BCH 212: GENERAL BIOCHEMISTRY II

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CARBOHYDRATE

- Carbohydrates are called carbohydrates because they are essentially hydrates of carbon (i.e. they are composed of carbon and water and have a composition of $(CH_2O)_{n.}$

- The major nutritional role of carbohydrates is to provide energy, and digestible carbohydrates provide 4 kilocalories per gram.

- No single carbohydrate is essential, but carbohydrates do participate in many required functions in the body.

- Organic compounds that contain CARBON, HYDROGEN, and OXYGEN in the ratio of 1 carbon atom and 1 oxygen atom for every 2 hydrogen atoms
- Carbohydrates are polyhydroxy aldehydes or ketones,
- or substances that yield such compounds on hydrolysis.
- Many, but not all, carbohydrates have the empirical formula $(CH_2O)_n$; some also contain nitrogen, phosphorus, or sulfur.

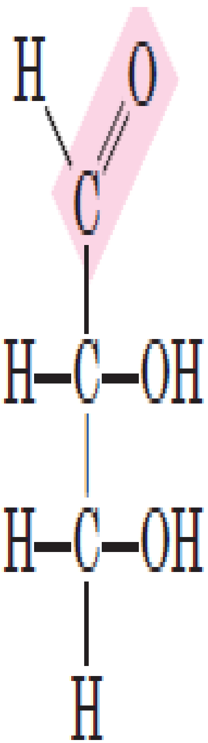
MAJOR CLASSES CARBOHYDRATES

- There are three major size classes of carbohydrates:
- monosaccharides,
- oligosaccharides, and
- polysaccharides

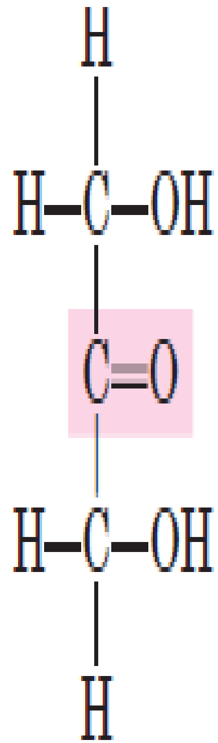
- **Monosaccharides**: those carbohydrates that cannot be hydrolyzed into simpler carbohydrates:

- They may be classified as trioses, tetroses, pentoses, hexoses, or heptoses, depending upon the number of carbon atoms; and

- aldoses or ketoses depending upon whether they have an aldehyde or ketone group.
- The brain consumes 120g of glucose/day



Glyceraldehyde, an aldotriose

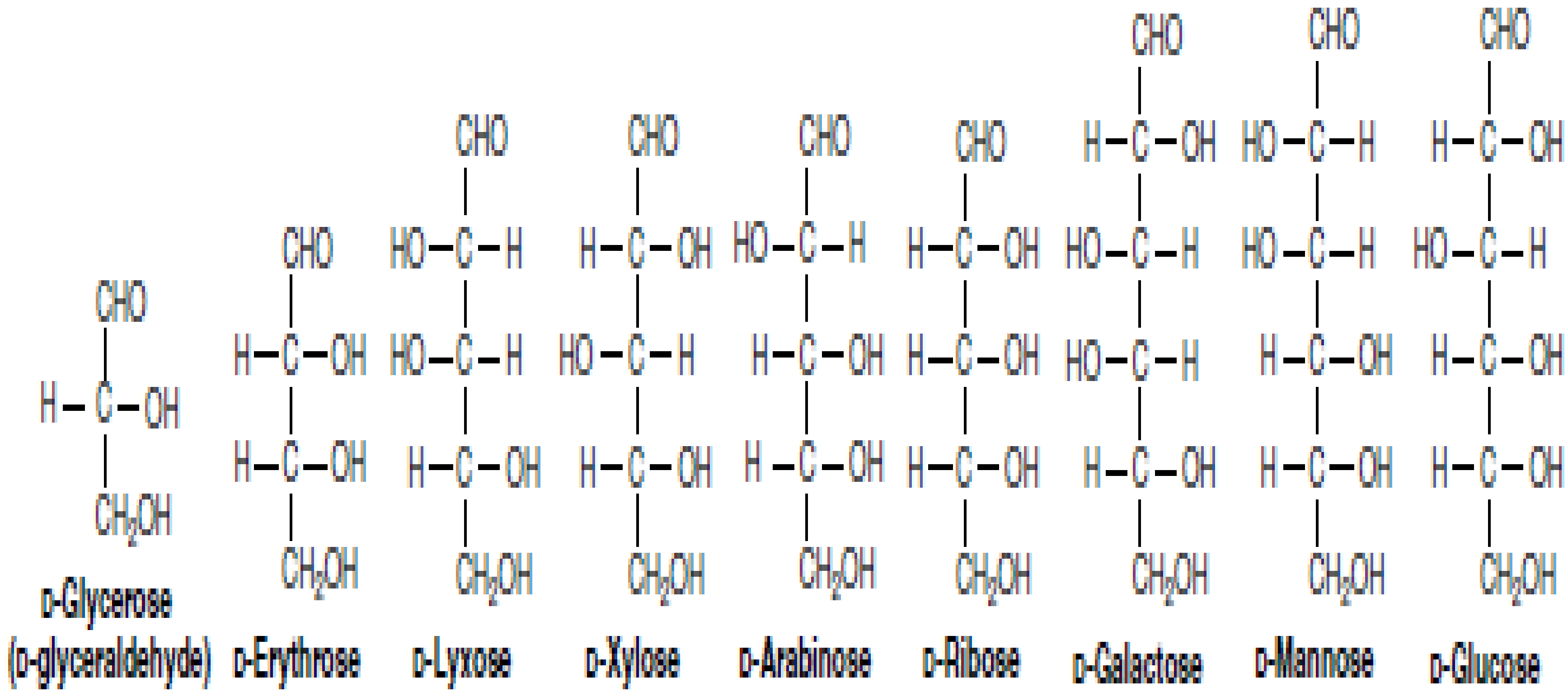


Dihydroxyacetone a ketotriose

D-Erythrose

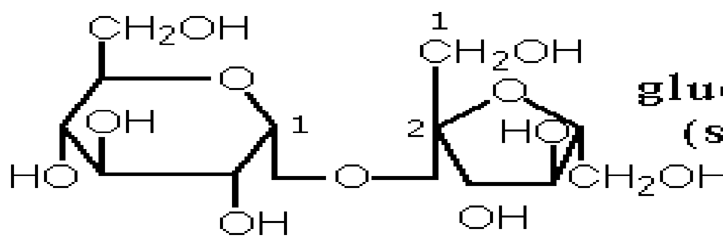
D-Erythrulose

Aldose sugars

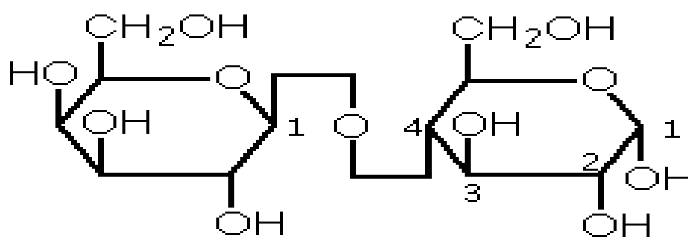


➢ Disaccharides

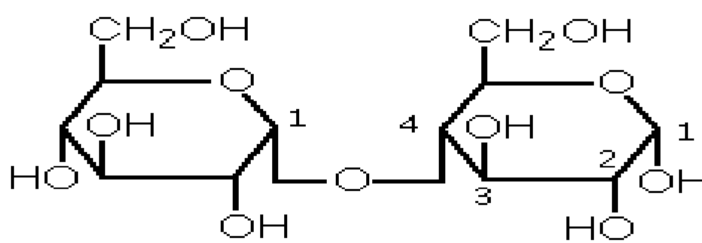
- These occur through the condensation of two monosaccharide units by a glycosidic linkage. Examples include maltose, lactose and sucrose.



glucose α 1-2 fructose
(sucrose)



galactose β 1-4 glucose
(lactose)



glucose α 1-4 glucose
(maltose)

- **Oligosaccharides**

- They contain 2-10 monosaccharides joined by glycosidic bonds. They can undergo further hydrolysis to form smaller units.
- Examples are disaccharide, trisaccharide, tetrasaccharide and pentasaccharides depending on the number of monosaccharides present.

