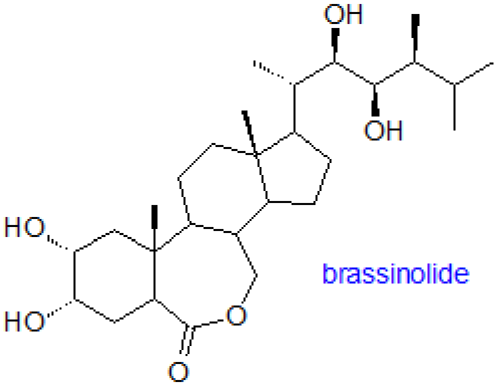


Biosynthesis of plant sterols via the cycloartenol intermediate

Cholesterol in plants is also produced from cycloartenol as the key intermediate. It is now established that the cholesterol biosynthetic pathway in tomato plants comprises 12 enzymes acting in 10 steps. Of these, half evolved through gene duplication and divergence from phytosterol biosynthetic enzymes, whereas others act reciprocally in both cholesterol and phytosterol metabolism. It is hoped that genetic manipulation of these enzymes will lead to plants that synthesise high value steroidal products.

Function: Like cholesterol, plant sterols are amphiphilic and are vital constituents of all membranes, and especially of the plasma membrane, the mitochondrial outer membrane and the endoplasmic reticulum. The three-dimensional structure of the plant sterols is such that there are planar surfaces at both the top and the bottom of the molecules, which permit multiple hydrophobic interactions between the rigid sterol and the other components of membranes. Indeed, they must determine the physical properties of membranes to an appreciable extent. It is believed that campesterol, β-sitosterol and 24-methylcholesterol (in this order) are able to regulate membrane fluidity and permeability in plant membranes by restricting the mobility of fatty acyl chains in a similar manner to cholesterol in mammalian cells, but stigmasterol has much less effect on lipid ordering and no effect on the permeability of membranes. In the plasma membrane, plant sterols associate with the glycosphingolipids such as glucosylceramide and glycosylinositolphosphoceramides inraft-like sub-domains, analogous to those in animal cells. The sterol glycosides are especially important in this context (see below).

Sterols are involved in how plant membranes adapt to changes in temperature and other biotic and abiotic stresses. For example, β-sitosterol is a precursor of stigmasterol via the action of a C22-sterol desaturase, and the ratio of these two sterols is important to the resistance of *A. thaliana* plants to low and high temperatures. In addition, plant sterols can modulate the activity of membrane-bound enzymes. Thus, stigmasterol and cholesterol regulate the activity of the Na^+/K^+-ATPase in plant cells, probably in a manner analogous to that of cholesterol in animal cells. Stigmasterol may be required specifically for cell differentiation and proliferation.



Perhaps surprisingly, cholesterol is a precursor for the biosynthesis of some steroidal saponins and alkaloids, for example the well-known steroidal glycoalkaloid in potato (α-solanine), as well as of other steroids including the phytoecdysteroids (in some species they are derived from lathosterol). While the physiological roles of ecdysteroids in plants has yet to be been confirmed, they are believed to enhance stress resistance by promoting health and vitality. Withanolides are complex oxysterols, which are believed to be defence compounds against insect herbivores. Certain sterols, such as campesterol in *A. thaliana*, are precursors of a family of nearly 70 polyhydroxy steroids that occur in minute amounts and act as growth hormones; they are collectively named brassinosteroids, including brassinolide illustrated. They have crucial importance for plant growth processes, including cell elongation, division, differentiation, immunity and development of reproductive organs in that they are involved in the regulation of innumerable genes and metabolic processes. They may even have some biomedical applications.

Oxidation: Phytosterols can be subjected to non-enzymatic oxidation with formation of oxysterols in a similar manner to that of cholesterol in animals, resulting in ring products such as hydroxy-, keto-, epoxy- and triol-derivatives, and further enzymic reactions can oxidize the side chain.

Lipids as signals, cofactors and pigments

Lipids are not just used as a passive component of membranes, or as a source of stored energy. They are involved in the process of signal transduction at the cell membrane, a process by which the interior components of the cell respond to a signal external to the cell, allowing the cell to respond to their local environment. Usually a chemical signal on the outside of the cell is the "primary messenger" that causes the cell to respond. Usually the chemical transmitter of information does not get into the cell. Rather it binds to surface receptors on the cell membrane surface. Somehow, the cells senses that a ligand is bound to the outside. Enzymes, usually in the membrane or at the intracellular surface of the lipid bilayer are activated. Many of these enzymes cleave lipids in the membrane. The cleaved fragments of the lipid molecules serve as intracellular signals or "secondary messengers" , which can bind to intracellular enzymes to activate intracellular processes. The following diagram shows some of the lipid mediators which are generated by the process and signal the cell to respond.

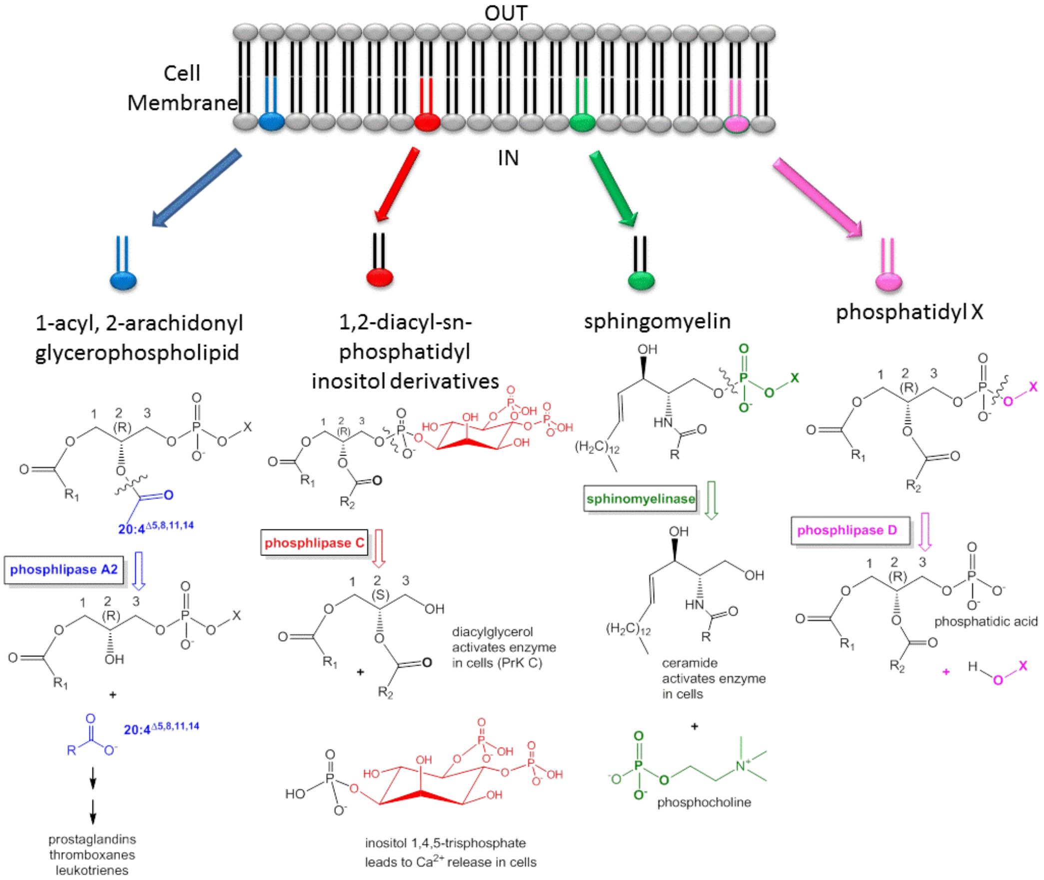
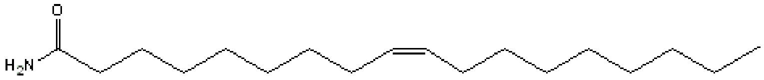


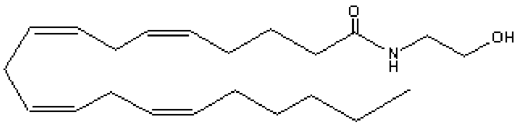
Figure: Lipids - More than Grease - Mediators in Signal Transduction

Recently, fatty acid amides have been shown to be potent mediators of neurological processes. In one interesting experiment, sheep were sleep deprived. Reasoning that the brain might release a biochemical signal into cerebrospinal fluid to induce sleep, scientists at Scripps removed some of this fluid and isolated a substance that was not found in rested sheep. On analysis, the structure was shown to be an amide of oleic acid.. Oleylethanolamide has been shown to bind to the peroxisome-proliferator-activated receptor-a (PPAR-a) which resides in the nucleus. This ligand, by affecting gene transcription, appears to regulate body weight and the feeling of fullness after eating (satiety) as it ieads to reduced eating.

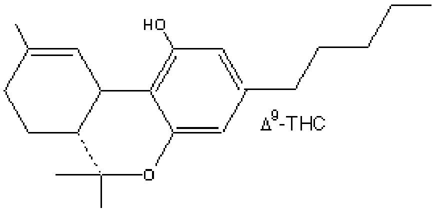
In an analogous fashion, people have sought the natural neurotransmitter which binds to the same receptor in the brain as THC, the active ingredient of marijuana. This was found several years ago and was shown to be the amide of arachidonic acid, called anandamide. See the figure below for structures.



oleamide -sleep inducing fatty acid amide



arachidonylethanolamide (anandamide)
endogenous THC-like ligand



Δ^9-THC

Figure: Fatty Acid Amides: Neurochemical Mediators

This fatty acid amide is an examples of a class of lipid derivatives called N-acylethanolamines (NAEs). These molecules, with acyl groups that vary in number of carbons and double bonds, are found widely in organisms in nature. Naturally occurring anandamide leads to increased food intake after a short period of reduced food intake. One of the known physiological effects of THC is increased food consumption (the munchies).

The isoprenoids include vitamins A, D, E, and K, first recognized as fatty materials essential to the normal growth of animals, and numerous biological pigments. Other "active" lipids serve as essential cofactors for enzymes, as electron carriers, or as intracellular signals. To illustrate the range of their structures and biological activities we will briefly describe a few of these compounds. In later chapters, their synthesis and biological roles will be considered in more detail.

Steroid Hormones Carry Messages between Tissues

The major groups of steroid hormones are the male and female sex hormones and the hormones of the adrenal cortex, cortisol and aldosterone (Fig. 9-15). All of these hormones contain an intact steroid nucleus. They are produced in one tissue and carried in the bloodstream to target tissues, where they bind to highly specific receptor proteins and trigger changes in gene expression and metabolism. Because of the very high affmity of receptor for hormone, very low concentrations of hormone (as low as 10^{-9} M) sufiice to produce the effect on target tissues.

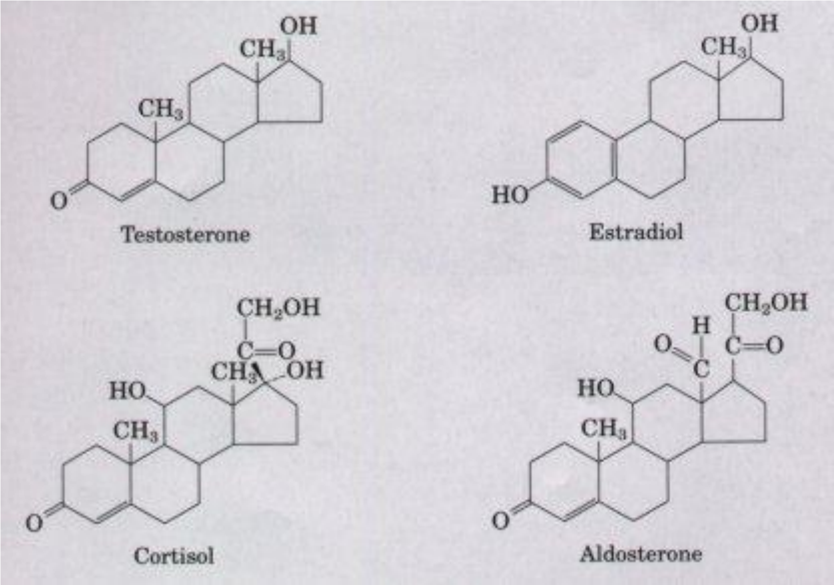


Figure 9-15 Steroids derived from cholesterol. Testosterone, the male sex hormone, is produced in the testes. Estradiol, one of the female hormones, is produced in the ovaries and placenta. Cortisol and aldosterone are hormones produced in the cortex of the adrenal gland; they regulate glucose metabolism and salt excretion, respectively

Hydrolysis of Phosphatidylinositol Produces Intracellular Messengers

Phosphatidylinositol and its phosphorylated derivatives (Fig. 9-16) are components of the plasma membranes of all eukaryotic cells. They serve as a reservoir of messenger molecules that are released inside the cell when certain extracellular signals interact with specific receptors in the plasma membrane. For example, when the hormone vasopressin binds to receptor molecules in the plasma membranes of cells in the kidney and the blood vessels, a specific phospholipase in the membrane is activated. This phospholipase breaks the bond between glycerol and phosphate in phosphatidylinositol-4,5-bisphosphate (Fig. 9-16), releasing two products: inositol-1,4,5-trisphosphate and diacylglycerol. Inositol-1,4,5-trisphosphate causes the release of Ca^{2+} sequestered in membrane-bounded compartments of the cell, triggering the activation of a variety of Ca^{2+}-dependent

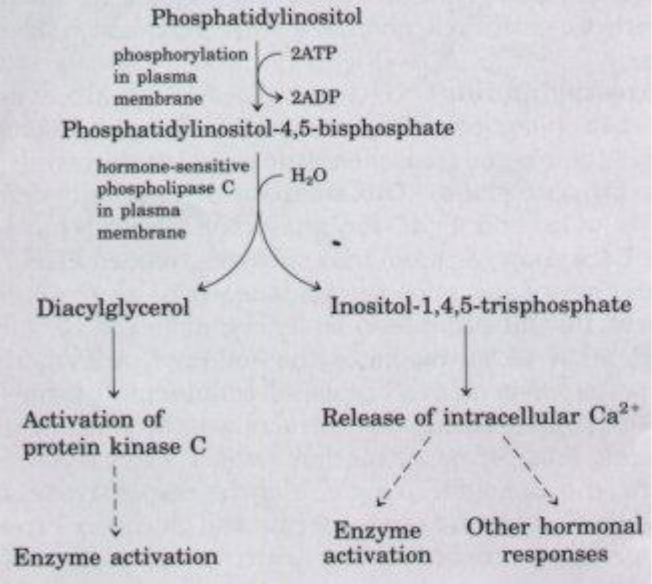


Figure 9-16 Phosphatidylinositol-4,5-bisphosphate, formed in the plasma membrane by phosphorylation of phosphatidylinositol, is hydrolyzed by a specific phospholipase C in response to hormonal signals. Both of the products

enzymes and hormonal responses. of hydrolysis act as intracellular messengers. Diacylglycerol binds to and activates an enzyme, protein kinase C, that transfers phosphate groups from ATP to several cytosolic proteins, thereby altering their enzymatic activities.

Eicosanoids Are Potent Biological Effectors

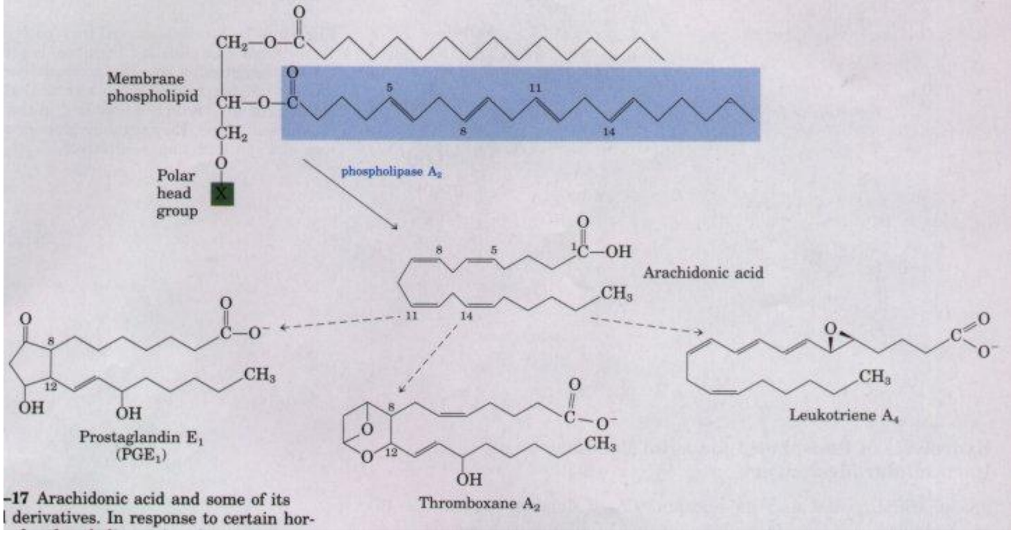


Figure 9-17 Arachidonic acid and some of its eicosanoid derivatives. In response to certain hormonal signals, phospholipase A_2 releases arachidonic acid (arachidonate at pH 7) from membrane phospholipids; arachidonic acid then serves as a precursor to various eicosanoids. These include prostaglandins such as PGE_1, in which carbon atoms 8 and 12 of arachidonic acid are joined to form the characteristic five-membered ring; thromboxane A_2, in which carbons 8 and 12 are joined and an oxygen atom is added to form the sixmembered ring; and leukotriene A, containing a series of three conjugated double bonds. Aspirin and ibuprofen block the formation of prostaglandins and thromboxanes from arachidonic acid.

Eicosanoids (Fig. 9-17) are fatty acid derivatives with a variety of extremely potent hormonelike actions on various tissues of vertebrate animals. Unlike hormones, they are not transported between tissues in the blood, but act on the tissue in which they are produced. This family of compounds is known to be involved in reproductive function; in the inflammation, fever, and pain associated with injury or disease; in the formation of blood clots and the regulation of blood pressure; in gastric acid secretion; and in a variety of other processes important in human health or disease. More roles for the eicosanoids doubtless remain to be discovered.

Eicosanoids are all derived from the 20-carbon polyunsaturated fatty acid arachidonic acid, $20:4(\Delta^{5,8,11,14})$ (Fig. 9-17), from which they take their general name (Greek eihosi, "twenty"). There are three classes of eicosanoids: prostaglandins, thromboxanes, and leukotrienes. Various eicosanoids are produced in different cell types by dif ferent synthetic pathways, and have different target cells and biological actions.

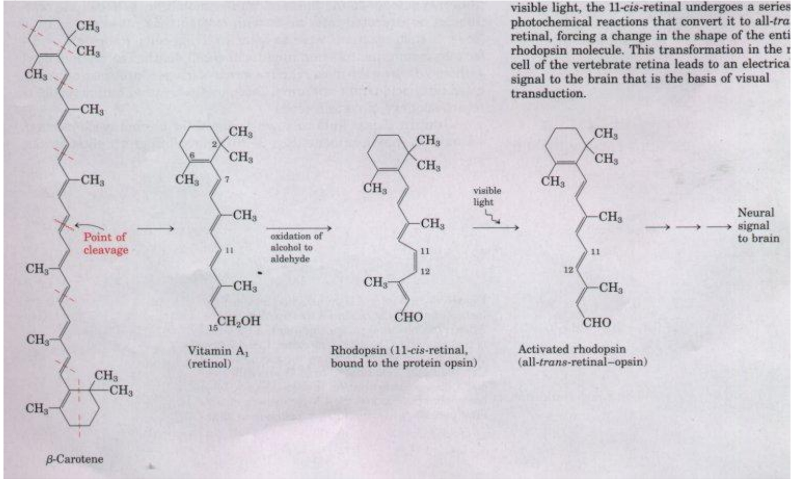
The prostaglandins (PG) (Fig. 9-17) all contain a five-membered ring of carbon atoms originally part of the chain of arachidonic acid. They derive their name from the tissue in which they were first recognized (the prostate gland). 'Iwo groups were originally defined: PGE, for ether-soluble, and PGF, for phosphate buffer-soluble (fosfczt in Swedish). Each contains numerous subtypes, named PGE_1,, PGE_2, etc. Prostaglandins are now known to act in many tissues by regulating the synthesis of the intracellular messenger molecule 3',5'-cyclic AMP (cAMP). Because cAMP mediates the action of many hormones, the prostaglandins affect a wide range of cellular and tissue functions. Some prostaglandins stimulate contraction of the smooth muscle of the uterus during labor or menstruation. Others affect blood flow to specific organs, the wake-sleep cycle, and the responsiveness of certain tissues to hormones such as epinephrine and glucagon. Prostaglandins in a third group elevate body temperature (producing fever) and cause inflammation, resulting in pain.

The thromboxanes, first isolated from blood platelets (also known as thrombocytes), have a six-membered ring containing an ether (Fig. 9-17). They are produced by platelets and act in formation of blood clots and the reduction of blood flow to the site of a clot.

Leukotrienes, found first in leukocytes, contain three conjugated double bonds (Fig. 9-17). They are powerful biological signals; for example, they induce contraction of the muscle lining the airways to the lung. Overproduction of leukotrienes causes asthmatic attacks. The strong contraction of the smooth muscles of the lung that occurs during anaphylactic shock is part of the potentially fatal allergic reaction in individuals hypersensitive to bee stings, penicillin, or various other agents.

Vitamins A, D, E, and K Are Fat-Soluble

During the first third of this century, a major focus of research in physiological chemistry was the identification of vitaminscompounds essential to the health of humans and other vertebrate animals that cannot by synthesized by these animals and must therefore be obtained in the diet. Early nutritional studies identified two general classes of such compounds: those soluble in nonpolar organic solvents (fat-soluble vitamins) and those that could be extracted from foods with aqueous solvents (water-soluble vitamins). Eventually the fat-soluble group was resolved into the four vitamins A, D, E, and K, all of which are isoprenoid compounds. Isoprenoids are synthesized by the condensation of isoprene units.



visible light, the 11-*cis*-retinal undergoes a series
photochemical reactions that convert it to all-*tra*
retinal, forcing a change in the shape of the enti
rhodopsin molecule. This transformation in the r
cell of the vertebrate retina leads to an electrica
signal to the brain that is the basis of visual
transduction.

Figure 9-18 Vitamin A_1 and its precursor, β-carotene. The isoprene structural units are set off by dashed red lines. Cleavage of β-carotene yields two molecules of vitamin A_1 (retinol). Oxidation at C-15 converts retinol to the aldehyde, retinal. Rhodopsin, a visual pigment widely employed in nature, consists of retinal and the protein opsin. In the dark, retinal of rhodopsin is in the 11-cis form. When a rhodopsin molecule is excited with visible light, the 11-cis-retinal undergoes a series of photochemical reactions that convert it to all-transretinal, forcing a change in the shape of the entire rhodopsin molecule. This transformation in the rod cell of the vertebrate retina leads to an electrical signal to the brain that is the basis of visual transduction.

Vitamin A (retinol) (Fig. 9-18) is a pigment essential to vision. It was first recognized as an essential nutritional factor for laboratory animals, and was later isolated from fish liver oils. Vitamin A itself does not occur in plants, but many plants contain carotenoids, lightabsorbing pigments that can be enzymatically converted into vitamin A by most animals. Figure 9-18 shows, for example, how vitamin A can be formed by cleavage of ,β-carotene, the pigment that gives carrots, sweet potatoes, and other yellow vegetables their characteristic color. Deficiency of vitamin A leads to a variety of symptoms in humans and experimental animals, which include dry skin, xerophthalmia (dry eyes), dry mucous membranes, retarded development and growth, sterility in male animals, and night blindness, an early symptom commonly used in the medical diagnosis of vitamin A deficiency.

