**SYLLABUS**

**Semester-VI**

| **16CHU603B** | **MOLECULES OF LIFE** | **4H 4C** |
|---|---|---|

**Instruction Hours/week: L:4 T:0 P:0** **Marks: Internal: 40 External: 60 Total:100**

**Scope**

The course deals with the molecules of life like carbohydrates, amino acids, peptides, proteins, enzymes, nucleic acids and lipids.

**Objectives**

The course enable the student to

1. Understand the structures of different types of carbohydrates
2. Understand the synthesis and functions of proteins
3. Understand the functions of enzymes
4. Understand the synthesis and functions of nucleic acid
5. Understand the classification of lipids and the concept of energy in biosystems

**Methodology**

Blackboard teaching, Powerpoint presentation and group discussion.

**UNIT I**

**CARBOHYDRATES**

Classification of carbohydrates, reducing and non-reducing sugars, General Properties of Glucose and Fructose, their open chain structure. Epimers, mutarotation and anomers. Determination of configuration of Glucose (Fischer proof). Cyclic structure of glucose. Haworth projections. Cyclic structure of fructose. Linkage between monosachharides, structure of disacharrides (sucrose, maltose, lactose) and polysacharrides (starch and cellulose) excluding their structure elucidation.

**UNIT II**

**AMINO ACIDS, PEPTIDES AND PROTEINS**

Classification *of Amino Acids,* Zwitterion structure and Isoelectric point. Overview of Primary, Secondary, Tertiary and Quaternary structure of proteins. Determination of primary structure of peptides, determination of N-terminal amino acid (by DNFB and Edman method) and C–terminal amino acid (by thiohydantoin and with carboxypeptidase enzyme). Synthesis of simple peptides (upto dipeptides) by N-protection (tbutyloxycarbonyl and phthaloyl) & C-activating groups and Merrifield solid phase synthesis.

**UNIT III**

**ENZYMES AND CORRELATION WITH DRUG ACTION**

Mechanism of enzyme action, factors affecting enzyme action, Coenzymes and cofactors and

their role in biological reactions, Specificity of enzyme action(Including stereospecificity), Enzyme inhibitors and their importance, phenomenon of inhibition(Competitive and Noncompetitive inhibition including allosteric inhibition). Drug action-receptor theory. Structure –activity relationships of drug molecules, binding role of –OH group,-NH2 group, double bond and aromatic ring,

**UNIT IV**

**NUCLEIC ACIDS**

Components of Nucleic acids: Adenine, guanine, thymine and Cytosine (Structure only), other components of nucleic acids, Nucleosides and nucleotides **(nomenclature**), Structure of polynucleotides; Structure of DNA (Watson-Crick model) and RNA(**types of RNA**), Genetic Code, Biological roles of DNA and RNA: Replication, Transcription and Translation.

**UNIT V**

**LIPIDS**

Introduction to lipids, classification. Oils and fats: Common fatty acids present in oils and fats, Omega fatty acids, Trans fats, Hydrogenation, Saponification value, Iodine number. Biological importance of triglycerides, phospholipids, glycolipids, and steroids (cholesterol).

**Concept of energy in Biosystems**

Calorific value of food. Standard caloric content of carbohydrates, proteins and fats. Oxidation of foodstuff (organic molecules) as a source of energy for cells. Introduction to Metabolism (catabolism, anabolism), ATP: the universal currency of cellular energy, ATP hydrolysis and free energy change. Conversion of food into energy. Outline of catabolic pathways of Carbohydrate- Glycolysis, Fermentation, Krebs Cycle. Overview of catabolic pathways of Fats and Proteins. Interrelationships in the metabolic pathways of Proteins, Fats and Carbohydrates.

**Suggested Texts:**

1. Morrison, R. T. & Boyd, R. N. *Organic Chemistry*. Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).
2. Finar, I. L. *Organic Chemistry*. Volume 1. Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).
3. Finar, I. L. *Organic Chemistry*. Volume 2. Dorling Kindersley (India) Pvt. Ltd. (Pearson Education).
4. Nelson, D. L. & Cox, M. M. *Lehninger's Principles of Biochemistry*. 7th Ed. W. H. Freeman.
5. Berg, J.M., Tymoczko, J.L. & Stryer, L. (2002). *Biochemistry*. W.H. Freeman.

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**ARPAGAM CADEMYOF HIGHER EDUCATION**
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**Established Under Section 3 of UGC Act 1956**

**COIMBATORE-21**

**DEPARTMENT OF CHEMISTRY**

**LECTURE PLAN**

**STAFF NAME**: B.Prabha **SUB.CODE**:16CHU603B

**SUBJECT NAME**: MOLECULES OF LIFE **SEMESTER**: VI

**CLASS**: III B.Sc., CHEMISTRY **SECTION:** A & B

| S.No | Lecture hour | Topics | Support material |
|---|---|---|---|
| | | **Unit - I** | |
| 1 | 1 | **Carbohydrates**: Classification of carbohydrates, reducing and non-reducing sugars | T1: 1128, T2: 503 |
| 2 | 1 | General properties of Glucose and Fructose, their open chain structure | T1: 1228-1230, T2: 507-510 |
| 3 | 1 | Epimers, mutarotation and anomers. | T1: 1233,1247,1250<br>T2: 510,514-515, T3: 286,306 |
| 4 | 1 | Determination of configuration of Glucose (Fischer proof) | T1: 1237-1240 |
| 5 | 1 | Cyclic structure of glucose (Haworth projections). Cyclic structure of fructose | T1: 1248-1250, T2: 516, T3: 293 |
| 6 | 1 | Linkage between monosaccharides, Structure of disaccharides (sucrose, maltose, lactose) | T1:1259-1260, 1263,1265<br>T2: 279-280 |
| 7 | 1 | Structure of polysaccharides (starch and cellulose) | T1: 1267,1274 |
| 8 | 1 | Recapitulation and discussion of important questions | |
| | **Total No of Hours Planned For Unit 1= 8** | | |
| | **Unit – II** | | |
| 1. | 1 | **Amino acids, Peptides and Proteins:** Classification of Amino acids, Zwitterion structure and Isoelectric point. | T1: 1206-1208, T2: 289, T3: 638, 651-652 |
| 2. | 1 | Primary, Secondary, Tertiary and Quaternary structure of proteins. | T3: 667 |
| 3. | 1 | Determination of primary structure of peptides | T1: 1226-1234 |

| | | | |
|---|---|---|---|
| 4. | 1 | Determination of N-terminal amino acid (by DNEB and Edman method) | T1: 1218-1221 |
| 5. | 1 | C-terminol amino acid (by thiohydantoin and Carboxypeptidase enzyme) | T3: 661 |
| 6. | 1 | Synthesis of simple peptides (upto dipeptides) by N-projection. | T1: 1222-1224, T3: 670 |
| 7. | 1 | C-activating groups and Merrifield solid phase synthesis | T1: 1224-1225, T3: 672 |
| 8. | 1 | Recapitulation and discussion of important questions | |
| | **Total No of Hours Planned For Unit 2 = 8** | | |
| | | **Unit – III** | |
| 1. | 1 | **Enzyme and Correlation with Drug action:** Mechanism of enzyme action, factors affecting enzyme action | R1: 186-187, 572 T1: 1333, T3: 214 |
| 2. | 1 | Coenzyme, cofactors and their role in biological reaction | R1: 184 |
| 3. | 1 | Specificity of enzyme action (Including Specificity) | T1:1333, R1:191 |
| 4. | 1 | Enzyme inhibitors and their importance, Phenomenon of inhibition (competitive, noncompetitive and allosteric inhibition) | R1: 201, 203, 210 |
| 5. | 1 | Drug action-receptor theory. Structure-activity relationship of drug molecules. | R1: 210 |
| 6. | 1 | Binding role of –OH, -$NH_2$, double bond and aromatic ring. | R1: 212-216 |
| 7. | 1 | Recapitulation and discussion of important questions | |
| | **Total No of Hours Planned For Unit 3 = 7** | | |
| | | **Unit – IV** | |
| 1. | 1 | **Nucleic Acids**: Components of Nucleic acids (Adenine, guanine, thymine and Cytosine (Structure only) | T1: 1357, T2: 811-812 |
| 2. | 1 | Other components of nucleic acids, Nucleosides and nucleotides (nomenclature) | T1: 1358, T2: 812-818 |
| 3. | 1 | Structure of polynucleotides, Structure of DNA (Watson-Crick model) | T2: 823 |
| 4. | 1 | Structure of RNA (types of RNA), Genetic Code | T1: 1363-1364, T2: 827-828 |
| 5. | 1 | Biological roles of DNA and RNA: Replication | T2: 824, T1: 1361 |
| 6. | 1 | Transcription and Translation | T2: 827, T1: 1361 |
| 7. | 1 | Recapitulation and discussion of important questions | |
| | **Total No of Hours Planned For Unit 4 = 7** | | |

| | | | |
|---|---|---|---|
| | | **Unit – V** | |
| 1. | 1 | **Lipids**: Introduction to lipids, Classification. Oils and Fats: common fatty acids present in oils and fats. | T1: 1180,1182 |
| 2. | 1 | Omega fatty acids, Trans fats, Hydrogenation, Saponification value, Iodine number. | R1: 345 |
| 3. | 1 | Biological importance of triglycerides, phospholipids, glycolipids and steroids (cholesterol) | T1: 1192, 1196-1198<br>R1: 824,829,831 |
| 4. | 1 | Concept of Energy in Biosystems. Caloric value of food. Standard caloric content of carbohydrates, proteins and fats. | R1:487 |
| 5. | 1 | Oxidation of foodstuff (organic molecules) as a source of energy for cells. Introduction to Metabolism (catabolism and anabolism) | R1: 487, 648, 652 |
| 6. | 1 | ATP: the universal currency of cellular energy, ATP hydrolysis and free energy change. Conversion of food into energy. | R1: 399 |
| 7. | 1 | Outline of catabolic pathways of Carbohydrate-Glycolysis, Fermentation, Kerbs Cycle. | R1: 616, 693-699, 615,528 |
| 8. | 1 | Catabolic pathways of Fats and Proteins. Interrelationships in the metabolic pathways of Proteins, Fats and Carbohydartes. | R1: 616,693,699,701 |
| 9. | 1 | ESE Question paper discussion | |
| 10. | 1 | ESE Question paper discussion | |
| | **Total No of Hours Planned For Unit 5 = 10** | | |
| **Total Hours Planned** | | **40** | |

**Text Books:**

1. Morrison R.T & Boyd R.N., (1992), Organic Chemistry, Dorling Kindersley Pvt. Ltd., (Pearson Education)
2. Finar I.L (2002), Organic Chemistry- Volume 1, Dorling Kindersley Pvt. Ltd., (Pearson Education)
3. Finar I.L (2002), Organic Chemistry- Volume 2, Dorling Kindersley Pvt. Ltd., (Pearson Education).

**Reference Books:**

1. Nelson D.L & Cox M.M, (2012), Lehninger's Principles of Biochemistry, 7th Edition
2. Berg J.M, Tymoczko J.L & Stryer L. (2002), Biochemistry. W.H. Freeman

## Unit-I
## Syllabus

Classification of carbohydrates, reducing and non-reducing sugars, General Properties of Glucose and Fructose, their open chain structure. Epimers, mutarotation and anomers. Determination of configuration of Glucose (Fischer proof). Cyclic structure of glucose. Haworth projections. Cyclic structure of fructose. Linkage between monosachharides, structure of disacharrides (sucrose, maltose, lactose) and polysacharrides (starch and cellulose) excluding their structure elucidation.

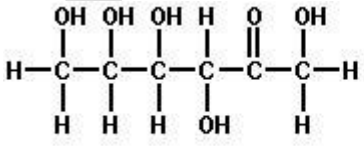
### Definition

**Carbohydrate**, class of naturally occurring compounds and derivatives formed from them. In the early part of the 19th century, substances such as wood, starch, and linen were found to be composed mainly of molecules containing atoms of carbon (C), hydrogen (H), and oxygen (O) and to have the general formula $C_6H_{12}O_6$; other organic molecules with similar formulas were found to have a similar ratio of hydrogen to oxygen. The general formula $C_x(H_2O)_y$ is commonly used to represent many carbohydrates, which means "watered carbon."

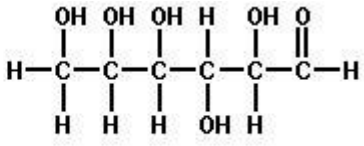
Carbohydrates are probably the most abundant and widespread organic substances in nature, and they are essential constituents of all living things. Carbohydrates are formed by green plants from carbon dioxideand water during the process of photosynthesis. Carbohydrates serve as energy sources and as essential structural components in organisms; in addition, part of the structure of nucleic acids, which contain genetic information, consists of carbohydrate.

### Classification and nomenclature

Although a number of classification schemes have been devised for carbohydrates, the division into four major groups—monosaccharides, disaccharides, oligosaccharides, and polysaccharides—used here is among the most common. Most monosaccharides, or simple sugars, are found in grapes, other fruits, and honey. Although they can contain from three to nine carbon atoms, the most common representatives consist of five or six joined together to form a chainlike molecule. Three of the most important simple sugars—glucose (also known as dextrose, grape sugar, and corn sugar), fructose (fruit sugar), and galactose—have the same molecular formula, ($C_6H_{12}O_6$), but, because their atoms have different structural arrangements, the sugars have different characteristics; i.e., they are isomers.



Fructose

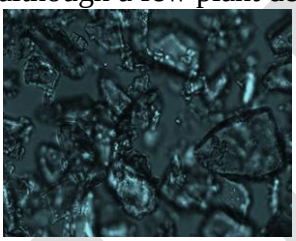


Glucose

Slight changes in structural arrangements are detectable by living things and influence the biological significance of isomeric compounds. It is known, for example, that the degree of sweetness of various sugars differs according to the arrangement of the hydroxyl groups (—OH) that compose part of the molecular structure. A direct correlation that may exist between taste and any specific structural arrangement, however, has not yet been established; that is, it is not yet

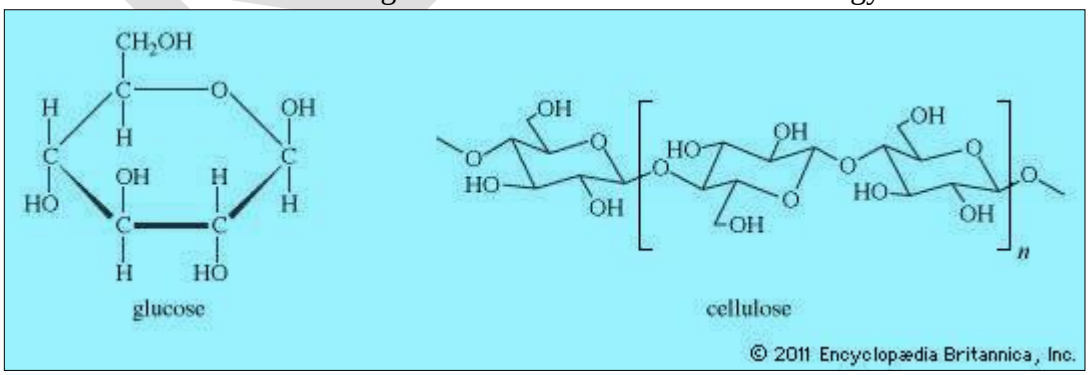
possible to predict the taste of a sugar by knowing its specific structural arrangement. The energy in the chemical bonds of glucose indirectly supplies most living things with a major part of the energy that is necessary for them to carry on their activities. Galactose, which is rarely found as a simple sugar, is usually combined with other simple sugars in order to form larger molecules.

Two molecules of a simple sugar that are linked to each other form a disaccharide, or double sugar. The disaccharide sucrose, or table sugar, consists of one molecule of glucose and one molecule of fructose; the most familiar sources of sucrose are sugar beets and cane sugar. Milk sugar, or lactose, and maltose are also disaccharides. Before the energy in disaccharides can be utilized by living things, the molecules must be broken down into their respective monosaccharides. Oligosaccharides, which consist of three to six monosaccharide units, are rather infrequently found in natural sources, although a few plant derivatives have been identified.



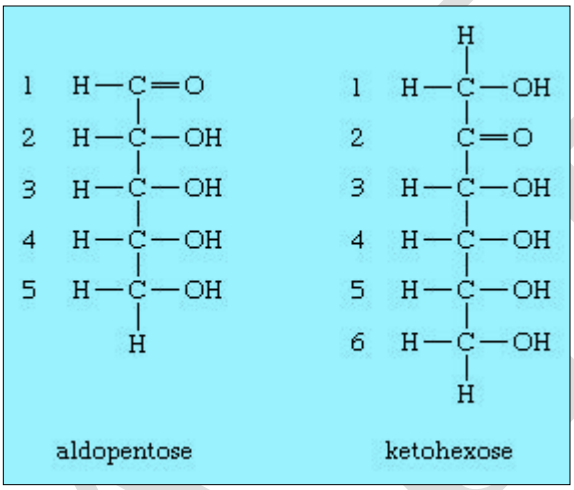
**lactose crystal**Lactose crystals are shown suspended in oil. Their distinct shape allows them to be identified in foods examined for research.© *Kayla Saslow, courtesy of the University of Wisconsin-Madison*

Polysaccharides (the term means many sugars) represent most of the structural and energy-reserve carbohydrates found in nature. Large molecules that may consist of as many as 10,000 monosaccharide units linked together, polysaccharides vary considerably in size, in structural complexity, and in sugar content; several hundred distinct types have thus far been identified. Cellulose, the principal structural component of plants, is a complex polysaccharide comprising many glucose units linked together; it is the most common polysaccharide. The starch found in plants and the glycogen found in animals also are complex glucose polysaccharides. Starch (from the Old English word *stercan*, meaning "to stiffen") is found mostly in seeds, roots, and stems, where it is stored as an available energy source for plants. Plant starch may be processed into foods such as bread, or it may be consumed directly—as in potatoes, for instance. Glycogen, which consists of branching chains of glucose molecules, is formed in the liver and muscles of higher animals and is stored as an energy source.



**Composition of cellulose and glucose** Cellulose and glucose are examples of carbohydrates. *Encyclopædia Britannica, Inc.*

The generic nomenclature ending for the monosaccharides is *-ose*; thus, the term *pentose* (*pent* = five) is used for monosaccharides containing five carbon atoms, and *hexose* (*hex* = six) is used for those containing six. In addition, because the monosaccharides contain a chemically reactive group that is either an aldehyde group or a keto group, they are frequently referred to as aldopentoses or ketopentoses or aldohexoses or ketohexoses. The aldehyde group can occur at position 1 of an aldopentose, and the keto group can occur at a further position (e.g., 2) within a ketohexose. Glucose is an aldohexose—i.e., it contains six carbon atoms, and the chemically reactive group is an aldehyde group.




**Biological significance**

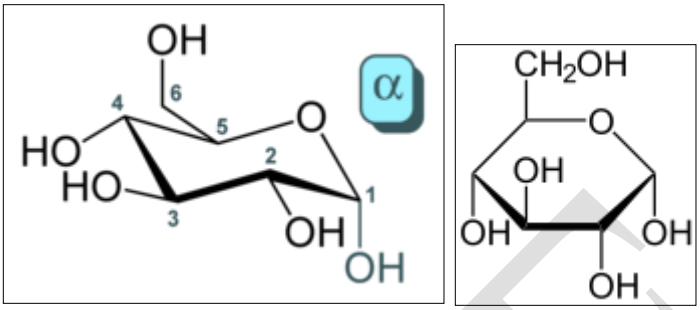
The importance of carbohydrates to living things can hardly be overemphasized. The energy stores of most animals and plants are both carbohydrate and lipid in nature; carbohydrates are generally available as an immediate energy source, whereas lipids act as a long-term energy resource and tend to be utilized at a slower rate. Glucose, the prevalent uncombined, or free, sugar circulating in the blood of higher animals, is essential to cell function. The proper regulation of glucose metabolism is of paramount importance to survival.