POLYSACCHARIDES

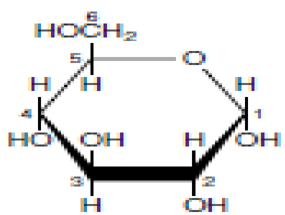
- **Polysaccharides** are carbohydrate polymers consisting of tens to hundreds to several thousand monosaccharide units.

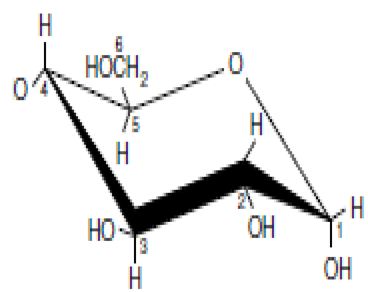
- All of the common polysaccharides contain glucose as the monosaccharide unit.

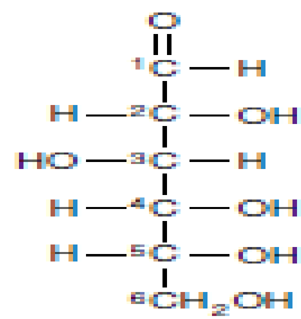
- Polysaccharides are synthesized by plants, animals, and humans to be stored for food, structural support, or metabolized for energy.

STRUCTURAL REPRESENTATION OF MONOSACCHARIDES

- Using glucose as a typical example, the structural formula can exist in three forms:
- straight-chain form; cyclic structure which is favoured on thermodynamic basis (Haworth projection); and chair form.







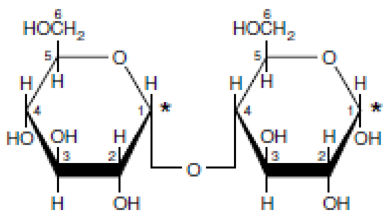
Isomerism in sugars

- Isomerism of molecules is also related to their chirality or asymmetric nature of the coordinating atoms present.
- The general formula for isomerism is 2^n, where n is the number of chiral carbon.

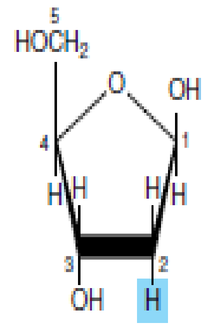
Various isomerisms

- D and L isomerism: designation of D (dextrorotatory) or L (Levorotatory) to sugar is determined by the orientation of the OH groups around the carbon atom adjacent to the terminal primary alcohol carbon.
- Optical isomerism: designated as + or –
- Pyranose and furanose ring structures

Maltose

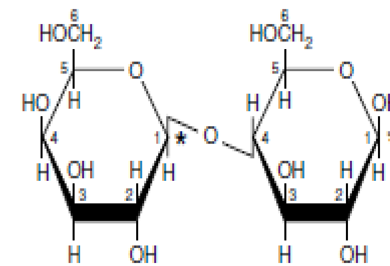


O-α-D-Glucopyranosyl-(1 → 4)-α-D-glucopyranose



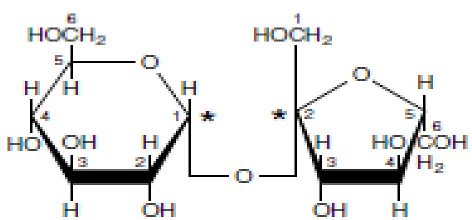
2-Deoxy-D-ribofuranose (β form)

Lactose



O-β-D-Galactopyranosyl-(1 → 4)-β-D-glucopyranose

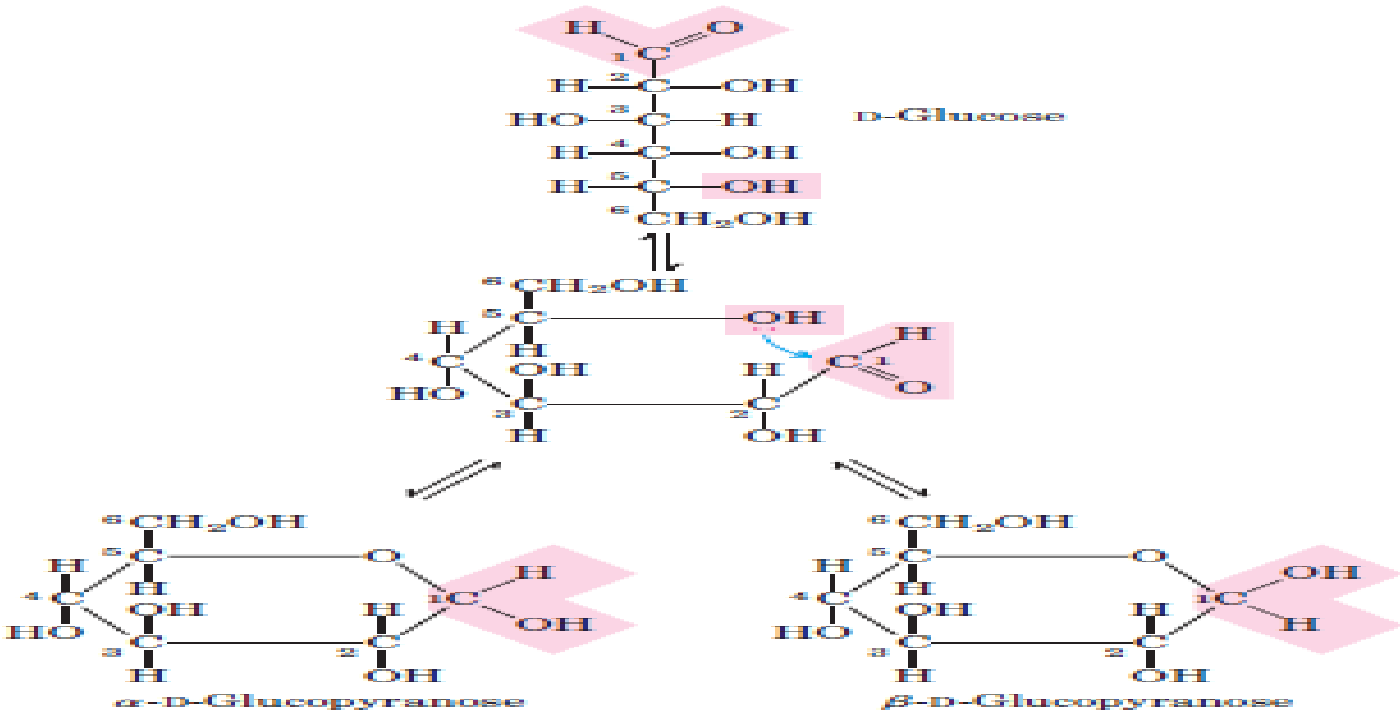
Sucrose



O-α-D-Glucopyranosyl-(1 → 2)-β-D-fructofuranoside

- Anomers:
- The ring structure of monosaccharides e.g D-glucose, is obtained from the intramolecular bond formation between an aldehyde group (C-1) and alcohol group (C-5) to form hemiacetal.
- This makes D-glucose to exist in two stereoisomers designated α and β. Also, bond formation between an ketone group and alcohol group results in hemiketal.

- α and β anomeric forms are interconvertible in aqueous solution by a process called **mutarotation**.



- Keto hexoses also occur as α and β isomers from the formation of hemiketal linkage from the reaction of hydroxyl group at C-5 or C-6 and keto group at C-2.
- Epimers: They are isomers that differ as a result of variations in configuration of the OH and H on carbon atoms 2, 3, and 4 of glucose. For instance, mannose and galactose are epimers of glucose at C-2 and C-4 respectively.
- Aldose-ketose isomerism: fructose is an isomer of glucose because they have the same molecular formula but different structural formula.

LIPID CHEMISTRY

- Lipids are naturally occurring heterogeneous compound which are relatively insoluble in water and soluble in non-polar solvents

- **Classification of lipids**

- **Simple lipids:** esters of fatty acids with various alcohols. E.g. fats and oil, waxes.
- **Complex lipids**: esters of fatty acids containing groups in addition to an alcohol and a fatty acid e.g Phospholipid and glycolipids
-

FATTY ACIDS

- These are aliphatic carboxylic acids containing long hydrocarbon chains ranging from C-4 to C-24, which may be saturated or unsaturated.
- Based on the bonds that exist within the hydrocarbon chains, fatty acids can be saturated or unsaturated.
- Saturated fatty acid is a long-chain carboxylic acid containing only C-C single bonds.
- Unsaturated fatty acid is a long-chain carboxylic acid containing one or more C-C double bonds

- Unsaturated fatty acids occur mostly in cis form e.g oleic acid rather than trans form e.g elaidic acid.