Vitamin D is a derivative of cholesterol and the precursor to a hormone essential in calcium and phosphate metabolism in vertebrate animals. Vitamin D_3, also called cholecalciferol, is normally formed in the skin in a photochemical reaction driven by the ultraviolet component of sunlight (Figure 9-19). It is also abundant in fish liver oils, and is added to commercial milk as a nutritional supplement. Vitamin D_3 itself is not biologically active, but it is the precursor of 1,25-dihydroxycholecalciferol, a potent hormone that regulates the uptake of calcium

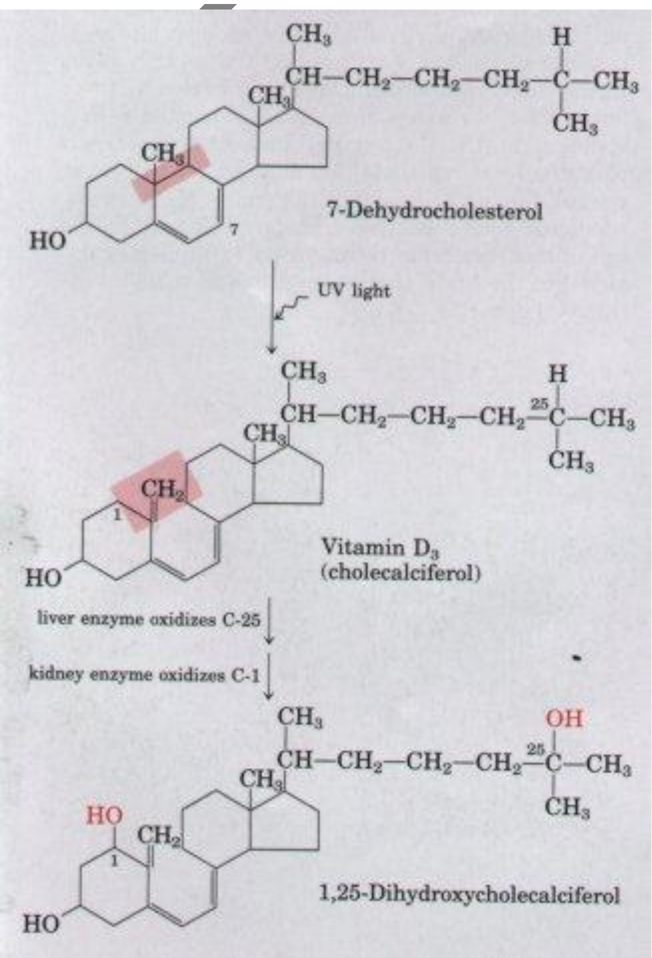


Figure 9-19 Vitamin D_3 production and metabolism. Vitamin D_3 is produced by irradiation of 7-dehydrocholesterol in the skin, and in the kidney is converted into the active hormone, 1,25-dihydroxycholecalciferol, which regulates the metabolism of Ca^{2+} and $P0_4^{3-}$. Dietary vitamin D prevents rickets, a disease once common in cold climates, where heavy clothing blocked the LTV component of sunlight necessary to vitamin

in the intestine and the balance of release and D_3production in skin deposition of bone calcium and phosphate. Deficiency of vitamin D leads to defective bone formation, resulting in the disease rickets.

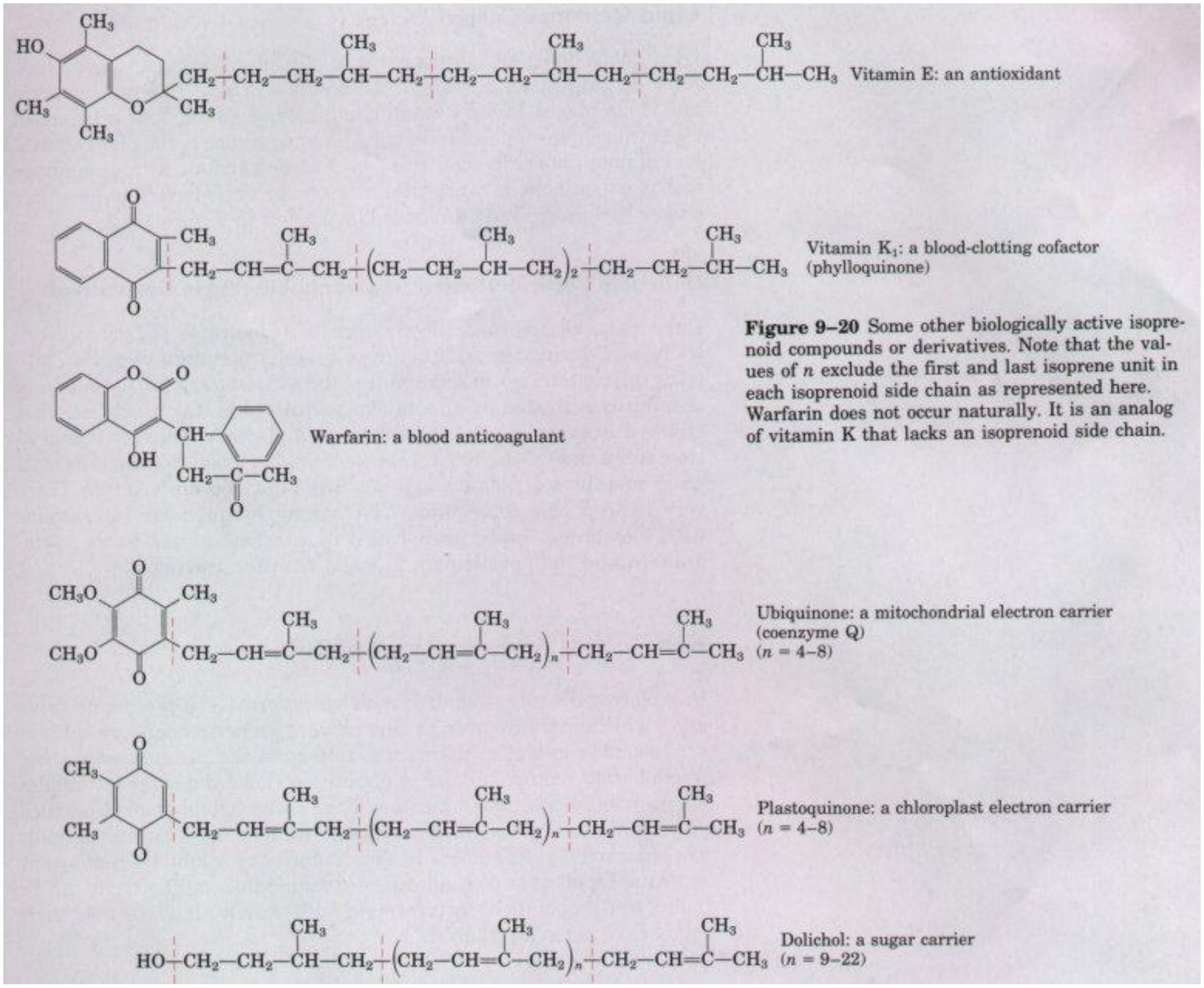


Figure 9-20 Some other biologically active isoprenoid compounds or derivatives. Note that the values of n exclude the first and last isoprene unit in each isoprenoid side chain as represented here. Warfarin does not occur naturally. It is an analog of vitamin K that lacks an isoprenoid side chain

Vitamin E (Fig. 9-20) is the collective name for a group of closely related lipids called tocopherols, all of which contain a substituted aromatic ring and a long hydrocarbon side chain. Tocopherols are found in hens' eggs and vegetable oils, and are especially abundant in wheat germ. Deficiency of vitamin E is very rare in humans, but when laboratory animals are fed diets depleted of vitamin E, they develop scaly skin, muscular weakness and wasting, and sterility.

Tocopherols can undergo oxidation-reduction reactions on the aromatic ring. The vitamin activity of tocopherols likely results from their ability to prevent oxidative damage to the lipids of cellular membranes. Recall the reactions of unsaturated fatty acids with oxygen that cause rancidity in foods. If such reactions were to occur in living cells, the resulting defects in membrane function might cause cell death. Tocopherols react with and destroy the most reactive forms of oxygen, protecting unsaturated fatty acids from oxidation. Tocopherols are used commercially to retard spoilage of certain foods.

Vitamin K is a lipid cofactor required for normal blood clotting. Vitamin K_1 (phylloquinone; Fig. 9-20) is found in green plant leaves,and a related form, vitamin K_2 (menaquinone), is formed by bacteria residing in the animal intestine. The vitamin acts in the formation of prothrombin, a blood plasma protein essential in blood-clot formation. Prothrombin is a proteolytic enzyme that splits specific peptide bonds in the blood protein fibrinogen, converting it to fibrin, the insoluble, fibrous protein that holds blood clots together. Deficiency of vitamin K results in slowed blood clotting, which can be fatal to a wounded animal. Henrik Dam and Edward A. Doisy are given credit for having independently discovered the antihemorrhaghic action of vitamin K.

Warfarin (Fig. 9-20) is a synthetic analog of vitamin K, which acts as a competitive inhibitor of prothrombin formation. It is extremely poisonous to rats, causing death by internal bleeding. Ironically, this potent rodenticide is also a valuable anticoagulant drug for the treatment of human patients in whom excessive blood clotting is dangeroussurgical patients and victims of coronary thrombosis.

Lipid Quinones Carry Electrons

Ubiquinone and plastoquinone (Fig. 9-20), also isoprenoid derivatives, function as electron carriers in the production of ATP in mitochondria and chloroplasts. In most mammalian tissues, ubiquinone (also called coenzyme Q) has ten isoprene units. Plastoquinone is the plant equivalent of ubiquinone. In their roles as electron carriers, both ubiquinone and plastoquinone can accept either one or two electrons and either one or two protons to be reduced, as shown in Figure 18-2.

Dolichols Form Activated, Hydrophobic Sugar Derivatives

During the assembly of the complex carbohydrates of bacterial cell walls, and during the addition of polysaccharide units to certain proteins (glycoproteins) in eukaryotes, the sugar units to be added are chemically activated by attachment to dolichols (Fig. 9-20), another group of isoprenoids. Dolichols from animals have between 17 and 21 isoprene units (85 to 105 carbon atoms), bacterial dolichols have 11 units, and those of plants and fungi have 14 to 24 isoprene units. These very hydrophobic compounds have strong hydrophobic interactions with membrane lipids, anchoring the attached sugars to the membrane where they participate in sugar-transfer reactions.

Possible Questions

2 marks

1. Define lipids
2. Draw the structure of sterols
3. List out the importance of glycerophospholipids
4. Brief about galactolipids
5. Write short notes on cofactors

8 marks

1. Given account of physical properties of fat
2. Write the structure and functions of galactolipids
3. Explain about the classification of lipids
4. Write the structure and functions of glycerophospholipids
5. Give an account on chemical properties of fat
6. Write the difference between galactolipids and sulpholipids
7. Write the structure, distribution and role of membrane lipids
8. Explain in detail about storage lipids
9. What is the role of lipids in bio membranes
10. Describe in detail plant steroids

Karpagam Academy of Higher Education
Department of Biochemistry
I B.Sc., Biochemistry
19BCU101- Molecules of life
Prepared By Dr. A. RAMAKRISHNAN

UNIT III

Question number	Question	Option I	Option II	Option III	Option IV		Answer
1	Fats are solids at	10^0C	20^0C	30^0C	40^0C		**20^0C**
2	Hydrolysis of vegetable oil gives	fatty acid & glycine	fatty acid & glycol	fatty acid & glycerol	fatty acid & glyoxal		**fatty acid & glycerol**
3	Fatty acid 18:1:9 is	Staric acid	Linoleic acid	Palmitic acid	**Oleic acid**		**Oleic acid**
4	Essential fatty acid is	lenoleic acid	Palmitic acid	Stearic acid	Myristic acid		**lenoleic acid**
5	The lipid which is also having hormonal function is	Vitamin A	Vitamin D	Stearic acid	Etanolamine		**Vitamin D**
6	Oils which do not solidify at low temperature contain	More of saturated fatty acids	more of unsaturated fatty acids	less ofunsaturated fatty acid	saturated		**more of unsaturated fatty acids**
7	The melting point of a fat is higher when it has	higher unsaturated fatty acids	higher short chain fatty acids	higher saturated fatty acids	lower saturated fatty acids		**higher saturated fatty acids**

8	The structure of lenoleic acid is represented by the symbol	18:00	18:19	18:2 ^{9,12}		8:3 ^{9,12,15}		**18:2** $^{\mathbf{9,12}}$
9	Butter contains	more of saturated fatty acid	more of unsaturated fatty acids	arachidonic acid		fatty acid & glyoxal		**more of saturated fatty acid**
10	Esters of fatty acids with higher alcoholsother than glycerol are said to be	Waxes	Fats	Both		cholestrol		**Waxes**
11	The combination of an amino alcohol, fatty acid & sialic acid form	Phospholipids	sulpholipids	Glycolipids		amino lipids		**Glycolipids**
12	The rate of fatty acid oxidation is increased by	Phospholipids	Glyco lipids	amino lipids		all of the above		**Phospholipids**
13	Cardiolipin found in mitochondria is formed from	Lipositol	Phosphotidyl ethanolamine	Phosphatidyl Glycerol		glycerol		**Phosphatidyl Glycerol**

14	Iodine value of an shows the extent of	Polymerisation	molecular size	unsaturation		**esterification**		**esterification**
15	Hydrolysis of fat by alkali is called	Saponification	acid number	iodine number		both b and c		**Saponification**
16	The number of milliliters of 0.1N KOH required to neutralize the insoluble fatty acids from 5gms of fat is called	Acid number	Acetyl number	Halogen number		**Polenske number**		**Polenske number**
17	Lecithin contains a nitrogenous base	Ethanolamine	choline	inositol		aminogroup		**choline**
18	Lecithin contains an unsaturated fatty acid at position	α	α+β	αβ		**β**		**β**
19	Lecithins are soluble in ordinary fat solvents except	Benzene	ethyl alcohol	methanol		metyl alcohol		**ethyl alcohol**

20	When lecithins are exposed to air	Black	Brown	yellow		Red		**Brown**
21	The most	phosphati	lecithins	cephalins		phosphatidyl serine		**lecithins**
22	Sphingosi	18 carbon	12 carbon	13 carbon		15 carbon		**18 carbon**
23	Lecithins combine to protein to form	phospoho protein	muco protein	lipo protein	glcoprotein	glycoprotein		**lipo protein**
24	Phosphotidyl inositol is found in	Cabbage	soybean	cauliflower	apples	Apples		**soybean**
25	Instead of ester link plasmalogins posses an eter link in position	β	α	γ	none	both alpha and beta		**α**
26	The alkyl radical in plasmologen is an alcohol	saturated	unsaturated	both	none	**all of the above**		**all of the above**
27	Spingosine is present in	cardiolipin	diacylglycerol	ceramide	lecithin	Lecithin		**cardiolipin**
28	The nitrogen base in the sphingomyelin is	choline	serine	ethanolamine	a complex amino alcohol	a complex amino alc		**choline**
29	The concentrations of sphingomyelins are increased in	Gaucher's disease	fabry' disease	febrile disease	Niemann-pick disease.	**Niemann-pick disease.**		**Niemann-**

30	Spingomyelins contain a complex amino alcohol named as	Sedddddrine	lyso lecithin	spingosine	glycol	Glycol		**spingosine**
31	Glcolipids contain an amino alcohol	spingosinse	iso spingosine	both	none	**all of the above**		**all of the above**
32	kerasin contains	nervonic acid	hydroxy nervonic acid	cerebronic acid	lignoceric acid	lignoceric acid		**nervonic acid**
33	Oxynervon contains	nervonic acid	hydroxy nervonic acid	cerebronic acid	lignoceric acid	lignoceric acid		**hydroxy nervonic acid**
34	Gaucher’s disease is characterized by the eye in	Lignoceric acid	nervonic acid	cerebronic acid	hydroxy nervonic acid	hydroxy nervonic aci		**cerebronic acid**
35	Gangliosides are the glycolipids occurring in	Liver	Brain	Kidney	Muscle	Muscle		**Brain**
36	The most abundant lipid is	Triglycerides	Waxes	phospholipid	cholesterol	Cholesterol		**Triglycerides**
37	Gangliosides are	Glycospingolipids	lipoproteins	glycophospholipid	none	waxes		**Glycospingolipids**
38	The lipoprotein which has the largest size and least density is	LDL	HDL	VLDL	Chylomicrons	**Chylomicrons**		**Chylomic**

39	Lipoproteins precent in cell membrane is by nature	hydrophobic	Hydrophilic	both	none	**all of the above**		**all of the above**
40	The density of lipoproteins increases as the protein content	rises	decreases	highly decreases	slightly & promptly decreases	slightly & promptly		**rises**
41	Lipo proteins may be identified more accurately by means of	Electrophoresis	centrifugation	Immuno electrophoresis	Ultra centrifugation	Ultra centrifugation		**Immuno electrophoresis**
42	Very low density lipo proteins are also known as	β-lipoprot - β -lipeins	preoproteins	α- lipo proteins	none	beta lipo protein		**preoproteins**
43	Adults ne	700	500	600		400		**700**
44	The protein moiety of lipoprotein is known as	Apoprotein	preprotein	post protein	pre protein	Pseudoprotein		Apoprotei
45	The β-lipoprotein fraction increases in severe	Diabetes mellitus	Uremia	nephritis	Uremia	muscular dystrophy		**Diabetes mellitus**

46	Adultration of butter can be tested by	Acid number	iodine nur	RM number	iodine number	All		**RM number**
47	Bee wax contains	Stearic acid	Myricyl pa	Oleic acid	Myricyl palmitate	Linolenic acid		**Myricyl p**
48	Rancidity occurs when fats are exposed to	air	moisture	light	moisture	**All**		**All**
49	A lipid containing steroid ring is	Plasmalogens	sphingomy	cholesterol	sphingomyelin	none		**cholesterol**
50	NANA is a component of	spingomyelin	gangliosid	cardiolipin	ganglioside	Plasmalogen		**cardiolipin**
51	The phospholipid containing an ether linkage at C1 is known as	Plasmalogens	Cardiolipin s	Cephalin	Cephalin	Lecithin		**Plasmalogen**
52	Which one of the following lipid has detergent activity	Triacylglycerides	Glycolipid	phospholipid	Glycolipid	Cholesterol		**Triacylglycerides**
53	The degree of adulteration of given oil is determined by measuring	saponifica	Acid number	RM number		iodine number		**RM number**

54	Fat serve a	metabolic	energy sto	enezyme activity		starch		**energy sto**
55	Lipid serv	cell memb	signaling	both a & b		cell membfane synth		**both a & b**
56	Hydrocarb	low tempe	high temp	low boiling point		high boiling point		**high temp**
57	Sphingom	brain	nerves tiss	both a & b		kidney		**both a & b**
58	Gangliosid	kidney	liver	brain		spleen		**brain**
59	Predomina	LDL	HDL	VLDL		sterol		**LDL**
60	Predomina	LDL	HDL	VLDL		sterol		**HDL**

pick disease.

rons

n

almitate

rage
b
erature
b

UNIT IV
SYLLABUS

Amino acids and Nucleic acids: Structure and classification, physical, chemical and optical properties of amino acids. Nucleotides - structure and properties. Nucleic acid structure – Watson-Crick model of DNA. Structure of major species of RNA - mRNA, tRNA and rRNA. Nucleic acid chemistry - UV absorption, effect of acid and alkali on DNA. Other functions of nucleotides - source of energy, component of coenzymes, second messengers.

Amino acids

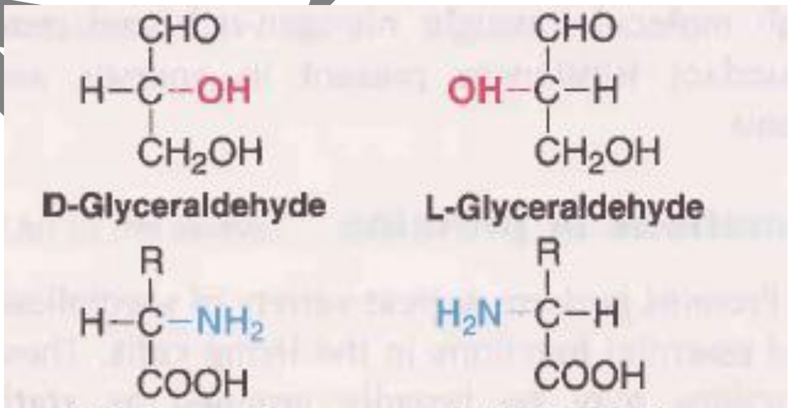
Amino acids are a group of organic compounds containing two functional groups amino and carboxyl. The amino group (-NH2) is basic while the carboxyl group (-COOH) is acidic in nature.

Structure and classification

There are different ways of classifying the amino acids based on the structure and chemical nature nutritional requirement, metabolic fate etc.

A. Amino acid classification based on the structure:

- A comprehensive classification of amino acids is based on their structure and chemical nature.
- Each amino acid is assigned a 3 letter or 1 letter symbol.
- These symbols are commonly used to represent the amino acids in protein structure.
- The 20 amino acids found in proteins are divided into seven distinct groups.
- The different groups of amino acids, their symbols and structures are given.
- The salient features of different groups are described next.