The ability of ruminants, such as cattle, sheep, and goats, to convert the polysaccharides present in grass and similar feeds into protein provides a major source of protein for humans. A number of medically important antibiotics, such as streptomycin, are carbohydrate derivatives. The cellulose in plants is used to manufacture paper, wood for construction, and fabrics.

**Reducing and Non-reducing Sugars**

The carbohydrates may also be classified as either reducing or non-reducing sugars. Cyclic acetals or ketals are not in equilibrium with their open chain carbonyl group containing forms in neutral or basic aqueous solutions. They cannot be oxidized by reagents such as Tollen's reagent ($Ag^+$, $NH_3$, $OH^-$) or $Br_2$. So, these are referred as non- reducing sugars. Whereas hemiacetals or hemiketals are in equilibrium with the open- chain sugars in aqueous solution. These compounds can reduce an oxidizing agent (eg. $Br_2$), thus, they are classified as a reducing sugar.

## Glucose




**Glucose** (also called **dextrose**) is a simple sugar with the molecular formula $C_6H_{12}O_6$. Glucose is the most abundant monosaccharide, a subcategory of carbohydrates. Glucose is mainly made by plants and most algae during photosynthesis from water and carbon dioxide, using energy from sunlight. There it is used to make cellulose in cell walls, which is the most abundant carbohydrate. In energy metabolism, glucose is the most important source of energy in all organisms. Glucose for metabolism is partially stored as a polymer, in plants mainly as starch and amylopectin and in animals as glycogen. Glucose circulates in the blood of animals as blood sugar. The naturally occurring form of glucose is D-glucose, while L-glucose is produced synthetically in comparably small amounts and is of lesser importance.

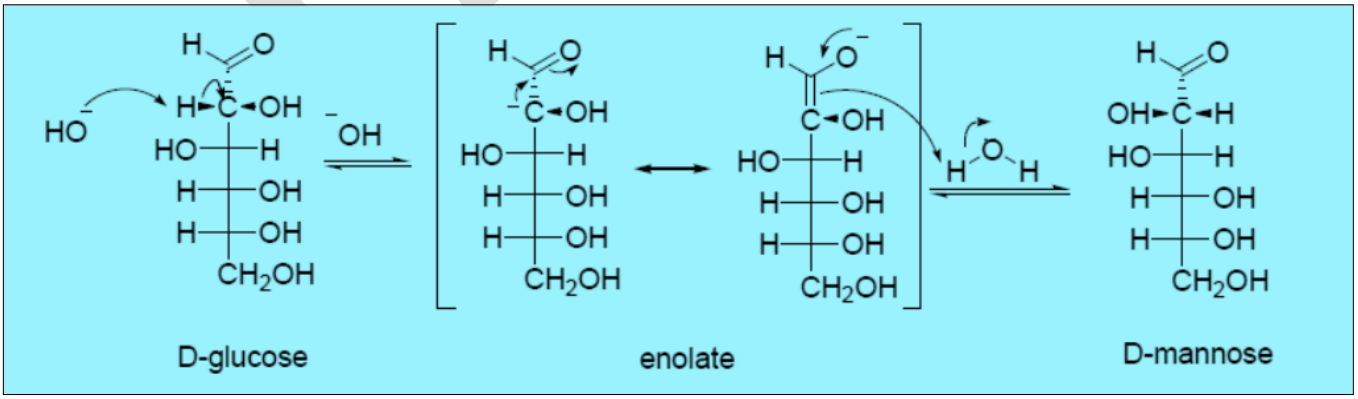
Glucose is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system. The name glucose derives through the French from the Greek γλυκός, which means "sweet," in reference to must, the sweet, first press of grapes in the making of wine. The suffix "-ose" is a chemical classifier, denoting a sugar.

***Reactions***

Monosaccharides contain *carbonyl* functional group and *alcohol* functional groups, so it can be oxidized or reduced and can react with nucleophiles to form corresponding products.

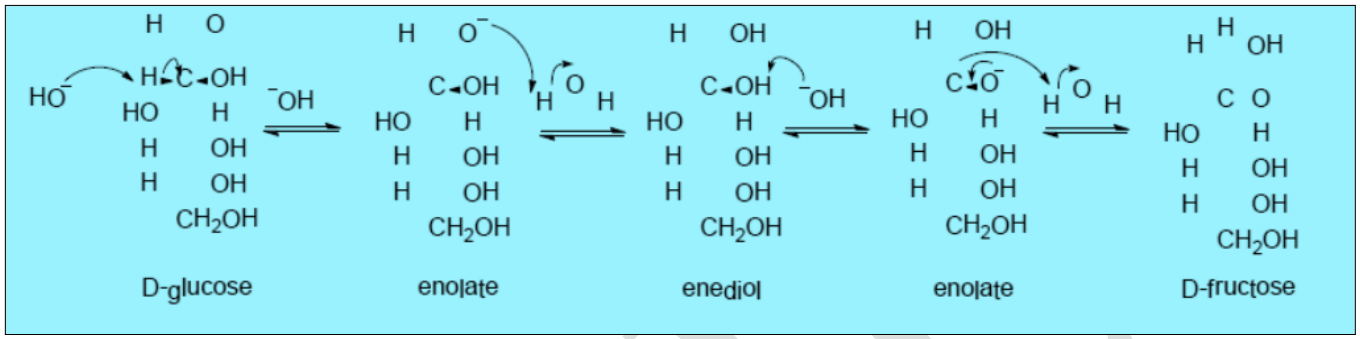
**Epimerization**

In the presence of base, D-glucose may be converted into D-mannose via the removal of hydrogen at C-2 carbon followed by protonation of the enolate



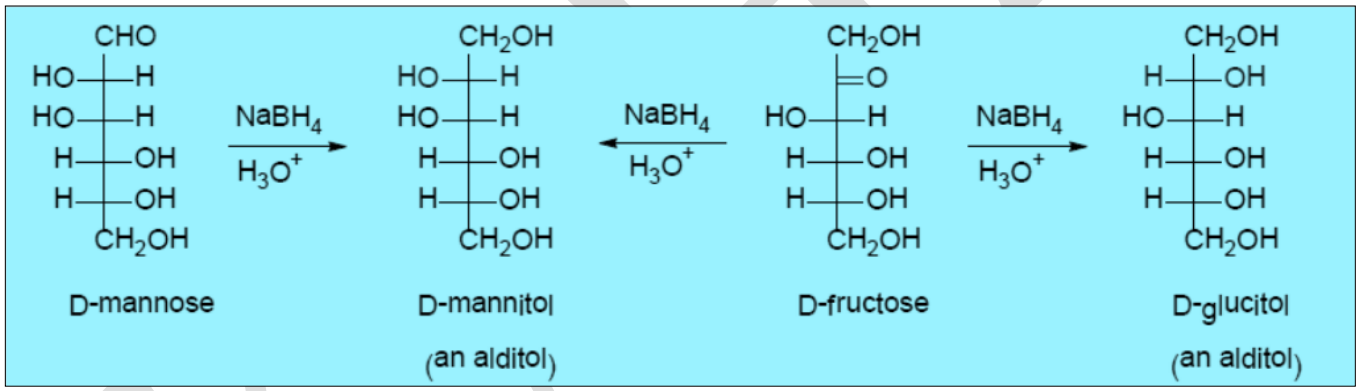
**Enediol Rearrangement**

The position of carbonyl group may shift via enediol intermediate under basic condition. For example, rearrangement of D-glucose gives D-fructose.



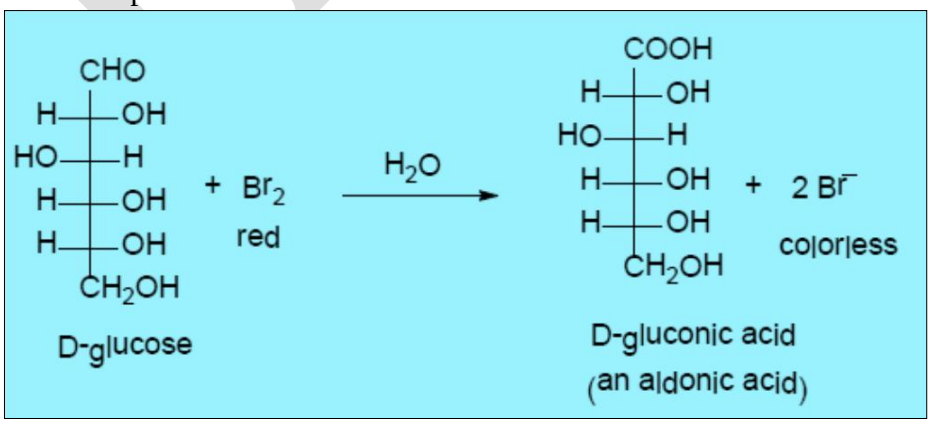

**Reduction**

The monosaccharide contains carbonyl group which can be reduced by the reducing agents such as $NaBH_4$. Reduction of aldose forms one alditol and ketose forms two alditols

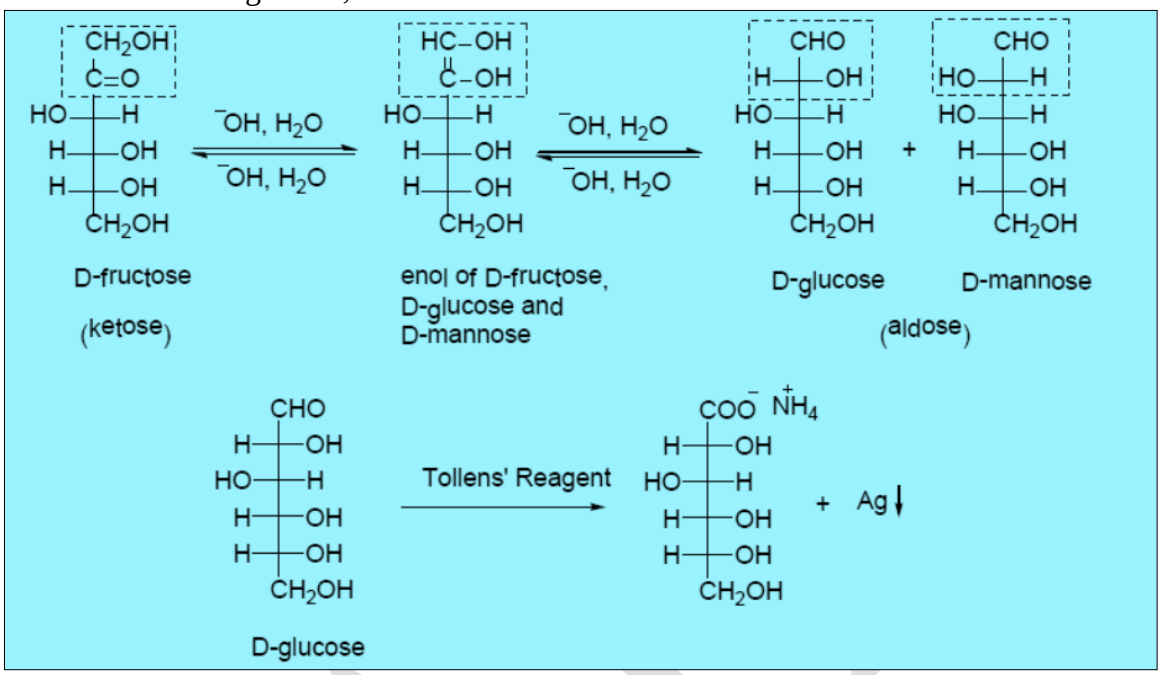



**Oxidation**

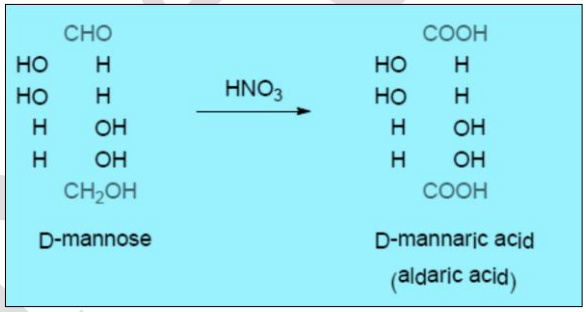
*Bromine water* oxidizes aldehyde functional group, but it cannot oxidize ketones or alcohols. Therefore, aldose can be distinguished from ketose by observing reddish-brown colour of bromine. The oxidized product is an *aldonic acid.*



*Tollen's reagent* can oxidize both aldose and ketose to aldonic acids. For example, the enol of both D-fructose and D-glucose, as well as the enol of D- mannose are same.

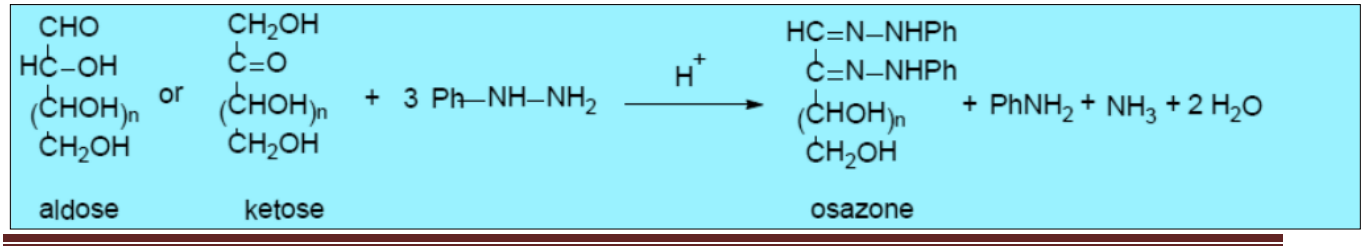



Both aldehyde and primary alcohol groups of an aldose are oxidized by strong oxidizing agent such as $HNO_3$. The oxidized product called an aldaric acid. Ketose also reacts with $HNO_3$ to give more complex product mixtures

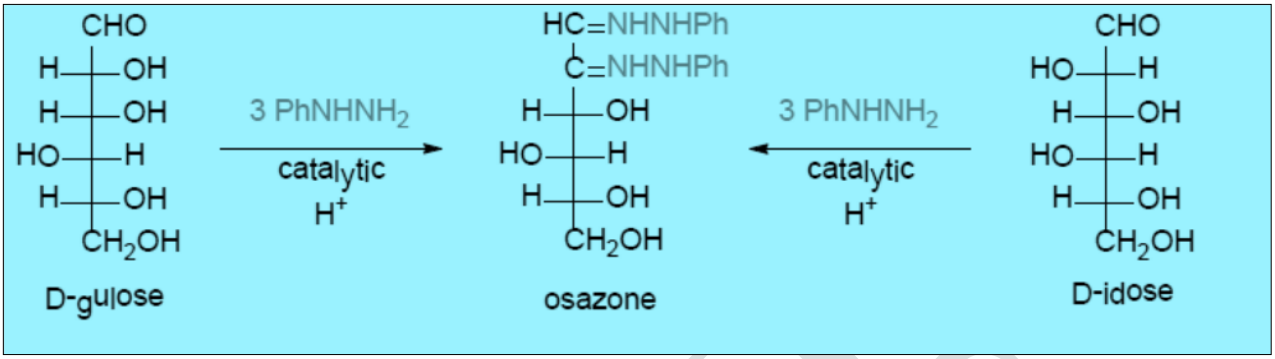



**Osazone Formation**

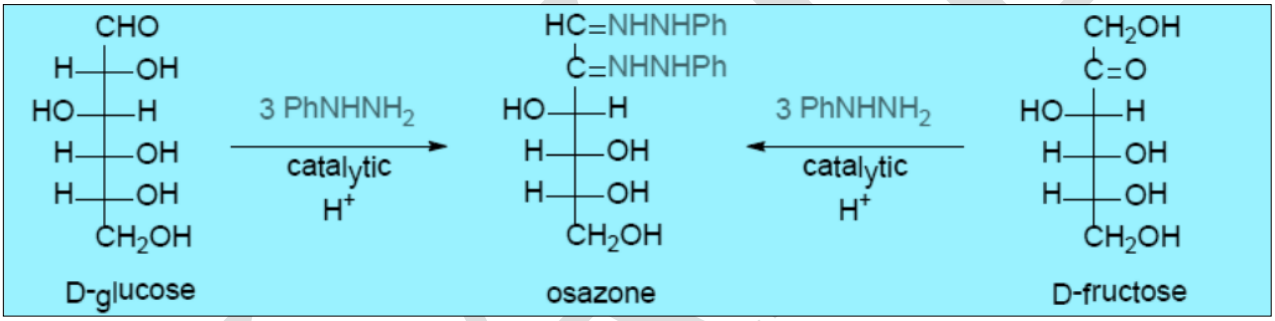
Aldose and ketose react with one equiv of phenylhydrazine to produce phenylhydrazones. In contrast, both C-1 and C-2 react with three equivalent of phenylhydrazine to form a bis-hydrazone known as an *osazone.*



The configuration at C-1 or C-2 is lost in the formation of osazone, C-2 epimers form identical osazones. For example, D-gluose and D-idose are C-2 epimers; both form the same osazone.

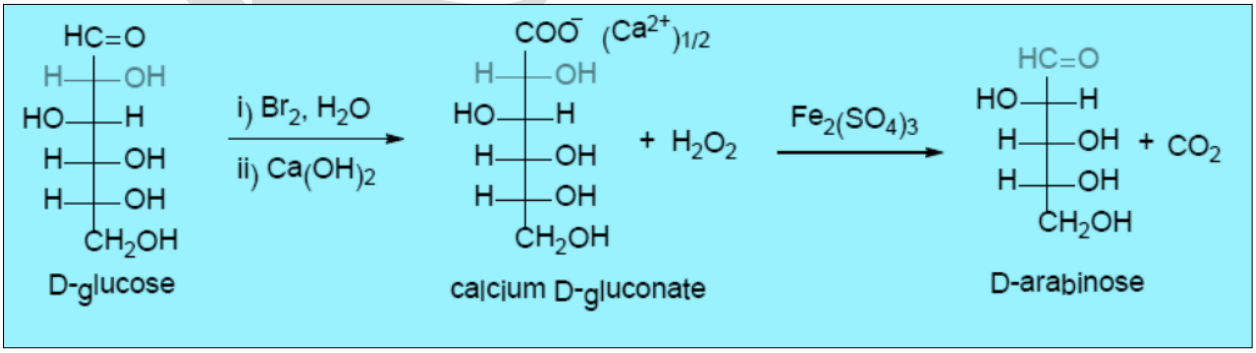



Ketose reacts with phenylhydrazine at C-1 and C-2 position to form osazone. D-Glucose and D-fructose form the same osazone




**The Ruff Degradation**

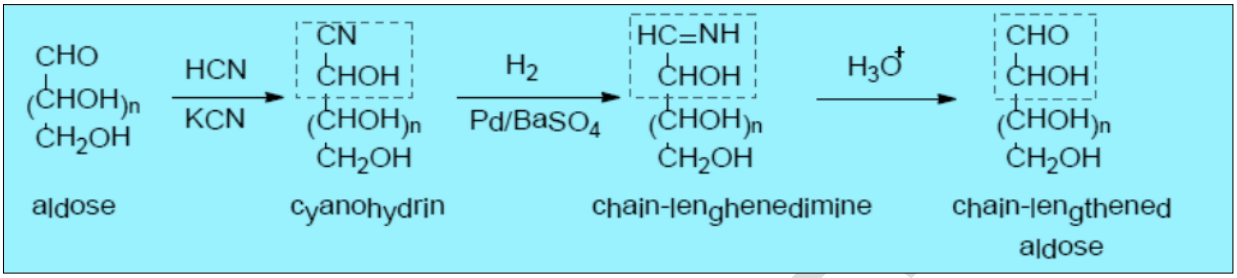
Aldose chain is shortened by oxidizing the aldehyde to –COOH, then decarboxylation. In the Ruff degradation, the calcium salt of an aldonic acid is oxidized with hydrogen peroxide. Ferric ion catalyzes the oxidation reaction, which cleaves the bond between C-1 and C-2, forming an aldehyde. The calcium salt of the aldonic acid prepared from oxidation of an aldose with an aqueous solution of bromine and then adding calcium hydroxide to the reaction mixture.