Properties of fatty acids

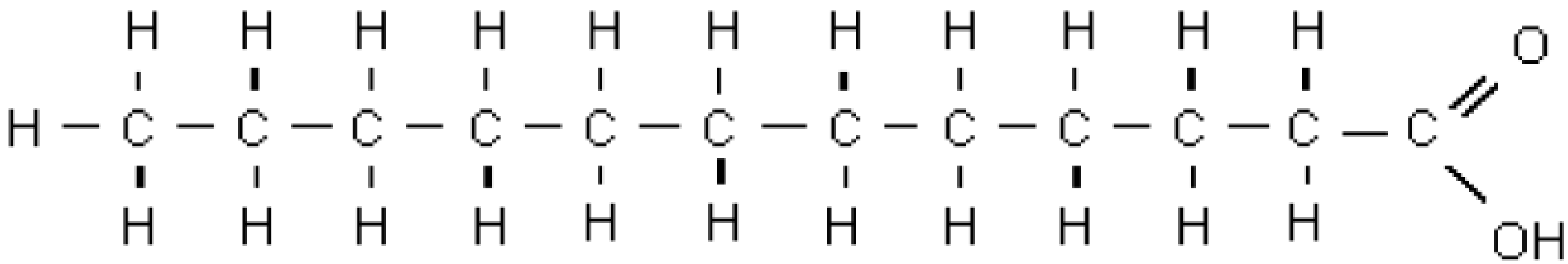
- Fatty acids are amphipathic, because of the Hydrophobic tail and Hydrophilic (–COOH) head
- The longer the hydrocarbon chain the higher the melting point of the fatty acid
- The greater the number of double bonds in the fatty acid the lower the melting point of the fatty acid
- Unsaturated fatty acids have substantially lower melting points than saturated fatty acids

Essential and non-essential fatty acids

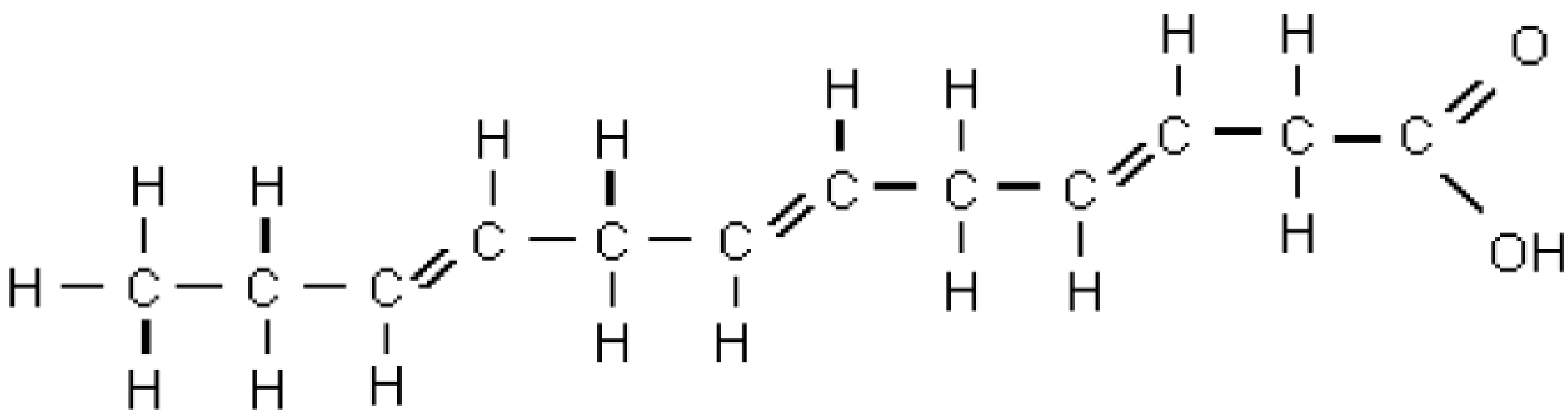
- Essential fatty acids are the ones that cannot be synthesized in the body and thus are obtained from the diet e.g. ω-3 and ω-6 fatty acids.
- Non-essential fatty acids can be synthesized in the human system and therefore do not come only from diet

NOMENCLATURE OF SATURATED FATTY ACID

- Systemic or IUPAC name of a fatty acid is formed by replacing the ending –e of alkane with suffix –oic acid to form a carboxylic acid
- Examples: 16C fatty acid: hexadecanoic acid (hexadecane), and 18C fatty acid: octadecanoic acid (octadecane)
- Fatty acid can also be named using α, β, γ, δ, ε, ζ, η, θ to describe the carbon positions.
- The carboxyl carbon is only assigned C-1 while from C-2 can now take α and C-3, β and so on. The terminal carbon atom in a fatty acid molecule is considered as ω-carbon or the n-carbon atom.



Saturated Fatty Acid



Unsaturated Fatty Acid

Common name	**Systematic name**	**Short-hand structural formula**
Valeric acid	Pentanoic acid	CH3(CH2)3COOH
Caproic acid	Hexanoic acid	CH3(CH2)4COOH
Caprylic acid	Octanoic acid	CH3(CH2)6COOH
Capric acid	Decanoic acid	CH3(CH2)8COOH
Lauric acid	Dodecanoic acid	CH3(CH2)10COOH
Myristic acid	Tetradecanoic acid	CH3(CH2)12COOH
Palmitic acid	Hexadecanoic acid	CH3(CH2)14COOH
Stearic acid	Octadecanoic acid	CH3(CH2)16COOH
Arachidic acid	Eicosanoic acid	CH3(CH2)18COOH
Behenic acid	Docosanoic acid	CH3(CH2)20COOH
Lignoceric acid	Tetracosanoic acid	CH3(CH2)22COOH

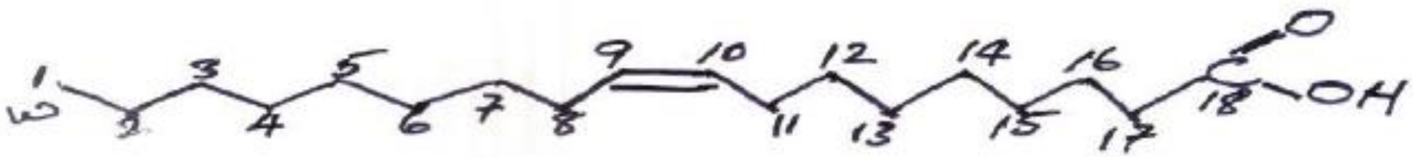
SYSTEMIC NOMENCLATURE OF UNSATURATED FATTY ACID

- Systemic nomenclature considers: number of carbon atoms in the fatty acid; number of double bonds; position of the double bonds
- The delta (Δ) numbering system is used to indicate the position of the double bond in fatty acids
- For examples, oleic acid: cis Δ9 octadecenoic acid (cis-9 octadecenoic acid); linoleic acid: is cis- Δ9,12-Octadecadienoic (cis-9,12- octadecadienoic acid) acid.

- Shortened form of nomenclature can be: 18:1; 9; for oleic acid. 18:2; 9, 12; for linoleic acid.

Omega numbering for unsaturated fatty acids

- ω-numbering system is used to indicate the position of the double bond by counting from the ω-carbon
- Oleic acid ω-9, C18:1 this implies it contains a double bond between C9 and C10 counting from the ω-C atom; C18:1 means 18 C atoms, one double bond.
- Linoleic acid: ω-6, C18:2, the double bond is between C6 and C7 from the ω-C atom end.