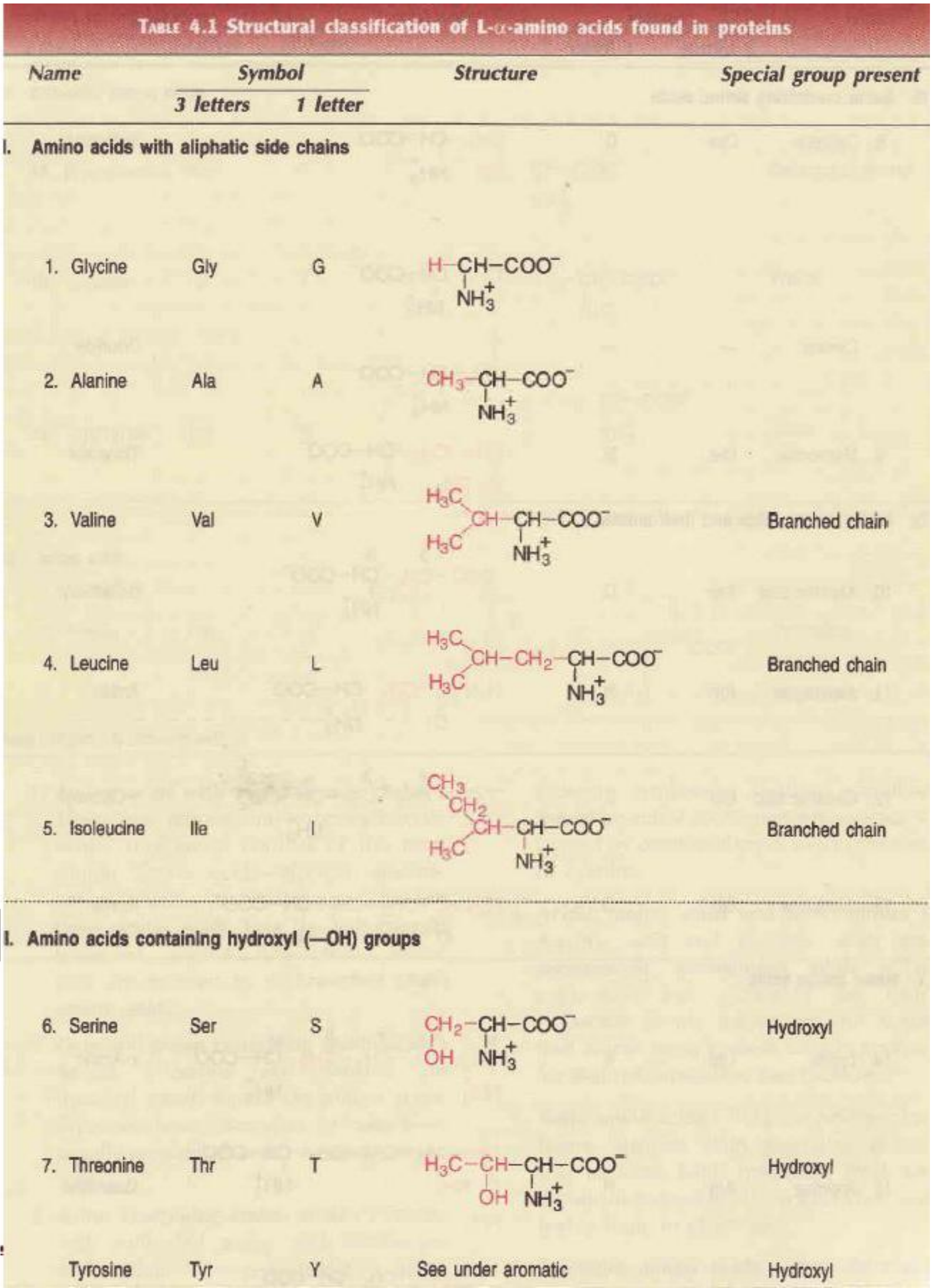
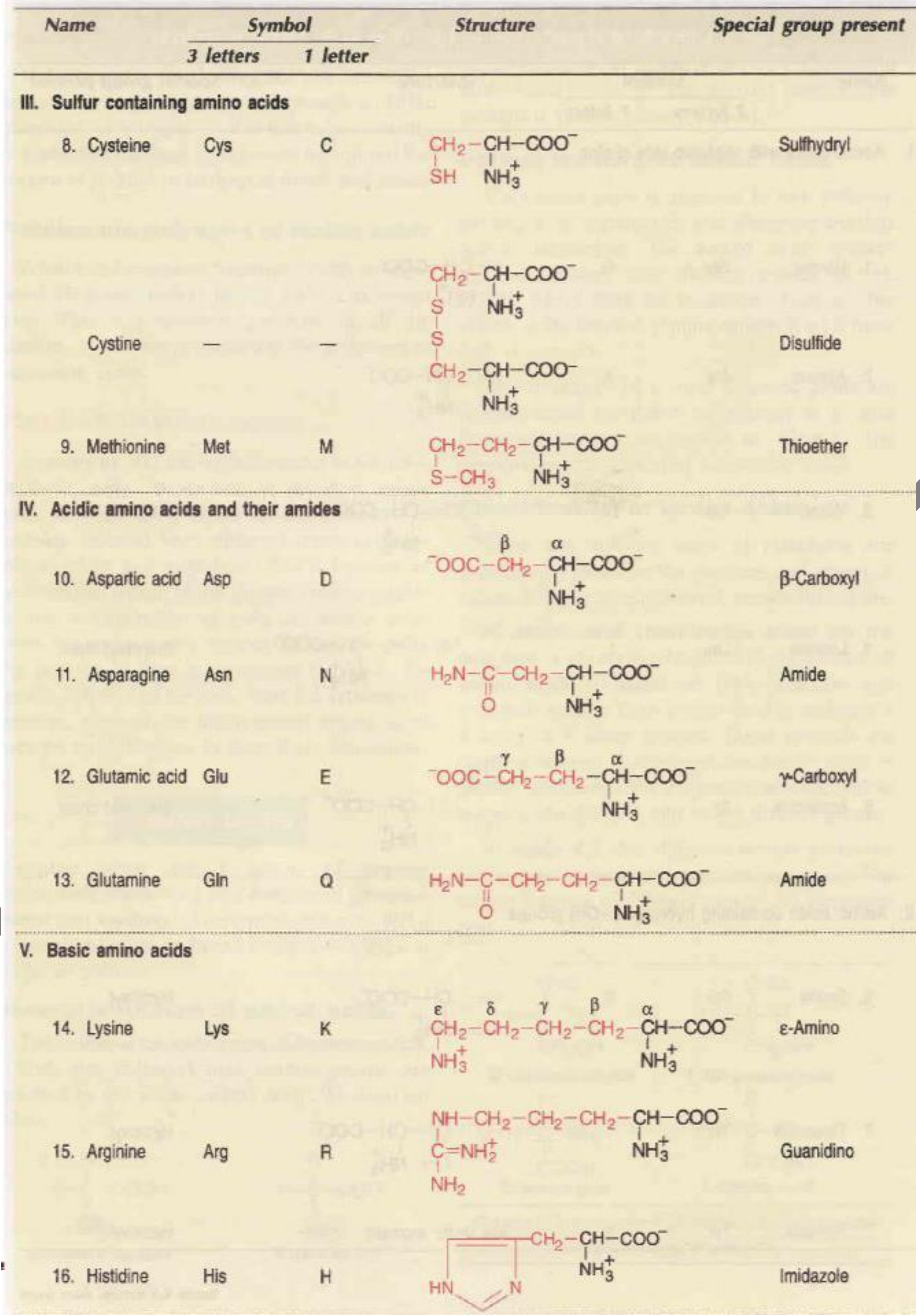
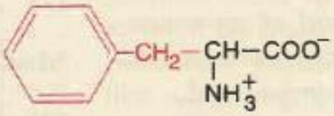
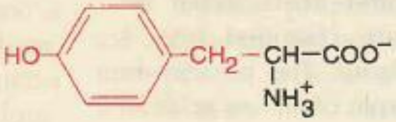
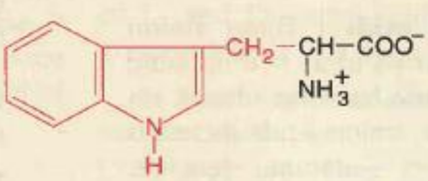
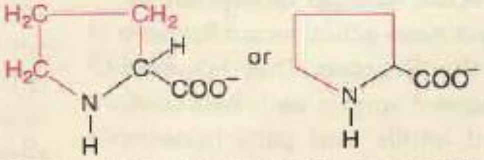


TABLE 4.1 Structural classification of L-α-amino acids found in proteins

Name	Symbol		Structure	Special group present
	3 letters	1 letter		
I. Amino acids with aliphatic side chains				
1. Glycine	Gly	G	$\mathrm{H{-}\underset{NH_3^+}{CH}{-}COO^-}$	
2. Alanine	Ala	A	$\mathrm{CH_3{-}\underset{NH_3^+}{CH}{-}COO^-}$	
3. Valine	Val	V	$\mathrm{{}^{H_3C}_{H_3C}{>}CH{-}\underset{NH_3^+}{CH}{-}COO^-}$	Branched chain
4. Leucine	Leu	L	$\mathrm{{}^{H_3C}_{H_3C}{>}CH{-}CH_2{-}\underset{NH_3^+}{CH}{-}COO^-}$	Branched chain
5. Isoleucine	Ile	I	$\mathrm{CH_3{-}CH_2{-}\underset{H_3C}{CH}{-}\underset{NH_3^+}{CH}{-}COO^-}$	Branched chain
I. Amino acids containing hydroxyl (—OH) groups				
6. Serine	Ser	S	$\mathrm{\underset{OH}{CH_2}{-}\underset{NH_3^+}{CH}{-}COO^-}$	Hydroxyl
7. Threonine	Thr	T	$\mathrm{H_3C{-}\underset{OH}{CH}{-}\underset{NH_3^+}{CH}{-}COO^-}$	Hydroxyl
Tyrosine	Tyr	Y	See under aromatic	Hydroxyl



Name	Symbol		Structure	Special group present
	3 letters	1 letter		
III. Sulfur containing amino acids				
8. Cysteine	Cys	C	$\underset{SH}{CH_2}-\underset{NH_3^+}{CH}-COO^-$	Sulfhydryl
Cystine	—	—	$\begin{array}{l} CH_2-\underset{NH_3^+}{CH}-COO^- \\ S \\ S \\ CH_2-\underset{NH_3^+}{CH}-COO^- \end{array}$	Disulfide
9. Methionine	Met	M	$\underset{S-CH_3}{CH_2}-CH_2-\underset{NH_3^+}{CH}-COO^-$	Thioether
IV. Acidic amino acids and their amides				
10. Aspartic acid	Asp	D	$^-OOC-\overset{\beta}{CH_2}-\underset{NH_3^+}{\overset{\alpha}{CH}}-COO^-$	β-Carboxyl
11. Asparagine	Asn	N	$H_2N-\underset{O}{\underset{\|}{C}}-CH_2-\underset{NH_3^+}{CH}-COO^-$	Amide
12. Glutamic acid	Glu	E	$^-OOC-\overset{\gamma}{CH_2}-\overset{\beta}{CH_2}-\underset{NH_3^+}{\overset{\alpha}{CH}}-COO^-$	γ-Carboxyl
13. Glutamine	Gln	Q	$H_2N-\underset{O}{\underset{\|}{C}}-CH_2-CH_2-\underset{NH_3^+}{CH}-COO^-$	Amide
V. Basic amino acids				
14. Lysine	Lys	K	$\underset{NH_3^+}{\overset{\varepsilon}{CH_2}}-\overset{\delta}{CH_2}-\overset{\gamma}{CH_2}-\overset{\beta}{CH_2}-\underset{NH_3^+}{\overset{\alpha}{CH}}-COO^-$	ε-Amino
15. Arginine	Arg	R	$\begin{array}{l} NH-CH_2-CH_2-CH_2-\underset{NH_3^+}{CH}-COO^- \\ C=NH_2^+ \\ NH_2 \end{array}$	Guanidino
16. Histidine	His	H	$-CH_2-\underset{NH_3^+}{CH}-COO^-$ HN N	Imidazole

Name	Symbol		Structure	Special group present
	3 letters	1 letter		
VI. Aromatic amino acids				
17. Phenylalanine	Phe	F		Benzene or phenyl
18. Tyrosine	Tyr	Y		Phenol
19. Tryptophan	Trp	W		Indole
VII. Imino acid				
20. Proline	Pro	P		Pyrrolidine

(Note : R group is shown in red)

- **Amino acids with aliphatic side chains:** These are monoamino monocarboxylic acids. This group consists of the most simple amino acids-glycine, alanine, valine, leucine and isoleucine. The last three amino acids (Leu, lle, Val) contain branched aliphatic side chains, hence they are referred to as branched chain amino acids.

- **Hydroxyl group containing amino acids:** Serine, threonine and tyrosine are hydroxyl group containing amino acids. Tyrosine-being aromatic in nature-is usually considered under aromatic amino acids.

- **Sulfur containing amino acids**: Cysteine with sulfhydryl group and methionine with thioether group are the two amino acids incorporated during the course of protein synthesis. Cystine, another important sulfur containing amino acid, is formed by condensation of two molecules of cysteine.

- **Acidic amino acids and their amides:** Aspartic acid and glutamic acids are dicarboxylic monoamino acids while asparagine and glutamine are their resoective amide derivatives. All these four amino acids possess distinct codons for their incorporation into proteins.
- **Basic amino acids**: The three amino acids lysine, arginine (with guanidino group) and histidine (with imidazole ring) are dibasic monocarboxylic acids. They are highly basic in character.
- **Aromatic amino acids:** Phenylalanine, tyrosine and tryptophan (with indole ring) are aromatic amino acids. Besides these, histidine may also be considered under this category.
- **lmino acids:** Proline containing pyrrolidine ring is a unique amino acid. It has an amino group (=NH), instead of an amino group (-NH2) found in other amino acids. Therefore proline is an aimino acid.

B. Classification of amino acids based on polarity:

- Amino acids are classified into 4 groups based on their polarity. The polarity in turn reflects the functional role of amino acids in protein structure.
- **Non-polar amino acids :** These amino acids are also referred to as hydrophobic (water hating). They have no charge on the 'R' group. The amino acids included in this group are - alanine, leucine, isoleucine, valine, methionine, phenylalanine, tryptophan and proline.
- **Polar amino acids with no charge on 'R' group:** These amino acids, as such, carry no charge on the 'R'group. They however possess groups such as hydroxyl, sulfhydryl and amide and participate in hydrogen bonding of protein structure. The simple amino acid glycine (where R = H) is also considered in this category. The amino acids in this group are glycine, serine, threonine, cysteine, glutamine, asparagine and tyrosine.
- **Polar amino acids with positive 'R' group:** The three amino acids lysine, arginine and histidine are included in this group.
- **Polar amino acids with negative 'R'group:** The dicarboxylic monoamino acids aspartic acid and glutamic acid are considered in this group.

C. Nutritional classification of amino acids:

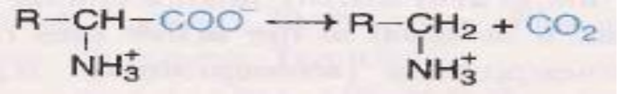
- The twenty amino acids are required for the synthesis of variety of proteins, besides other biological functions.
- However, all these 20 amino acids need not be taken in the diet. Based on the nutritional requirements amino acids are grouped into two classes essential and nonessential.

- **Essential or indispensable amino acids:** The amino acids which cannot be synthesized by the body and, therefore, need to be supplied through the diet are called essential amino acids. They are required for proper growth and maintenance of the individual. The ten amino acids listed below are essential for humans.
- **Non - essential or dispensable amino acids :** The body can synthesize about '10 amino acids to meet the biological needs, hence they need not be consumed in the diet. These are-glycine, alanine, serine, cystein e, aspartate,a sparagnie, glutamate, glutamine, tyrosine and proline.

D. Amino acid classification based on their metabolic fate:

- The carbon skeleton of amino acids can serve as a precursor for the synthesis of glucose.
- From metabolic view point, amino acids are divided into three
- **Glycogenic amino acids:** These amino acids can serve as precursors for the formation of glucose or glycogen. e.g. alanine, aspartate, glycine, methionine etc.
- **Ketogenic amino acids**: Fat can be synthesized from these amino acids. Two amino acids leucine and lysine are exclusively ketogenic.
- **Glycogenic and ketogenic amino acids:** The four amino acids isoleucinep, henylalanine, tryptophan, tyrosine are precursors for synthesis of glucose as well as fat.

Chemical reactions of amino acids:
The general reactions of amino acids are mostly due to the presence of two functional groups namely carboxyl (-COOH) group and amino (-NH2) group.
1. Amino acids form salts (-COONa) with bases and esters (-COOR') with alcohols.
2. **Decarboxylation:** Amino acids undergo decarboxylation to produce corresponding amines.
3. This reaction assumes significance in the living cells due to the formation of many biologically important amines.



$$\underset{NH_3^+}{R-CH}-COO^- \longrightarrow \underset{NH_3^+}{R-CH_2} + CO_2$$

4. These include histamine, tyramine and y-amino butyric acid (CABA) from the amino acids histidine, tyrosine and glutamate, respectively.

5. Reaction with ammonia: The carboxyl group of dicarboxylic amino acids reacts with NH3 to form amide

☐ Aspartic acid + NH, ------ Asparagine
☐ Glutamic acid + NH. ------Glutamine

Reactions due to -NH$_2$ group:
The amino groups behave as bases and combine with acids (e.g. HCI) to form salts (-NHiCl-).

4. Reaction with ninhydrin : The a-amino acids react with ninhydrin to form a purple, blue or pink colour complex (Ruhemann's purple).

- Amino acid + Ninhydrin ----- Keto acid + NH$_3$+CO$_2$+Hydrindantin
- Hydrindantin + NH$_3$ + Ninhydrin- ---- Ruhemann's purple

- Ninhydrin reaction is effectively used for the quantitative determination of amino acids and proteins.

6. **Colour reactions of amino acids:** Amino acids can be identified by specific colour reactions

7. Transamination: Transfer of an amino group from an amino acid to a keto acid to form a new amino acid is a very important reaction in amino acid metabolism.

8. Oxidative deamination: The amino acids undergo oxidative deamination to liberate free ammonia.

Physical, chemical and optical properties of amino acids

An amino acid is an organic molecule with an amino group (-NH2) and a carboxyl group (-COOH). The most frequent and of greatest interest are those amino acids forming part of proteins. Two amino acids are combined in a condensation reaction between the amino group and the carboxyl group of another amino acid, releasing one molecule of water and forming an amide bond is called peptide bond**;** these two amino acids form a dipeptide. If you join a third amino acid is formed one tripeptide and so on, to form a polypeptide. This reaction occurs naturally within cells, in ribosomes.

All components of the protein amino acids are L-alpha-amino acids. This means that the amino group is attached to the carbon adjacent to the carboxyl group (alpha carbon) or, in other words, both the carboxyl and the amino attached to the same carbon; also this one unite alpha carbon hydrogen and a chain (usually called side chain or radical R) of variable structure, which determines the identity and properties of each of the different amino acids.

The human body is made up by 20 percent protein. Proteins play in almost all biological processes a key role. Amino acids are the basis of proteins.

Since much of our cells, muscles and tissues are composed of amino acids, they are part of many important functions in our body: the amino acids give the cell not only its structure, but are also responsible for transporting and storing all kind of vital nutrients. Amino acids influence the functions of organs, glands, tendons or arteries. They are essential in wound healing and tissue repair, especially muscles, bones, skin and hair, as well as eliminating the negative impacts associated with metabolic disorders of all types.

The human body is made up by 20 percent protein. Proteins play in almost all biological processes a key role. Amino acids are the basis of proteins.

Physical Properties of Amino acids:

1. Solubility:

Most of the amino acids are usually soluble in water, and insoluble in organic solvents.

2. Melting Point:

Amino acids are generally melt at higher temperature of ten above 200^0C.

3. Taste:

Amino acids may be sweet (Gly, Ala & Val), tasteless (Leu) or Bitter (Arg & Ile).

4. Optical Properties:

All amino acids possess optical isomers due to the presence of asymmetric α-carbon atoms.

5. Zwitter ion and Isoelectric point:

The name zwitter is derived from the German word which means “hybrid”. Zwitter ion (or) dipolar ion is a hybrid molecule containing positive & negatively ionic groups. Basically the proton shifts from carboxyl group to amino group of the self molecule at normal pH cellular levels.

6. Titration Curve of Glycince:

Glycine is optically inactive, simplest amino acid because which have no asymmetric carbon atom. Acid-Base titration involves the gradual addition (or) removal of protons. It has three different stages when the Glycine undergoes acid-base titration.

Since much of our cells, muscles and tissues are composed of amino acids, they are part of many important functions in our body: the amino acids give the cell not only its structure, but are also responsible for transporting and storing all kind of vital nutrients. Amino acids influence the functions of organs, glands, tendons or arteries.They are essential in wound healing and tissue repair, especially muscles, bones, skin and hair, as well as eliminating the negative impacts associated with metabolic disorders of all types.

Chemical Properties of Amino acids:

Chemical reactions of amino acids due to carboxyl and amino groups:

I) Due to Carboxyl group:

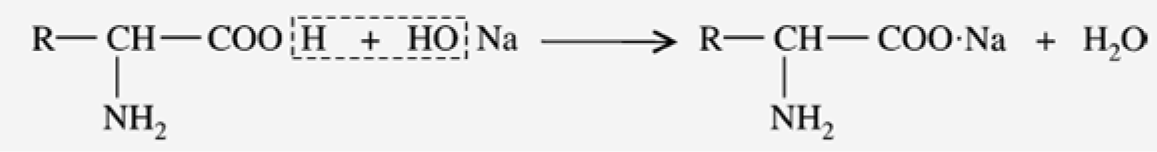
a) Decarboxylation:

The amino acids will undergo alpha decarboxylation to form the corresponding “amines”. Thus important amines are produced from amino acids.

- **Histidine** → Histamine + CO_2
- **Tyrosine** →Tyramine + CO_2
- **Tryptophan** →Tryptamine + CO_2
- **Lysine** →Cadaverine + CO_2
- **Glutamic acid** → Gamma Amino Butyric Acid (GABA) + CO_2

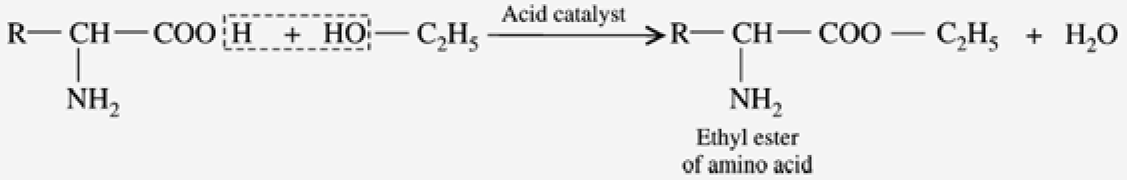
b) Reaction with Alkalies (Salt formation):

The carboxyl group of amino acids can release a H^+ ion with the formation of Carboxylate (COO^-) ions. These may be neutralized by cations like Na^+ and Ca^{+2} to form Salts. Thus amino acids react with alkalies to form "Salts".



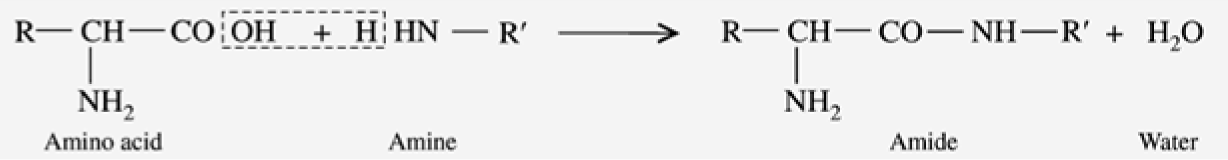
c) Reaction with Alcohols (Esterification) :

When the amino acids is reacted with alcohol to form, "Ester". The esters are volatile in contrast to the form amino acids.



d) Reaction with Amines:

Amino acid reacts with Amines to form "Amides".



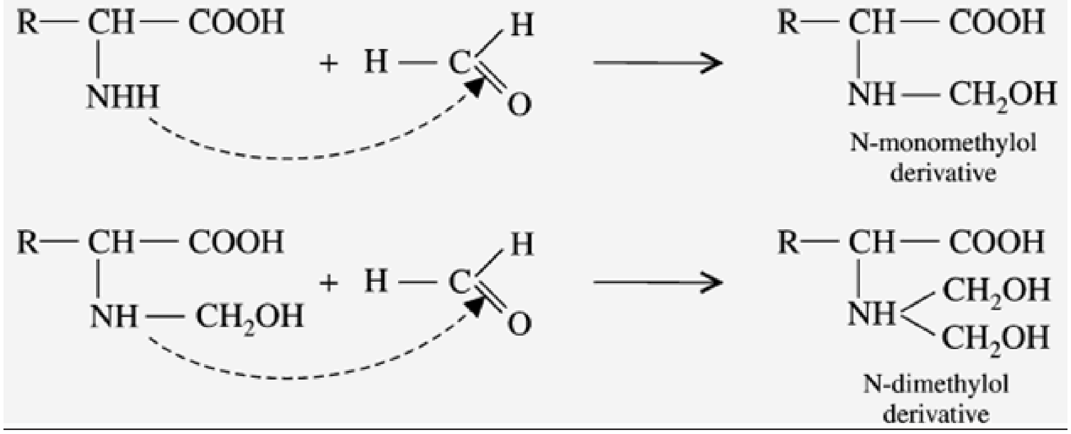
II) Due to Amino group:

a) Reaction with Mineral acids (Salt formation)

When the amino acids are treated with mineral acids (like HCl), it forms "Acid Salts".

b) Reaction with Formaldehyde:

When the amino acid reacts with two molecules of Formaldehyde it forms "N-dimethylol derivative" (Hydroxy-methyl derivative). This reaction is done in two steps. These derivatives are insoluble in water and resistant to attack by microorganisms.

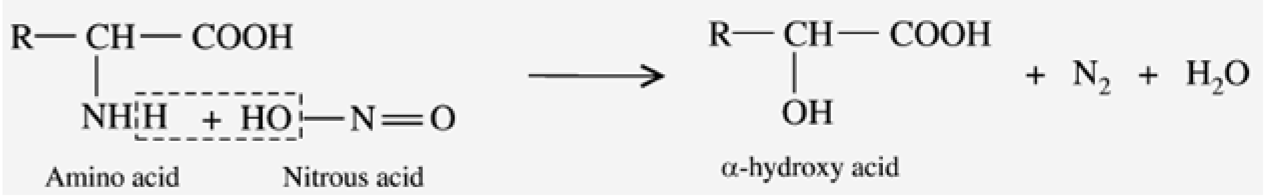


c) Reaction with Benzaldehyde:

When the amino acid reacts with Benzaldehyde, it gives “Schiff’s base”.