**The Kiliani–Fischer Synthesis**

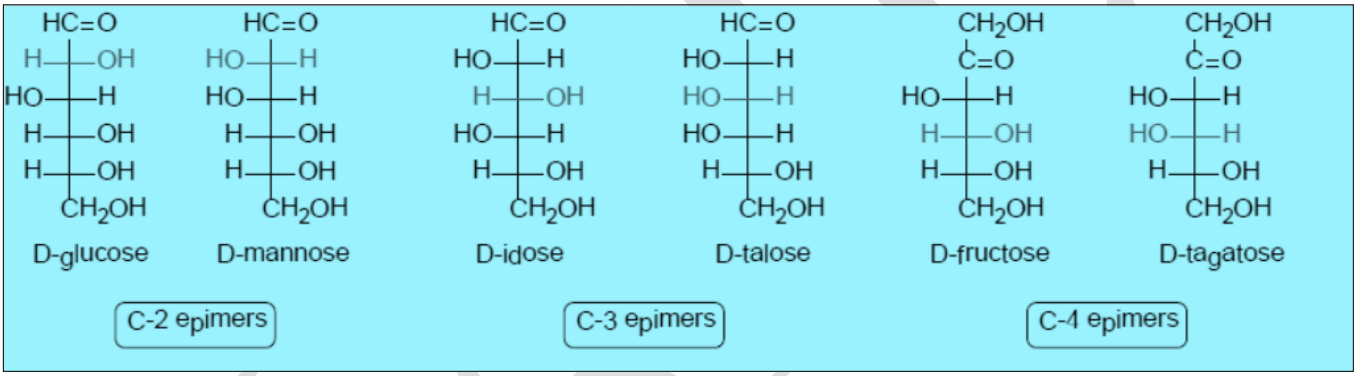
An aldose carbon chain can be increased by one carbon in a Kiliani–Fischer synthesis. It is the

opposite of Ruff Degradation reaction. This synthesis leads to formation of a pair of C-2 epimers.




## Epimers

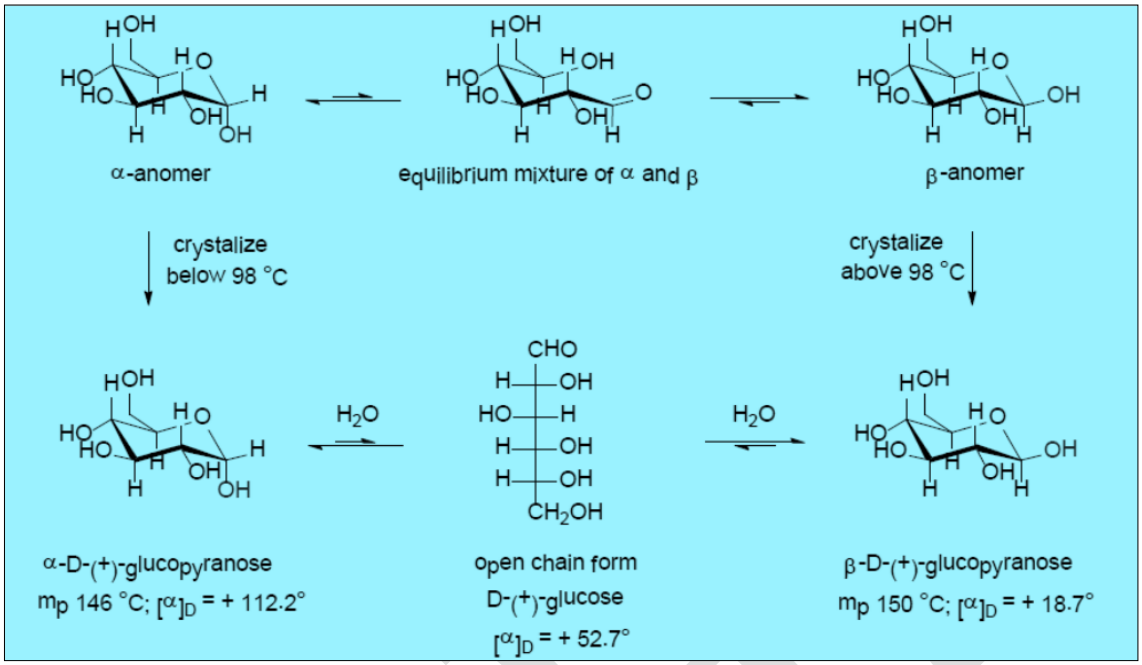
***Epimers*** are stereoisomers that differ in configuration of only one asymmetric carbon of enantiomers or diastereomers. Example, D-glucose and D-mannose are C-2 epimers and D-glucose and D-talose are C-3 epimers. D-fructose and D-tagatose are C-4 epimers of ketohexoses.




## Mutarotation

Normally D-(+)-glucose has a melting point of 146 °C. However, when D-(+)-glucose is crystallized by evaporating an aqueous solution kept above 98 °C, a second form of D- (+)-glucose with a melting point of 150 °C can be obtained. When the optical rotations of these two forms are measured, they are found to be significantly different, but when an aqueous solution of either form is allowed to stand, its rotation changes. The specific rotation of one form decreases and the other increases, until both solutions show the same value.

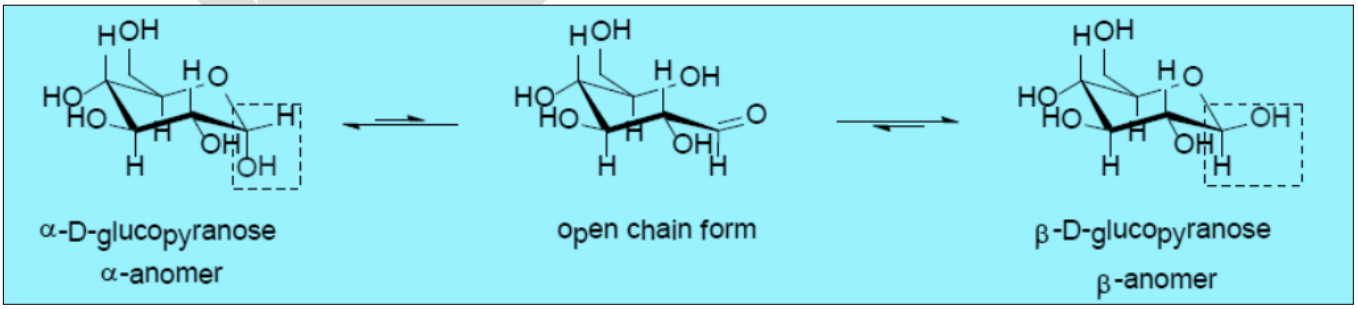
For example, a solution of D-(+)-glucose (mp 146 °C) specific rotation gradually decreases from an initial value of + 112.2° to + 52.7°, while The D-(+)- glucose (mp 150 °C) specific rotation gradually increases from an initial value of + 18.7° to + 52.7°. The three forms of glucose reach equilibrium concentrations with the specific rotation of +52.7. This change ("mutation") in the specific rotation toward equilibrium is called ***mutarotation.***



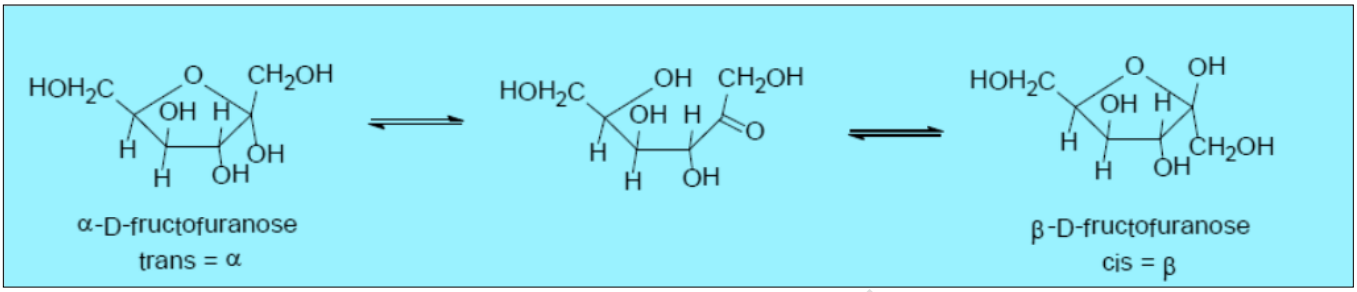

**Anomeric Effect**

When a pyranose or furanose ring closes, the hemiacetal carbon atom is converted from a flat carbonyl group to an asymmetric carbon. Depending on which face of the (protonated) carbonyl group is attacked, the hemiacetal –OH group can be directed either up or down. These two orientations of the hemiacetal –OH group give diastereomeric products called anomers, and the hemiacetal or acetal carbon atom is called the anomeric carbon atom. The preference of certain substituents bonded to the anomeric carbon for the axial position is called the anomeric effect. *Ano* is Greek for "upper"; thus, anomers

iffer in configuration at the upper-most asymmetric carbon. The anomeric carbon is the only carbon in the molecule that is bonded to two oxygen atoms. The anomer with the anomeric –OH group down (axial) is called the *α*-anomer, and the one with the anomeric –OH group up (equatorial) is called the *β*-anomer.




In fructose, the *α*-anomer has the anomeric - OH group down, *trans* to the terminal – $CH_2OH$ group, while the *β*-anomer has it up, *cis* to the terminal –$CH_2OH$ group




**The Fischer proof of the structure of (+)-glucose**

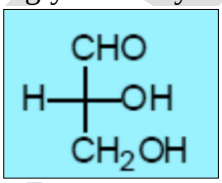
Started in 1888, 12 years after the proposal that carbon was tetrahedral, and thus had stereoisomers.

Tools:

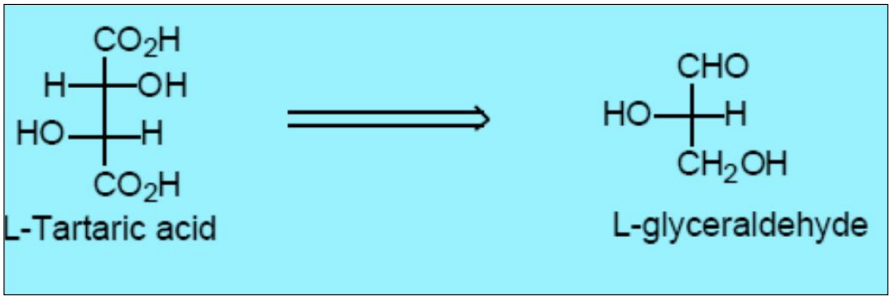
- melting points
- optical rotation (determine whether a molecule is optically active)
- chemical reactions

Fischer knew:

- (+)-glucose is an aldohexose.
- Therefore, there are 4 stereocenters and $2^4$ = 16 stereoisomers (8 D-sugars and 8 L-sugars)
- At this time could not determine the actual configuration (D or L) of sugars
- Fischer arbitrarily assigned D-glyceraldehyde the following structure.

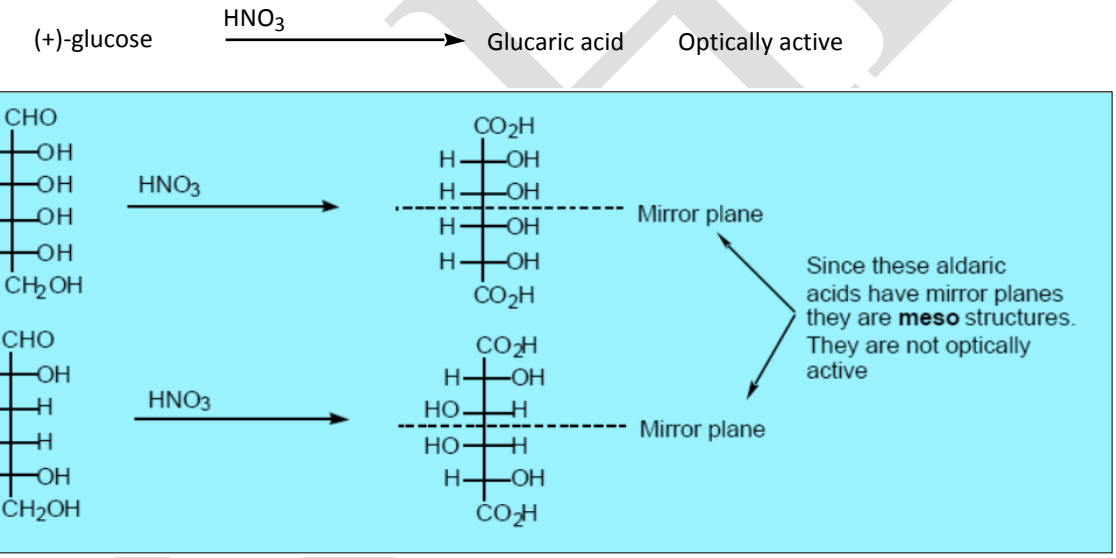


- In 1951 Fischer was shown to have guessed correctly.

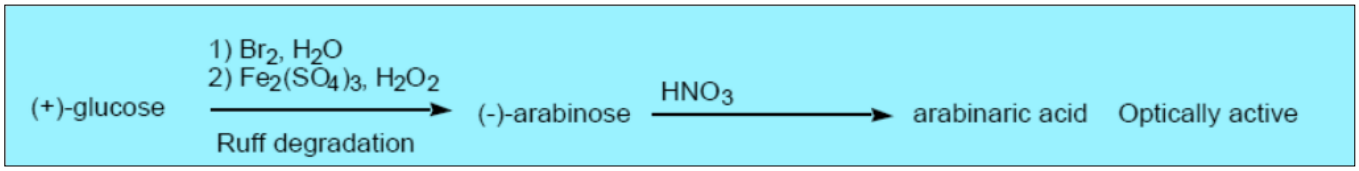


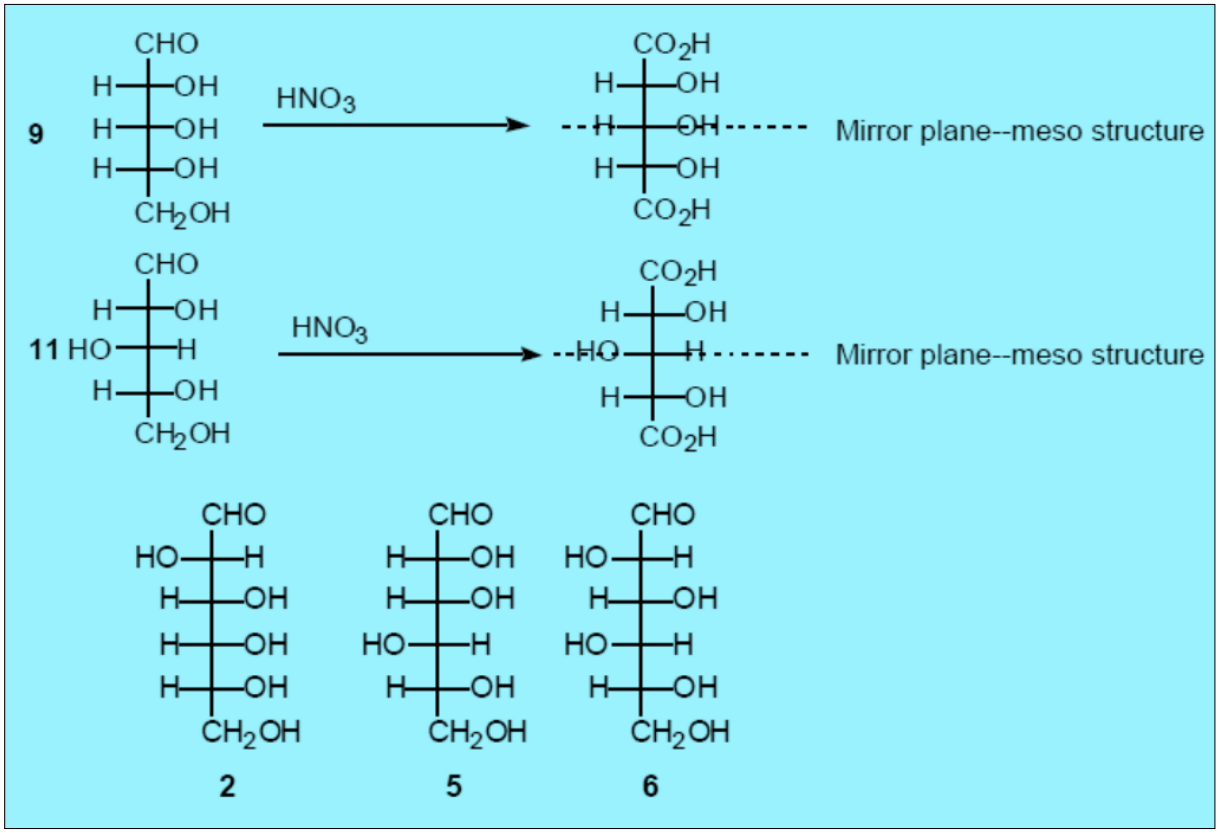

Which of the 8 D-aldohexoses is (+)-glucose???

1) Oxidation of (+)-glucose with nitric acid gives an aldaric acid, glucaric acid, that is optically active. Therefore (+)-glucose cannot have structures **1** or **7**, which would give optically inactive aldaric acids.