ω9 C18:1

ω6 C18:2

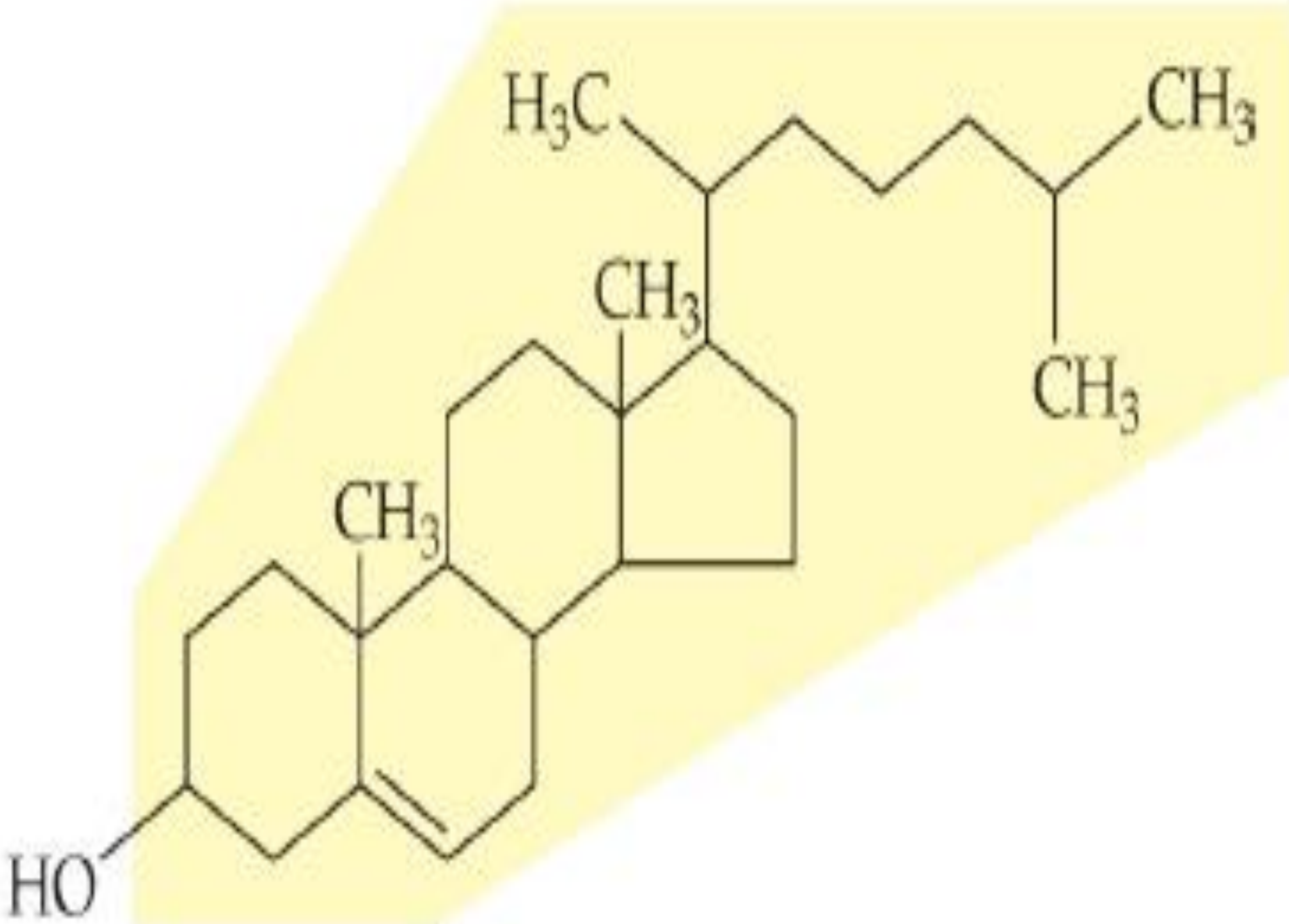
ω3 C18:4

Polyunsaturated fatty acids

- Polyunsaturated fatty acids are categorized into three series based on the omega nomenclature.
- ω-9 fatty acids e.g. oleic acid
- ω-6 fatty acids e.g. linoleic acid and arachidonic acid
- ω-3 fatty acids e.g. α-linoleic acid (18:3;9,12,15) and timnodonic acid

BLOOD LIPIDS AND LIPOPROTEINS

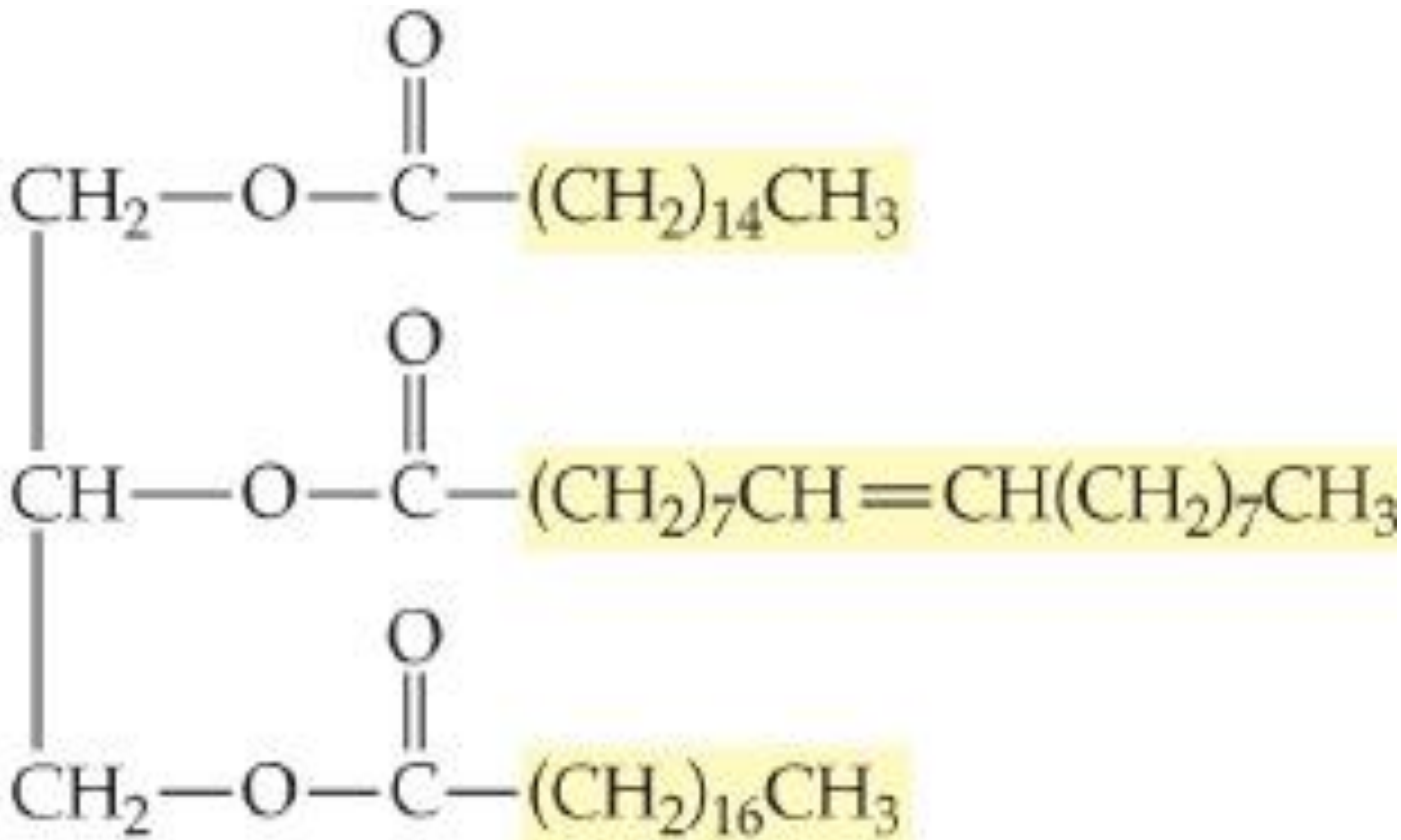
- **Cholesterol and triglycerides** are the major blood lipid as well as the **phospholipids.**
- Cholesterol is an important lipid found in the cell membrane. It is a sterol formed from the combination of steroid and an alcohol.
- The fluidity of the cell membrane is owed to cholesterol. Cholesterol is insoluble in the blood and so must be carried by a specific protein to facilitate its movement in the blood.



Cholesterol, a steroid

- **Triglycerides or triacylglycerols**

- They are carboxylic acids triesters of glycerol, a three-carbon trialcohol. They are the stored form of fat in the body esp. in the adipocytes.
- Short-chain unsaturated triglycerides are liquid at room temperature. Whereas long-chain saturated triglycerides are solid at room temperature.