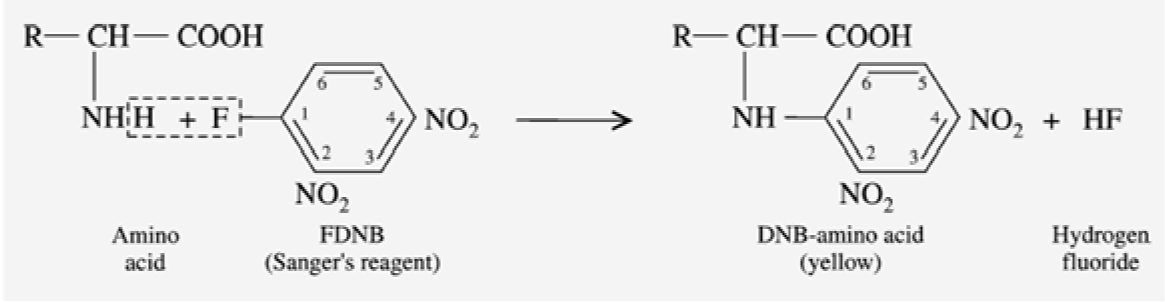
d) Reaction with Nitrous acid (Van slyke reaction):

When the amino acids react with Nitrous acid (HNO2) to liberate N2 gas and to produce the corresponding “α-hydroxyl acid”. The imino acids Proline and Hydroxyproline do not respond to this reaction.



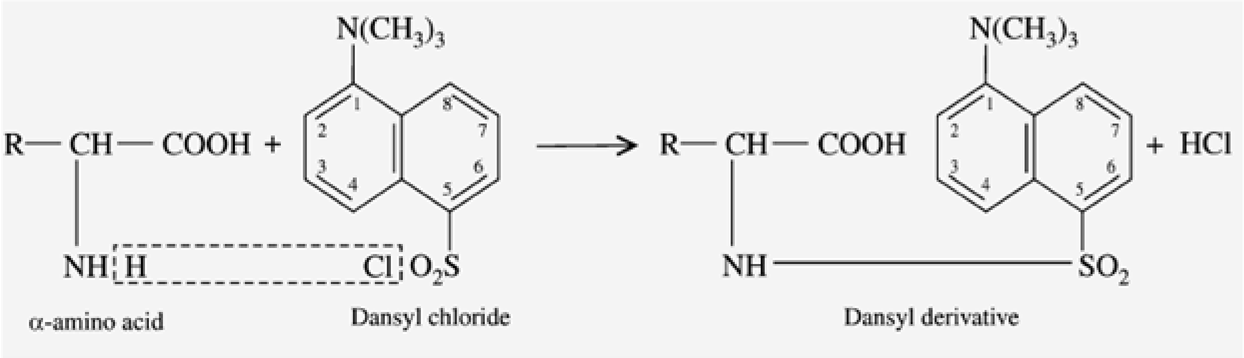
e) Reaction with Sanger’s reagent:

“1-flouro-2,4-dinitrobenzene” is called Sanger’s reagent (FDNB). In mildly alkaline solution, sanger’s reagent reacts with α-amino acid to produce Yellow colored derivative, DNB-amino acid.



f) Reaction with DANSYl Chloride:

DANSYl chloride means “Dimethyl Amino Naptha Sulphonyl Chloride”. When the amino acid reacts with DANSYl chloride reagent, it gives a “Flourescent DANSYl derivative”.



g) Reaction with acylating agents (Acylation):

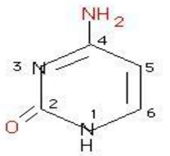
When the amino acids react with "Acid chloride" and acid anhydride (Pthalic anhydride) in alkaline medium it gives "pthaloyl amino acid".

Nucleotides - structure and properties

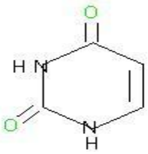
Structure of purines and pyrimidines:

Purines:

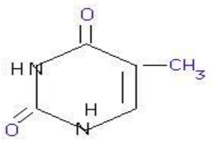
- A purine is a heterocyclic aromatic organic compound, consisting of a pyrimidine ring fused to an imidazole ring.
- Adenine = 6-amino purine
- Guanine = 2-amino-6-oxy purine
- Hypoxanthine = 6-oxy purine
- Xanthine = 2,6-dioxy purine
- Adenine and guanine are found in both DNA and RNA.
- Hypoxanthine and xanthine are not incorporated into the nucleic acids as they are being synthesized but are important intermediates in the synthesis and degradation of the purine nucleotides.
  - Uracil = 2,4-dioxy pyrimidine
  - Thymine = 2,4-dioxy-5-methyl pyrimidine
  - Cytosine = 2-oxy-4-amino pyrimidine
  - Orotic acid = 2,4-dioxy-6-carboxy pyrimidine



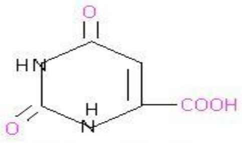
Cytosine



Uracil



Thymine

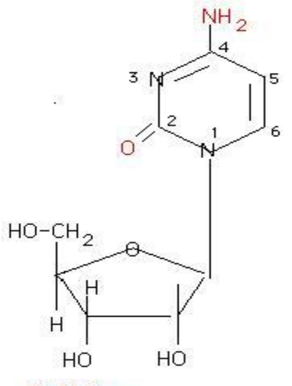


Orotic Acid

- Cytosine is found in both DNA and RNA.
- Uracil is found only in RNA.
- Thymine is normally found in DNA.
- Sometimes tRNA will contain some thymine as well as uracil.

Nucleosides

- If a sugar, either ribose or 2-deoxyribose, is added to a nitrogen base, the resulting compound is called a nucleoside.
- Carbon 1 of the sugar is attached to nitrogen 9 of a purine base or to nitrogen 1 of a pyrimidine base.
- The names of purine nucleosides end in -osine and the names of pyrimidine nucleosides end in -idine.
- The convention is to number the ring atoms of the base normally and to use l', etc. to distinguish the ring atoms of the sugar.
- Unless otherwise specificed, the sugar is assumed to be ribose.
- To indicate that the sugar is 2'-deoxyribose, a d- is placed before the name.
  - Adenosine
  - Guanosine
  - Inosine - the base in inosine is hypoxanthine
  - Uridine
  - Thymidine
  - Cytidine



Cytidine

Nucleotides

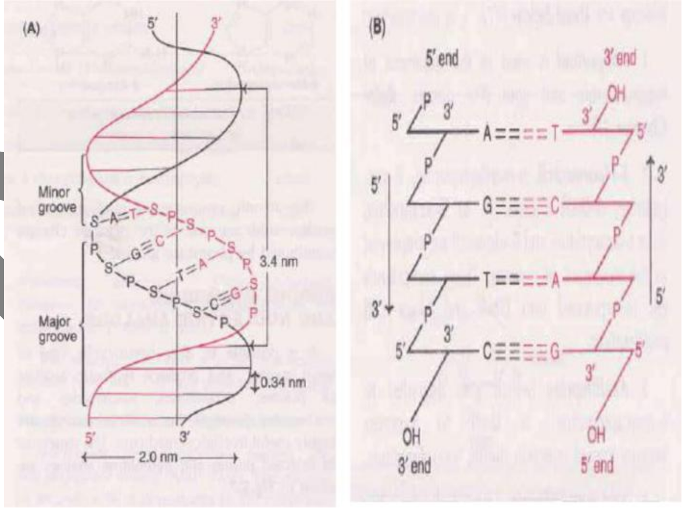
- Adding one or more phosphates to the sugar portion of a nucleoside results in a nucleotide.
- Generally, the phosphate is in ester linkage to carbon 5' of the sugar.
- If more than one phosphate is present, they are generally in acid anhydride linkages to each other.
- If such is the case, no position designation in the name is required.

- If the phosphate is in any other position, however, the position must be designated.
- For example, 3'-5' cAMP indicates that a phosphate is in ester linkage to both the 3' and 5' hydroxyl groups of an adenosine molecule and forms a cyclic structure.
- 2'-GMP would indicate that a phosphate is in ester linkage to the 2' hydroxyl group of a guanosine. Some representative names are:
    - AMP = adenosine monophosphate = adenylic acid
    - CDP = cytidine diphosphate
    - dGTP = deoxy guanosine triphosphate
    - dTTP = deoxy thymidine triphosphate (more commonly designated TTP)
    - cAMP = 3'-5' cyclic adenosine monophosphate

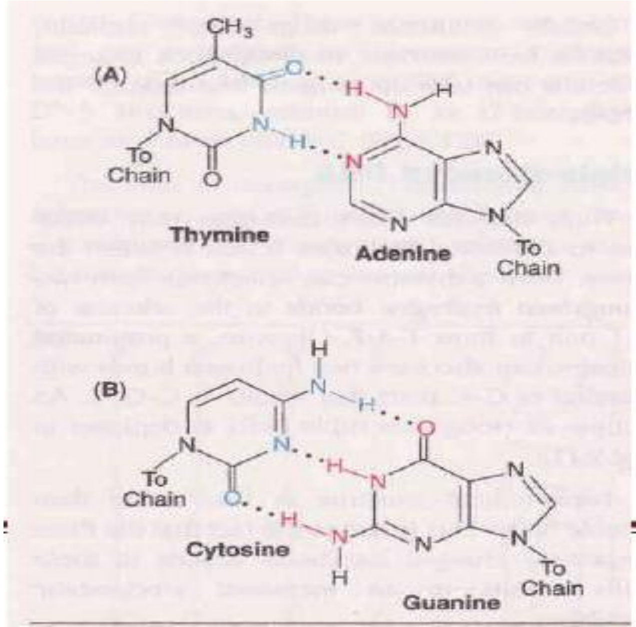
Nucleic acid structure – Watson-Crick model of DNA

DNA:

- DNA is a polymer of deoxyribonucleotides (or simply deoxynucleotides).
- It is composed of monomeric units namely deoxyadenylate (dAMP), eoxyguanylate (dGMP), deoxycytidylate(dCMP) and deoxythymidylate(d TMP) (It may be noted here that some authors prefer to use TMP for deoxythymidylate, since it is found only in DNA).
- The details of the nucleotide structure are given above.
- The double helical structure of DNA was proposed by lames Watson and Francis Crick in 1953 (Nobel Prize, 1962).
- The elucidation of DNA structure is considered as a milestone in the era of modern biology.
- The structure of DNA double helix is comparable to a twisted ladder.



(A) Watson-Crick model of DNA helix (B) Complementary base pairing in DNA helix.

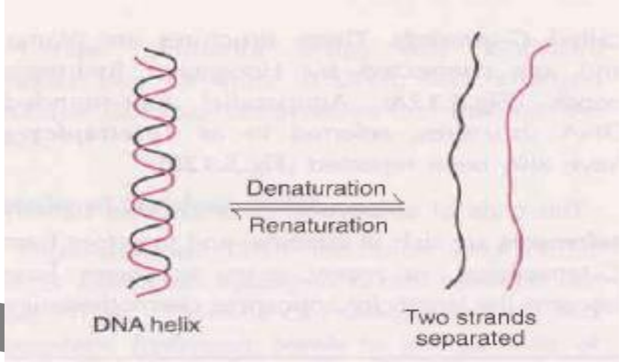


Complementary base paring in DNA (A) Thymine pairs with adenine by 2 hydrogen bonds

(B) Cytosine pairs with guanine by 3 hydrogen bonds.

- The DNA is a right handed double helix.
- It consists of two polydeoxyribonucleotide chains (strands) twisted around each other on a common axis.
- The two strands are antiparallel, i.e., one strand runs in the 5' to 3' direction while the other in 3'to 5'direction.T his is comparable to two parallel adjacent roads carrying traffic in opposite direction.
- The width (or diameter) of a double helix is 20 A^o (2 nm).
- Each turn (pitch) of the helix is 34 A'' (3.4 nm) with 10 pairs of nucleotides each pair placed at a distance of about 3.4 A^o.
- Each strand of DNA has a hydrophilic deoxyribose phosphate backbone (3'-5' phosphor diester bonds)o n the outside (periphery) of the molecule while the hydrophobic bases are stacked inside (core).
- The two polynucleotide chains are not identical but complementary to each other due to base pairing.
- The two strands are held together by hydrogen bonds formed by complementary base pairs.
- The A-T pair has 2 hydrogen bonds while G-C pair has 3 hydrogen bonds. The G = C is stronger by about 50% than A=T.
- The hydrogen bonds are formed between a purine and a pyrimidine only.

- If two purines face each other, they would not fit into the allowable space. And two pyrimidines would be too far to form hydrogen bonds.
- The only base arrangement possible in DNA structure, from spatial considerations is A-T, T-A, G-C and C-C.
- The complementary base pairing in DNA helix proves Chargaffs rule.
- The content of adenine equals to that of thymine (A = T) and guanine equals to that of cytosine (G = C). 10.
- The genetic information resides on one of the two strands known as template strand or sense strand.
- The opposite strand is antisense strand.
- The double helix has (wide) major grooves and (narrow) minor grooves along the phosphodiester backbone.
- Proteins interact with DNA at these grooves, without disrupting the base pairs and double helix.
- The two strands of DNA helix are held together by hydrogen bonds.
- Disruption of hydrogen bonds (by change in pH or increase in temperature) results in the separation of polynucleotide strands.
- This phenomenon of loss of helical structure of DNA is known as denaturation.
- The phosphodiester bonds are not broken by denaturation.
- Loss of helical structure can be measured by increase in absorbance at 260 nm (in a spectrophotometer).



Denaturation and renaturation of DNA.

- Melting temperature (Tm) is defined as the temperature at which half of the helical structure of DNA is lost.
- Since C-C base pairs are more stable (due to 3 hydrogen bonds) than A-T base pairs(2 hydrogen bonds), the Tm is greater for DNAs with higher C-C content.
- Thus, the Tm is 65°C for 35% G-C content while it is 70°C for 50% G-C content.
- Formamide destabilizes hydrogen bonds of base pairs and, therefore, lowers Tm.

- This chemical compound is effectively used in recombinant DNA experiments.

Renaturation:

- Renaturation or reannealing is the process in which the separated complementary DNA strands can form a double helix.

Structure of major species of RNA - mRNA, tRNA and rRNA

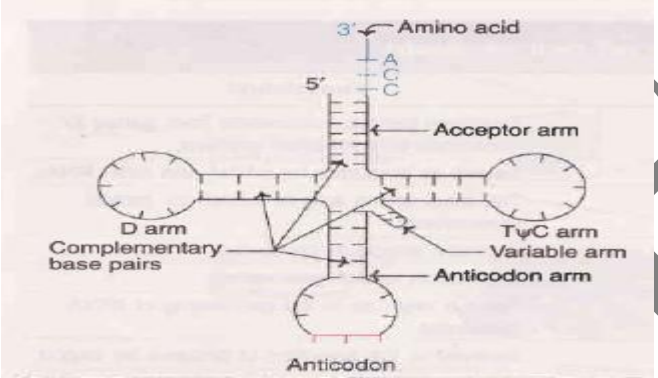
RNA:

- **Ribonucleic acid** or **RNA**, is one of the three major macromolecules (along with DNA and proteins) essential for all known forms of life.

TYPES OF RNA:

- The three major types of RNAs with their respective cellular composition are given below
    1. Messenger RNA (mRNA): 5-1O"/"
    2. Transfer RNA (tRNA): 10-200/"
    3. Ribosomal RNA (rRNA): 50-80%
- The mRNA is synthesized in the nucleus (in eukaryotes) as heterogeneous nuclear RNA (hnRNA).
- hnRNA, on processing, liberates the functional mRNA which enters the cytoplasm to participate in protein synthesis.
- mRNA has high molecular weight with a short half-life.
- The eukaryotic mRNA is capped at the S'-terminal end by 7- methylguanosine triphosphate.
- It is believed that this cap helps to prevent the hydrolysis of mRNA by 5'-exonucleases.
- Further,t he cap may be also involved in the recognition of mRNA for protein synthesis.
- The 3'-terminal end of mRNA contains a polymer of adenylate residues (20-250 nucleotides) which is known as poly (A) tail.
- This tail may provide stability to mRNA, besides preventing it from the attack of 3'-exonucleases.mRNA molecules often contain certain modified bases such as 6-methyladenylatesin the internal structure.
- Transfer RNA (soluble RNA) molecule contains 71-80 nucleotides (mostly 75) with a molecular weight of about 25,000.
- There are at least2 0 species of tRNAs, corresponding to 20 amino acids present in protein structure.
- The structure of tRNA (for alanine) was first elucidated by Holley.
- The structure of IRNA, depicted in resembles that of a clover leaf tRNA contains mainly four arms, each arm with a base paired stem.

1. The acceptor arm: This arm is capped with a sequence C CA (5'to 3'). The amino acid is attached to the acceptor arm.
2. The anticodon arm: This arm, with the three specific nucleotide bases (anticodon), is responsible for the recognition of triplet codon of mRNA. The codon and anticodon are complementary to each other.



Structure of transfer RNA.

3. The D arm : It is so named due to the presence of dihydrouridine.
4. The T□C arm : This arm contains a sequence of T, pseudouridine (represented by Psi, □) and C.
5. The variable arm : This arm is the most variable in tRNA. Based on this variability, tRNAs are classified into 2 categories :
(a) Class I tRNAs : The most predominant (about 75"/") form with 3-5 base pairs length"
(b) Class ll tRNAs : They contain 13-20 base pair long arm.

- Base pairs in tRNA : The structure of tRNA is maintained due to the complementary base pairing in the arms.
- The four arms with their respective base pairs are given below
  - The acceptor arm - 7 bp
  - The T□C arm - 5 bp
  - The anticodon arm - 5 bp
  - The Darm -4bp

Ribosomal RNA (rRNA)

- The ribosomes are the factories of protein synthesis.

- The eukaryotic ribosomes are composed of two major nucleoprotein complexes- 60S subunit and 40S subunit.
- The 605 subunit contains 28S rRNA, 55 rRNA and 5.8S rRNA while the 40S subunit contains 18S rRNA.
- The function of rRNAs in ribosomes is not clearly known.
- It is believed that they play a significant role in the binding of mRNA to ribosomes and protein synthesis.
- RNA is a polymer of ribonucleotides held together by 3',5'-phosphodiester bridges.
- Although RNA has certain similarities with DNA structure, they have specific differences.
- **Pentose:** The sugar in RNA is ribose in contrast to deoxyribose in DNA.
- **Pyrimidine :** RNA contains the pyrimidines uracil in place of thymine (in DNA).
- **Single strand:** RNA is usually a singlestranded polynucleotide. However, this strand may fold at certain places to give a doublestranded structure, if complementary base pairs are in close proximity.
- **Chargaff's rule-not obeyed:** Due to the single-stranded nature, there is no specific relation between purine and pyrimidines contents. Thus the guanine content is not equal to cytosine (as is the case in DNA).
- **Susceptibility to alkali hydrolysis:** Alkali can hydrolyse RNA to 2',3'-cyclic diesters. This is possible due to the presence of a hydroxyl group at 2' position. DNA cannot be subjected to alkali hydrolysis due to lack of this group.
- **Orcinol colour reaction :** RNAs can be histologically identified by orcinol colour reaction due to the presence of ribose.

Functions of RNA

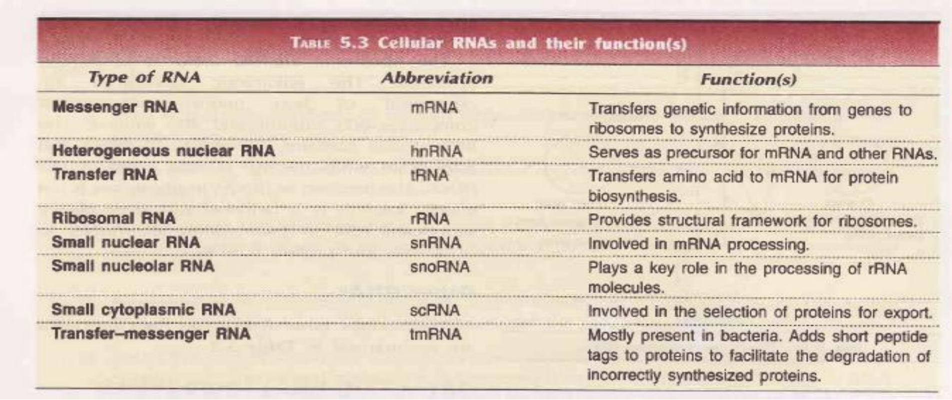


TABLE 5.3 Cellular RNAs and their function(s)

Type of RNA	Abbreviation	Function(s)
Messenger RNA	mRNA	Transfers genetic information from genes to ribosomes to synthesize proteins.
Heterogeneous nuclear RNA	hnRNA	Serves as precursor for mRNA and other RNAs.
Transfer RNA	tRNA	Transfers amino acid to mRNA for protein biosynthesis.
Ribosomal RNA	rRNA	Provides structural framework for ribosomes.
Small nuclear RNA	snRNA	Involved in mRNA processing.
Small nucleolar RNA	snoRNA	Plays a key role in the processing of rRNA molecules.
Small cytoplasmic RNA	scRNA	Involved in the selection of proteins for export.
Transfer–messenger RNA	tmRNA	Mostly present in bacteria. Adds short peptide tags to proteins to facilitate the degradation of incorrectly synthesized proteins.

Nucleic acid chemistry

Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are made up of nucleic acids found in the nuclei of living cells. They are the vehicles of genetic inheritance.

Nucleic acids are condensation polymers of nucleotides. To understand their functions you will find it helpful to look at how their molecules are built up and the structures of these molecules.

The building blocks

Three types of chemicals make up the building blocks for nucleic acids.

Phosphates

These are based on the inorganic acid H_3PO_4 (phosphoric acid).

Two important reactions of the hydroxyl groups in phosphoric acid are:

- with alcohols to form ester groups
- with amines to form amide groups

Sugars

The sugars in DNA and RNA are pentoses.

- in **DNA** the sugar is **deoxyribose**
- in **RNA** the sugar is **ribose**

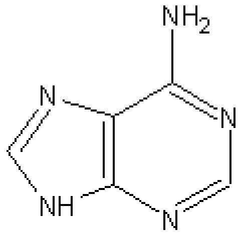
Both these sugars have hydroxyl groups. Ribose has four and deoxyribose has three (hence the prefix 'deoxy'). These groups can react with carboxylic acids and phosphoric acid to form esters.

Organic bases

There are four organic bases involved in the formation of DNA molecules:

- adenine and guanine (both purines containing two rings in their structures)
- thymine and cytosine (both pyrimidines containing only one ring in their structures)

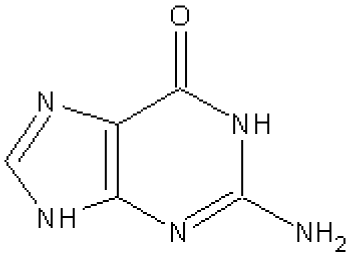
adenine



(A)

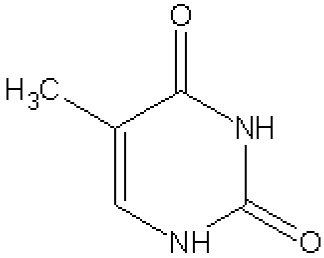
A and G are double-ring **purine**bases.

guanine



(G)

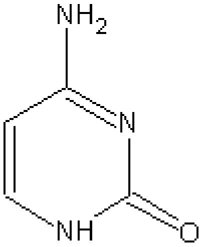
thymine



(T)

T and C are single-ring **pyrimidine** bases.

cytosine



(C)

UV absorption

- The effect of ozone and ultraviolet (UV) radiations upon the UV absorption spectra of solutions (buffered at pH 7.0–7.2) of nucleic acids, and the nucleotides, nucleosides, purines, and pyrimidines of nucleic acids have been studied, and in a few instances the effects of both agents in various combinations were tested.
- Without exception, ozonation of the above compounds quickly reduces the absorption maximum at or near 2600 A. and usually induces an increase in absorption at wavelengths shorter than 2400 A., but has much less effect on their absorption at wavelengths longer than 2800 A.
- The effects of ozone on nucleic acid are probably compounded of the effects of ozone on the constituent purines and pyrimidines, each of which appears to be individually affected.
- UV has little effect on the absorption spectra of all of the above compounds, a measurable change appearing only after prolonged irradiation.
- UV causes a decrease in absorption by nucleic acids at the 2600-A. peak and an increase at wavelengths shorter than 2400 A. and longer than 2800 A.
- Exposure of adenine to UV causes an increased absorption over the entire range, but neither adenosine nor adenylic acid was markedly affected by comparable doses.
- UV has little effect on absorption by guanosine or guanylic acid.
- Of the pyrimidines tested, uracil was most sensitive to UV, and its sensitivity was greater in the combined form of uridine or uridylic acid. The main effect of UV on the absorption spectrum of nucleic acid may therefore be attributable to the change it induces in uracil.