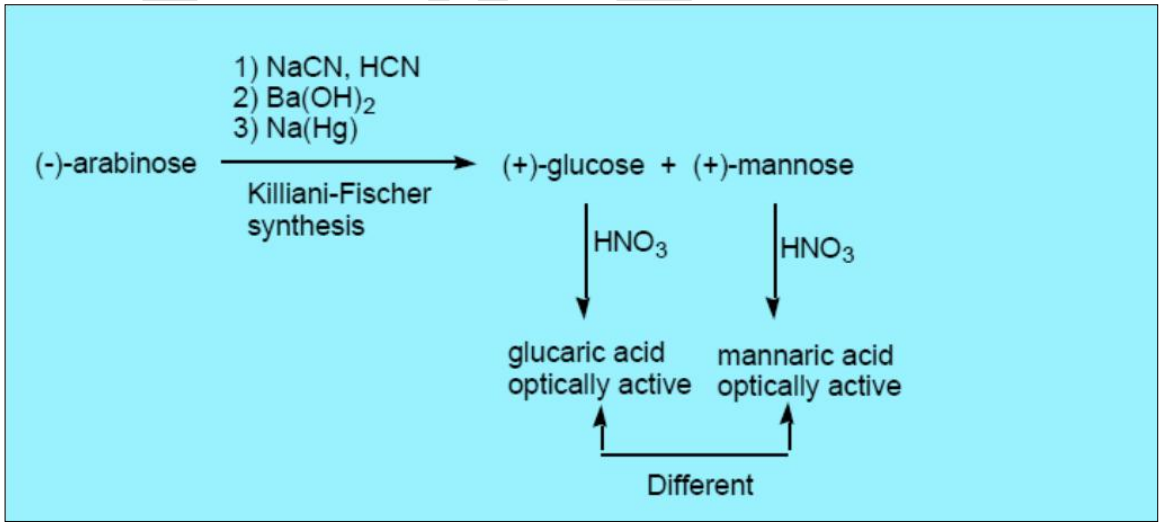


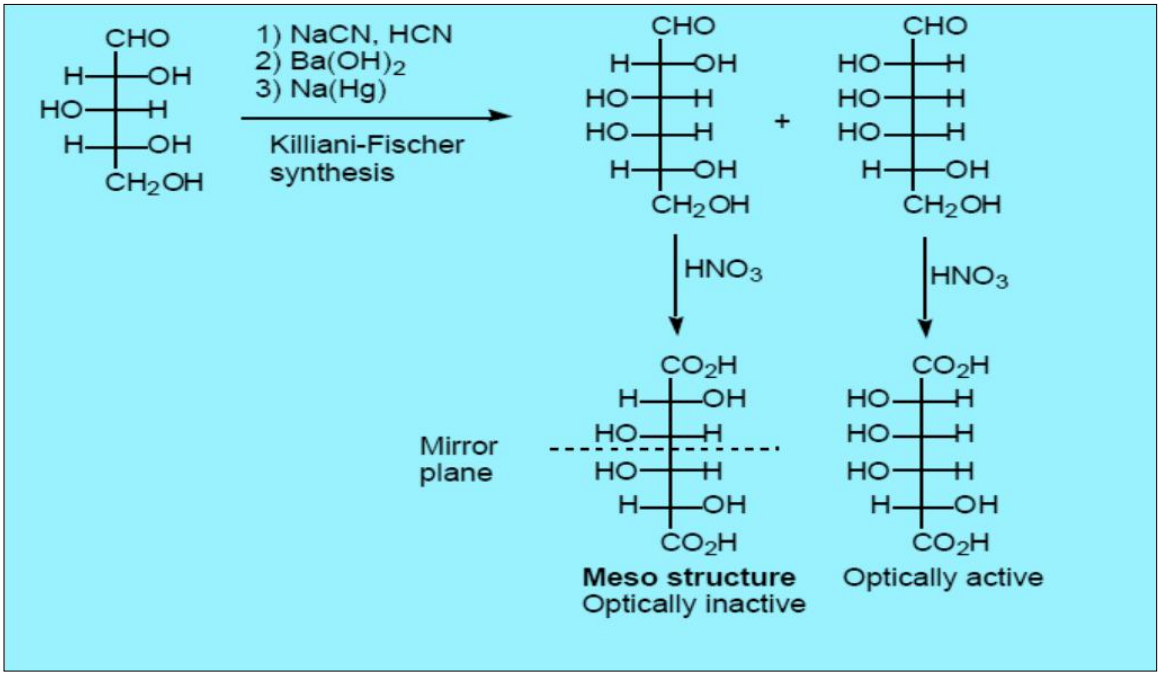

2) Ruff degradation of (+)-glucose gives (-)-arabinose. Oxidation of (-)-arabinose with nitric acid gives arabanaric acid, which is optically active. Therefore, (-)-arabinose cannot have structures **9** or **11**, which would give optically inactive aldaric acids. If arabinose cannot be **9** or **11**, (+)-glucose cannot be **2** (**1** was already eliminated), **5** or **6**, which would give **9** or **11** in a Ruff degradation.



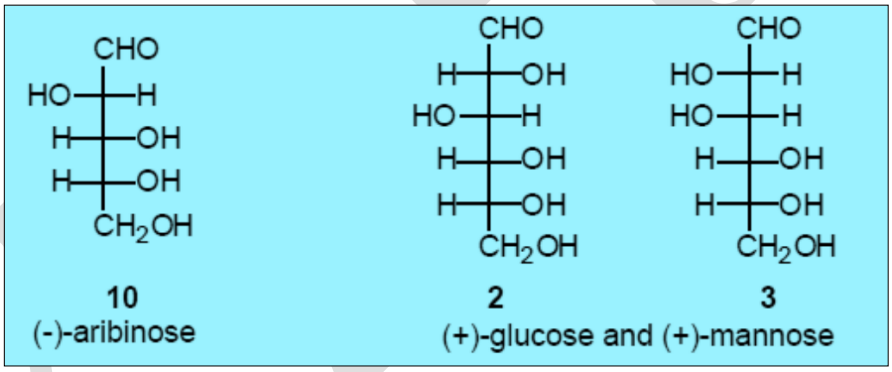



3) Killiani-Fischer chain extension of (-)-arabinose gives (+)-glucose and (+)-mannose. Both of which give optically active aldaric acids when oxidized with nitric acid. Therefore, (-)-arabinose cannot be structure **12**. **12** would give **7** and **8** in a Killiani- Fischer chain extension. **8** would give an optically active aldaric acid, but **7** would give an optically inactive aldaric acid.



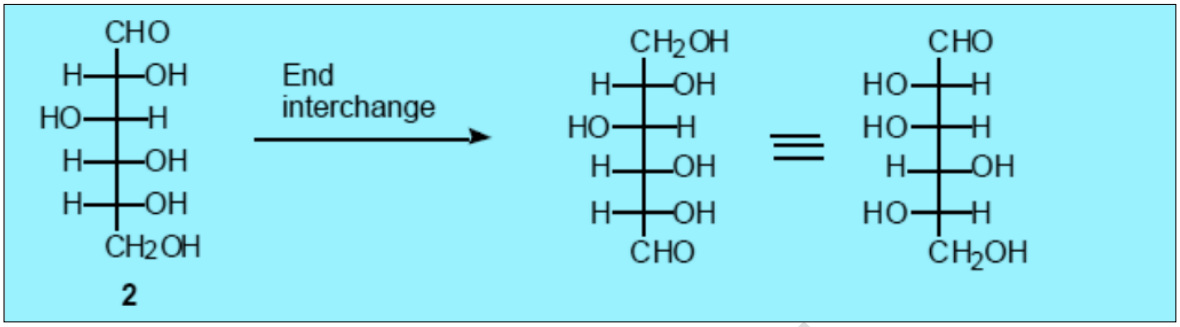


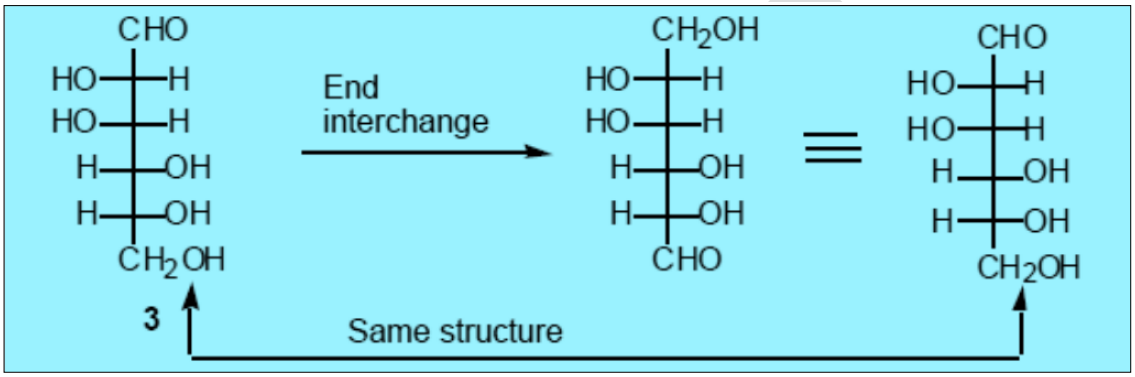

4) The structure of arabinose is **10**. Therefore the structures of (+)-glucose and (+)- mannose are **2** and **3**, but which is which????

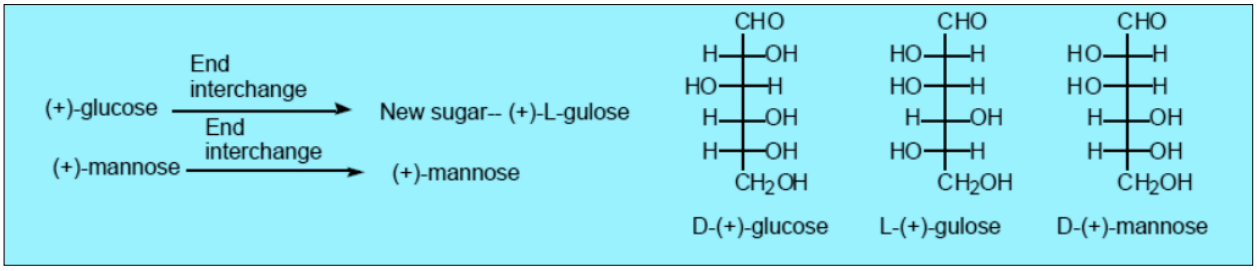



Fischer had previously developed a method to interchange the ends of a sugar (the aldehyde is converted to a $CH_2OH$ and the $CH_2OH$ is converted to an aldehyde, but we won't worry about how this is done). Fischer reasoned that if ends of **2** were

interchanged, a new L-aldohexose would be obtained. On the other hand, if the ends of **3** were interchanged, the product would be the same (structure **3**). When the ends of (+)-glucose were interchanged a new sugar was obtained, which Fischer named L-gulose. When the ends of (+)-mannose were interchanged, the product was (+)-mannose. **Therefore the structure of (+) glucose is structure 2, and strucutre 3 is (+)-mannose.**

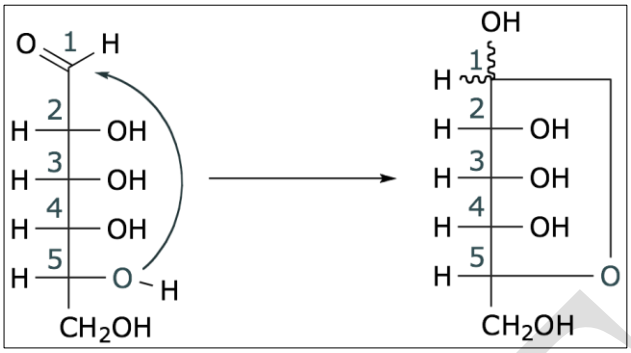



Aldoses contain an aldehyde group and hydroxyl groups, and they undergo intramolecular reactions to form cyclic hemiacetals. These five-membered and six-membered cyclic hemiacetals are often more stable than the open-chain form of the sugar.

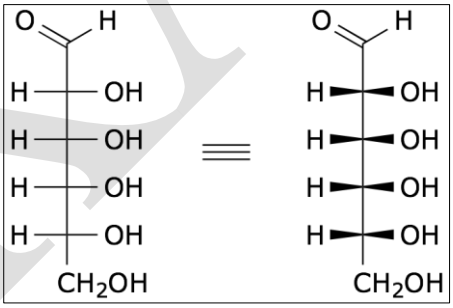
In D-allose, nucleophilic attack on the carbonyl carbon of the aldehyde group by the hydroxyl group on carbon five (C-5) gives a six-membered ring cyclic hemiacetal. The new bond that forms between the oxygen atom on C-5 and the hemiacetal carbon atom C-1 is usually shown by using a box in the Fischer projection. This cyclic structure is called the pyranose ring form of the sugar.



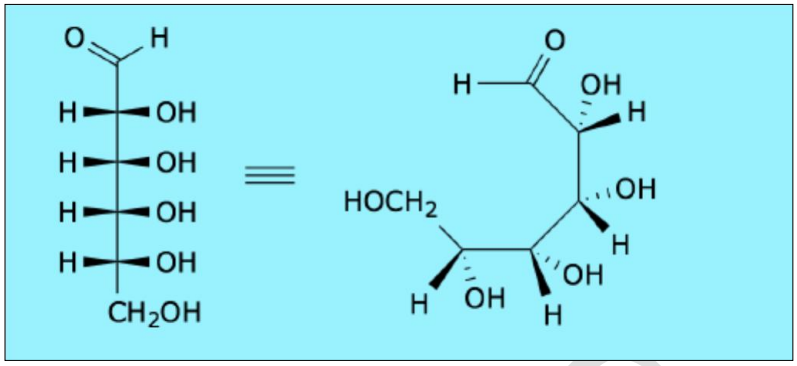
When the cyclic hemiacetal forms, the C-1 carbon atom becomes a new stereogenic center and can have either an *R*- or an *S*-configuration. To illustrate the ambiguity in the configuration at this new stereogenic center, squiggly lines are used in the Fischer projection to connect the hydrogen and the hydroxyl group to C-1.

A Fischer projection can illustrate the structure of the cyclic hemiacetal form of a sugar, but it lacks something aesthetically as far as representing the six-membered ring in the structure. In addition, this type of Fischer projection gives little information about the orientation of the groups on C-2 through C-5 in the cyclic form of the sugar.

Sugar structures drawn using a flat polygon to represent the ring are called Haworth structures. Drawing the correct Haworth structure of the cyclic hemiacetal form of the sugar from a Fischer projection of the acyclic form of a sugar is not difficult as long as you follow a few guidelines. Recall that a Fischer projection represents a fully eclipsed conformation of the molecule, in which all of the horizontal bonds are oriented out of the plane and all of the vertical bonds are oriented into the plane. In the Fischer projection for D-allose, all of the horizontal bonds are oriented coming out of the plane as shown.



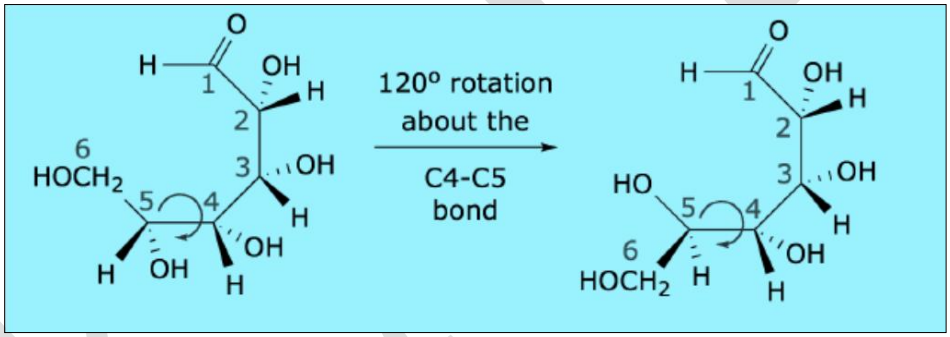
The vertical carbon-carbon bonds in the Fischer projection of D-allose are all oriented into the plane. It is easier to see the orientation of the vertical carbon-carbon bonds if you turn the structure $90^{o}$ to the right and look at a side view of the structure.



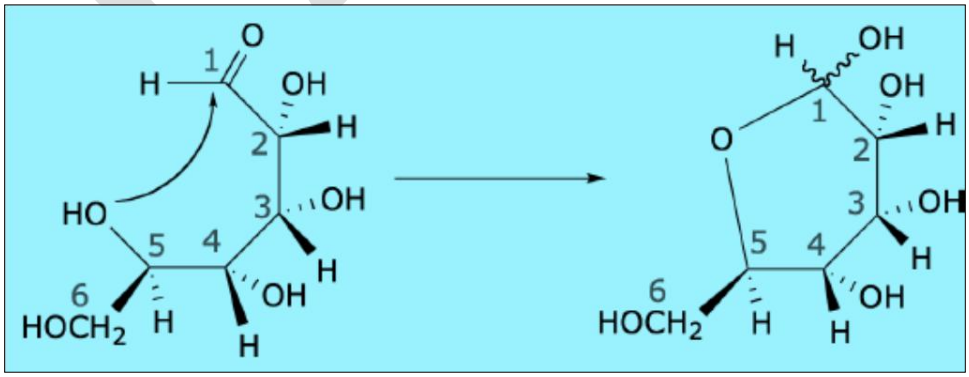
Turning the structure 90o to the right orients the hydroxyl groups on C-2 through C-5 into the plane defined by the carbon atom backbone. This side view of the molecule gives a better perspective of the eclipsed conformation of the sugar than does the Fischer projection. In addition, this perspective makes it easier to see how the cyclic hemiacetal forms.

To form the hemiacetal, the hydroxyl group on C-5 must be properly aligned with the sugar's carbonyl carbon for nucleophilic attack. Rotating $120^{o}$ around the bond between C-4 and

C-5 moves the C-5 hydroxyl group into the same plane as the carbonyl group. This conformational change moves the -$CH_2OH$ group on C-5 from its orientation in the same plane as the carbon atoms to out of the plane toward you, and

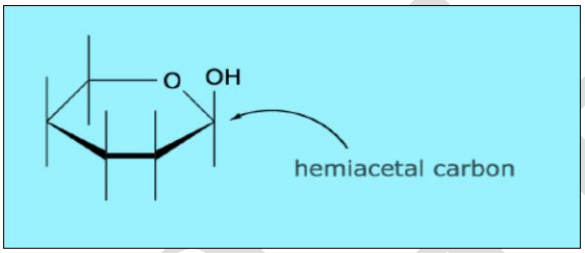



the C-5 hydroxyl group is now positioned properly for intramolecular nucleophilic attack on the carbonyl group. This gives the six-membered ring cyclic hemiacetal.

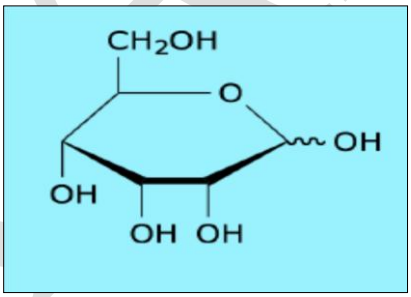


This cyclization process creates a new stereogenic center at the hemiacetal carbon C-1, which is also called the anomeric carbon. Squiggly lines are used to represent the bonds to the H and OH on the hemiacetal carbon atom because this new stereogenic center could have either an *R*- or an *S*-configuration. These steps illustrate how the sugar's cyclic hemiacetal structure forms, but we still need to draw the ring as a flat hexagon to get the Haworth structure of the sugar.

In a Haworth structure of a pyranose ring hemiacetal, the oxygen atom in the ring is usually drawn in the upper right-hand position of the hexagon, with the hemiacetal carbon to the right of this position. The bonds to the groups attached to the ring carbons are drawn using vertical lines to indicate whether a group is oriented to the top-face or to the bottom-face of the ring.