A triacylglycerol

CLASSIFICATION OF AND FUNCTIONS OF LIPOPROTEINS

- Cholesterol and other lipids are carried on plasma lipoproteins.
- Cholesterol and cholesteryl esters, like triacylgycerols and phospholipids are relatively insoluble in water, but must be transported within the body.
- Therefore, they are carried in the blood plasma as lipoproteins.
- Lipoproteins are spherical complexes with hydrophobic lipids in the core and hydrophilic amino side chains at the surface which interacts with the aqueous environment.

- **Chylomicrons**: are the largest lipoproteins and the least dense which contain a high proportion of triglyceride.
- The apolipoproteins of chylomicrons are apoB-48, apoE, and apoC-II.
- **Very low density lipoproteins (VLDL)**: Excess fatty acids and carbohydrates are converted to triacylglycerols in the liver and packaged with specific apolipoproteins into VLDL.
- These lipoproteins are transported in the blood from the liver to muscle and adipose tissue, where activation of lipoprotein lipase by apoC-II causes the release of free fatty acids from the VLDL triglycerides.

- **Intermediate density lipoproteins (IDL)**: The loss of triglyacylglycerol converts some VLDL to VLDL remnant known as IDL.
- **Low density lipoproteins (LDL)**: Further removal of triglycerides from the VLDL yields LDL which is very rich in cholesterol and cholesteryl esters and also apoB-100 as the major apolipoprotein.
- LDL facilitates the movement of cholesterol to the extrahepatic tissues that have specific plasma membrane receptors that recognize apoB-100.

- **High density lipoprotein (HDL)**: It contains apoA-I, apoC-I, apoC-II and other apolipoproteins, as well as the enzyme lecithin-cholesterol acyl transferase (LCAT), which catalyzes the formation of cholesteryl esters from lecithin (phosphatidylcholine) and cholesterol.
- It facilitates the transport of fatty acids from extrahepatic tissues to the liver.

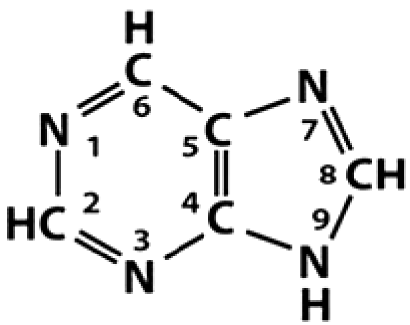
CHEMISTRY OF NUCLEIC ACIDS

- Nucleic acids are formed by the combination of nucleotide molecules through sugar-phosphate bonds known as phosphodiester linkages.
- They are categorized into two, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).
- They are composed of nitrogenous bases, ribose sugar backbone and phosphate group(s). These three components are referred to as nucleotides.

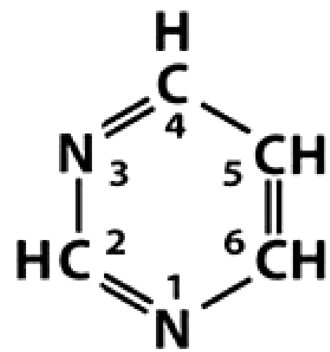
Nitrogenous Bases

- Bases are either pyrimidine or purine. Pyrimidines are six-membered ring consisting of other atoms in addition to carbon atoms.

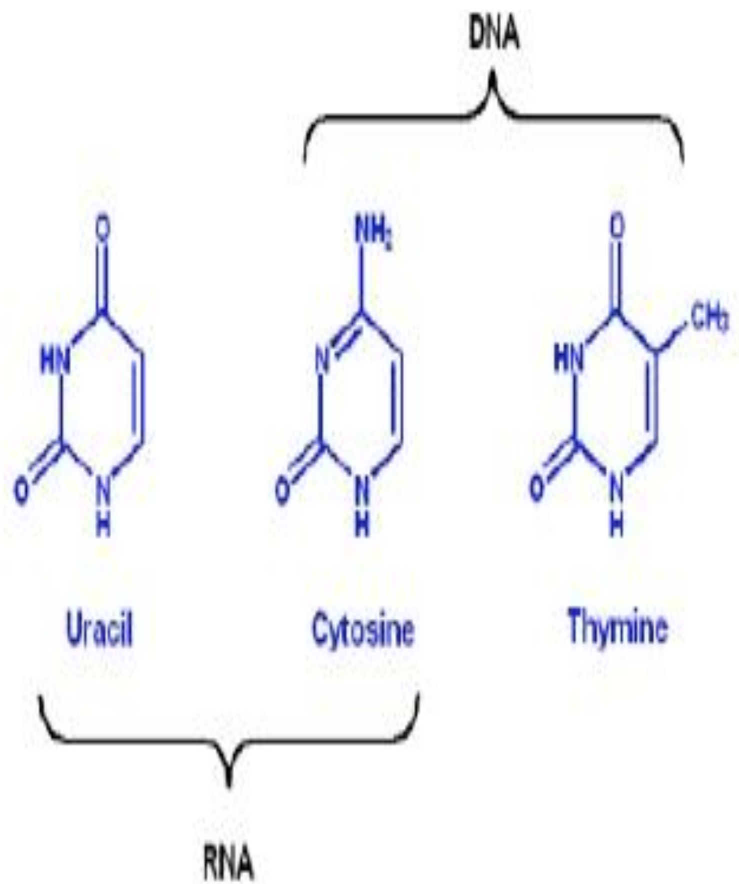
- Examples are cytosine (C), thymine (T) and uracil (U). Purines are pyrimidine linked to an imidazole ring, e.g. guanine (G) and adenine (A).

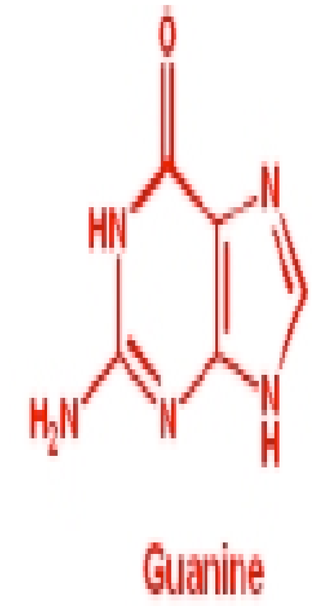


Purine

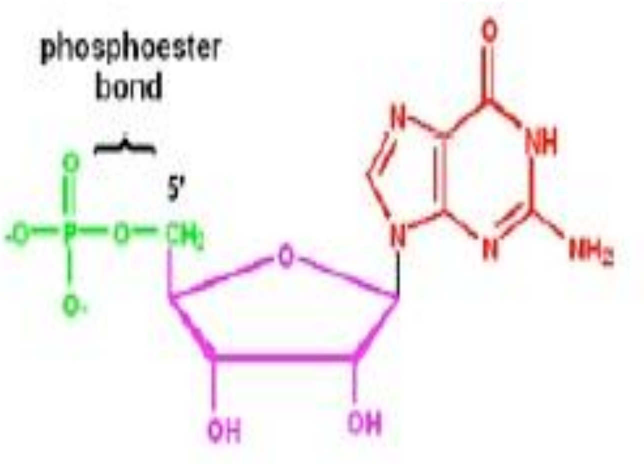


Pyrimidine

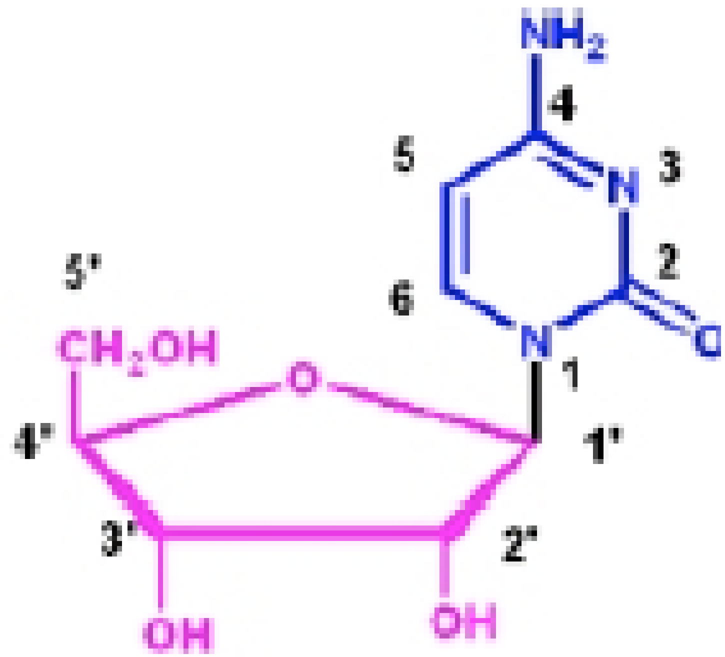

DNA
NH2
O
O
HN
N
CH3
HN
O
N
H
O
N
H
O
N
H
Uracil
Cytosine
Thymine
RNA


NH2
O
N
N
HN
N
N
N
H
H2N
N
N
H
Adenine
Guanine

- Nucleotides?
- Nucleosides?