Effect of acid and alkali on DNA

Ordinarily each DNA molecule inside your cells contains two strands joined together by interactions called hydrogen bonds. Change in conditions, however, can "denature" the DNA and cause these strands to separate. Adding strong bases, like NaOH, dramatically increases the pH, thus decreasing the hydrogen ion concentration of the solution and denaturing double-stranded DNA.

The chemical difference between RNA and DNA polymers (the absence of the 2' hydroxyl group) results in differences between the reaction of DNA and RNA to alkaline conditions. Because ribose has both 2' and 3' hydroxyl groups, the 2' hydroxyl can "attack" the phosphodiester bond in the presence of hydroxyl (OH-) radicals, which results in the phosphate backbone being broken. Because DNA does not have a 2' hydroxyl group, DNA polymers cannot undergo this alkaline clevage.

Effects of pH

The hydroxide ion concentration and pH have a direct correlation, meaning the higher the pH, the higher the hydroxide concentration. Likewise, the lower the hydrogen ion concentration falls. At high pH, then, the solution is rich in hydroxide ions, and these negatively-charged ions can pull hydrogen ions off of molecules like the base pairs in DNA. This process disrupts the hydrogen bonding that holds the two DNA strands together, causing them to separate.

RNA vs. DNA

Unlike RNA, DNA lacks a hydroxyl group on the 2' position in each sugar group. This difference makes DNA much more stable in alkaline solution. In RNA, the hydroxyl group on the 2' position can give up a hydrogen ion to the solution at high pH, creating a highly reactive alkoxide ion that attacks the phosphate group holding two neighboring nucleotides together. DNA does not suffer from this defect and thus enjoys remarkable stability at high pH.

Alkaline lysis

Molecular biologists often make use of alkaline denaturation to isolate plasmid DNA from bacteria. Plasmids are little loops of DNA separate from the bacterial chromosome. In an alkaline lysis miniprep, biologists add detergent and sodium hydroxide to bacteria suspended in solution. The detergent dissolves the bacterial cell membrane while the sodium hydroxide boosts the pH and makes the solution highly alkaline. As the broken cells release their contents, the DNA inside separates into its component strands, or denatures.

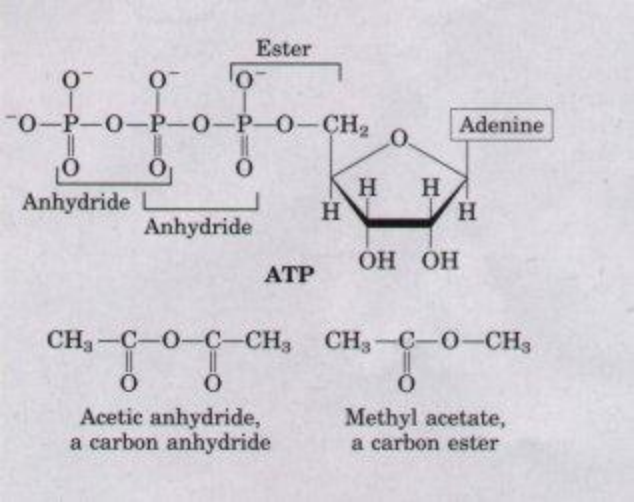
Reannealing

Once the biologist extracts the DNA from the cell, he adds another reagent to return the solution to a more neutral pH and precipitate the detergent. The change in pH allows the plasmid strands to reanneal; the bulky chromosome, however, cannot do the same, so the biologist can remove it together with the detergent, denatured proteins and other assorted junk, leaving the plasmid behind. Alkaline lysis does not completely purify the plasmid

DNA; rather, it serves as a "quick and dirty" way to extract it from the cell and remove most other contaminants.

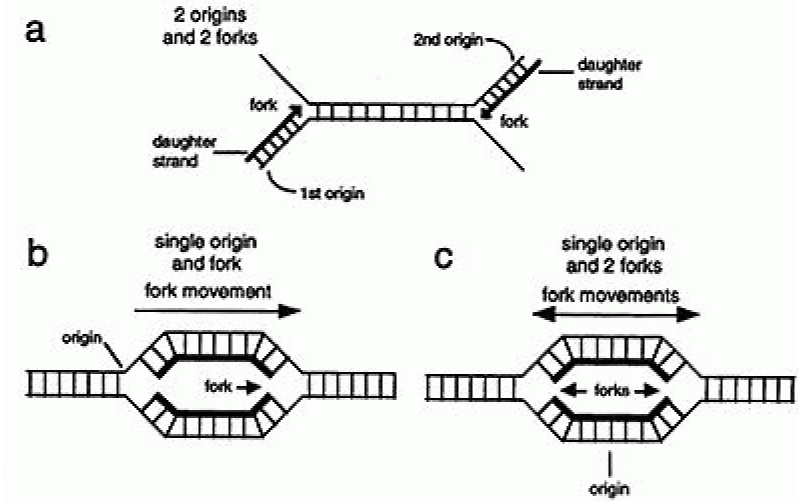
Other Functions of Nucleotides

In addition to their roles as the subunits of nucleic acids, nucleotides have a variety of other functions in every cell: as energy carriers, components of enzyme cofactors, and chemical messengers.



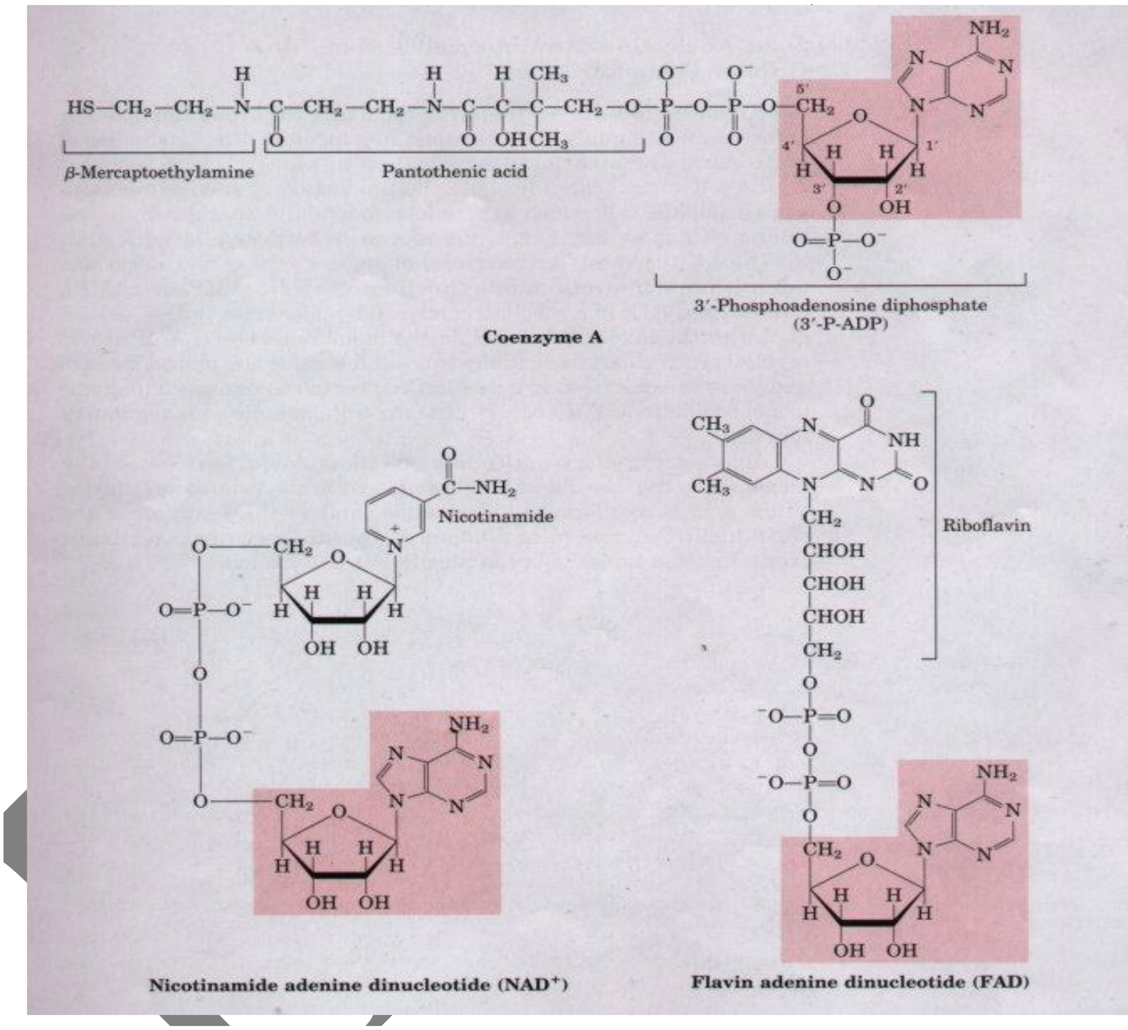
Source of Energy

NTP's are used in the synthesis of RNA primers andATP is used as an energy source for some of theenzymes needed to initiate and sustain DNA synthesis at the replication fork. The nucleotide that is to be incorporated into the growing DNA chain is selected by base pairing with the template strand of the DNA.



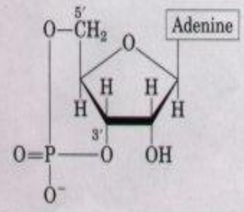
Component of coenzymes

Cofactors, mostly metal ions or coenzymes, are inorganic and organic chemicals that assist enzymes during the catalysis of reactions. Coenzymes are non-protein organic molecules that are mostly derivatives of vitamins soluble in water by phosphorylation; they bind apoenzyme to proteins to produce an active holo enzyme.

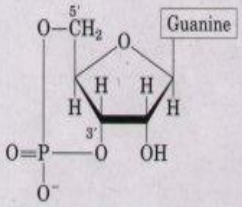


Second messengers

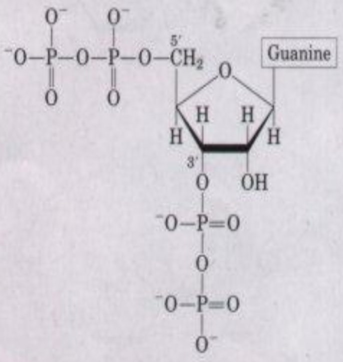
Second messengers are intracellular signaling molecules released by the cell in response to exposure to extracellular signaling molecules—the first messengers. Second messengers trigger physiological changes such as proliferation, differentiation, migration, survival, and apoptosis. They are one of the triggers of intracellular signal transductioncascades.



Adenosine 3′,5′-cyclic monophosphate
(cyclic AMP; cAMP)



Guanosine 3′,5′-cyclic monophosphate
(cyclic GMP; cGMP)



Guanosine 3′-diphosphate,5′-diphosphate
(guanosine tetraphosphate)
(ppGpp)

Examples of second messenger molecules include cyclic AMP, cyclic GMP, inositol trisphosphate, diacylglycerol, and calcium. First messengers are extracellular factors, often hormones or neurotransmitters, such as epinephrine, growth hormone, and serotonin. Because peptide hormones and neurotransmitters typically are biochemically hydrophilicmolecules, these first messengers may not physically cross the phospholipid bilayer to initiate changes within the cell directly—unlike steroid hormones, which usually do. This functional limitation necessitates the cell to devise signal transduction mechanisms to transduce first messenger into second messengers, so that the extracellular signal may be propagated intracellularly. An important feature of the second messenger signaling system is that second messengers may be coupled downstream to multi-cyclic kinase cascades to greatly amplify the strength of the original first messenger signal. For example, RasGTP signals link with the Mitogen Activated Protein Kinase (MAPK) cascade to amplify the allosteric activation of proliferative transcription factors such as Myc and CREB.

Secondary messenger systems can be synthesized and activated by enzymes, for example, the cyclases that synthesize cyclic nucleotides, or by opening of ion channels to allow influx of metal ions, for example Ca^{2+} signaling. These small molecules bind and activate protein kinases, ion channels, and other proteins, thus continuing the signaling cascade.

There are three basic types of secondary messenger molecules:

- Hydrophobic molecules: water-insoluble molecules such as diacylglycerol, and phosphatidylinositols, which are membrane-associated and diffuse from the plasma membraneinto the intermembrane space where they can reach and regulate membrane-associated *effector proteins*
- Hydrophilic molecules: water-soluble molecules, such as cAMP, cGMP, IP_3, and Ca^{2+}, that are located within the cytosol
- Gases: nitric oxide (NO), carbon monoxide (CO) and hydrogen sulfide (H_2S) which can diffuse both through cytosol and across cellular membranes.

These intracellular messengers have some properties in common:

- They can be synthesized/released and broken down again in specific reactions by enzymes or ion channels.
- Some (such as Ca^{2+}) can be stored in special organelles and quickly released when needed.
- Their production/release and destruction can be *localized*, enabling the cell to limit space and time of signal activity.
  - There are several different secondary messenger systems (cAMP system, phosphoinositol system, and arachidonic acid system), but they all are quite similar in overall mechanism, although the substances involved and overall effects can vary.
  - In most cases, a ligand binds to a membrane-spanning receptor protein molecule. The binding of a ligand to the receptor causes a conformation change in the receptor. This conformation change can affect the activity of the receptor and result in the production of active second messengers.
  - In the case of G protein-coupled receptors, the conformation change exposes a binding site for a *G-protein*. The G-protein (named for the GDP and GTP molecules that bind to it) is bound to the inner membrane of the cell and consists of three subunits: alpha, beta and gamma. The G-protein is known as the "transducer."
  - When the G-protein binds with the receptor, it becomes able to exchange a GDP (guanosine diphosphate) molecule on its alpha subunit for a GTP (guanosine triphosphate) molecule. Once this exchange takes place, the alpha subunit of the G-protein transducer breaks free from the beta and gamma subunits, all parts remaining membrane-bound. The alpha subunit, now free to move along the inner membrane, eventually contacts another membrane-bound protein - the "primary effector."
  - The primary effector then has an action, which creates a signal that can diffuse within the cell. This signal is called the "second (or secondary) messenger." The secondary messenger may then activate a "secondary effector" whose effects depend on the particular secondary messenger system.
  - Calcium ions are one type of second messengers and are responsible for many important physiological functions including muscle contraction, fertilization and neurotransmitter release. The ions are normally bound or stored in intracellular components (such as the endoplasmic reticulum) and can be released during signal transduction. The enzyme phospholipase C produces diacylglycerol and inositol trisphosphate, which increases calcium ion permeability into the membrane. Active G-protein open up calcium channels to let calcium ions enter the plasma membrane. The other product of phospholipase C, diacylglycerol, activates protein kinase C, which assists in the activation of cAMP (another second messenger).

Possible Questions

2 marks

1. Define amino acids
2. Draw the structure of glycine
3. Draw the structure of proline
4. Write short notes on aliphatic amino acids
5. Write notes on different types of RNA

8 marks

1. Explain in detail about
    - i. aromatic amino acids
    - ii. unusual amino acids
2. Draw the structure of purines
3. Write about the classification of amino acids
4. Draw the structure of pyrimidines and explain in detail
5. Describe the structure and properties of aliphatic amino acids
6. Explain in detail about double helix structure of DNA
7. Explain the structure and properties of aromatic and basic groups of amino acids
8. Briefly describe the different forms of DNA
9. Discuss in detail about tRNA
10. Discuss in detail about rRNA

Karpagam Academy of Higher Education
Department of Biochemistry
I B.Sc., Biochemistry
19BCU101- Molecules of life
Prepared By Dr. A. RAMAKRISHNAN

Question number	**Question**	**Option I**	**Option II**	**Option III**		**Option IV**		**Answer**
1	Out of 200 different amino acids found in nature the number of aminoacids present in protein	20	25	43	30	30		**20**
2	At iso electric pH amino acids exist as	anion	cation	zwitter ion	A&B	a&b		**zwitter ion**
3	Ampholytes have	only positive charges	only negative charges	both positive & negative charges	none	all of the above		all of the above

4	The ionisable groups of amino acids atleast	1				4		**2**
5	The ionisable groups of amino acids exist almost entirely as the conjugated base at	6.6	6.8	7.2	7.4	7.4		**7.4**
6	The melting point of amino acid is above	100^{0}C	180^{0}C	200^{0}C	220^{0}C	220^{0}C		**200^{0}C**
7	Amino acids are insoluble in	Lactic acid	cholorofo rm	ethanol	benzene	benzone		**benzone**

8	the reagent for the detection of amino acid is	Molisch's reagent	Dicholoro phenol indo phenol	ninhydrin	none	both a and b		**ninhydrin**
9	Which among the following is an essential amino acid	Cysteine	leucine	tyrosine	Aspartic acid	Aspartic acid		**leucine**
10	The neutral amino acid is	leucine	lysine	proline	serine	serine		**leucine**
11	Which amino acid is a lipotropic factor?	Lysine	leucine	tryptophan	methionine	tryptophan		**methionine**
12	The basic amino acid	Glycine	Histidine	proline	serine	Cysteine		**Histidine**
13	Which among the following is a nutritionally essential amino acid for man?	Alanine	Glycine	tyrosine	tryptophan	imidazole group		**tryptophan**
14	All amino acids are optically active	Glycine	serine	threonine	tryptophan	methyl group		**Glycine**

15	Which one of the following amino acid does not contain sulphur	methionine	cystine	Lysine	Cysteine	Ketones		**Lysine**
16	Arginine has a	Thiol group	Guanidine group	phenolic group	imidazole group	Serine		**Guanidine group**
17	Formaldehyde reacts with amino acid	Carboxyl group	amino group	hydroxyl group	methyl group	methyl group		**amino group**
18	Ninhydrin reaction is specific to	Amino & carboxylic acid	carboxylic acid	Aldehydes	Ketones	Ketones		**Amino & carboxylic acid**
19	Serotonin is derived in the body from the following amino acid	Phenyl alanine	histidine	tryptophan	Serine	Serine		**tryptophan**
20	The amino acid which contains a indole group is	Histidine	arginine	attulin	glycine	Tryptophan		**Tryptophan**
21	The amino acid which contains a guanidine group is	Histidine	arginine	attulin	attulin	Ornithine		**arginine**

22	The amino acid which synthesises many hormones	Valine	alanine	Phenylalanine	alanine	Histidiene		**alanine**
23	Sakaguchi reaction is answered by	cystine	ornithine	arginine	arginine	Arginino succinic acid		**arginine**
24	The isoelecrtic point of an amino acid depends on its	optical rotation	dissociation constant	diffusion coeffient	diffusion coeffient	chain length		**optical rotation**
25	The amino acids exist as zwitter ions when they are in	solid state	acidic solution	alkaline solutio	alkaline solutio	neutral solution		**solid state**
26	are absorbed into portal circulation	are absorbed into portal circulation	are absorbed into lymph	are excreted to the extent of 50%	are excreted to the extent of 50%	converted into glucose in the intestine		**are absorbed into portal circulation**
27	An amino acid which contains a disulfide bond is	lysine	methionine	homocysteine	homocysteine	Cystine		**Cystine**
28	Amino acids are insoluble in	Acetic acid	Chloroform	Ethanol	Ethanol	Benzene		**Benzene**

29	Owing to the opposite reactions depending on the acidity or alkalinity of the solution, the amino acid sare called	Amphibolic	Ampholytic	Both	None	ambhipathic		**Ampholytic**
30	This protein has a pigment as the prosthetic group	heme	haemoglobin	hematin	Collagen	Collagen		**haemoglobin**
31	The backbone of nucliec acid structure is contributed by	Hydrophobic forces	hydrogen bonds	phosphodiester linkages	ionic bonds	ionic bonds		**phosphodiester linkages**
32	The pyrimidine base of the DNA is	cytosine	Guanine	Uracil	Adenine	Adenine		**cytosine**
33	There are three hydrogen bonds between Cytosine and	Adenine	guanine	cytosine		thymine		**thymine**

34	An increased melting temperature for duplex DNA results from a high content of	Adenine & Guanine	Cytosine &thymine	Adenine &thymine		Cytosine &guanine		**Cytosine &guanine**
35	The base which is absent in RNA is	Cytosine	Uracil	thymine		Adenine		**thymine**
36	The following facts are true of all transfer (t)RNA except that	the 5' end is phosphorylated	they are single chains	methylated bases are found	the anticodon loop is identical	the anticodon loop is identical		**the anticodon loop is identical**
37	Z-DNA was discovered by	Watson& Crick	Hoogsten	Chargaff	Chargaff	warg &Rich		**Hoogsten**
38	The base sequence at the end of all tRNA is	CCA	CAA	CCC	CCC	AAA		**CCA**
39	Deoxy ribose has no oxygen in	5' position	2' position	3' position	4' position	4' position		**2' position**
40	Among the RNA's which of the following is very unstable	rRNA	tRNA	mRNA	5SRNA	5SRNA		**mRNA**

41	Ribose is linked with purine by	C_1 to N_1	C_1 to N_9	C_5 to N_9	C_1 to N_7	C_1 to N_7		**C_1 to N_9**
42	mRNA has complementary sequence of	C-DNA	t-RNA	RNA	r-RNA	r-RNA		**t-RNA**
43	The higher percentage of RNA found is	Nucleus	Mitochondria	microsomes	golgibodies	golgibodies		**Nucleus**
44	RNA is easily hydrolysed by base due to	presence of OH group in position 2 of the ribose	Differences in the bases	Low molecular weight	none	both a and b		**presence of OH group in position 2 of the ribose**
45	The best role of purine & pyrimidine nucleotides is to serve as the monomeric precursors of	RNA	DNA	Both	None	all of the above		**Both**
46	Melting temperature or Tm is high in DNA containing	rich in A, T pair	rich in G,C pair	Both in equal ratio	None	All		**rich in G,C pair**

47	The purine nucleotides act as the components of	FAD+	NAD+	NADP+	All	All		
48	When pancreatic deoxyribonuclease attacks DNA, the product obtained is	3’ phosphonucleotide	5’ phosphonucleotide	5’3’ phosphodiesters	2’3’ phosphodiesters	2’3’ phosphodiesters		**5’3’ phosphodiesters**
49	The pyrimidine nucleotides act as the high energy intermediates	UDPG	ATP	ADP		GDP		**UDPG**
50	The chemical name of thymine	2-Oxy –4-amino pyrimidine	2,4-dioxy –5-methyl pyrimidine	2,4-dioxy pyrimidine		Purine		**2,4-dioxy –5-methyl pyrimidine**
51	S1 nuclease	degrades double stranded DNA	degrades single stranded DNA	degrades RNA & DNA hybrid		degrades s	**degrades single stranded DNA**	
52	An increased melting temperature for duplex DNA results from a high content of	A+G	C+T	A+T		G+C	**G+C**	**G+C**