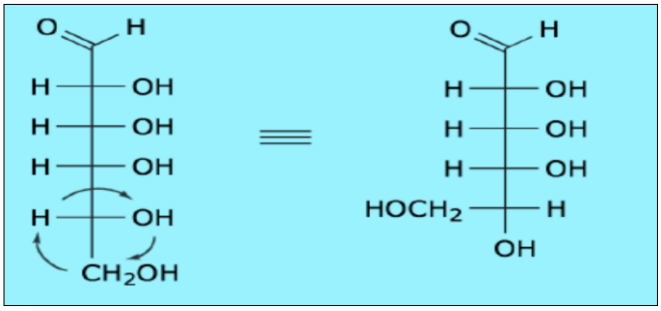



The configurations at the stereogenic centers in a Haworth structure of a sugar determine the identity of the sugar. The previous cyclic structure for D-allose shows that the hydroxyl groups on C-2, C-3, and C-4 are all oriented toward the bottom face of the ring, while the $CH_2OH$ group on C-5 is oriented toward the top face of the ring. Placing these groups on the structure gives the following Haworth structure for D-allose. (The hydrogens on the ring's carbon atoms are not shown for clarity's sake, and again, the ambiguity in the configuration at C-1 is shown by using a squiggly line).



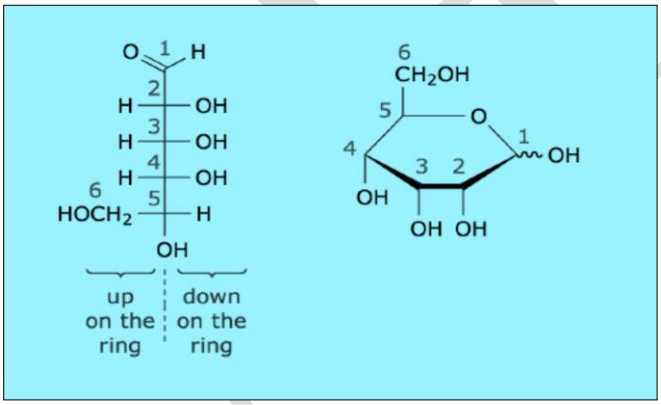

**Drawing a Haworth Structure from a Fischer Projection**

The most important thing to keep straight in drawing the correct Haworth structure of a sugar is that the stereochemistry at C-2 through C-5, because a change in the configuration at any of these stereogenic centers changes the identity of the sugar. As we saw in the analysis above, a conformational change is needed to get the C-5 hydroxyl group in the proper orientation far attack on the carbonyl group. We can illustrate this conformational change on the Fischer projection of the sugar as a rotation about the C4–C5 bond, swapping the positions of the H, the OH, and the $CH_2OH$ groups on C-5. The second Fischer projection below is simply a different conformation of the same sugar as the first one.

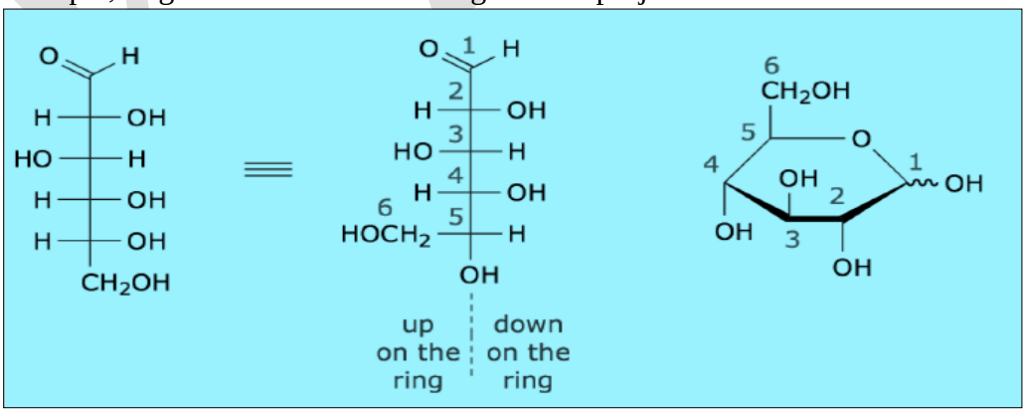


The second Fischer projection has the proper conformation for cyclic hemiacetal formation. Recall that to view this cyclization we turned the structure $90^{o}$ to the right. This turn takes all of the groups that are on the right-hand side of the backbone in the Fischer projection and orients them into the plane, while all of the groups on the left-hand side of the backbone are now oriented out of the plane. Since the orientations of these groups are retained when the cyclic

hemiacetal forms, any group on the right-hand side in the Fischer projection will be on the bottom face of the Haworth structure, while all of the groups on the left-hand side of the Fischer projection will be on the top face of the Haworth structure. Numbering the carbon atoms in the Fischer projection and on the Haworth structure makes it easy to put the groups on the ring carbons in the proper orientation.



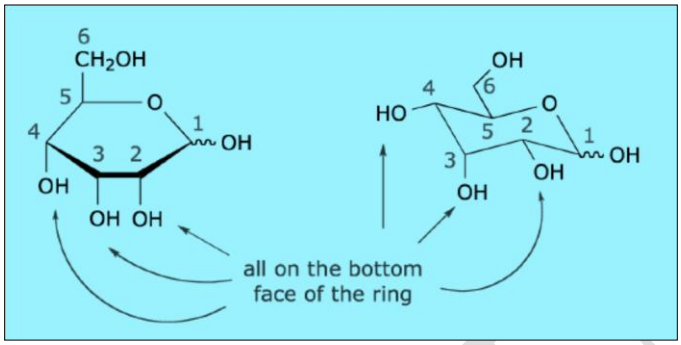

As a second example, D-glucose has the following Fischer projection and Haworth structure:




**Drawing a Sugar's Chair Conformation from a Haworth Structure or Fischer Projection**

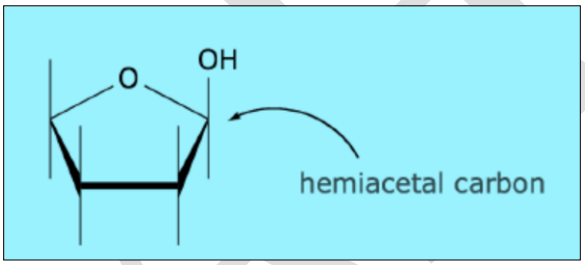
If you have either the Haworth structure or the Fischer projection of the sugar, drawing the chair conformation of the sugar is easy as long as you remember the orientations of the axial and equatorial

bonds on each carbon atom of the chair conformation. For example, given the Haworth structure, the chair conformation for D-allose is:

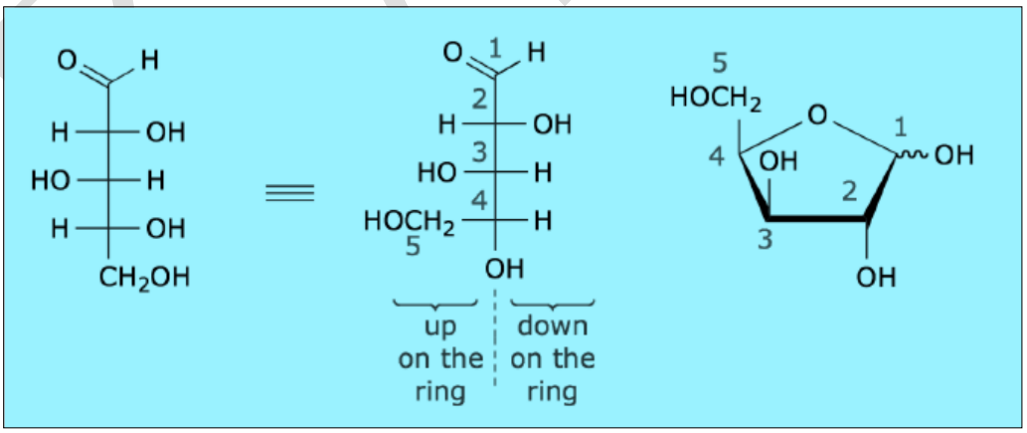



**Furanose Ring systems**

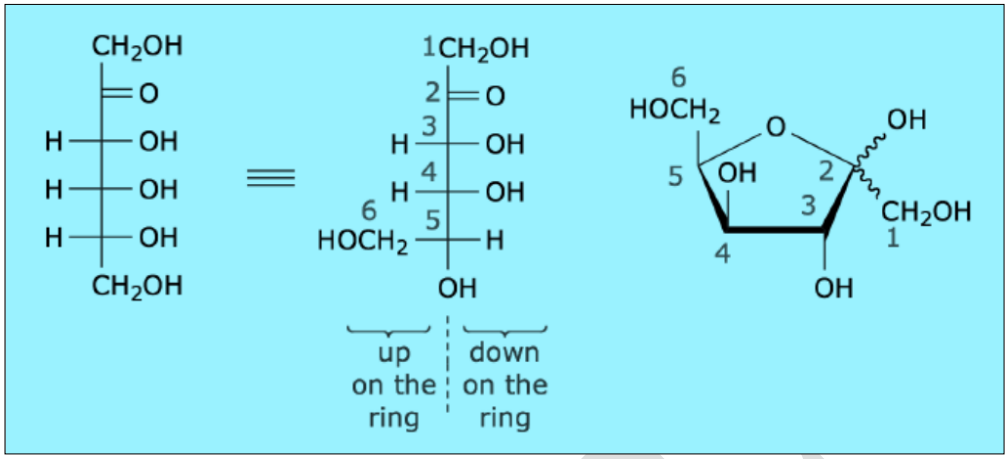
Many sugars (ketohexoses, aldopentoses, and in some cases even aldohexoses) form five- membered ring cyclic hemiacetals, which are called furanose ring forms. These cyclic hemiacetal structures form through exactly the same process was previously outlined for the formation of the pyranose rings of aldohexoses. In the furanose systems, a pentagon is used to represent the cyclic hemiacetal, with the oxygen atom at the apex of the pentagon.




The Fischer projection and the Haworth structure for the aldopentose D-xylose are given below.




The Fischer projection and the Haworth structure for furanose ring form of the ketohexose D- sorbose are shown below. Note that in the cyclic hemiacetal form of this keto-sugar, the anomeric carbon is C-2, not C-1 as it was in the previous examples.



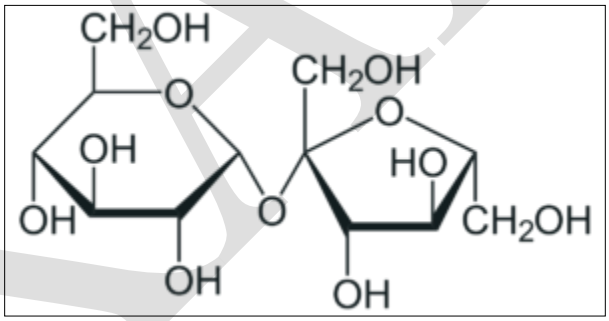

**Disaccharides**

Disaccharides are sugars (carbohydrate molecules) that form when two simple sugars i.e. monosaccharides combine to form a disaccharide.

Cyclic monosaccharides react with alcohols to form acetals and ketals. Sometimes this alcohol is actually a carbohydrate since they function very similarly to alcohols. So when this happens individual monosaccharides link together to make an acetal. This linkage is known as *glycosidic linkage.*

This linkage is an oxide linkage formed by the loss of a water molecule. When two monosaccharides are linked together by glycosidic linkage the resulting product is a disaccharide. Now let us take a look at some common and important disaccharides.

**Sucrose**



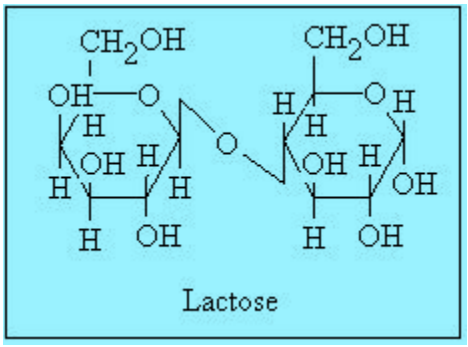

This is the most important disaccharide. It is popularly known as *table sugar*. Sucrose is found in all photosynthetic plants. It is commercially obtained from sugarcane and sugar beets via an industrial process. Let us take a look at some chemical properties of sucrose

- The molecular formula of sucrose is **$C_{12}H_{22}O_{11}$.**
- If sucrose goes through acid catalysed hydrolysis it will give one mole of D-Glucose and one mole of D-Fructose.
- The chemical structure of sucrose comprises of α form of glucose and β form of fructose
- The glycosidic linkage is α linkage because the molecule formation is in α orientation
- Sucrose is a non-reducing sugar. As you can see from the structure it is combined (linked) at the hemiacetal oxygen and does not have a free hemiacetal hydroxide

- Since has no free hemiacetal hydroxide it does not show mutarotation (α to β conversion). Sucrose also does not form osazones for the same reason.

- We can prove the structural formula of sucrose by hydrolysing it with α-glycosidase enzymes which only hydrolyses α glucose. This test is positive for sucrose.

**Lactose**

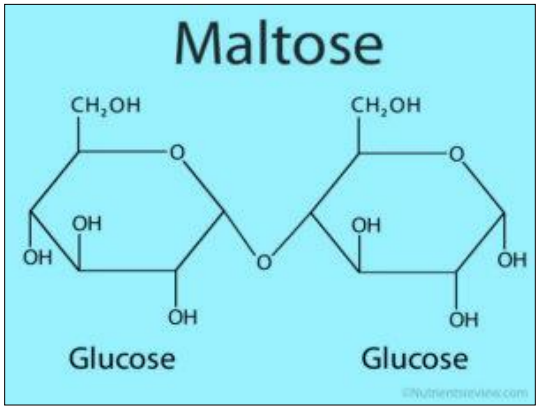



This is a disaccharide you may already be familiar with. Lactose is the primary ingredient found in the milk of all mammals. Unlike the majority of saccharides, lactose is not sweet to taste. Lactose consists of one galactose carbohydrate and one glucose carbohydrate. These are bound together by a 1-4 glycosidic bond in a beta orientation.

If you look at the structure of lactose you will see that there is one significant difference between galactose and glucose. Galactose's fourth carbon has a different orientation in galactose than in sucrose. If it was not so the resulting molecule would have just been sucrose (glucose+glucose) instead of lactose.

Also from the structure, we can notice that lactose is a reacting sugar since it has one free hemiacetal hydroxide. So when we react Lactose with bromine water it will give monocarboxylic acid.

**Maltose**




Maltose is another disaccharide commonly found. It has two monosaccharide glucose molecules bound together, The link is between the first carbon atom of glucose and the fourth carbon of another glucose molecule. This, as you know, is the one-four glycosidic linkage. Let us look at a few of its properties

- On acid catalysed hydrolysis one mole of maltose gives two moles of D-glucose.
- Maltose has a free hemiacetal hydroxide, hence it undergoes mutarotation. It exists as both α-Maltose and also β-Maltose

- For the same reasons it also gives a positive test with Benedicts and Tollens reagent.

**Polysaccharides**

The polysaccharides are the most abundant carbohydrates in nature and serve a variety of functions, such as energy storage or as components of plant cell walls. Polysaccharides are very large polymers composed of tens to thousands of monosaccharides joined together by glycosidic linkages. The three most abundant polysaccharides are starch, glycogen, and cellulose. These three are referred to as *homopolymers* because each yields only one type of monosaccharide (glucose) after complete hydrolysis. *Heteropolymers* may contain sugar acids, amino sugars, or noncarbohydrate substances in addition to monosaccharides. Heteropolymers are common in nature (gums, pectins, and other substances). The polysaccharides are nonreducing carbohydrates, are not sweet tasting, and do not undergo mutarotation.

**Starch**

Starch is the most important source of carbohydrates in the human diet and accounts for more than 50% of our carbohydrate intake. It occurs in plants in the form of granules, and these are particularly abundant in seeds (especially the cereal grains) and tubers, where they serve as a storage form of carbohydrates. The breakdown of starch to glucose nourishes the plant during periods of reduced photosynthetic activity. We often think of potatoes as a "starchy" food, yet other plants contain a much greater percentage of starch (potatoes 15%, wheat 55%, corn 65%, and rice 75%). Commercial starch is a white powder.

Starch is a mixture of two polymers: amylose and amylopectin. Natural starches consist of about 10%–30% amylase and 70%–90% amylopectin. Amylose is a linear polysaccharide composed entirely of D-glucose units joined by the α-1,4-glycosidic linkages we saw in maltose (part (a) of Figure 5.1.1). Experimental evidence indicates that amylose is not a straight chain of glucose units but instead is coiled like a spring, with six glucose monomers per turn (part (b) of Figure). When coiled in this fashion, amylose has just enough room in its core to accommodate an iodine molecule. The characteristic blue-violet color that appears when starch is treated with iodine is due to the formation of the amylose-iodine complex. This color test is sensitive enough to detect even minute amounts of starch in solution.

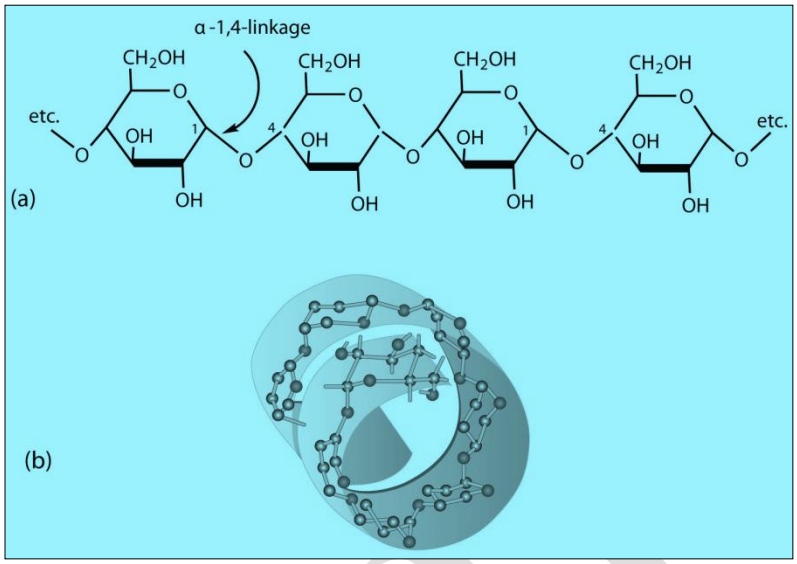



***Figure:*** *Amylose. (a) Amylose is a linear chain of α-D-glucose units joined together by α-1,4-glycosidic bonds. (b) Because of hydrogen bonding, amylose acquires a spiral structure that contains six glucose units per turn.*

Amylopectin is a branched-chain polysaccharide composed of glucose units linked primarily by α-1,4-glycosidic bonds but with occasional α-1,6-glycosidic bonds, which are responsible for the branching. A molecule of amylopectin may contain many thousands of glucose units with branch points occurring about every 25–30 units (Figure). The helical structure of amylopectin is disrupted by the branching of the chain, so instead of the deep blue-violet color amylose gives with iodine, amylopectin produces a less intense reddish brown.