Guanosine 5' monophosphate
(5'-GMP)
(Guanylic acid)



Nucleoside and nucleotides nomenclature

- Nucleoside: Add suffix “idine” to pyrimidine, and “osine” to purine.
- For example, pyrimidine: cytosine becomes cytidine, uracil becomes uridine and thymine becomes thymidine; purine: adenine becomes adenosine, guanine becomes guanosine.
- Nucleotides are guanylate, cytidylate, uridylate, adenylate, and thymidylate.

Importance of nucleotides

- ATP formation which is a major source of energy in the cell
- GTP, UTP, CTP are sources of energy in certain metabolic pathways
- Formation of coenzymes NAD, NADP, FAD and coenzyme A
- cAMP acts as a second messenger inside the cell for many hormones and cGMP act as a cellular mediator.
- Some nucleotides are important regulators for many metabolic reactions
- Nucleotides act as carriers of activated intermediates such as: a- UDP- glucose in synthesis of glycogen b- CDP choline in synthesis of phospholipids c- GDP mannose in synthesis of glycoproteins.

- **Deoxyribonucleic acid (DNA)**: This is a polymeric molecule comprising of repeating nucleotide subunits.
- The sugar backbone present is 2-deoxyribose i.e. oxygen atom at carbon position 2 is removed.
- The bases contain in DNA are cytosine, guanine, adenine, thymine.
- **Ribonucleic acid (RNA)**: It is also a polymeric molecule that consists of repeating nucleotide subunits but differ from DNA in structure and function

- RNA has two major structural differences: each of the ribose rings contains a 2´-hydroxyl; and RNA uses uracil instead of thymine

MAJOR CLASSES OF RNA

- **Ribosomal RNA (rRNA)**: This comprises 65 to 70% of the mass of the ribosome.
- It is the intricate cellular machinery that synthesizes proteins.
- Three of the rRNAs (5S, 5.8S and 28S) are components of 60S ribosomal particle.
- The 40S ribosomal subunit contains only 18S rRNA. The rRNAs assemble with ribosomal protein subunits in the nucleus

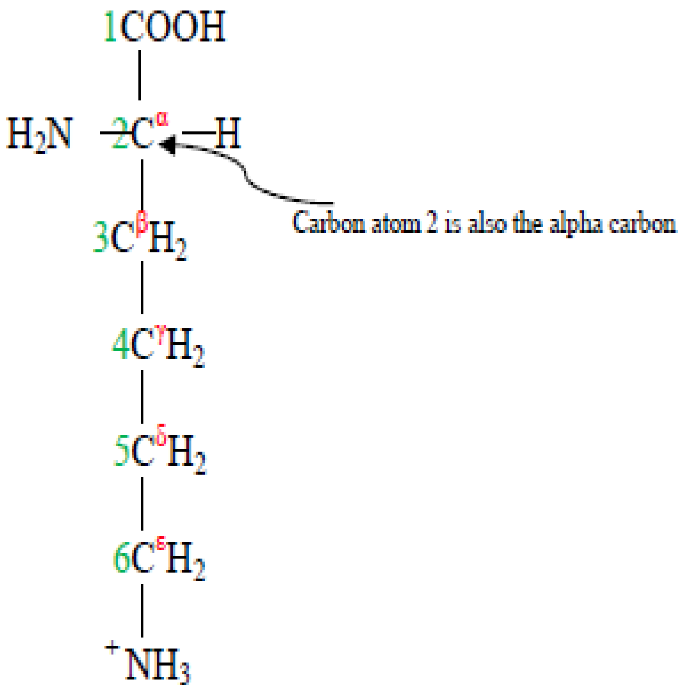
- **Transfer RNA (tRNA)**: This is the next most abundant forms of RNA and accounts for about 15% of the total RNA. It is also referred to as 4S RNA.
- It reads the genetic information encoded in the mRNA and transfers the appropriate amino acid to the growing polypeptide chain in the course of protein synthesis.

- **Messenger RNA (mRNA)**: This encodes the amino acid sequence of one or more polypeptides specified by the DNA.
- mRNA functions in the delivery of genetic information to the cytoplasm where protein synthesis occurs;
- it serves as a template for translation by ribosomes during protein synthesis.

Chemistry and structure of amino acids

- Amino acids are the building block of proteins
- They are referred to as α-amino carboxylic acid except proline.The simplest of them is amino acetic acid, called glycine.
- Glycine serve as the parent structure for other standard or common amino acids as its side chain (R group) is substituted on the α-carbon atom to produce the remaining standard amino acids.
- For instance, alanine has methyl side chain.
- With the exception of glycine, all common amino acids are chiral compounds.

Numbering of carbon atoms in amino acids



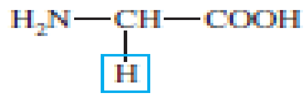
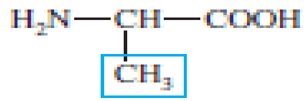
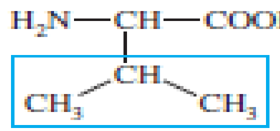
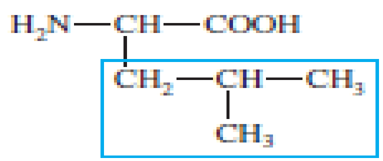
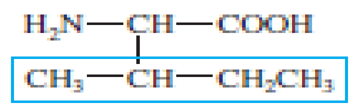
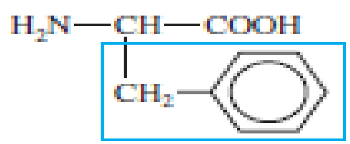
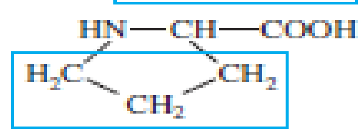
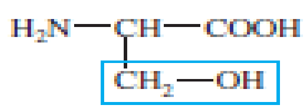
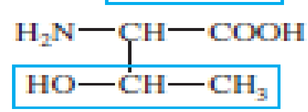
Stereochemistry of amino acids

- Stereochemistry of proteins explains the three-dimensional arrangement of the constituent atoms of the molecule in space.
- The configuration of simple sugar and amino acids are specified by L, D system.
- Various compounds formed from the different spatial arrangement of the compound are called its stereoisomers.
- Stereoisomers that are mirror images of each other are called enantiomers. If otherwise, they are called diastereomers

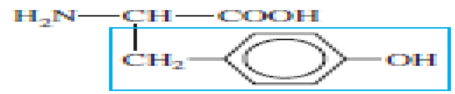
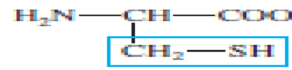
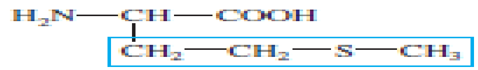
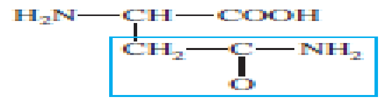
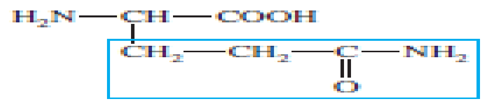
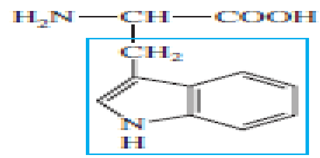
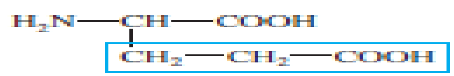
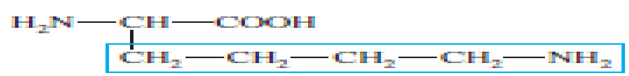
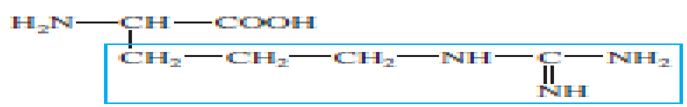
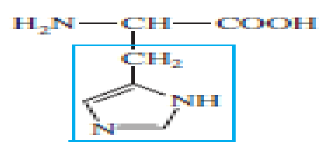
Standard amino acids