53	The strucutre of RNA is in the form of	Hairpin loop	clover-leaf like structure	double helical structure		alpha helix	none	**clover-leaf like structure**
54	6-Amino purine is	Guanine	adenine	cytosine		adenine	methionine	**adenine**
55	The chemical name of 2-amino –6- oxy purine	Adenine	xanthine	guanine		Cytosine	hypoxanthine	**guanine**
56	The lactom form is the predominant tautomer of	uracil	cytosine	xanthine	adenine	Guanine		**uracil**
57	N7-methyl guanine has been found more recently in the nucleic acids of the cells of	Bacteria	yeast	mammals	plant	plants		**mammals**
58	Hypoxanyhine and ribose contitute	Adenosine	inosine	guanosine		cytidine		**inosine**
59	Thymine and deoxy ribose form	deoxycytidine	deoxyadenosine	deoxythymidine		deoxywidine		**deoxythymidine**
60	The most abundant intracellular free nucletide	ATP	FAD	NAD+		NADP+		**ATP**

61	The concentration of ATP in living mammalian cells in mm is near	0.2	0.3	0.4		1	**1**	
62	The intracellular cAMP concentration in are µm near	3	2	1	1	0.5		**1**
63	The epinelisation of galactose to glucose & vice versa take place by	UTP	CTP	GTP	GTP	ATP		**UTP**
64	The biosynthesis of phosphoglycerides in animal tissue requires	ATP	GTP	CTP		TPP		**GTP**
65	The chemical name 4-hydro-xypyrazole pyrimidines is used for	Thioguanine	mercaptopurine	Axatheeopurine		Allopurinol		**Allopurinol**
66	Transforming factor is	RNA	DNA	tRNA	none	r-RNA		**DNA**

67	Guanosine nucletide is held by the cytosine nucletide by the number of hydrogen bonds	1	2	3	4	4		**2**
68	Within single turn of DNA the number of base pairs exists	4	6	8	10	10		**10**
69	Each turn of DNA structure has a pitch in nm of	1.4	2.4	3.4	4.4	4.4		**3.4**
70	The double stranded DNA molecule loses its viscosity upon	Denaturation	Filteration	sedimentation	concentration	concentration		**Denaturation**

UNIT V
SYLLABUS

Vitamins: Structure and active forms of water soluble and fat soluble vitamins, deficiency diseases and symptoms, hypervitaminosis

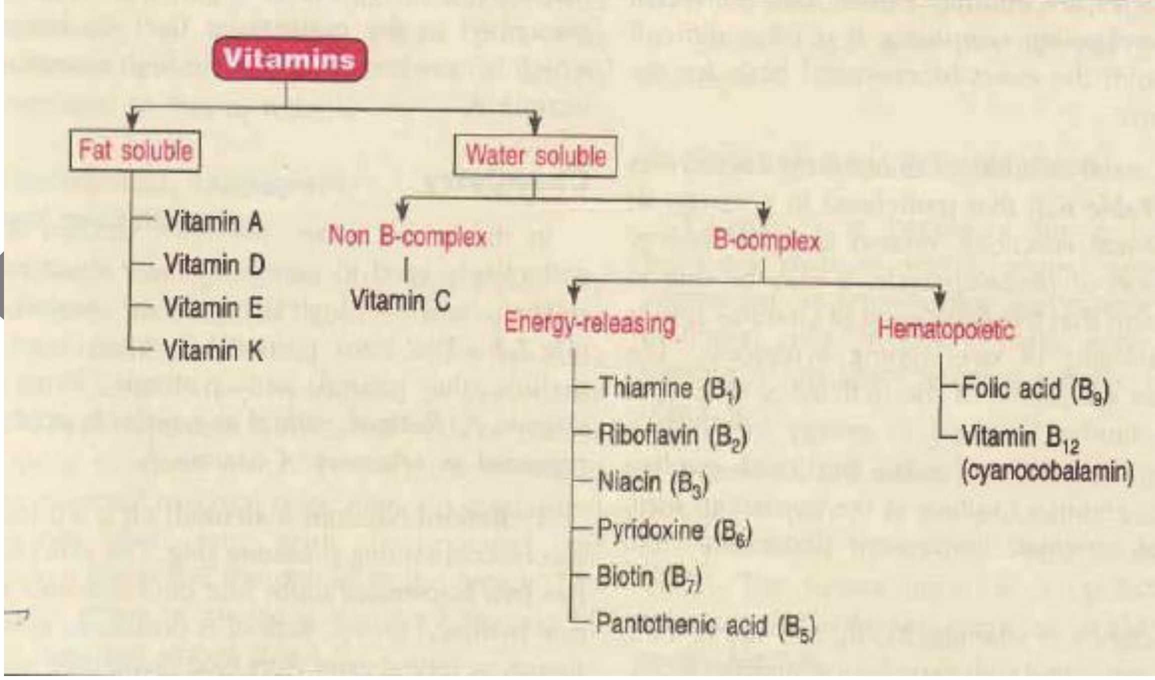
Vitamins
Structure and active forms of water soluble and fat soluble vitamins - deficiency diseases and symptoms

Definition:

Vitamins are natural substances found in plants and animals and known as Essential nutrients for human beings.

Classification of vitamins:

- Vitamins are classified according to their solubility, namely: the fat-solubles and the water solubles.
- Fat-soluble vitamins include vitamin A, D, E, and K, while the water-soluble vitamins include vitamins C or ascorbic acid and B complex which include thiamin, riboflavin, niacin, pyridoxine, cobalamin, panthotenic and folic acid, chlorine, inositol, and biotin.



Classification of Vitamins

Fat soluble vitamins:

- The fat-soluble vitamins include vitamins A, D, E and K - since they are soluble in fat and are absorbed by the body from the intestinal tract.

- The human body has to use bile acids to absorb fat-soluble vitamins.
- Once these vitamins are absorbed, the body stores them in body fat.
- When you need them, your body takes them out of storage to be used.
- Eating fats or oils that are not digested can cause shortages of fat-soluble vitamins.

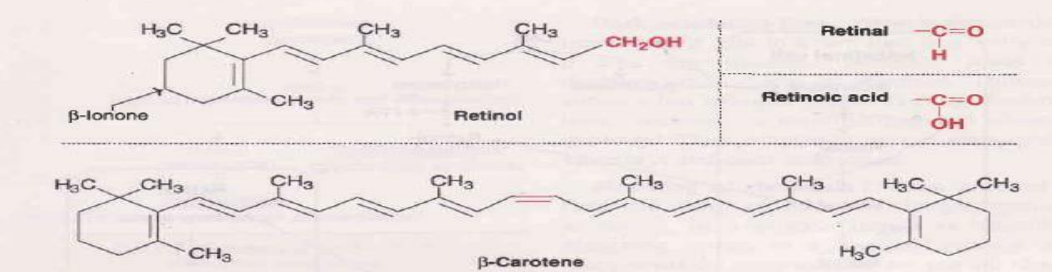
Characteristics of the vitamins are:

Most of the vitamins have been artificially synthesized.

Some of vitamins are soluble in water and others are fat-soluble.

- Some vitamins are synthesized in the body.
- Some members of vitamin B complex are synthesized by microorganisms in the intestinal tract.
- Vitamins are partly destroyed and are partly excreted.
- Vitamins can be stored in the body to some extent, for example the fat-soluble vitamins are stored in the liver and subcutaneous tissue.
- Vitamins can perform their work in very small quantities.
- Hence, the total daily requirement is usually very small.
- The fat soluble vitamin A, as such is present only in foods of animal origin. However, its provitamins carotenes are found in plants.
- In the recent years, the term vitamin A is collectively used to represent many structurally related and biologically active molecules.
- The term retinoids is often used to include the natural and synthetic forms of vitamin A. Retinol, retinal and retinoic acids are regarded as vitamers of vitamin A.

1. **Retinol (vitamin A alcohol):** It is a primary alcohol containing p-ionone ring. The side chain has two isoprenoid units, four double bonds and one hydroxyl group. Retinol is present in animal tissues as retinyl ester with long chain fatty acids.
2. **Retinal (vitamin A aldehyde):** This is an aldehyde form obtained by the oxidation of retinol. Retinal and retinol are interconvertible. Previously, the name retinine was used for retinal.
3. **Retinoic acid (vitamin A acid):** This is produced by the oxidation of retinal. However, retinoic acid cannot give rise to the formation of retinal or retinol.
4. **β-Carotene (provitamin A):** This is found in plant foods. It is cleaved in the intestine to produce two moles of retinal. in humans, this conversion is inefficient, hence β-carotene possesses about one-sixth vitamin A activity compared to that of retinol.



Structures of vitamin A and related compounds (Red color represents the substituents groups in the respective compounds).

Sources:

Vitamin A: liver, vitamin A fortified milk and dairy products, butter, whole milk, cheese, egg yolk. Provitamin A: carrots, leafy green vegetables, sweet potatoes, pumpkins, winter squash, apricots, cantaloupe.

Physiological Functions:

Helps to form skin and mucous membranes and keep them healthy, thus increasing resistance to infections; essential for night vision; promotes bones and tooth development. Beta carotene is an antioxidant and may protect against cancer.

Deficiency

- **Deficiency manifestations of the eyes:** Night blindness (nyctalopia) is one of the earliest symptoms of vitamin A deficiency. The individuals have difficulty to see in dim light since the dark adaptation time is increased. Prolonged deficiency irreversibly damages a number of visual cells. Severe deficiency of vitamin A leads to xerophthalmia

- **Effect on reproduction**: The reproductive system is adversely affected in vitamin A deficiency generation of germinal epithelium leads to sterility in males.

- **Effect on skin and epithelial cells:** The skin becomes rough and dry. Keratinization of epithelial cells of gastrointestinal act, urinary tract and respiratory tract is noticed. This leads to increased bacterial infection. Vitamin A deficiency is associated with formation of urinary stones

Symptoms

Mild: nausea, irritability, blurred vision. Severe: growth retardation, enlargement of liver and spleen, loss of hair, bone pain, increased pressure in skull, skin changes. Mild: night blindness, diarrhea, intestinal infects ions, impaired vision.

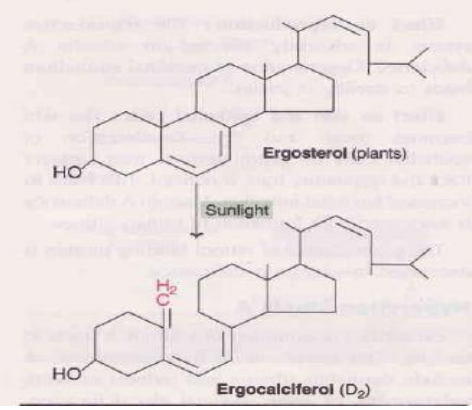
Severe: inflammation of eyes, keratinization of skin and eyes. Blindness in children.

VITAMIN D:

Vitamin D is a fat soluble vitamin. It resembles sterols in structure and functions like a hormone.

Chemistry:

Ergo calciferol (Vitamin D2) is formed ergosterol and is present in plants. Ergocalciferol and cholecalciferol are sources of for vitamin D activity and referred to as provitamins.



Formation of ergocalciferol from ergosterol

Absorption, transport and storage:

- Vitamin D is absorbed in the small intestine for which bile is essential.
- Through lymph, vitamin D enters the circulation bound to plasma □2-globulin and is distributed throughout the body.
- Liver and other tissues stores small amounts of vitamin D

Sources

- Good sources of vitamin D include fatty fish, fish liver oils, egg yolk etc. Milk is not a good source of vitamin D.

Vitamin D can be provided to the body in three ways:

1. Exposure of skin to sunlight for synthesis of vitamin D
2. Consumption of natural foods;
3. by irradiating foods (like yeast) that contain precursors of vitamin D and fortification of foods (milk, butter etc.)

- Calcitriol is the biologically active form of vitamin D.
- It regulates the plasma levels of calcium and phosphorus.
- Calcitriol acts at 3 different levels ie., Intestine, bone and kidney to maintain plasma calcium.
- Calcitriol increases the intestinal absorption of calcium and phosphorus.
- In the intestinal cells calcitriol binds with a cytosolic receptor to from a calcitriol, receptor complex.
- This complex approaches the nucleus and interacts with a specific DNA leading to the synthesis of a specific calcium binding protein.
- The protein increases the calcium uptake by intestine.

Action of calcitriol on the bone:

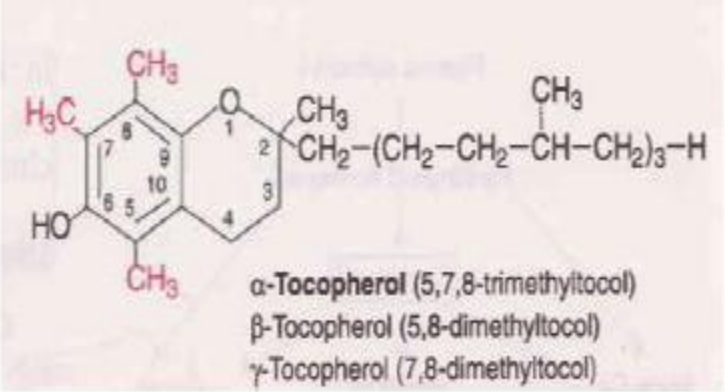
- In the osteoblasts of bone, calcitriol stimulate calcium uptake for deposition as calcium phosphate.
- Thus calcitriol is essential for bone formation. Calcitriol along with PTH increases mobilization of Ca and Po4 from the bone.
- This causes elevation of plasma Ca and Po4 levels.

Action of calcitriol on the kidney:

- Calcitriol is also involved in minimizing the excretion of ca and Po4 through the kidney, by decreasing their excretion and enhancing reabsorption.
- Calcitriol is now considered as a hormone because calcitriol is produced in the kidney which acts on target organs; intestine, bone and kidney.
- The calcitriol action is similar to steroid hormones. Calcitriol acts in association with other hormone PTH.
- Deficiency of vitamin D leads to demineralization of bone.
- The result is rickets in children and osteomalacia in adults.

- Rickets is characterized by bone deformities ie. Enlarged wrists and ankles, bowed legs and knock knees.
- Biochemically, in rickets, there is decrease in serum calcium and phosphours as well as increase in serum alkaline phosphates.
- In osteomalacia, bones become softer and become susceptible to fractures.
- Renal rickets is seen in patients with chronic renal failure due to decreased synthesis of calcitriol in kidney.
- Hyper vitaminosis D may lead to hyper calcemia. Hyper phosphatemia, anorexia, vomiting, nausea and diarrhoea etc.
- Vitamin E (tocopherol) is a naturally occurring antioxidant.
- It is essential for normal reproduction in many animals, hence known as anti-sterility vitamin.

Chemistry:
Vitamin E is a group of tocopherols. About 8 tocopherols have been identified among these tocopherol is the most active.



Structure of α-tocopherol

Absorption, transport and storage:
Vitamin E is absorbed along with fat in the small intestine. Bile salts are necessary for the absorption. In the liver, it is incorporated into lipoproteins (VLDL and LDL) and transported. Vitamin E is stored in adipose tissue, liver and muscle. The normal plasma level of tocopherol is less than 1 mg/dl.

Biochemical functions

- Most important function of vitamin E is that it acts as an antioxidant.
- The biochemical functions of vitamin E related either directly or indirectly to its antioxidant property.
- Vitamin E is essential for the membrane structure and integrity of the cell.
- It prevents the peroxidation of polyunsaturated fatty acids in various tissues.
- It protects RBC from hemolysis.
- It is closely associated with reproductive functions and prevents sterility.
- Vitamin E protects liver from being damaged by toxic compounds such as carbon tetrachloride.

- It works in association with vitamins A, C and □ carotene, to delay the onset of cataract.
- High intake of vitamin E (200 – 300 mcg / day) protects against the development of heart diseases.
- Many vegetable oils are rich sources of vitamin E.
- Wheat germ oil, cotton seed oil, peanut oil, corn oil and sunflower oil are the good source of this vitamin.
- It is also present in meat, milk, butter and eggs.

Deficiency symptoms

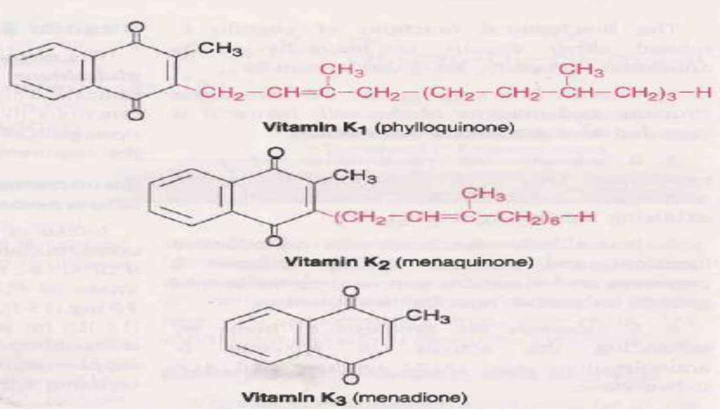
The symptoms of vitamin E deficiency vary from one animal species to another. In many animals, the deficiency is associated with sterility, degenerative changes in muscle, megaloblastic anaemia and changes in central nervous system Severe symptoms of vitamin E deficiency are not seen in humans except increased fragility of erythrocyte and minor neurological symptoms,

Toxicity of vitamin E:

Among the fat soluble vitamins (A, D, E, K), vitamin E is the least toxic. No toxic effect has been reported even after ingestion of 300 mg/ day for 23 years

VITAMIN K:

- Vitamin K is the only fat soluble vitamin with a specific coenzyme function.
- It is required for the production of blood clotting factors essential for coagulation (in German-Koagulation; hence the name K for this vitamin).
- Vitamin K is present in different forms.
- Vitamin K_1 (Phylloquinone) is present in plants.
- Vitamin K_2 (menaquinone) is produced by the intestinal bacteria and animals.
- Vitamin K_3 (menadione) is a synthetic form.



Structure of Vitamin K

Absorption, transport and storage:

- Vitamin K is taken in the diet or synthesized by the intestinal bacteria.

- Its absorption takes place along with fat (chylomicrons) and is dependent on bile salts.
- Vitamin K is transported along with LDL and is stored mainly in liver and, to a lesser extent, in other tissues.

Biochemical functions

Vitamin K is essential for the maintenance of normal levels of various blood clotting factors such as prothrombin, factor VII factor, IX and factor X. Vitamin K acts as a coenzyme for the carboxylation of glutamic acid residues present in the proteins.

Sources

Cabbage, cauliflower, tomatoes, alfa alfa, spinach and other green vegetables are good sources. It is also present in egg yolk, meat, liver, cheese and dairy products

Deficiency symptoms

- The deficiency of vitamin K is uncommon, since it is present in the diet in sufficient quantity and/or is adequately synthesized by the intestinal bacteria.
- However, vitamin K deficiency may occur due to its faulty absorption (lack of bile salts), loss of vitamin into feces (diarrheal diseases) and administration of antibiotics (killing of intestinal flora).
- Deficiency of vitamin K leads to the lack of active prothrombin in the circulation. The result is that blood coagulation is adversely affected.
- The individual bleeds profusely even for minor injuries. The blood clotting time is increased

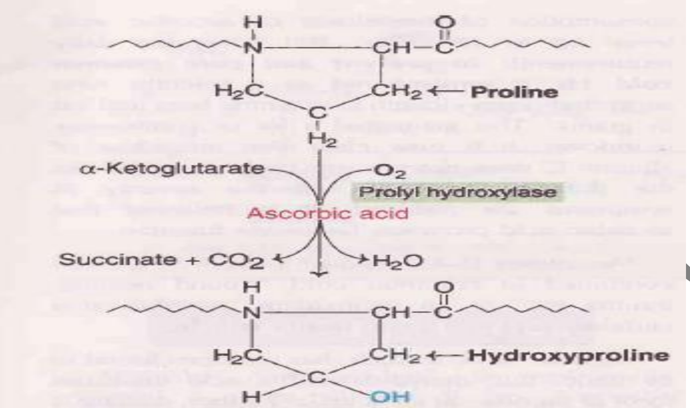
WATER SOLUBLE VITAMINS:

Characteristics:

- They are polar molecules.Diverse chemical nature or no similarity of chemical structure between them.
- Not stored in body except Vitamin B_{12}.
- Act as a co-enzyme of different enzyme catalyze reaction except Vitamin C acts as an enzymes.
- Synthesized from plant tissue such as cereals, green leafy vegetables, meat milk ets.,
- Except cobalamine stored in liver and not synthesized in plant tissue.

ASCORBIC ACID (Vitamin C)

- Vitamin C is a water soluble Vitamin.
- Important role in human health and disease.
- Vitamin C is also known as ascorbic acid or antiscurvy factor.
- Isolation of vitamin C Zilva during 1917-1927.
- Haworth and co-workers in 1933 established chemical structure of ascorbic acid.
- Synthesis of vitamin C reported in 1933 Haworth and co-workers in England.
- Chemical structure of L-ascorbic acid and L-dehydroascorbic acid.
- Structure of L-ascorbic acid derivative of hexose called L-glucose.



Ascorbic acid dependent hydroxylation of proline of protocollagen.

Sources

- Citrus fruits, gooseberry (amla), guava/ green vegetables (cabbage, spinach), tomatoes, potatoes (particularly skin) are rich in ascorbic acid.
- High content of vitamin C is found in adrenal gland and gonads.
- Milk is a poor source of ascorbic acid.
- Very sensitive to reversible oxidation (ascorbic acid □□ dehydroascorbic acid involved in the oxidation reduction reactions of the cell.
- Conversion of folic acid to folinic acid (citrovorum factor).
- The hydroxylation of steroids in the adrenal cortex.
- Metabolism of tyrosine and phenylalanine and also in tryptophan.
- Required for the absorption of ion and incorporation of plasma iron is ferritin.
- Involved in the formation of neorepinephrine.

Deficiency and symptoms

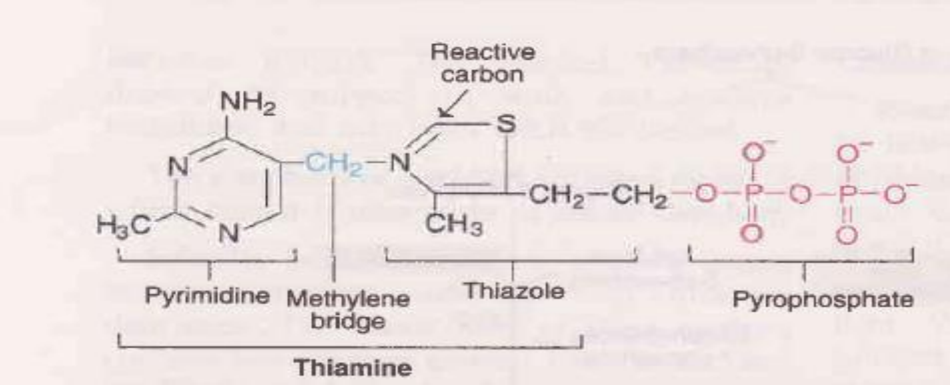
- The deficiency of ascorbic acid results in scurvy.
- This disease is characterized by spongy and sore gums, loose teeth, anemia, swollen joints, fragile blood vessels; decreased immunocompetence delayed wound healing, sluggish hormonal function of adrenal cortex and gonads, hemorrhage, osteoporosis etc.
- Most of these symptoms are related to impairment in the synthesis of collagen and/or the antioxidant property of vitamin C.