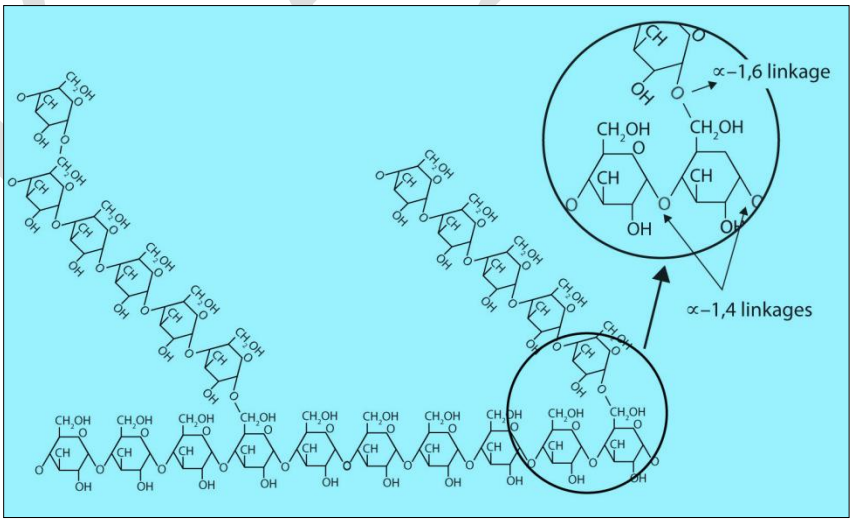



***Figure****: Representation of the Branching in Amylopectin and Glycogen. Both amylopectin and glycogen contain branch points that are linked through α-1,6-linkages. These branch points occur more often in glycogen.*

Dextrins are glucose polysaccharides of intermediate size. The shine and stiffness imparted to clothing by starch are due to the presence of dextrins formed when clothing is ironed. Because of their characteristic stickiness with wetting, dextrins are used as adhesives on stamps, envelopes, and labels; as binders to hold pills and tablets together; and as pastes. Dextrins are more easily digested than starch and are therefore used extensively in the commercial preparation of infant foods.

The complete hydrolysis of starch yields, in successive stages, glucose:

starch → dextrins → maltose → glucose

In the human body, several enzymes known collectively as amylases degrade starch sequentially into usable glucose units.

**Glycogen**

Glycogen is the energy reserve carbohydrate of animals. Practically all mammalian cells contain some stored carbohydrates in the form of glycogen, but it is especially abundant in the liver (4%–8% by weight of tissue) and in skeletal muscle cells (0.5%–1.0%). Like starch in plants, glycogen is found as granules in liver and muscle cells. When fasting, animals draw on these glycogen reserves during the first day without food to obtain the glucose needed to maintain metabolic balance.

About 70% of the total glycogen in the body is stored in muscle cells. Although the percentage of glycogen (by weight) is higher in the liver, the much greater mass of skeletal muscle stores a greater total amount of glycogen.

Glycogen is structurally quite similar to amylopectin, although glycogen is more highly branched (8–12 glucose units between branches) and the branches are shorter. When treated with iodine, glycogen gives a reddish brown color. Glycogen can be broken down into its D-glucose subunits by acid hydrolysis or by the same enzymes that catalyze the breakdown of starch. In animals, the enzyme phosphorylase catalyzes the breakdown of glycogen to phosphate esters of glucose.

**Cellulose**

Cellulose, a fibrous carbohydrate found in all plants, is the structural component of plant cell walls. Because the earth is covered with vegetation, cellulose is the most abundant of all carbohydrates, accounting for over 50% of all the carbon found in the vegetable kingdom. Cotton fibrils and filter paper are almost entirely cellulose (about 95%), wood is about 50% cellulose, and the dry weight of leaves is about 10%–20% cellulose. The largest use of cellulose is in the manufacture of paper and paper products. Although the use of noncellulose synthetic fibers is increasing, rayon (made from cellulose) and cotton still account for over 70% of textile production.

Like amylose, cellulose is a linear polymer of glucose. It differs, however, in that the glucose units are joined by β-1,4-glycosidic linkages, producing a more extended structure than amylose (part (a) of Figure 5.1.3). This extreme linearity allows a great deal of hydrogen bonding between OH groups on adjacent chains, causing them to pack closely into fibers (part (b) of Figure). As a result, cellulose exhibits little interaction with water or any other solvent. Cotton and wood, for example, are completely insoluble in water and have considerable mechanical strength. Because cellulose does not have a helical structure, it does not bind to iodine to form a colored product.

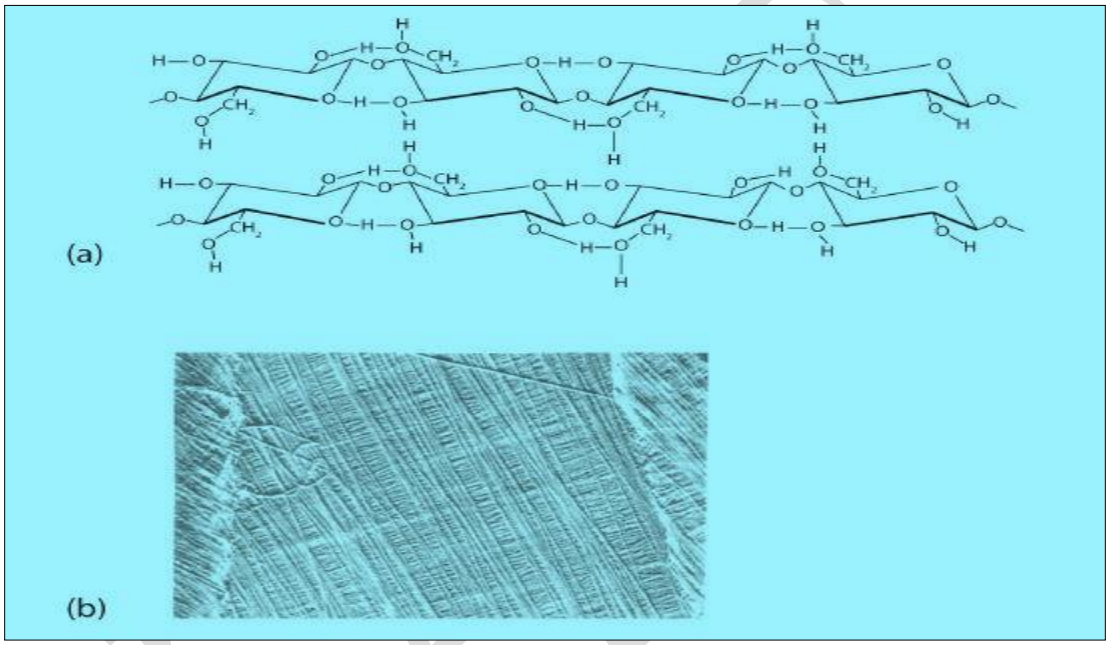



***Figure**: Cellulose. (a) There is extensive hydrogen bonding in the structure of cellulose. (b) In this electron micrograph of the cell wall of an alga, the wall consists of successive layers of cellulose fibers in parallel arrangement.*

Cellulose yields D-glucose after complete acid hydrolysis, yet humans are unable to metabolize cellulose as a source of glucose. Our digestive juices lack enzymes that can hydrolyze the β-glycosidic linkages found in cellulose, so although we can eat potatoes, we cannot eat grass. However, certain microorganisms can digest cellulose because they make the enzyme cellulase, which catalyzes the hydrolysis of cellulose. The presence of these microorganisms in the digestive tracts of herbivorous animals (such as cows, horses, and sheep) allows these animals to degrade the cellulose from plant material into glucose for energy. Termites also contain cellulase-secreting microorganisms and thus can subsist on a wood diet. This example once again demonstrates the extreme stereospecificity of biochemical processes.

## SUGGESTING MATERIALS

**Text Books:**

1. Morrison R.T & Boyd R.N., (1992), Organic Chemistry, Dorling Kindersley Pvt. Ltd., (Pearson Education)
2. Finar I.L (2002), Organic Chemistry- Volume 1, Dorling Kindersley Pvt. Ltd., (Pearson Education)
3. Finar I.L (2002), Organic Chemistry- Volume 2, Dorling Kindersley Pvt. Ltd., (Pearson Education).

**Reference Books:**

1. Nelson D.L & Cox M.M, (2012), Lehninger's Principles of Biochemistry, 7th Edition
2. Berg J.M, Tymoczko J.L & Stryer L. (2002), Biochemistry. W.H. Freeman

## POSSIBLE QUESTIONS

### Section A **20x 1 = 20 marks**

1. The general formula of monosaccharides is
a. **$C_nH_{2n}O_n$** b. $C_{2n}H_nO_n$ c. $C_nH_2O_n$ d. $C_nH_{2n}O_{2n}$
2. The aldose sugar is
a. Ribulose **b. Glycerose** c. Erythrulose d. Dihydroxyacetone3
3. Polysaccharides are
a. Oils b. Acids **c. Polymers** d. Proteins
4. Two sugars which differ from one another only in the configuration at alpha position is called
a. **Epimers** b. Anomers c. Optical isomer d. Stereoisomer
5. The most important epimer of glucose is
a. Fructose b. Arabinose c. Xylose d**. Galactose**
6. alpha-D-glucose and beta-D-glucose are
a. Stereoisomers b. Epimers **c. Anomers** d. Keto-aldol pair
7. The Change in specific rotation values of sugars is called as
a. Optical isomerism **b. Mutarotation** c. Epimerisation d. Isomerisation
8. Compounds having same structural formula but differing in spatial configuration are known as
a. **Stereoisomers** b. Anomers c. Isomers d. Epimers
9. The carbohydrate of blood group substance is
a. Sucrose **b. Fucose** c. Arabinose d. Maltose
10. Sucrose consists of
a. Glucose + Glucose **b. Glucose + Fructose** c. Glucose+Galactose d. Glucose+Mannose
11. The mutarotation refers to change in
a. **Optical rotation** b. Conductance c. Chemical properties d. $P^H$
12. A disaccharide formed by 1,1-glycosidic linkage between their monosaccharide unit is
a. Lactose b. Sucrose **c. Trehalose** d. Maltose
13. Which of the following is a heteroglycan
a. Dextrins b. Agar **c. Inulin** d. Chitin
14. Glucose on oxidation does not give
a. **Glycoside** b. Glucosaccharic acid c. Gluconic acid d. Glucoric acid
15. A positive seliwanoff's test is obtained with
a. Glucose **b. Fructose** c. Maltose d. Lactose
16. Which of the following is not form osazone
a. **Sucrose** b. Glucose c. Fructose d. Maltose
17. ADH test is based on the measurement of
a. Specific gravity of urine b. Concentration of urea in urine
c.Concentration of urea in blood d. Volume of urine in ml/minute
18. The specific gravity of urine normally in the ranges from
a. 0.900-0.999 **b. 1.003-1.030** c. 1.000-1.001 d. 1.101-1.120
19. Number of stereoisomers present in glucose is
a. 4 b. 8 **c. 16** d.12
20. The following which one gave malose on hydrolysis
a. Sucrose **b. Starch** c. Glucose d. Galactose

**Section-B (2 Marks)**

1. What is Carbohydrates?
2. How to identify the reducing and non-reducing sugar?
3. Draw a structure of sucrose, maltose and lactose?
4. Define: mutarotation
5. What is Anomeric effect?
6. Define: Epimers
7. What are stereoisomers and optical isomers?
8. Draw a structure of starch?
9. List out the properties of cellulose?
10. Write any four properties of disaccharides?

**Section-C (6 Marks)**

1. Classify the types of carbohydrates
2. Briefly explain the general properties of D-Glucose
3. Given an account of Fischer proof to determine the configuration of D-glucose
4. Explain the cyclic structure of D-glucose based on Haworth projection
5. Distinguish between mono, di and poly saccharides
6. Write a structure and properties of
   i) Sucrose ii) Maltose iii) Lactose
7. Explain the type of linkage present in starch and cellulose
8. Write a note on
   i) Mutarotation ii) Epimers
9. How to prepare D-glucose from aldopentose?
10. Starting with Glucose to prepare
    i) D-Mannose
    ii) Glucaric acid
    iii) Alpha- Glutinol
    iv) D- Fructose

**16CHU603B**
**Karpagam Academy of Higher Education**
**Coimbatore-21**

**(For the candidate admitted on 2016 onwards)**
**Department of Chemistry**
**VI- semester**
**Molecules of Life**

| Unit-I (Multiple Choice Questions Each Carry 1 Mark). | | | | | | |
|---|---|---|---|---|---|---|
| S.No | Questions | Option A | Option B | Option C | Option D | Answer |
| 1 | The general formula of monosaccharides is | $C_nH_{2n}O_n$ | $C_{2n}H_nO_n$ | $C_nH_2O_n$ | $C_nH_{2n}O_{2n}$ | $C_nH_{2n}O_n$ |
| 2 | The aldose sugar is | Ribulose | Glycerose | Erythrulose | Dihydroxyacetone | Glycerose |
| 3 | Polysaccharides are | Oils | Acids | Polymers | Proteins | Polymers |
| 4 | Two sugars which differ from one another only in the configuration at alpha position is called | Epimers | Anomers | Optical isomer | Stereoisomer | Epimers |
| 5 | The most important epimer of glucose is | Fructose | Arabinose | Xylose | Galactose | Galactose |
| 6 | alpha-D-glucose and beta-D-glucose are | Stereoisomers | Epimers | Anomers | Keto-aldol pair | Anomers |
| 7 | The Change in specific rotation values of sugars is called as | Optical isomerism | Mutarotation | Epimerisation | Isomerisation | Mutarotation |
| 8 | Compounds having same structural formula but differing in spatial configuration are known as | Stereoisomers | Anomers | Isomers | Epimers | Stereoisomers |
| 9 | The carbohydrate of blood group substance is | Sucrose | Fucose | Arabinose | Maltose | Fucose |
| 10 | Sucrose consists of | Glucose + Glucose | Glucose + Fructose | Glucose+Galactose | Glucose+Mannose | Glucose + Fructose |
| 11 | The mutarotation refers to change in | Optical rotation | conductance | Chemical properties | pH | Optical rotation |
| 12 | A disaccharide formed by 1,1-glycosidic linkage between their monosaccharide unit is | Lactose | Sucrose | Trehalose | maltose | Trehalose |
| 13 | which of the following is a heteroglycan | Dextrins | Agar | Inulin | Chitin | Agar |
| 14 | Glucose on oxidation does not give | Glycoside | Glucosaccharic acid | Gluconic acid | Glucoric acid | Glycoside |
| 15 | A positive seliwanoff's test is obtained with | Glucose | Fructose | Maltose | Lactose | Fructose |
| 16 | Which of the following is not form osazone | Sucrose | Glucose | Fructose | Maltose | Sucrose |
| 17 | ADH test is based on the measurement of | Specific gravity of urine | Concentration of urea in urine | concentration of urea in blood | Volume of urine in ml/minute | Specific gravity of urine |

| | | | | | | |
|---|---|---|---|---|---|---|
| 18 | The specific gravity of urine normally in the ranges from | 0.900-0.999 | 1.003-1.030 | 1.000-1.001 | 1.101-1.120 | 1.003-1.030 |
| 19 | Number of stereoisomers present in glucose is | 4 | 8 | 16 | 12 | 16 |
| 20 | The following which one gave malose on hydrolysis | Sucrose | Starch | Glucose | Galactose | Starch |
| 21 | alpha-D-glucuronic acid is present in | Hyaluronic acid | Chondroltin sulphate | | Heparin | Heparin |
| 22 | An L-isomer of monosaccharide formed in human body | L-Fructose | L-Xylose | L-Xylulose | L-Erythrose | L-Xylulose |
| 23 | The smallest monosaccharide having furanose ring structure is | Erythrose | Glucose | Fructose | Ribase | Glucose |
| 24 | Iodine give a red colour with | Starch | Dextrin | Inulin | Glycogen | Glycogen |
| 25 | Amylose is a constituent of | Starch | Cellulose | Glycogen | Dextrin | Starch |
| 26 | Branching occurs in glycogen approximetly after every | Five glucose units | Ten glucose units | Fifteen glucose units | Twenty glucose units | Ten glucose units |
| 27 | Glucose-6-phosphatase is not present in | Liver and kidney | Kidney and muscles | Kidney & adipose tissue | Muscles & adipose tissue | Muscles & adipose tissue |
| 28 | Glucose uptake by liver cell is | Energy consuming | A satuated process | insulin-dependent | insulin-independent | insulin-independent |
| 29 | Active uptake of glucose is inhibited by | Ouabain | Phlorrizin | Digoxin | Alloxan | Phlorrizin |
| 30 | Tautomerisation is | Shift of Hydrogen | Shift of Carbon | Shiift of Nitogen | Removal of Oxygen | Shift of Hydrogen |
| 31 | Excessive intake of ethanol increases the ratio: | NADH : $NAD^+$ | $NAD^+$ : NADH | $FADH_2$ : FAD | FAD : $FADH_2$ | NADH : $NAD^+$ |
| 32 | Glycogenin is | Uncoupler of oxidative phosphorylation | Polymer of glycogen molecles | Protein primer for glycogen synthesis | Intermediate in glycogen breakdown | Protein primer for glycogen synthesis |
| 33 | Animal fat is in general | Poor in saturated and rich in polyunsaturated fatty acids | Rich in saturated and poor in polysaturated fatty acids | Rich in saturated and polysaturated fatty acids | Poor in saturated and polysaturated fatty acids | Rich in saturated and poor in polysaturated fatty acids |
| 34 | Obseity increases the risk of | Hypertension | Diabetes mellitus | Cardiovascular disease | All of these | All of these |
| 35 | Heavy proteinuria occurs in | Acute glomerulonephritis | Acute pyelonephritis | Nephroslerosis | Nephrotic syndrome | Acute pyelonephritis |
| 36 | The general formula of polysaccharides is | $[C_6H_{12}O_6]_n$ | $[C_6H_{10}O_5]_n$ | $[C_6H_{12}O_5]_n$ | $[C_6H_{19}O_6]_n$ | $[C_6H_{10}O_5]_n$ |
| 37 | The intermediate in hexose monophosphate shunt is | D-Ribolose | D-Arobinose | D-xylose | D-lyxose | D-Ribolose |

| | | | | | | |
|---|---|---|---|---|---|---|
| 38 | Honey contains the hydrolytic product of | Lactose | Maltose | Inulin | Starch | Inulin |
| 39 | Galctose on oxidaton with con. $HNO_3$ produces | Gluconic acid | Saccharic acid | Saccharolactone | Mucicacic acid | Mucicacic acid |
| 40 | Cellulose is made up of the moluceles of | Alpha Glusose | Beta Glucose | Alpha Mannose | Beta Mannose | Alpha Glusose |
| 41 | What is the range of glucose unit present in amylose | 100-200 | 200-300 | 300-400 | 500-600 | 300-400 |
| 42 | N-acetylneuraminic acid is an example of | Sialic acid | Mucic acid | Glucuronic acid | Hippuric acid | Glucuronic acid |
| 43 | Benedict's test is likely to give weakly positive result with concentrated urine due to the action of | urea | Uric acid | Ammonium salt's | Phosphates | Uric acid |
| 44 | The general test for detection of carbohydrates is | Iodine test | Molisch test | Osazone test | Muliken's test | Molisch test |
| 45 | Glycogen syntheiase activity is depressed by | Glucose | Insulin | Cyclic AMP | Fructokinase | Cyclic AMP |
| 46 | The conversion of alanine to glucose is termed | Glycolysis | Oxidative decarbaxylation | Specific dynamic action | Gluconegenesis | Gluconegenesis |
| 47 | Under anaerobic condition the glycolysis one mole of glucose yield how many moles of ATP | one | Two | Eight | Thirty | Two |
| 48 | Glucose will be converted into fatty acids if the diet has excess of | Carbohydrates | Proteins | Fat | Vitamins | Carbohydrates |
| 49 | Among the following which one is specific test for ketohexose | Selwanoff's test | Osazone test | Molisch test | Schiff test | Selwanoff's test |
| 50 | Cane sugar (Sucrose) injected into blood is | Changed to fructose | Changed to glucose | No significant change | Changed to glucose and fructose | No significant change |
| 51 | Our body can get pentoses from | Glycolyic pathway | Uromic acid pathway | TCA cycle | HMP shunt | HMP shunt |
| 52 | The normal glucose tolerance curve reaches peak is | 15 min | 1 hour | 2 hour | 1 and half hour | 1 hour |
| 53 | The tissue with the highest total glycogen content are | Muscle and kidneys | kidneys and liver | liver and muscle | Brain and Liver | liver and muscle |
| 54 | The total glycogen content of the body is about | 100g | 200g | 300g | 500g | 300g |
| 55 | The total glucose in the body is | 10-15g | 20-30g | 40-50g | 60-80g | 20-30g |
| 56 | Glycogen is present in all body tissue except | Liver | Brain | Kidney | Stomach | Brain |
| 57 | Iodine test is positive for starch, dextrin and | Mucoprotein | Agar | Glycogen | Cellulose | Agar |
| 58 | Humar heart muscle contains | D-arabinose | D-ribose | D-xylose | D-lyxose | D-xylose |
| 59 | Starch and glycogen are polymers of | Fructose | Mannose | alpha-D-glucose | Galactose | alpha-D-glucose |

| | | | | | | |
|---|---|---|---|---|---|---|
| 60 | Reduction of glucose with Ca2+ in water produces | Sorbital | Dulcitol | Mannitol | Glucuronic acid | Sorbital |