- These are the common amino acids found in proteins and they are essentially 20

The Standard Amino Acids

Name	Symbol	Abbreviation	Structure	Functional Group in Side Chain
side chain is nonpolar, H or alkyl				
glycine	G	Gly		none
alanine	A	Ala		alkyl group
*valine	V	Val		alkyl group
*leucine	L	Leu		alkyl group
*isoleucine	I	Ile		alkyl group
*phenylalanine	F	Phe		aromatic group
proline	P	Pro		rigid cyclic structure
side chain contains an —OH				
serine	S	Ser		hydroxyl group
*threonine	T	Thr		hydroxyl group

The Standard Amino Acids (continued)

Name	Symbol	Abbreviation	Structure	Functional Group in Side Chain
tyrosine	Y	Tyr		phenolic —OH gro
side chain contains sulfur				
cysteine	C	Cys		thiol
*methionine	M	Met		sulfide
side chain contains nonbasic nitrogen				
asparagine	N	Asn		amide
glutamine	Q	Gln		amide
*tryptophan	W	Trp		indole
side chain is acidic				
aspartic acid	D	Asp		carboxylic acid
glutamic acid	E	Glu		carboxylic acid
side chain is basic				
*lysine	K	Lys		amino group
*arginine	R	Arg		guanidino group
*histidine	H	His		imidazole ring

*essential amino acid

Classification based on polarity

- **Amino Acids with Nonpolar Side Chains**
- Examples are Glycine, Alanine, Valine, Leucine, Isoleucine, Methionine, Proline, Phenylalanine and Tryptophan
- **Amino Acids with Polar Side Chains**
- **Uncharged polar R groups**: e.g. **Serine** and **Threonine** - are polar because of their hydroxyl groups.
- **Asparagine** and **Glutamine** – the polarity is due to the presence of amide-bearing R groups.
- **Tyrosine** – has an OH functional group attached to benzene ring. This OH is hydrophilic.
- **Cysteine** – its thiol or (SH) group is responsible for its polarity

- **Charged polar R groups**

- At physiological pH, **Lysine**, **Arginine** and **Histidine** are positively charged due to their terminal ammonium, guanidinium, and the imidazolium groups respectively
- **Aspartic acid** and **Glutamic acid** are negatively charged above pH 3

Classification based on nutritional requirements

- **Essential amino acids**: Examples include Arg, Val, Met, Leu, Thr, Phe, His, Ile, Lys, and Trp.
- Dietary proteins that contain all the essential amino acids in the right proportion is said to be complete proteins e.g. fish, meat and egg.
- The proteins that are seriously deficient in one or several amino acids are called incomplete proteins e.g. plant proteins.

Rare and unusual amino acids

- For example, 4-hydroxyproline and 5-hydroxylysine, GABA (γ-amino butyric acid), β-alanine, D-glutamic acid, Ornithine, citrulline, homoserine are unusual amino acids.
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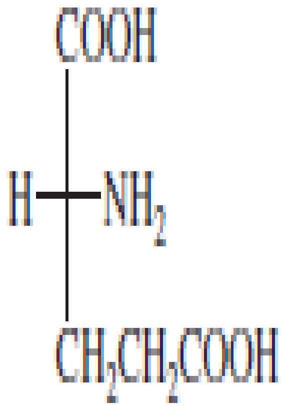
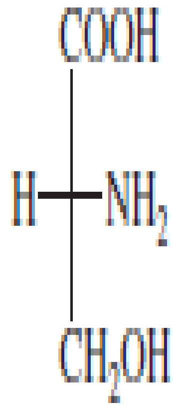
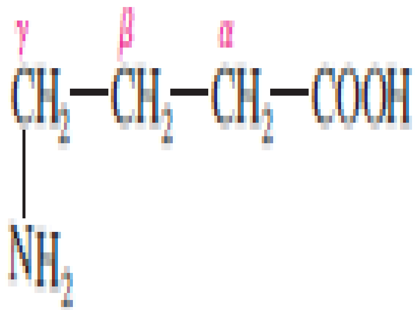