VITAMINS B-COMPLEX:

VITAMIN B_1 (Thiamine)

- Sulfur containing and nitrogen containing rings attached to carbon atoms Part of nerve cell membranes—synthesize and regulate neurotransmitters.
- Functions in energy metabolism—vitamin portion of TPP; plays role in decarboxylation and helps form Acetyl Co A from pyruvate

- Thiamine contains a pyrimidine ring and a thiazole ring held by a methylene bridge.
- Thiamine is the only natural compound with thiazole ring.
- The alcohol (OH) group of thiamine is esterfied with phosphate (2 moles) to form the coenzyme, thiamine pyrophosphate (TPP or cocarboxylase).
- The pyrophosphate moiety is donated by ATP and the reaction is catalyzed by the enzyme thiamine pyrophosphate transferase



Structure of thiamine and thiamine catalyses the oxidative decarboxylation Pyrophosphate (TPP)

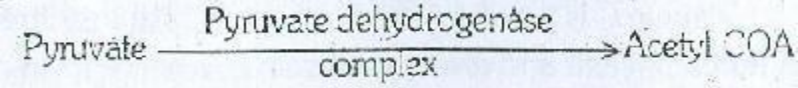
Sources

- Cereals, pulses, oil seeds, nuts and yeast are good sources.
- Thiamine is mostly concentrated in the outer layer (bran) of cereals Polishing of rice removes about 80% of thiamine.
- Vitamin B, is also present in animal foods like pork, liver, heart, kidney, milk etc.
- In the parboiled (boiling of paddy with husk) and milled rice, thiamine is not lost in polishing.
- Since thiamine is a water soluble vitamin, it is extracted into the water during cooking process. Such water should not be discarded.

Biochemical functions

The coenzyme TPP is intimately connected with the energy releasing reactions in the carbohydrate metabolism.

- The enzyme pyruvate dehydrogenase complex catalyses the irreversible conversion of Pyruvate to acetyl CoA. This reaction is depended on TPP.



$$\text{Pyruvate} \xrightarrow[\text{complex}]{\text{Pyruvate dehydrogenase}} \text{Acetyl COA}$$

- The enzyme a ketoglutarate dehydrogenase of the citric acid cycle requires TPP.
- TPP is also used as a coenzyme with transketolase in the hexose monophosphate shunt.
- Thee branched chain a ketoacid dehydrogenase catalyzes the oxidative decarboxylation of branched..chain amino acids to the respective ketoacids. This enzyme requires TPP.

- TPP plays an important role in the transmission of nerve impulse.

Deficiency

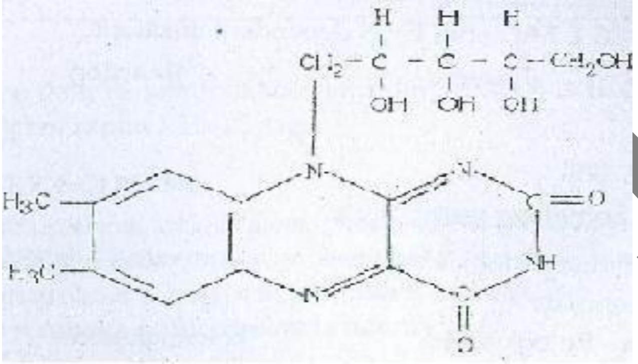
- Heavy alcohol consumption with inadequate food consumption; alcohol interferes with absorption (Wernicke-Korsakoff syndrome); poor and elderly at risk for not eating sufficient energy.
- Beri Beri
  Impaired muscle contractions
  Impaired cardiac function, edema and muscle twitches
  Decreased neurological function and memory loss

VITAMIN B$_2$ (Riboflavin)

Riboflavin through its coenzymes takes part in a variety of cellular oxidation reduction reactions.

Chemistry:

Riboflavin contains an isoalloxazine ring with a ribitol side chain.



Structure of Riboflavin

Sources

Milk and milk products, meat, eggs, liver, kidney are rich sources. Cereals, fruits, vegetables and fish are moderate sources.

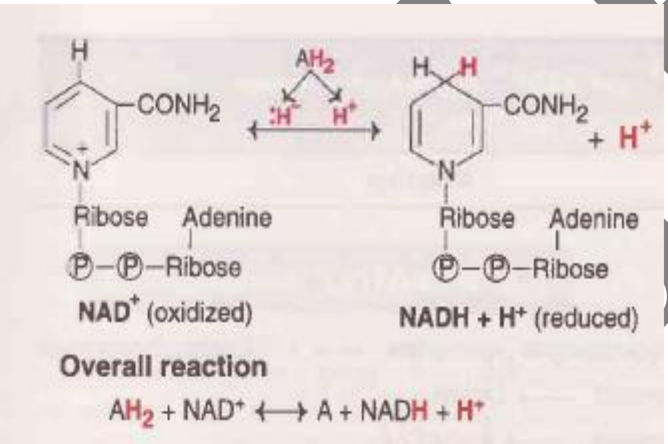
Biochemical functions

- The flavin coenzymes (mostly FAD) participate in many oxidation reduction reactions` responsible for energy production.
- FMN and FAD undergo identical reversible reactions, accepting two hydrogen atoms to form FM NH2 or FADH2.
- The coenzymes FMN and FAD are associated with certain enzyme involved in carbohydrate, lipid, protein and purine metablism besides the electron transport.
- Few examples are shown in the table.
- Riboflavin deficiency symptoms include cheilosis (fissures at the corners of the mouth), glossitis (tongue smooth and purplish) and dermatitis.
- Riboflavin deficiency as such is uncommon.
- It is mostly seen along with other vitamin deficiencies.
- Chronic alcoholics are susceptible to 82 deficiencies.

- Assay of the enzyme glutathione reductase in erythrocytes will be useful in assessing riboflavin deficiency.
- **Antimetabolite:** Galactoflavin is an antimetabolite of riboflavin

VITAMIN B_3 (Niacin)

- Niacin or nicotinic acid is also known as pellagra preventive factor of Goldenberg.
- The coenzymes of niacin (NAD^+ and $NADP^+$) can be synthesized by the essential amino acid tryptophan.
- Niacin is a pyridine derivative. Structurally pyridine 3 carboxylic acid.
- The amide form of niacin is known as niacinamide or nicotinamide.
- Dietary nicotinamide, niacin and an essential amino acid, tryptophan contribute to the synthesis of the coenzyme NAD and NADP. 60 mgs of tryptophan is equivalent to 1 mg of niacin for the synthesis of niacin.



Mechanism of oxidation and reduction of nicotinamide coenzyme-NAD^+

Sources

- Rich sources include liver, yeast, whole grains, cereals, pulses like beans and peanuts.
- On an average 1g of good quality protein containing about 60 mg of tryptophan is equivalent to 1 mg of niacin for the synthesis of nicotinamide coenzyme.

Biochemical functions:

☐ The coenzymes NAD^+ and $NADP^+$ are involved in a variety of oxidation reduction reactions.

☐ They accept hydride ion (hydrogen atom and one electron: H^-) and undergo reduction in the pyridine ring.

☐ This results in the neutralization of positive charges.

☐ The nitrogen atom and the fourth carbon atom of nicotinamide ring participate in the reaction.

☐ While one atom of hydrogen (as hydride ion) from the substrate (AH_2) is accepted by the coenzyme, the other hydrogen ion (H^+) is released in to the surrounding medium.

☐ This reaction is reversed when NADH is oxidized to NAD+. NADP+ also functions like NAD^+ in the oxidation-reduction reactions.

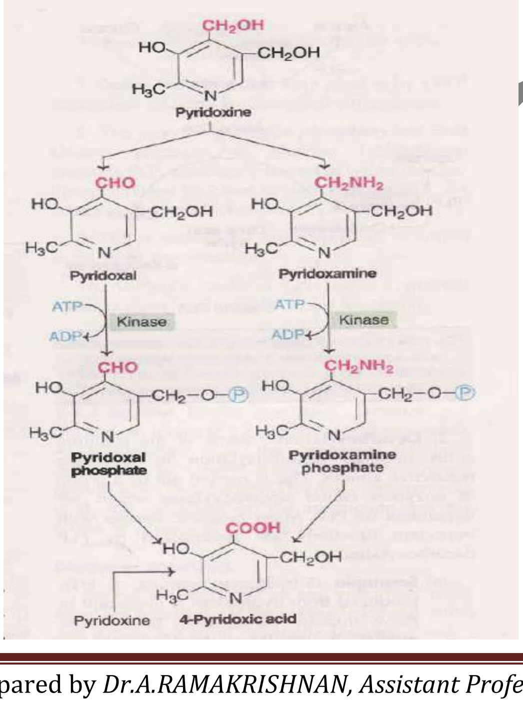
- A large number of enzymes (about 40) belonging to the class oxidoreductases are dependent on NAD^+ or $NADP^+$.
- The coenzymes are loosely bound to the enzymes and can be separated easily by dialysis.
- NAD^+ and $NADP^+$ participate in almost all the metabolisms (carbohydrate lipid, protein etc.).
- Some enzymes are exclusively dependent on NAD^+ whereas some require only $NADP^+$.
- A few enzymes can use either NAD^+ or $NADP^+$. Selected examples of enzymes and the reactions they catalyse.
- NADH produced is oxidized in the electron transport chain to generate ATP.
- ADPH is also important for many biosynthetic reactions as it donates reducing equivalents
- Niacin deficiency results in a condition called pellagra (rough skin).
- The diseases pellagra involves skin, gastrointestinal tract and central nervous system.
- The symptoms of pellagra are commonly referred to as three D’s ie. Dermatitis (Inflammation of skin), dementia (anxiety, poor memory), diarrohea (dysentery) and rarely to fourth D (death).

VITAMIN B_6 (Pyridoxine)

Vitamin $B_6$is used to collectively represent the three compounds namely pyridoxine, pyridoxal and pyridoxamine.

Chemistry:

- Vitamin B_6 compounds are pyridine derivatives. They differ from each other in the structure of a functional group attached to 4th carbon in the pyridine ring.
- Pyridoxine is a primary alcohol.
- Pyridoxal is an aldehyde.
- Pyridoxamine is an amine.
- The active form of vitamin B_6 is the coenzyme pyridoxal 5 phosphate (PLP)



Pyridoxine, its derivatives and coenzyme

Sources:

Animal sources such as egg yolk, fish, milk, meat are rich in $B_{6.}$ Wheat, corn, cabbage, roots, tubers are good vegetables sources.

Biochemical functions:

- Pyridoxal phosphate (PLP) the coenzyme of vitamins B_6 is found attached to the amino group of lysine in the enzyme.
- PLP is closely associated with the metabolism of amino acids. PLP participate in reactions like transmination, decarboxylation, deamination, transsulfuration etc.
- Transamination: PLP is involved in the transmination reaction converting amino acid to keto acids.
  - Decarboxylation: Some α amino acids undergo decarboxylation to form respective amines. This is carried out by decarboxylases which require PLP.
  - Pyridoxal Po_4 (PLP) is required for the synthesis of amino levulinic acid precursor of heme synthesis.
- Vitamin B_6 is an energy releasing vitamin. It integrates carbohydrate and amino acid metabolism.
  - PLP plays an important role in the metabolism of sulfur containing amino acids.
  - Since is synthesized from glycine by a PLP dependent enzyme hydroxyl methyltransferase.
  - Vitamin B_6 is required for absorption of amino acids.

Deficiency and symptoms:

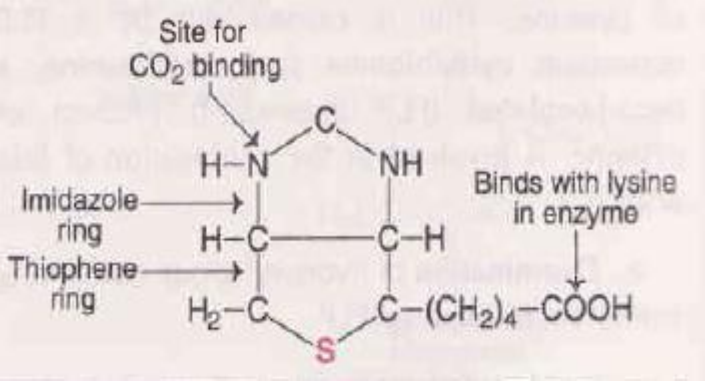
- Pyridoxine deficiency is associated with neurological symptoms such as depression, irritability, nervousness and mental confusion.
- Convulsions and peripheral neuropathy are observed in several deficiencies.

VITAMIN B_7 (Biotin)

Biotin (formerly known as anti-egg white injury factor, vitamin 87 or vitamin H) is a sulfur containing B –complex vitamin. It directly participates as a coenzyme in the carboxylation reactions.

Chemistry:

Biotin is heterocyclic sulfur containing monocarboxylic acid. The structure is formed by fusion of imidazole and thiophene rings with a valeric acid side chain (Biotin is covalently bound to e-amino group of lysine to form biocytin in the enzymes. Biocytin may be regarded as the coenzyme of biotin.



Structure of biotin with binding sites

Sources

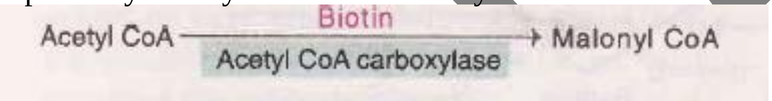
Biotin is widely distributed in both animal and plant foods. The rich sources are liver, kidney, egg yolk, milk, tomatoes, grains etc.

Biochemical functions

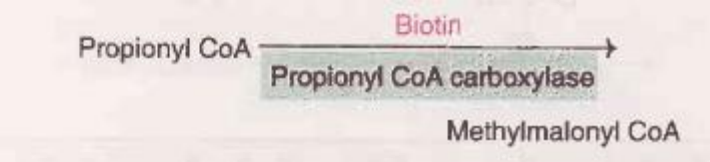
- Biotin serves as a carrier of CO_2 in carboxylation reactions.
- The reaction catalyzed by pyruvate carboxylase, converting pyruvate to oxaloacetate has been investigated in detail.
- This enzyme has biotin bound to the apoenzyme linked to the e-amino group of lysine, forming the active enzyme (holoenzyme) Biotin-enzyme reacts with CO2 in presence of ATP (provides energy) to form a carboxybiotin-enzyme complex.
- This high energy complex hands over the CO_2 to pyruvate (carboxylation reaction) to produce oxaloacetate.
- As a coenzyme, biotin is involved in various metabolic reactions.

1. Gluconeogenesis and citric acid cycle: The conversion of pyruvate to oxaloacetate by biotin dependent pyruvate carboxylase (described above) is essential or the synthesis of glucose from many non-carbohydrate sources. Oxaloacetate so formed is also required for the continuous operation of citric acid cycle.

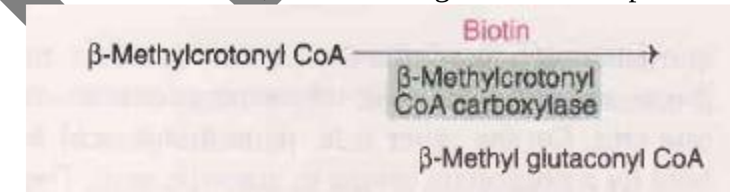
2. Fatty acid synthesis: Acetyl CoA is the starting material for the synthesis of fatty acids. The very first step in fatty acid synthesis is a carboxylation reaction.



3. Propionyl CoA is produced in the metabolism of certain amino acids (valine, isoleucine, threonine etc.) and degradation of odd chain fatty acids. Its further metabolism is dependent on biotin.



In the metabolism of leucine, the following reaction is dependent on biotin.



Deficiency and symptoms

- The symptoms of biotin deficiency include anemia, loss of appetite, nausea, dermatitis, glossitis etc.

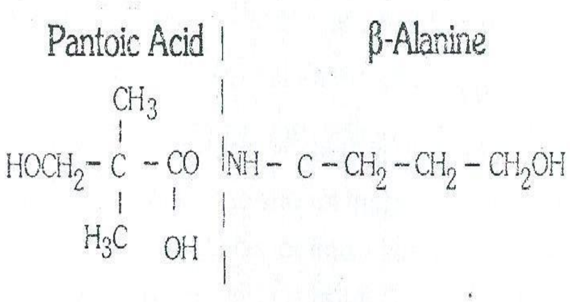
- Biotin deficiency may also result in depression, hallucinations, muscle pain and dermatitis, Biotin deficiency is uncommon, since it is well distributed in foods and also supplied by the intestinal bacteria.
- The deficiency may however, be associated with the following two causes.
- Destruction of intestinal flora due to prolonged use of drugs such as sulfonamides.
- High consumption of raw eggs.
- The raw egg white contains a glycoprotein -avidin, which tightly binds with biotin and blocks its absorption from the intestine.
- An intake of about 20 raw eggs per day is needed to produce biotin deficiency symptoms in humans.
- Consumption of an occasional raw egg will not result in deficiency.

Pantothenic acid

Pantothenic acid is widely distributed in nature. Its metabolic role as coenzyme A is well known.

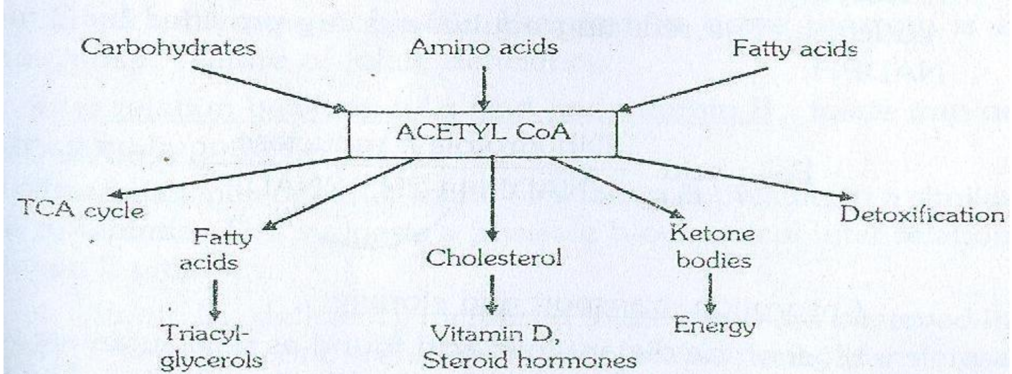
Chemistry:

Pantothenic acid consists of two components pantothenic acid and □ alanine held together by a peptide linkage.



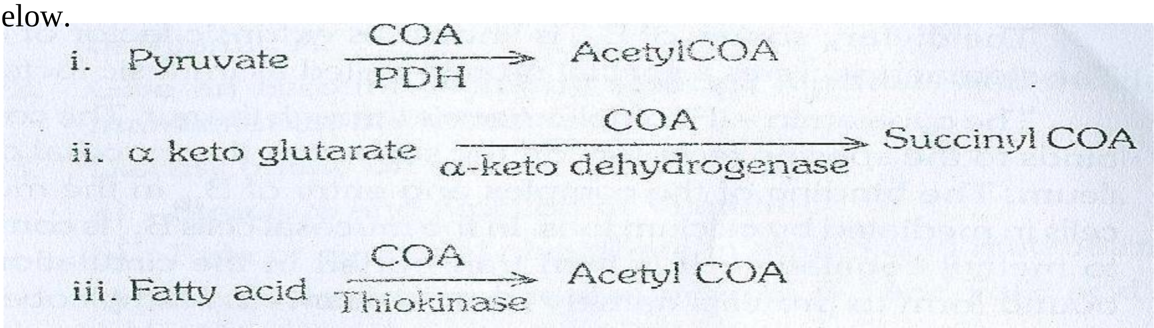
Biochemical functions:

- The functions of pantothenic acid are excreted through coenzyme A or CoA.
- Coenzyme A is the central molecule involved in all the metabolisms (carbohydrate, lipid and protein) and hence it is called as a coenzyme of metabolic integration.



Coenzyme A – Metabolic Integration

Metabolic integration due to coenzyme A. coenzyme A serves as a carrier activated acetyl groups. A few examples of enzymes involved in the participation of coenzyme A are given below.



i. Pyruvate $\xrightarrow[\text{PDH}]{\text{COA}}$ AcetylCOA

ii. α keto glutarate $\xrightarrow[\alpha\text{-keto dehydrogenase}]{\text{COA}}$ Succinyl COA

iii. Fatty acid $\xrightarrow[\text{Thiokinase}]{\text{COA}}$ Acetyl COA

Sources

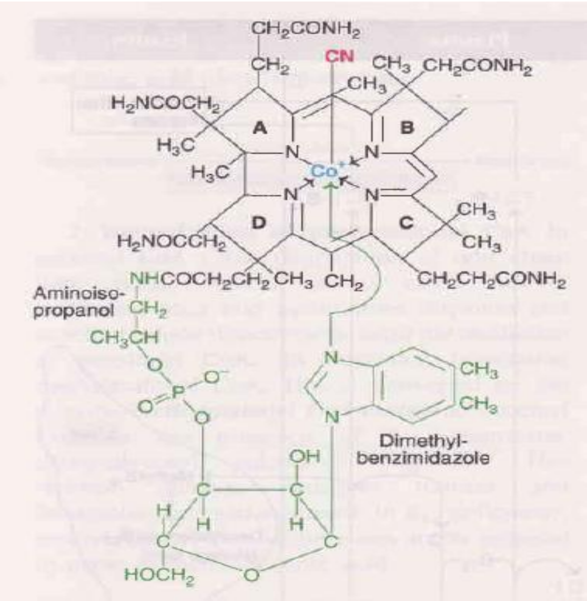
- Pantothenic acid is one of the most widely distributed vitamins found in plants and animals. The rich sources are egg, liver, meat, yeast, milk, etc.
- It is a surprise to biochemists that despite the involvement of pantothenic acid (as coenzyme A) in a great number of metabolic reactions, its deficiency manifestations have not been reported in humans.
- This may be due to the widespread distribution of this vitamin or the symptoms of pantothenic acid may be similar to other vitamin deficiencies Dr. Gopalan a world renowned nutritionist from India, linked the burning feet syndrome (pain and numbness in the toes, sleeplessness, fatigue etc.) with pantothenic acid deficiency.
- Pantothenic acid deficiency in experimental animals results in anemia, fatty liver, decreased steroid synthesis etc.

VITAMIN B_{12} (Cyanocobalamin)

- Vitamin B_{12} is also known as anti-pernicious anemia vitamin.
- It is a unique vitamin, Synthesized by only microorganisms and not by animals and plants.
- It was the last vitamin to be discovered.

Chemistry

- Due to the presence of a cyano group and a cobalt atom, vitamin B_{12} is also referred to as Cyanocobalamin.
- The structure of vitamin B_{12} consists of a corrin ring with a central cobalt atom.
- Cyanide (predominant) in Cyanocobalamin(B_{12a})
- Hydroxyl in hydroxycobalamin (B_{12b})
- Nitrite in nitrocobalamin (B_{12c}).
  (a) 5’ -Deoxyadenosyl cobalamin, cyanide is replaced by 5' deoxyadenosine forming an unusual carbon cobalt bond.
  (b) Methylcobalamin in which cyanide is replaced by methyl group.



Structure of vitamin B_{12} (Cyanocobalamin)

Biochemical functions:

- About ten enzymes requiring vitamin B_{12} have been identified. Most of them are found inbacteria (glutamate mutase, ribonucleotide reductase etc.).
- There are only two reactions in mammals that is dependent on vitamin B_{12}.
- **Synthesis of methionine from homocysteine**: Vitamin B_{12}, as Methylcobalamin is used in this reaction. This is an important reaction involving Ns-methyl tetrahydrofolate from which tetrahydrofolate is liberated (enzyme-homocysteine methyltransferase or npthionine syntheses). This metabolic step signifies the interrelation between vitamin B_{12} folic acid.
- **Isomerization of methymalonyl CoA to succinyl CoA**: The degradation of odd chain fatty acids, certain amino acids and pyrimidines produce directly or through the mediation of propionyl CoA, an important compound methylmalonyl CoA. This is converted by the enzyme methylmalonyl CoA mutase to succinyl CoA in the presence of B_{12} coenzyme, deoxyadenosyl cobalamin.
- This reaction involves hydrogen transfer and intramolecular rearrangement. In $_{B12}$ deficiency, methylmalonyl CoA accumulates and is excreted in urine as methylmalonic acid.

Sources

Liver, Kidney, egg fish and milk are good sources of vitamin B_{12}.