**Unit-II**
**Syllabus**

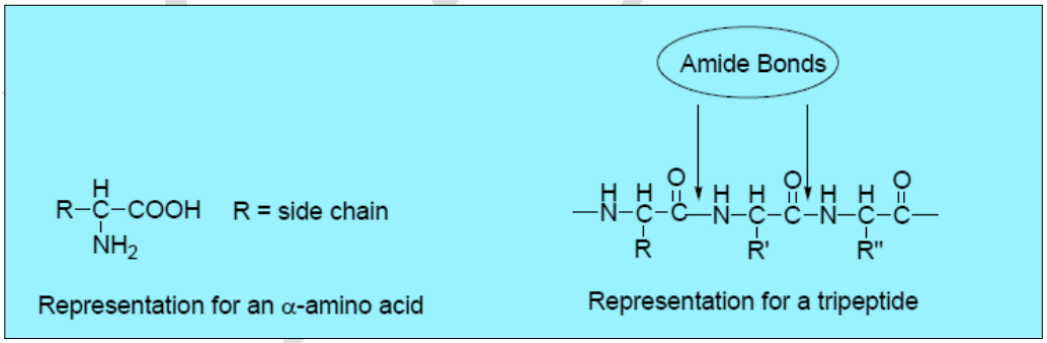
**AMINO ACIDS, PEPTIDES AND PROTEINS**

Classification *of Amino Acids,* Zwitterion structure and Isoelectric point. Overview of Primary, Secondary, Tertiary and Quaternary structure of proteins. Determination of primary structure of peptides, determination of N-terminal amino acid (by DNFB and Edman method) and C–terminal amino acid (by thiohydantoin and with carboxypeptidase enzyme). Synthesis of simple peptides (upto dipeptides) by N-protection (tbutyloxycarbonyl and phthaloyl) & C-activating groups and Merrifield solid phase synthesis.

# Amino Acids

## *Introduction*

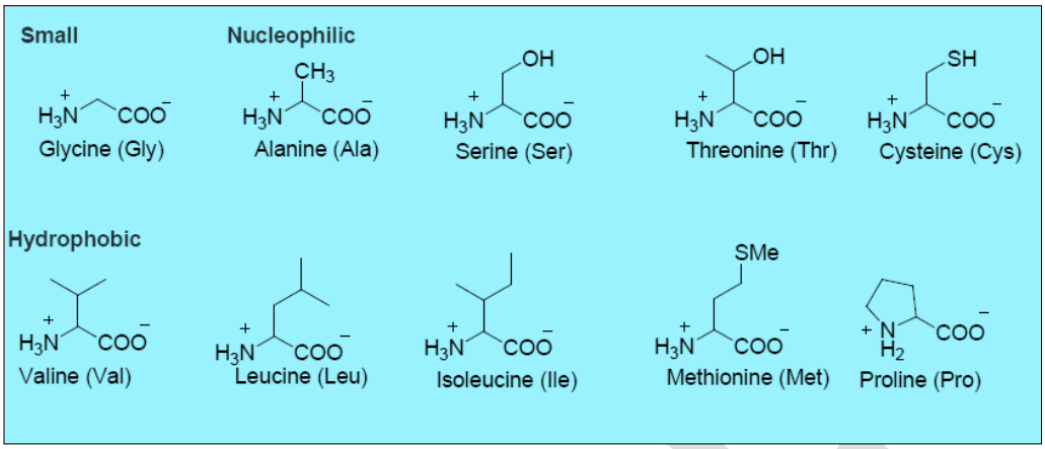
In nature three kinds of polymers occur: (i) polysaccharides, (ii) proteins and (iii) nucleic acids. This section discusses proteins and peptides that are polymers of α-amino acids linked together by amide bonds. Scheme 1 shows representation for an α-amino acid and peptide. The repeating units in peptide is called amino acid residue. Proteins are polypeptides that are made up of 40-100 amino acids.

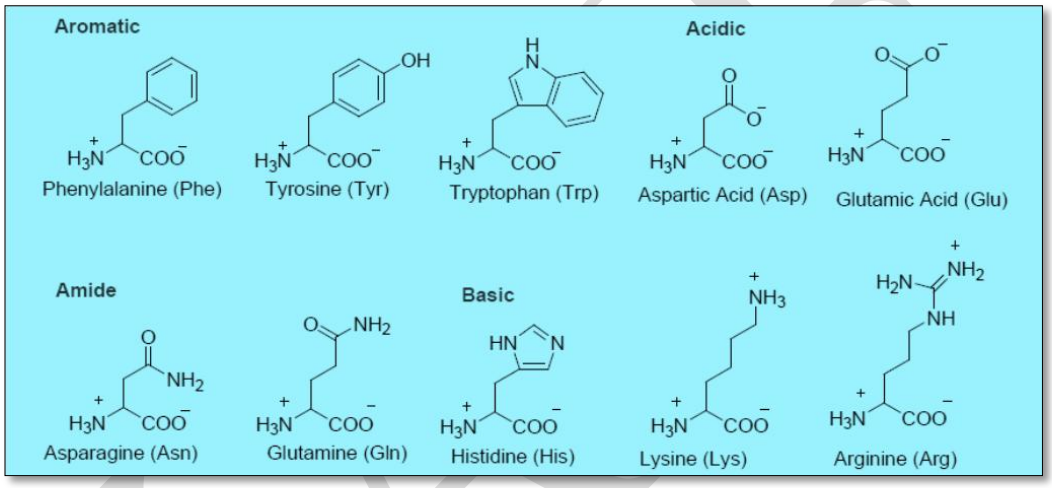



Classification of Amino Acids

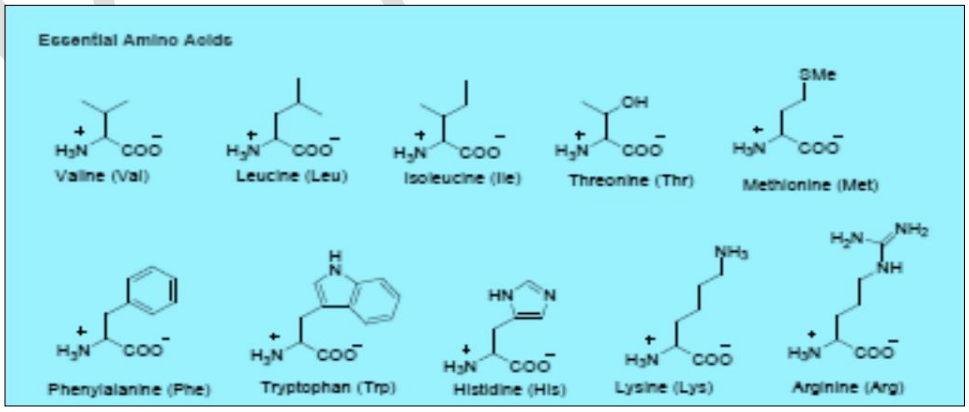
α-Amino Acids

The structures of the 20 most common naturally occurring amine acids are shown in below. They differ only in the side chain attached to the α-carbon. Among them, ten are essential amino acids.



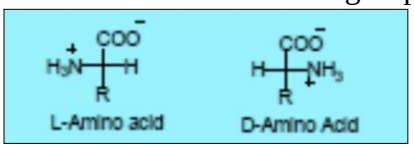

These amino acids are to be obtained from diets because we either cannot synthesize them at all or cannot synthesize them in adequate amounts.




***Configuration α-Amino Acids***

In 19 of the 20 naturally occurring α-amino acids, except glycine, the α-carbon is an asymmetric center. Thus, they can exit as enantiomers, and the most amino acids found in nature have L-configuration. Following figure shows the Fischer projection of an amino acid with a carboxyl

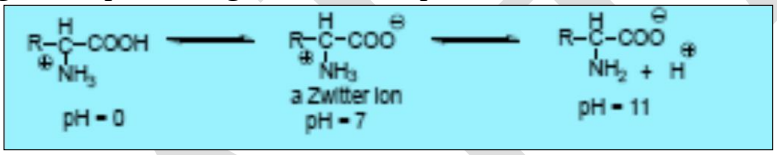
group on the top and the R group on the bottom of the vertical axis is an L-amino acid if the amino group is on the left and a D-amino acid if the amino group is one the right.




***Acid-Base Properties α-Amino Acids***

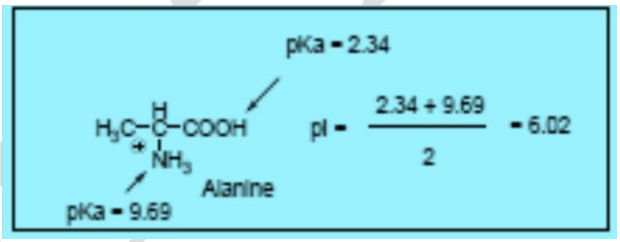
Amino acid has a carboxyl group and amino group, and each group can exist in an acidic or basic form, depending on the pH of the solution in that the amino acid is dissolved. In addition, some amino acids, such as glutamate, also contain ionizable side chain.

The pKa values of the carboxyl group and the protonated amino group of the amino acids approximately are 2 and 9, respectively (Scheme 5). Thus, both groups will be in their acidic forms in highly acidic medium (pH ~ 0). At pH 7, the pH of the solution is greater than the pKa of the carboxyl group, but less than the pKa of the protonated amino group. Hence, the carboxyl group will be in its basic form and the amino group in its acidic form (called Zwitter ion). In strongly basic medium (pH 11), both groups will be in basic form. Thus, an amino acid can never exist as an uncharged compound, regardless of the pH of the medium.

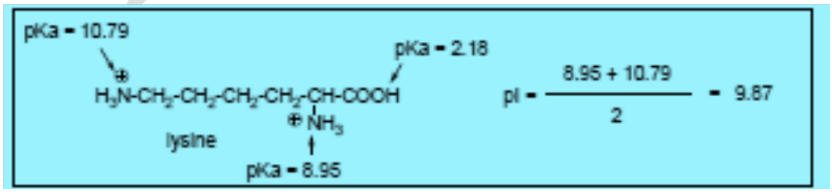



***The isoelectric point***

The isoelectric point (pI) of an amino acid is the $P^H$ where it has no net charge. For example, the pI of an amino acid that does not possess an ionizable side chain is midway between its two pKa values.



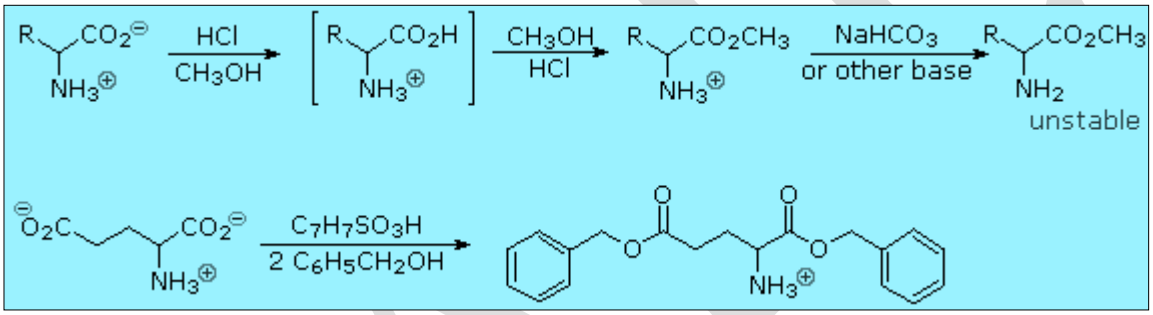

In case of an amino acid that contains an ionizable side chain, the pI is the average of the pKa values of the similarly ionizing groups. For example, see pI of lysine.



## Reactions of α-Amino Acids

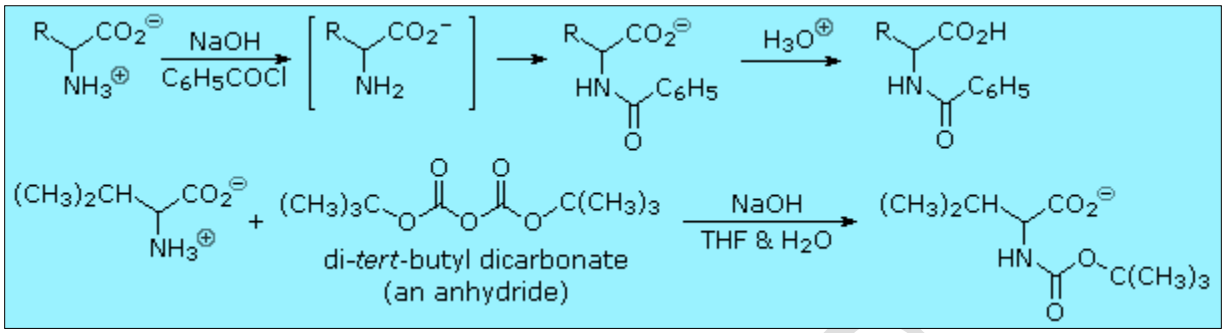
### 1. Carboxylic Acid Esterification

Amino acids undergo most of the chemical reactions characteristic of each function, assuming the pH is adjusted to an appropriate value. Esterification of the carboxylic acid is usually conducted under acidic conditions, as shown in the two equations written below. Under such conditions, amine functions are converted to their ammonium salts and carboxyic acids are not dissociated. The first equation is a typical Fischer esterification involving methanol. The initial product is a stable ammonium salt. The amino ester formed by neutralization of this salt is unstable, due to acylation of the amine by the ester function. The second reaction illustrates benzylation of the two carboxylic acid functions of aspartic acid, using p-toluenesulfonic acid as an acid catalyst. Once the carboxyl function is esterified, zwitterionic species are no longer possible and the product behaves like any 1°-amine.



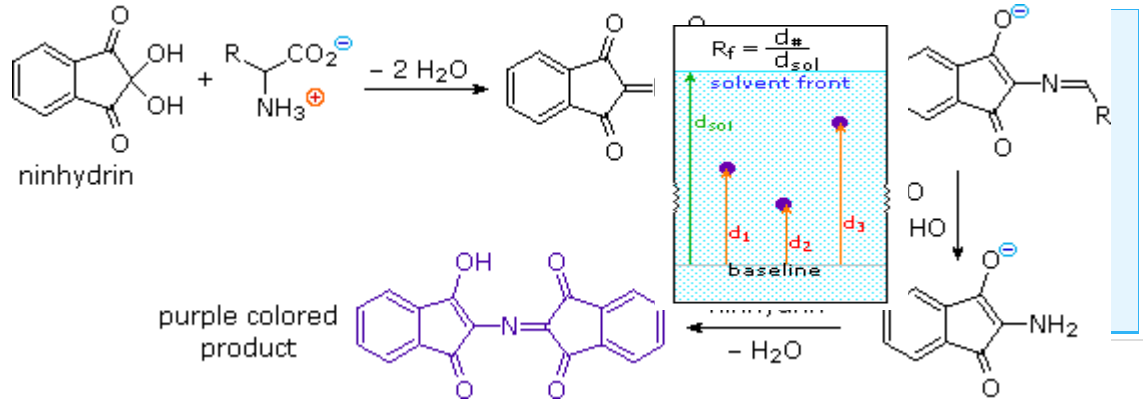

### 2. Amine Acylation

In order to convert the amine function of an amino acid into an amide, the pH of the solution must be raised to 10 or higher so that free amine nucleophiles are present in the reaction system. Carboxylic acids are all converted to carboxylate anions at such a high pH, and do not interfere with amine acylation reactions. The following two reactions are illustrative. In the first, an acid chloride serves as the acylating reagent. This is a good example of the superior nucleophilicity of nitrogen in acylation reactions, since water and hydroxide anion are also present as competing nucleophiles. A similar selectivity favoring amines was observed in the Hinsberg test. The second reaction employs an anhydride-like reagent for the acylation. This is a particularly useful procedure in peptide synthesis, thanks to the ease with which the t-butylcarbonyl (**t-BOC**) group can be removed at a later stage. Since amides are only weakly basic ( $pK_a$~ -1), the resulting amino acid derivatives do not display zwitterionic character, and may be converted to a variety of carboxylic acid derivatives.




### 3. The Ninhydrin Reaction

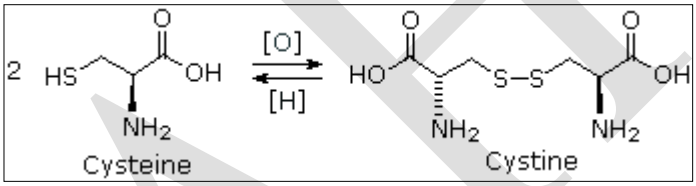
In addition to these common reactions of amines and carboxylic acids, common alpha-amino acids, except proline, undergo a unique reaction with the triketohydrindene hydrate known as ninhydrin. Among the products of this unusual reaction (shown on the left below) is a purple colored imino derivative, which provides as a useful color test for these amino acids, most of which are colorless. A common application of the ninhydrin test is the visualization of amino acids in **paper chromatography**. As shown in the graphic on the right, samples of amino acids or mixtures thereof are applied along a line near the bottom of a rectangular sheet of paper (the baseline). The bottom edge of the paper is immersed in an aqueous buffer, and this liquid climbs slowly toward the top edge. As the solvent front passes the sample spots, the compounds in each sample are carried along at a rate which is characteristic of their functionality, size and interaction with the cellulose matrix of the paper. Some compounds move rapidly up the paper, while others may scarcely move at all. The ratio of the distance a compound moves from the baseline to the distance of the solvent front from the baseline is defined as the retardation (or retention) factor $\mathbf{R_f}$. Different amino acids usually have different $R_f$'s under suitable conditions. In the example on the right, the three sample compounds (1, 2 & 3) have respective $R_f$ values of 0.54, 0.36 & 0.78.