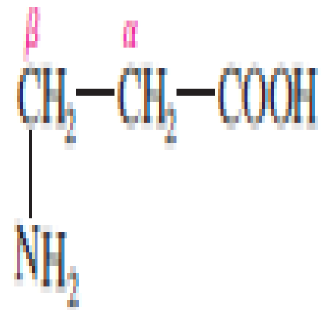
D-glutamic acid



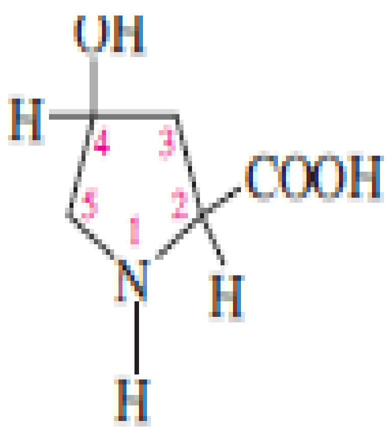
D-serine



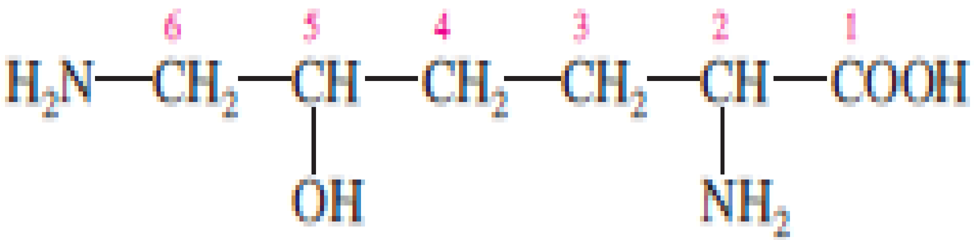
γ-aminobutyric acid



β-alanine



4-hydroxyproline



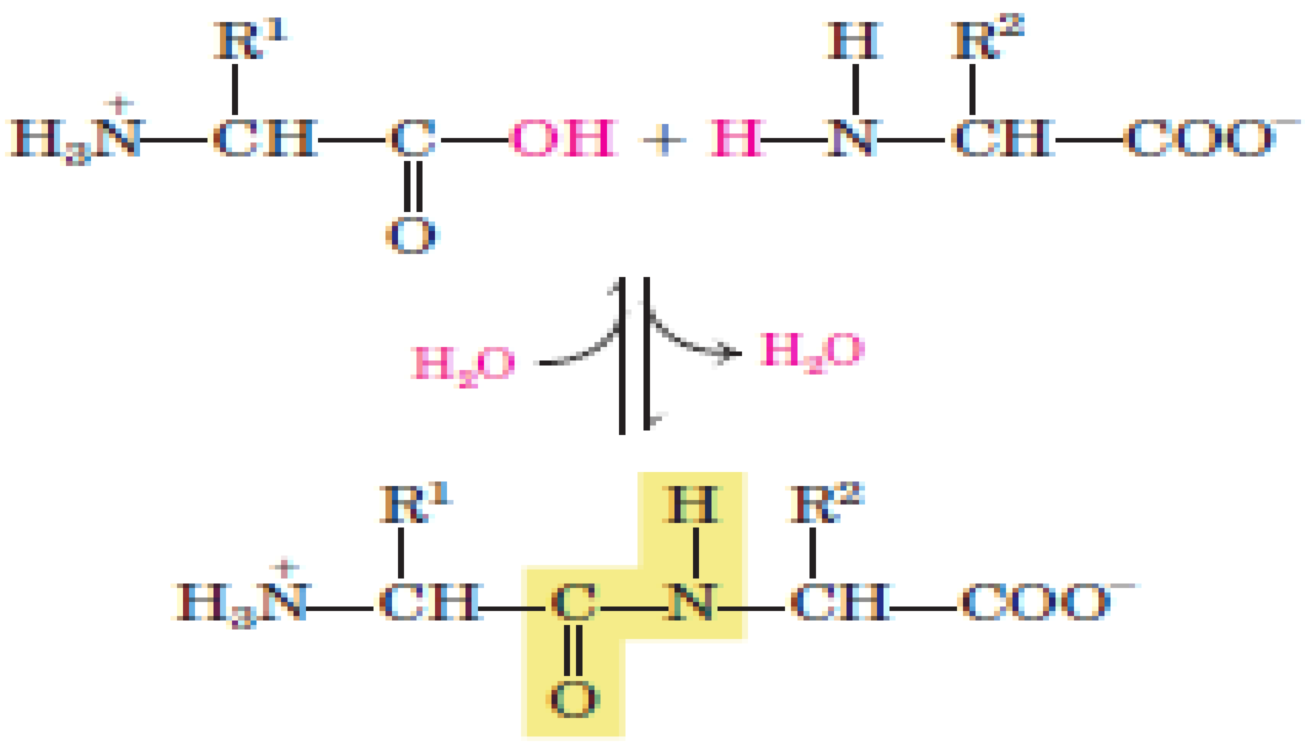
5-hydroxylysine

Classificaition of protein based on shape and size

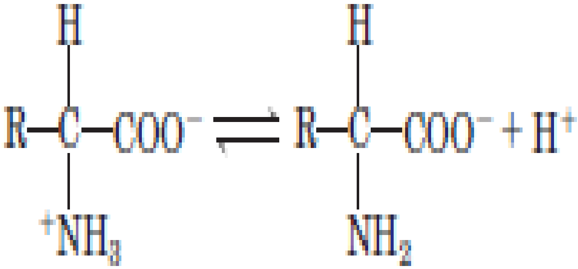
- **Fibrous proteins**
  - These are proteins that exist as long fibres. They are tough and water-insoluble. Examples involve alpha keratin found in hair, skin; beta-keratin
- **Globular proteins**
  - These are mostly water-soluble and fragile in nature. Examples include enzymes, haemoglobin hormones and antibodies

Structural organization of proteins

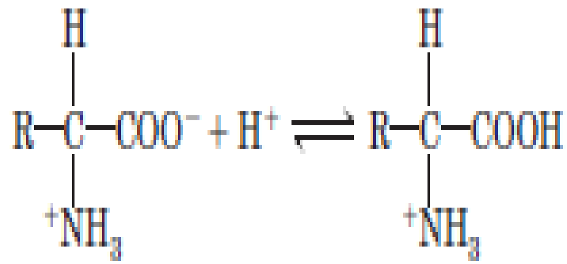
- Primary structure: The primary structure of protein is the linear order of amino acid or its sequence in a given protein.
- Proteins are linear polymers formed by covalent linkage of α-carboxyl group of an amino acid and α-amino group of another amino acid by a peptide bond.


R1
H3N+—CH—C—OH + H—N—CH—COO−
H
R2
O
H2O
H2O
R1
H
R2
H3N+—CH—C—N—CH—COO−
O

- **Amphoteric nature of amino acids**: This is the ability of amino acid in aqueous solution to exist either as acid or base.
- This amino acid is said to be dipolar ion or zwitterion.



Zwitterion



Zwitterion

- **Secondary structures**
- These are the interactions of about tens amino acid residues to give rise to regular repeating structures.
- Each of these regular repeats is called a helix.
- The two main types of secondary structure are the α-helix and the ß-sheet.

- **The α-helix** is a right-handed coiled strand.
- Some amino acids have high helix forming tendencies. These include methionine, alanine, leucine, glutamate, and lysine.
- While others such as proline, glycine, and aspartate are negatively disposed to α-helix formation.
- **Beta strands:** these are the most fundamental helix, having essentially a 2D backbone of folds like pleating skirt.

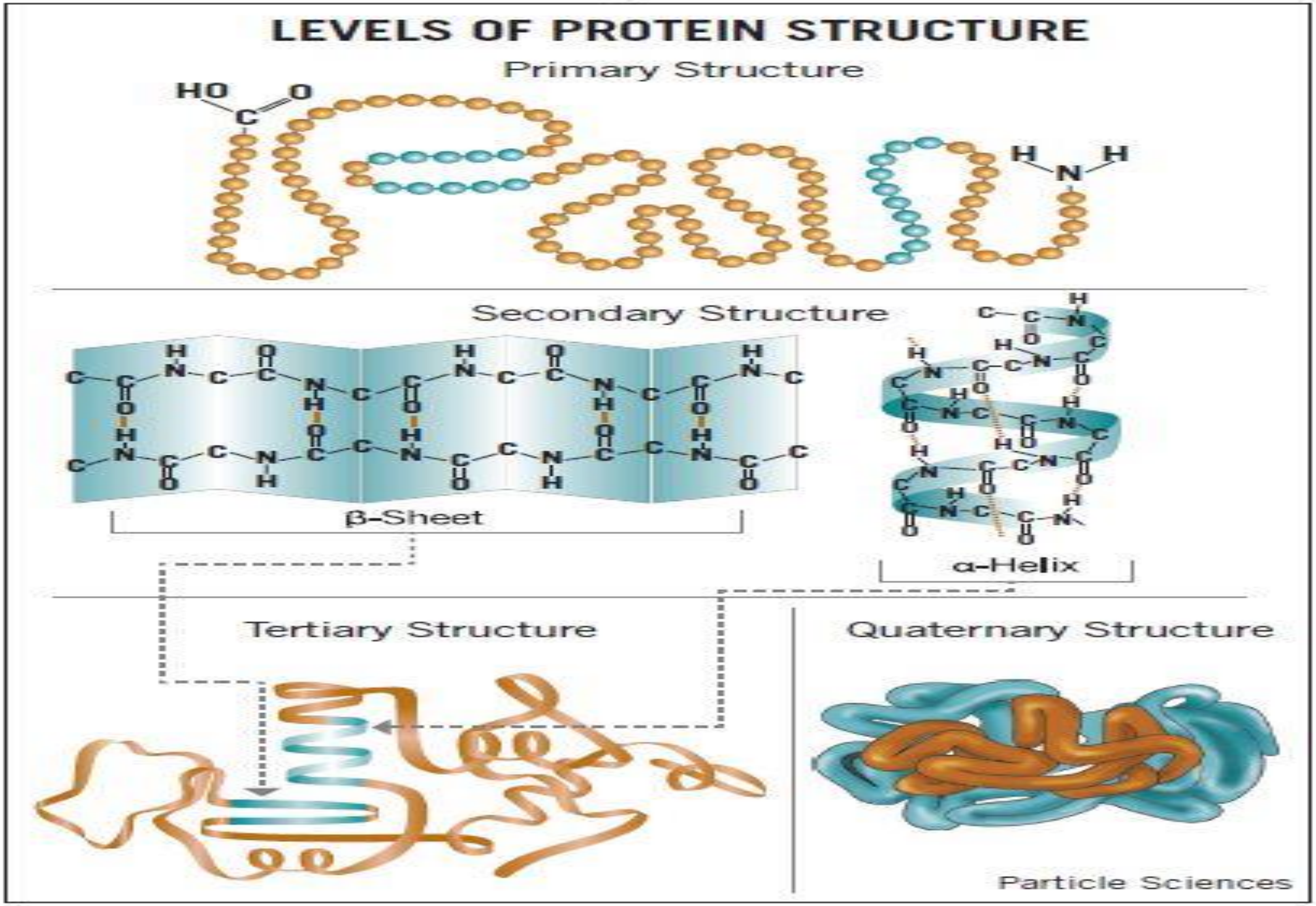
Tertiary Structure

- The overall three-dimensional shape of an entire protein molecule is the tertiary structure.
- It is the overall folding pattern of a single covalently linked molecule.
- The characteristic bond type are: hydrophobic and others- hydrogen, ion pair, van der Waals, and disulphide.

Quaternary Structure

- This is the association of two or more independent proteins via non-covalent forces to form a multimeric protein. That is, many protein subunits come together to form the quaternary structure.
- This subunits may be homodimers or heterodimers.
- The quaternary structure refers to how these protein subunits interact with each other and arrange themselves to form a larger aggregate protein complex
- The final shape of the protein complex is also stabilized by various interactions, like hydrogen-bonding, disulfide-bridges and salt bridges.

Figure 2


LEVELS OF PROTEIN STRUCTURE
Primary Structure
Secondary Structure
β-Sheet
α-Helix
Tertiary Structure
Quaternary Structure
Particle Sciences