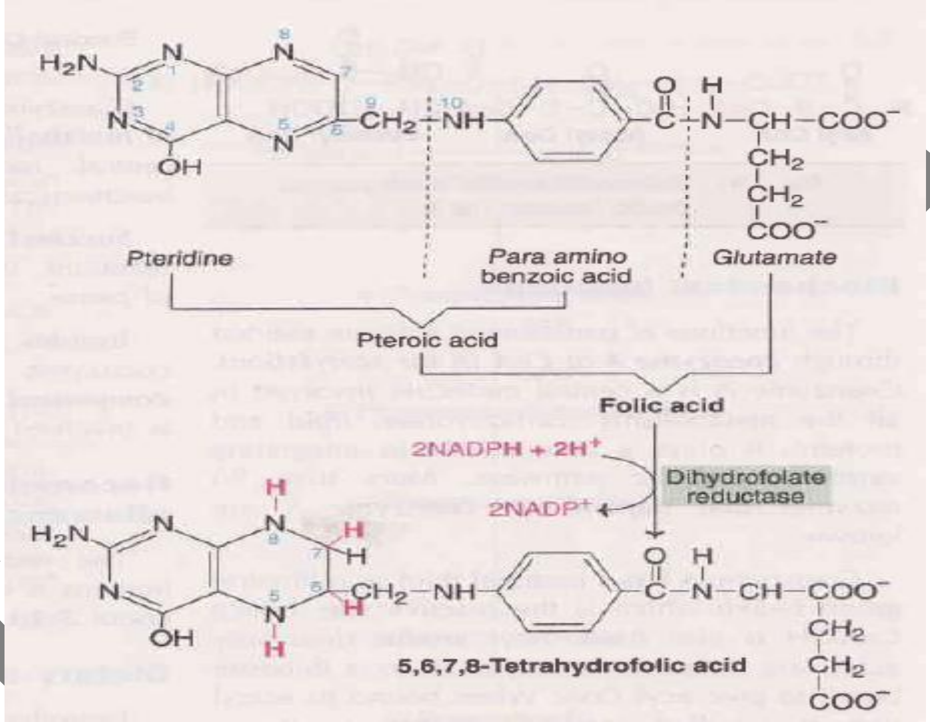
Deficiency and symptoms

- The most important disease associated with B_{12} deficiency pernicious anemia.
- It is characterized by low hemoglobin level decreased number of erythrocytes and neurological manifestation vitamin B_{12} deficiency is also associated with neuron degeneration and demyelization of nervous system.
- The symptoms are numbness in fingers and toes.
- Folic acid is abundantly found in green leafy vegetables.

- It is important for one carbon metabolism and is required for synthesis of certain amino acids, purines and the pyrimidines and thymine.

Chemistry

- Folic acid consists of three components pteridine ring, p-amino benzoic acid (PABA) and Glutamic acid (1 to 7 residues).
- Folic acid mostly has one glutamic acid residue and is known as pteroyl-glutamic acid (PGA).
- The active form of folic acid is tetrahydrofolate (THF or FH_4).
- It is synthesized from folic acid by the enzyme dihydrofolate reductase.
- The reducing equivalents are provided by 2 moles of NADPH.
- The hydrogen atoms are present at positions 5, 6, 7 and 8 of THF.



Conversion of folic acid to tetrahydrofolic acid (THF)

Biochemical functions

- Tetrahydrofolate (THF or FH_4) the coenzyme of folic acid is actively involved in the one carbon metabolism, many important compounds are synthesized in one carbon metabolism.
- Purines which are incorporated into DNA and RNA.
- Pyrimidines nucleotide-deoxy thymidilic acid is involved in the synthesis of DNA.
- Glycine, serine, ethanolamine and choline are produced.
- N formylmethionine, the initiator of protein biosynthesis is formed.

Sources
The rich sources are green leafy vegetables, whole grains, cereals, liver, kidney, yeast and eggs.

Deficiency and symptoms:

- Folate deficiency results in complications nearly identical to those described for vitamin B_{12} deficiency.
- The most pronounced effect of folate deficiency on cellular processes is upon DNA synthesis.
- This is due to impairment in dTMP synthesis which leads to cell cycle arrest in S-phase of rapidly proliferating cells, in particular hematopoietic cells.
- The result is megaloblastic anemia as for vitamin B_{12} deficiency.
- The inability to synthesize DNA during erythrocyte maturation leads to abnormally large erythrocytes termed macrocytic anemia.
- Folate deficiencies are rare due to the adequate presence of folate in food.
- Poor dietary habits as those of chronic alcoholics can lead to folate deficiency.
- The predominant causes of folate deficiency in non-alcoholics are impaired absorption or metabolism or an increased demand for the vitamin.
- The predominant condition requiring an increase in the daily intake of folate is pregnancy.
- This is due to an increased number of rapidly proliferating cells present in the blood.
- The need for folate will nearly double by the third trimester of pregnancy.
- Certain drugs such as anticonvulsants and oral contraceptives can impair the absorption of folate.
- Anticonvulsants also increase the rate of folate metabolism.

Hypervitaminosis
Hypervitaminosis is a condition of abnormally high storage levels of vitamins, which can lead to toxic symptoms. Specific medical names of the different conditions are derived from the vitamin involved: an excess of vitamin A, for example, is called hypervitaminosis A. Hypervitaminoses are primarily caused by fat-soluble vitamins (D, E, K and A), as these are stored by the body for longer period than the water-soluble vitamins. Generally, toxic levels of vitamins stem from high supplement intake and not from natural food. Toxicities of fat-soluble vitamins can also be caused by a large intake of highly fortified foods, but natural food rarely deliver dangerous levels of fat-soluble vitamins. The Dietary Reference Intake recommendations from the United States Department of Agriculture define a "tolerable upper intake level" for most vitamins

Causes
With few exceptions, like some vitamins from B-complex, hypervitaminosis usually occurs more with fat-soluble vitamins (D, E, K and A or 'DEKA'), which are stored in the liver and fatty tissues of the body. These vitamins build up and remain for a longer time in the body than water-soluble vitamins. Conditions include:

- Hypervitaminosis A
- Hypervitaminosis D
- Hypervitaminosis E

- Hypervitaminosis K, unique as the true upper limit is less clear as is its bioavailability.

According to Williams' Essentials of Diet and Nutrition Therapy it is difficult to set a DRI for vitamin K because part of the requirement can be met by intestinal bacterial synthesis.

- Reliable information is lacking as to the vitamin K content of many foods or its bioavailability. With this in mind the Expert Committee established an AI rather than an RDA.
- This RDA (AI for men age 19 and older is 120 µg/day, AI for women is 90 µg/day) is adequate to preserve blood clotting, but the correct intake needed for optimum bone health is unknown. Toxicity has not been reported.

High-dosage A; high-dosage, slow-release vitamin B_3; and very high-dosage vitamin B_6 alone (i.e. without vitamin B complex) hypervitaminoses are sometimes associated with side effects that usually rapidly cease with supplement reduction or cessation.

High doses of mineral supplements can also lead to side effects and toxicity. Mineral-supplement poisoning does occur occasionally, most often due to excessive intake of iron-containing supplements.

Individual hypervitaminosis: The features of hypervitaminosis are usually due to exaggerations of their normal physiological and biochemical actions.

1. Hypervitaminosis A:

It may occur as acute and chronic. In acute cases the features of hypervitaminosis are mainly due to exaggeration of their normal physiological and biochemical actions. Features in acute case are dizziness, headache, and lassitude, Irritability, pain abdomen, nausea, visual disturbances like diplopia, and bulging fontanels in infants, pruritus and excoriation of skin all over the body. Chronic cases are manifested by low grade fever, alopecia, dry fissured lip, ache in bones and joints, hyperostosis, anorexia, weight loss, hepatosplenomegaly, papilloedema, pseudotumour cerebri, if daily 25,000 IU or more vitamin A is consumed for many days. Other features suggestive of raised intracranial pressure, such as bulging fontanels (in an infant), papilloedema and diplopia, may also occur. Anemia and thrombocytopenia have also been described.Complications include: Hypocalcaemia, Hypercalciuria and renal stones. It may be unwise to give vitamin A supplements to older patients with good diets, particularly if at risk of osteoporosis.Experimentally chronic condition is produced when we take in excess of 50,000 units/day for more than three months. Complications include Hypocalcaemia, Hypercalciuria, renal stones and benign intracranial hypertension. Management is by stopping the supplements. If there are changes in mental state, admission to hospital is required. As far as prognosis is concerned, mortality is rare. Once identified, the prognosis is good. The yellow coloration of skin will reverse with time.

2. Hypervitaminosis D:

Usually this is caused by excessive ingestion or over prescription of prescribed medications such as calcium with vitamin D. occasionally there is increased calcitriol production as in hyperparathyroidism or malignancy including some renal adenomas, sarcomas and lymphomas. In sarcoidosis there is a hypersensitivity to vitamin D.

Excessive levels of vitamin D do not result from excessive exposure to sunlight because of further breakdown of D3 into products which have no effect on calcium metabolism. Recent concerns about vitamin D deficiency have led to increased use of supplements. Most symptoms occur because of secondary hypercalcaemia with increased bone resorption and hypercalciuria. They include: Polyuria, Polydipsia, Vomiting, Anorexia, and Lethargy, Dehydration, Constipation, Hypertension, Tetany, Seizures can be fatal. The traditional description of hypercalcaemia is stones, bones and groans. Hypervitaminosis D is also recognized as a cause of depression.In children it can result in dental enamel hypoplasia and focal pulp calcification.Investigations include serum calcium and phosphate and 25 hydroxy-vitamin D and 1, 25 dihydroxy-vitamin D levels. Management is by stopping the supplements and treats the cause. Bisphosphonates such as pamidronate may be used to treathypercalcaemia. Glucocorticoids are occasionally used for a short while in severe cases of vitamin D intoxication. Complications may include nephrolithiasis, nephrocalcinosis (calcium oxalate and calcium phosphate are radio opaque stones), calcinosis of the joints and peri articular tissues, and chronic kidney disease. As far as Prognosis is concerned renal disease is usually reversible if recognized early. An outbreak of hypervitaminosis D associated with the over fortification of milk from a home-delivery dairy.

3. Hypervitaminosis E:

Vitamin E is present in a great many foods, particularly vegetable oils, unprocessed cereal grains, nuts and seeds. There is no evidence of any adverse effects from consuming vitamin E in food. However, high doses of alpha-tocopherol supplements can affect blood clotting inhibit platelet aggregation and cause hemorrhage. Studies have also shown an increase in all-cause mortality associated with vitamin E supplements.

Vitamin E, 3 or 4 decades ago it appeared to be 'a vitamin in search of a deficiency'. Its importance had been demonstrated only for reproductive efficacy in rats. Vitamin E (alpha tocopherol) is a fat-soluble vitamin which acts as an antioxidant and disposes of free radicals. Problems only usually occur after a very large overdose.The recommended daily dose is 30 mg per day, and side-effects are usually experienced at doses above 1 g/kg. Excess of vitamin E inhibits vitamin K, causes increased bleeding and impaired immune system leading to necrotic enter-colitis. Bruising and bleeding with increased prothrombin time is mediated by the inhibition of vitamin K-dependent carboxylase, and reversed by administering vitamin K. Platelet thromboxane production is also reduced. Some studies have also reported fatigue, weakness, headache and gastrointestinal upset. Management includes stop the supplements. Consider vitamin K if prothrombin time is prolonged.

4 Hypervitaminosis B-complex:

In many cases skin changes, intestinal ulcers, fatty liver, hyperglycemia, hyperuricaemia, nausea and indigestion are found.

i). Thiamine (B1): Over dose produce curare like action, paralysis. Blocks nerve transmission. Restlessness, convulsions, labored respiration, death (respiratory paralysis and cardiac failure).Disrupt other B-Vitamins, disrupt insulin and thyroid functions.

ii). Riboflavin (B2): Over dose produces bright yellow urine, fatigue, vomiting, itching, numbness, burning or prickling sensation, sensitivity to light and hypotension occurs.

iii). Niacin (B3): Overconsumption of niacin causes flushing syndrome, hyperemia of skin, Pruritus, GIT disturbances and acanthosis nigricans. More than 3gm niacin daily causes aggravation of bronchial asthma, gout and fasting hyperglycemia. Low blood pressure, light headedness, insomnia, liver damage, peptic ulcer, skin rash, altered liver function tests may occur.

iv). Pantothenic acid (B 5): Overdose produce diarrhea, GIT problems, water retention may occur.

v). Pyridoxine (B6): Vitamin B6 is a water-soluble vitamin and one of eight B vitamins. As such, it might be considered safe but at doses over 200 micrograms per day it can cause neurological disorders when taken over a prolonged period.It used to be prescribed extensively for carpal tunnel syndrome and premenstrual tension. A sensory neuropathy mimicking multiple sclerosis may be seen, if B6 more than 2 gm is taken daily Progressive ataxia, impaired vision and vibration senses, and loss of deep tendon reflexes are seen. Preserved motor strength, perioral numbness and clumpsy limbs are present. Loss of appetite, stomach upset and skin lesions also occurs.

High intakes of vitamin B6 from food sources have not been reported to cause adverse effects. However, long-term use of supplements can cause severe and progressive sensory neuropathy with ataxia. The severity of symptoms is dose-dependent and the symptoms usually stop when the supplements are discontinued. Other adverse effects of excessive vitamin B6 intake include painful skin rashes, photosensitivity, nausea and heart burn.Symptoms include excessive doses damage sensory nerves. This can cause paraesthesia in the hands and feet, difficulty walking (poor co-ordination, 'staggering'), reduced sensation to touch, temperature, and to vibration and tiredness. Management is by stopping the vitamin B6 resolves symptoms in all cases. Failure to do so suggests another cause for symptoms. Vitamin B6 functions in protein and amino acid metabolism. Pyridoxine is the treatment for isoniazid overdose. It is also used by body builders with varying results, depending on dosage.

vi). Biotin (B 7) (vitamin H): Biotin causes Scurfy skin due to hyperkeratosis of superficial follicular epithelium.

vii). Folic acid (B 9): Folic acid is useful for the RBC and DNA production. Over dosage produce convulsions in epileptics. Inhibit hepatic alcohol dehydrogenase. Stomach, sleep and skin problems occurs.

viii). Cobalamine (B12): Over dose of B12 causes reduction in size of vascular controlled reflexes, palpitation, tingling sensation and numbness of limbs.

ix). Ascorbic acid (C): Vitamin C is found in citrus fruits and vegetables. An anti-oxidant and reducing agent, its controversial uses include treatment of upper respiratory tract infections and cancer. The worst effect is the formation of oxalate stone in the kidney. It may also cause uricosuria. Large doses if taken by pregnant women that induce the metabolic enzymes in the fetus and this may lead to rebound scurvy. Absorption of vitamin B12 is interfered with high doses of vitamin C. Vitamin C interferes with healthy antioxidant, pro-oxidant balance in body. In thalassemia or hemochromatosis increased iron overload occurs. Premature infants get hemolytic anemia due to the fragility of RBC.

x). Choline:

More than 3.5 gm/day in take causes skin rash and increased blood sugar.

Possible Questions

2 marks

1. Write short notes on Vitamin A
2. Mention the symptoms of Vitamin K
3. List out fat soluble vitamins
4. Draw the structure of Vitamin D
5. List out water soluble vitamins
6. How Vitamin D is provided to the body? List out the three ways

8 marks

1. Describe the structure and physiological functions of Vitamin A and D
2. What are all the source and functions of Vitamin C?
3. Explain in detail about structure and active form of Vitamin A
4. What are all the sources and functions of Vitamin K?
5. Explain in detail about Vitamin K its sources, deficiency and symptoms
6. Discuss in detail Vitamin D
7. Write in details about deficiency and symptoms of Vitamin C
8. Discuss about hypervitaminosis
9. Explain the sources of Vitamin B complex
10. Brief about Vitamin E

Karpagam Academy of Higher Education
Department of Biochemistry
I B.Sc., Biochemistry
19BCU101- Molecules of life
Prepared By Dr. A. RAMAKRISHNAN

UNIT-V

Question number	Question	Option I	Option II	Option III		Option IV	Answer
1	Metyl malonic aciduria is seen in a defiency of	Vitamin B6	folic acid	thiamin	thiamin	vitamin B12	**Vitamin B6**
2	What is caused by thiamin defiency	nyctalopia	Scurvy	Rickets	Rickets	Beri beri	**Scurvy**
3	retinal and retinal binding protein (RBP) are bound with this protein	albumin	prealbumin	a2 globulin	a2 globulin	b globulin	**prealbumin**
4	Megaloblastic anemia is caused by the defiency of	folic acid	vitamin B6	iron	iron	protein	**folic acid**
5	This vitamin acts as antioxidant	vitamin A	vitamin D	vitamin E	vitamin E	vitamin K	**vitamin E**

6	Calcitriol is	hydroxy cholecalciferol	25 hydroxy cholecalciferol	24,25 di hydroxy cholecalciferol	24,25 di hydroxy cholecalciferol	1, 25 dihydroxy cholecalciferol	**24,25 di hydroxy cholecalciferol**
7	25 hydroxilation of vitamin D3 takes place in	Liver	Intestines	Kidneys	Intestines	Pancreas	**Kidneys**
8	The egg injury factor in raw egg white is	biotin	avidin	albumin	B	calcium salts	**avidin**
9	the human species can biosynthesize	vitamin C	Vitamin B12	vitamin A	B	Niacin	**Vitamin B12**
10	Retina contains this photo sensitive pigment	rhodopsin	opsin	retinal	melanin	melanin	**rhodopsin**
11	Antixerophthalmic vitamin	Vitamin B1	Vitamin B2	Vitamin B6	Vitamin A	Vitamin A	**Vitamin A**
12	One of the following is not a symptom of Addison's disease	hypoglycemia	hyponatremia	hypokalemia	hypochloremia	hypochloremia	**hypoglycemia**
13	Gammaxane is an antimetabolite of	Thiamine	Riboflavin	Pyridoxine	Inositol	Inositol	**vitamin B12**
14	Sulpha drugs are antimetabolites of	vitamin K	pyridoxine	folic acid	vitamin B12	vitamin B12	**folic acid**

15	Pyridoxine defiency may lead to convulsions as it is needed for the synthesis of	GABA	PABA	EFA	SAM	SAM	**GABA**
16	This abnormal metabolite may be responsible for the neurological manifestation of pernicious anemia	taurine	metyl malonic acid	xanthurenic acid	phenyl pyruvic acid	phenyl pyruvic acid	**metyl malonic acid**
17	Choic acid is not required for the formation of	lecithins	acetyl choline	sphigomyelin	sphigomyelin	cholic acid	**cholic acid**
18	Biotin is required for the reaction of Co2 with	water	acetyl CoA	ammonia	ammonia	incorporaion of carbon 6 in purine	**acetyl CoA**
19	A defiency of folate leads to	megaloblastic anemia	aplastic anemia	pernicious anemia	pernicious anemia	hypochromaic microcytic anemia	**megaloblastic anemia**
20	A deficiency of Iron leads to	megaloblastic anemia	aplastic anemia	pernicious anemia	pernicious anemia	hypochromaic microcytic anemia	**hypochromaic microcytic anemia**

21	Vitmin B12 initially binds to the proteins known as	Transcobalamine I	R. proteins	Transcobalamine II	Transcobalamine II	Intrinsic factor of castle	**R. proteins**
22	Extrinsic factor of castle is	vitamin B12	glycoprotein	Sigma proteins	R-protein	R-protein	**R-protein**
23	Antiracnite vitamin is	vitamin A	vitamin D	vitamin E	vitamin E	vitamin K	**vitamin D**
24	Angular stomatitis is due to	Ariboflavinosis	Def. Of vitamin C	Def. Of vitamin B1	Def. Of vitamin B1	Def. Of folate	**Def. Of vitamin B1**
25	Prothrombin time is prolonged by administering	Vitamin K	Dicoumarol	Calcium	Calcium	Prothrombin	**Dicoumarol**
26	This vitamin acts as an antioxidant	Vitamin A	Vitamin D	Vitamin E	Vitamin E	Vitamin K	**Vitamin E**
27	This is a photo labile vitamin	thiamin	riboflavin	niacin’	niacin’	cholecalciferol	**riboflavin**
28	Convulsive episodes occur when there is a severe defiency of	pyridoxine	folic acid	thiamine	thiamine	riboflavin	**pyridoxine**

29	Metastatic calcification is seen in hypervitaminosis	A	K	D	D	E	**D**
30	The anti vitamin for para amino benzoic acid is	aminopterin	dicoumarol	sulphanamides	sulphanamides	thiopanic acid	**sulphanamides**
31	Severe pantothenic acid defiency defiency in man has beeb reported to cause	burning feet syndrome	Scurvy	cataract	cataract	xerophthalmia	**burning feet syndrome**
32	cholesterol is a precursor in the biogenesis of	Vitamin A	Vitamin E	Vitamin E	Vitamin K	Vitamin D	**Vitamin D**
33	This Vitamin is a potent antioxidant of Vitamin A	Vitamin B	Vitamin D	Vitamin D	Vitamin E	Vitamin K	**Vitamin D**
34	Convulsions and delirium could be caused by a defiency of	thiamine	glutamate	glutamate	niacin	magnesium	**magnesium**

35	In the muscle cells these ions move with glucose	calcium	magnesium	sodium		potassium	**potassium**
36	In the intestinal cells these ions move with glucose	Calcium	magnesium	sodium		potassium	**sodium**
37	Selenium is contained in	Glutathione redutase	Glutathione peroxidase	Glutamate dehyderogenase		Glutamin synthetase	**Glutathione peroxidase**
38	Soon after absorbtion copper is bound to	a1 globulin	b globulin	albumin		prealbumin	**albumin**
39	Electrolytes in sweat are increased considerably in	Diabetes mellitus	Peptic ulcer	Fibrocystic disease of pancrease		Infective hepatitis	**Fibrocystic disease of pancrease**
40	The most potent cortical hormone concerned with the retention of sodium in the body is	cortisone	Deoxy cortisone	progesterone		aldosterone	**aldosterone**
41	Ceruloplasmin contains	Iron	Magnesium	H+ ion concentration		Copper	**Copper**

42	Metabolism of sodium is influenced by the action of	Thyroxine	Glutathione	Insulin		Adrenocortical steroids	**Adrenocortical steroids**
43	The major pathway of calcium excretion under normal condition is	Intestinal tract	Kidneys	Liver		Sweat	**Kidneys**
44	Rice polishings contain this vitamin	riboflavin	niacin	thiamin		vitamin B12	**thiamin**
45	In beri beri there will be accumulation of in blood	Aceto acetic acid	Beta hydroxy butyric acid	Pyruvic acid		Metyl malonic acid	**Pyruvic acid**
46	The significant ocular lesion in ariboflavinosis is	keratomalacia	Bitot’s spots	Vascularisation of cornea		Lachrymal metaplasis	**Vascularisation of c**
47	Irradiation of food rises the content of	Vitamin A	niacin	Vitamin D		Vitamin K	**niacin**
48	Defiency of the mineral results in endemic goiter	selenium	fluorine	iodine		molybdenum	**iodine**

49	One among the following minerals is not a micronutrient for human beings	manganese	magnesium	mercury		molybdenum	**mercury**	
50	Wilson’s disease is characterized by the deposition of one of the following minerals in the tissue	Fe	Cu	Hg		Ag	**Cu**	
51	Progesteron causes retention of	sodium	potassium	Zinc		Copper	**sodium**	
52	Biotin is w	animal foo	plant food	both a and b		milk	**both a and b**	
53	Pantothen	beta alani	alpha alan	gamma alanine		omega alanine		**beta alan**
54	last vitami	Vitamin C	Vitamin K	Vitamin B_{12}		Vitamin A	**Vitamin B_{12}**	
55	Methylcob	hydroxyl g	carboxyl g	amino group		methyl group		**methyl gr**
56	Purines w	STS	SNP	EST	DNA and RNA.		**DNA and RNA.**	
57	Folic acid	cauliflowe	cabbage	green leafy vegetable		tumeric	**green leafy vegetabl**	
58	Macro mi	0.01%	0.02%	0.03%		0.04%	**0.01%**	
59	Trace min	20	30	50		100	**100**	
60	About ___	100%	99%	88%		77%	**99%**	

ornea

ine

oup

es