### 4. Oxidative Coupling

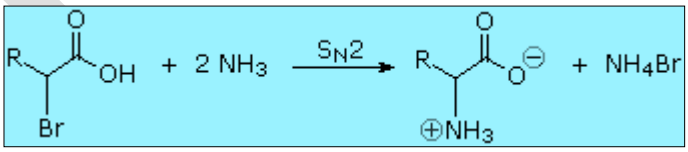
The mild oxidant iodine reacts selectively with certain amino acid side groups. These include the phenolic ring in tyrosine, and the heterocyclic rings in tryptophan and histidine, which all yield products of electrophilic iodination. In addition, the sulfur groups in cysteine and methionine are also oxidized by iodine. Quantitative measurement of iodine consumption has been used to determine the number of such residues in peptides. The basic functions in lysine and arginine are onium cations at pH less than 8, and are unreactive in that state. Cysteine is a thiol, and like most thiols it is oxidatively dimerized to a disulfide, which is sometimes listed as a distinct amino acid under the name **cystine**. Disulfide bonds of this kind are found in many peptides and proteins. For example, the two peptide chains that constitute insulin are held together by two disulfide links. Our hair consists of a fibrous protein called keratin, which contains an unusually large proportion of cysteine. In the manipulation called "permanent waving", disulfide bonds are first broken and then created after the hair has been reshaped. Treatment with dilute aqueous iodine oxidizes the methionine sulfur atom to a sulfoxide.

**Cysteine-Cystine Interconversion**



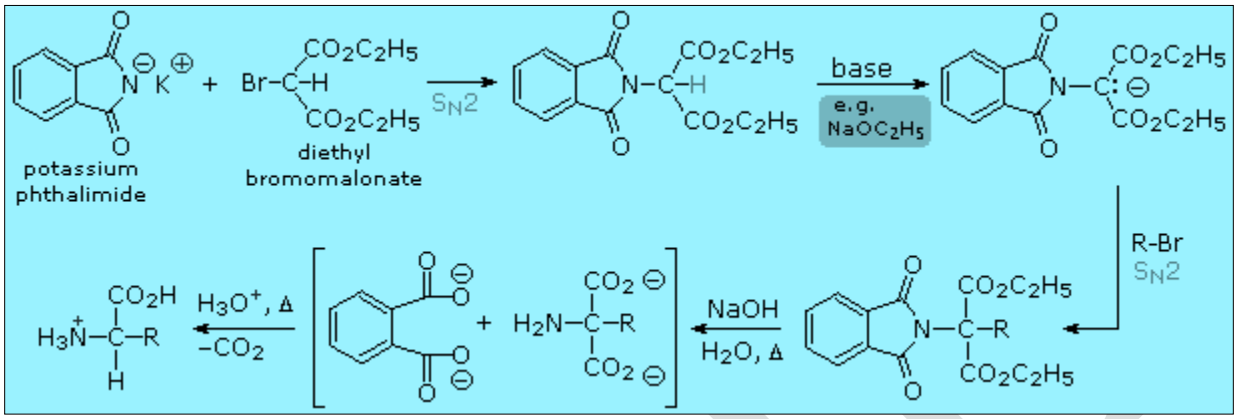

### Synthesis of α-Amino Acids

**1)** Amination of alpha-bromocarboxylic acids, illustrated by the following equation, provides a straightforward method for preparing alpha-aminocarboxylic acids. The bromoacids, in turn, are conveniently prepared from carboxylic acids by reaction with $Br_2$ + $PCl_3$. Although this direct approach gave mediocre results when used to prepare simple amines from alkyl halides, it is more effective for making amino acids, thanks to the reduced nucleophilicity of the nitrogen atom in the product. Nevertheless, more complex procedures that give good yields of pure compounds are often chosen for amino acid synthesis.

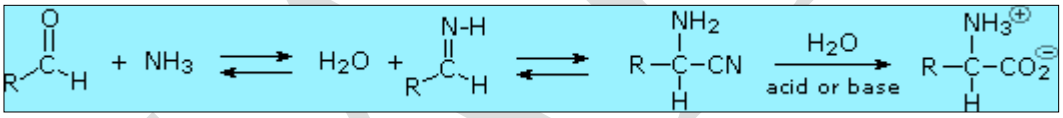



**2)** By modifying the nitrogen as a phthalimide salt, the propensity of amines to undergo multiple substitutions is removed, and a single clean substitution reaction of 1º- and many 2º-alkylhalides takes place. This procedure, known as the Gabriel synthesis, can be used to advantage in aminating bromomalonic esters, as shown in the upper equation of the following scheme. Since the phthalimide substituted malonic ester has an acidic hydrogen (colored orange), activated by the

two ester groups, this intermediate may be converted to an ambident anion and alkylated. Finally, base catalyzed hydrolysis of the phthalimide moiety and the esters, followed by acidification and thermal decarboxylation, produces an amino acid and phthalic acid (not shown).



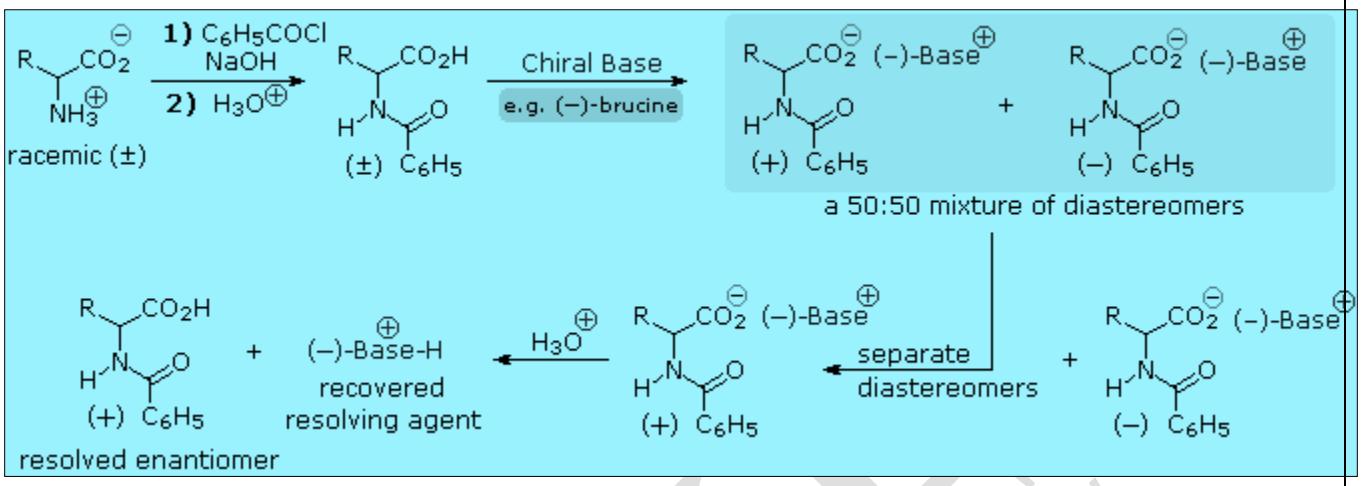

**3)** An elegant procedure, known as the **Strecker synthesis**, assembles an alpha-amino acid from ammonia (the amine precursor), cyanide (the carboxyl precursor), and an aldehyde. This reaction (shown below) is essentially an imino analog of cyanohydrin formation. The alpha-amino nitrile formed in this way can then be hydrolyzed to an amino acid by either acid or base catalysis.




**4) Resolution**

The three synthetic procedures described above, and many others that can be conceived, give racemic amino acid products. If pure **L** or **D** enantiomers are desired, it is necessary to resolve these racemic mixtures. A common method of resolving racemates is by diastereomeric salt formation with a pure chiral acid or base. This is illustrated for a generic amino acid in the following diagram. Be careful to distinguish charge symbols, shown in colored circles, from optical rotation signs, shown in parenthesis.

In the initial display, the carboxylic acid function contributes to diastereomeric salt formation. The racemic amino acid is first converted to a benzamide derivative to remove the basic character of the amino group. Next, an ammonium salt is formed by combining the carboxylic acid with an optically pure amine, such as brucine (a relative of strychnine). The structure of this amine is not shown, because it is not a critical factor in the logical progression of steps. Since the amino acid moiety is racemic and the base is a single enantiomer (levorotatory in this example), an equimolar mixture of diastereomeric salts is formed (drawn in the green shaded box). Diastereomers may be separated by crystallization, chromatography or other physical manipulation, and in this way one of the isomers may be isolated for further treatment, in this illustration it is the (+):(-) diastereomer. Finally the salt is broken by acid treatment, giving the resolved (+)-amino acid derivative together with the recovered resolving agent (the optically active amine). Of course, the same procedure could be used to obtain the (-)-enantiomer of the amino acid.




Since amino acids are amphoteric, resolution could also be achieved by using the basic character of the amine function. For this approach we would need an enantiomerically pure chiral acid such as tartaric acid to use as the resolving agent. By clicking on the above diagram, this alternative resolution strategy will be illustrated. Note that the carboxylic acid function is first esterified, so that it will not compete with the resolving acid.

Resolution of aminoacid derivatives may also be achieved by enzymatic discrimination in the hydrolysis of amides. For example, an aminoacylase enzyme from pig kidneys cleaves an amide derivative of a natural L-amino acid much faster than it does the D-enantiomer. If the racemic mixture of amides shown in the green shaded box above is treated with this enzyme, the L-enantiomer (whatever its rotation) will be rapidly converted to its free zwitterionic form, whereas the D-enantiomer will remain largely unchanged. Here, the diastereomeric species are transition states rather than isolable intermediates. This separation of enantiomers, based on very different rates of reaction, is called **kinetic resolution**.

**Peptide Synthesis**

In order to synthesize a peptide from its component amino acids, two obstacles must be overcome. The first of these is statistical in nature, and is illustrated by considering the dipeptide Ala-Gly as a proposed target. If we ignore the chemistry involved, a mixture of equal molar amounts of alanine and glycine would generate four different dipeptides. These are: **Ala-Ala, Gly-Gly, Ala-Gly & Gly-Ala**. In the case of tripeptides, the number of possible products from these two amino acids rises to eight. Clearly, some kind of selectivity must be exercised if complex mixtures are to be avoided.

The second difficulty arises from the fact that carboxylic acids and 1º or 2º-amines do not form amide bonds on mixing, but will generally react by proton transfer to give salts (the intermolecular equivalent of zwitterion formation).

From the perspective of an organic chemist, peptide synthesis requires selective acylation of a free amine. To accomplish the desired amide bond formation, we must first deactivate all extraneous amine functions so they do not compete for the acylation reagent. Then we must selectively activate the designated carboxyl function so that it will acylate the one remaining free amine. Fortunately, chemical reactions that permit us to accomplish these selections are well known.

First, the basicity and nucleophilicity of amines are substantially reduced by amide formation. Consequently, the acylation of amino acids by treatment with acyl chlorides or anhydrides at pH > 10, as described earlier, serves to protect their amino groups from further reaction.

Second, acyl halide or anhydride-like activation of a specific carboxyl reactant must occur as a prelude to peptide (amide) bond formation. This is possible, provided competing reactions involving other carboxyl functions that might be present are precluded by preliminary ester formation. Remember, esters are weaker acylating reagents than either anhydrides or acyl halides, as noted earlier.

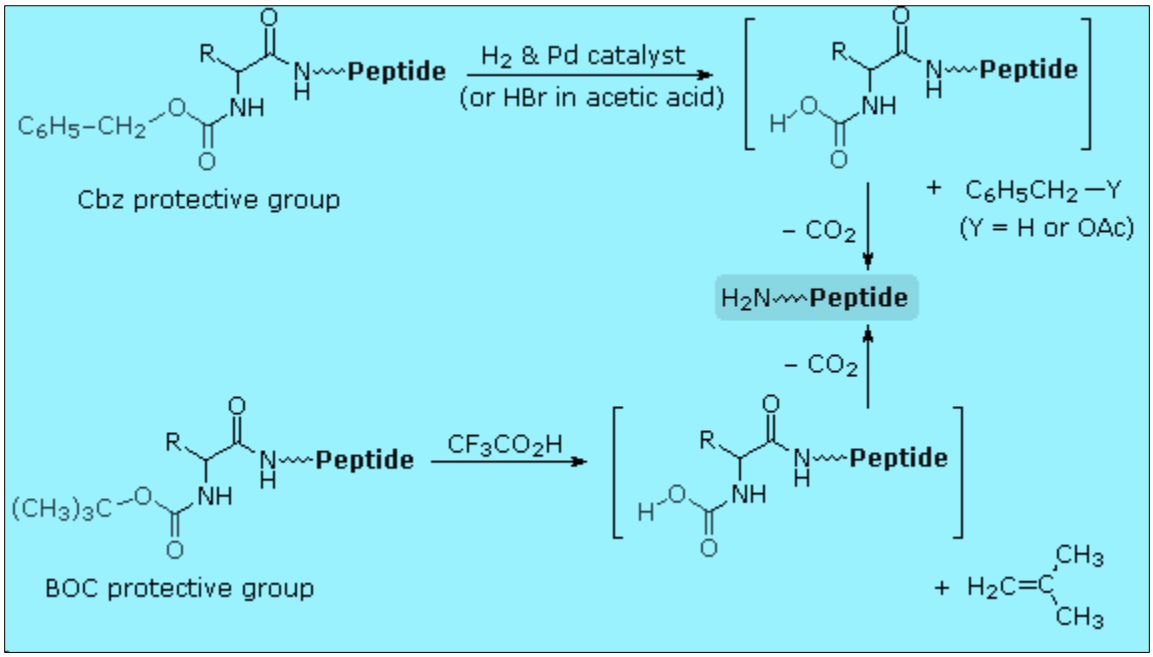
Finally, dicyclohexylcarbodiimide (DCC) effects the dehydration of a carboxylic acid and amine mixture to the corresponding amide under relatively mild conditions. The structure of this reagent and the mechanism of its action have been described. Its application to peptide synthesis will become apparent in the following discussion.

The strategy for peptide synthesis, as outlined here, should now be apparent. The following example shows a selective synthesis of the dipeptide Ala-Gly.

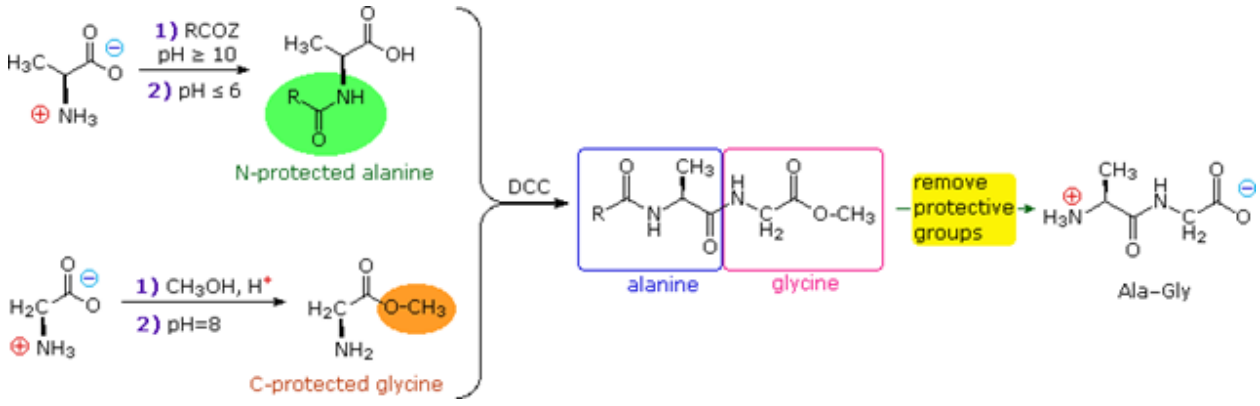
An important issue remains to be addressed. Since the N-protective group is an amide, removal of this function might require conditions that would also cleave the just formed peptide bond. Furthermore, the harsh conditions often required for amide hydrolysis might cause extensive racemization of the amino acids in the resulting peptide. This problem strikes at the heart of our strategy, so it is important to give careful thought to the design of specific N-protective groups. In particular, three qualities are desired:

1. The protective amide should be easy to attach to amino acids.
2. The protected amino group should not react under peptide forming conditions.
3. The protective amide group should be easy to remove under mild conditions.

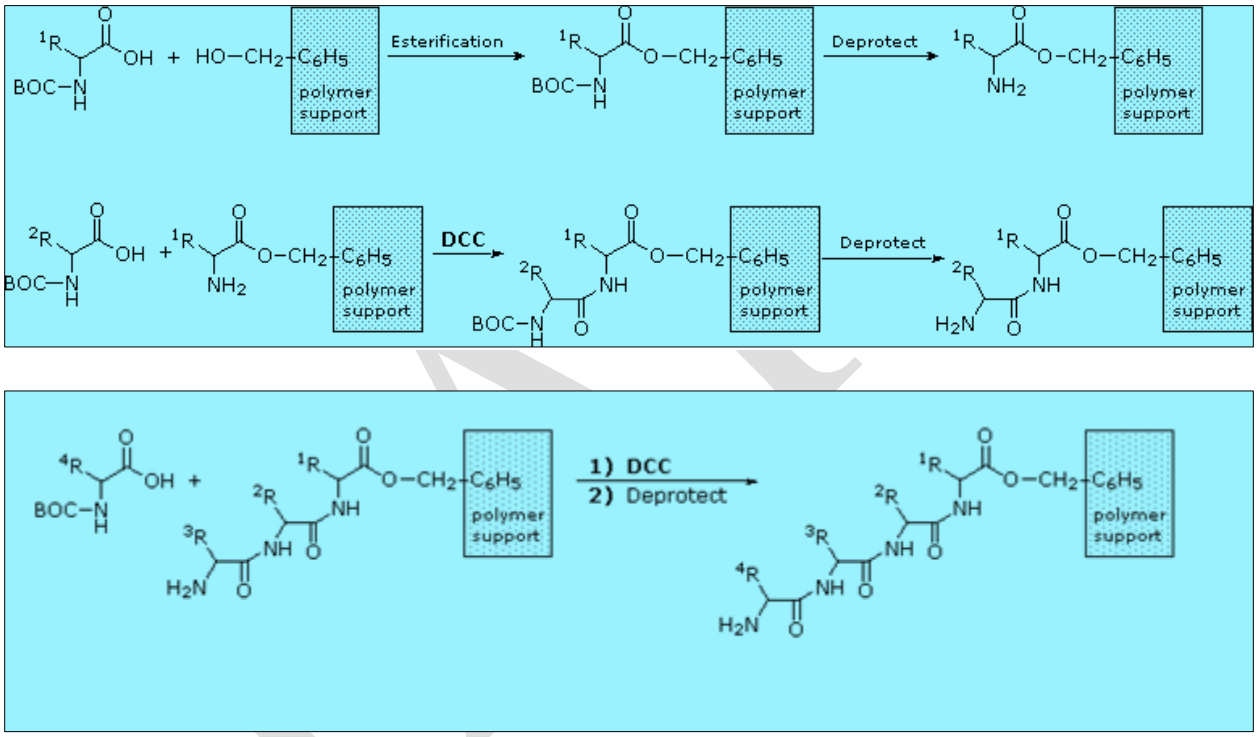
A number of protective groups that satisfy these conditions have been devised; and two of the most widely used, **carbobenzoxy** (Cbz) and **t-butoxycarbonyl** (BOC or t-BOC), are described here.




The reagents for introducing these N-protective groups are the acyl chlorides or anhydrides shown in the left portion of the above diagram. Reaction with a free amine function of an amino acid occurs rapidly to give the "protected" amino acid derivative shown in the center. This can then be used to form a peptide (amide) bond to a second amino acid. Once the desired peptide bond is created the protective group can be removed under relatively mild non-hydrolytic conditions. Equations showing the protective group removal will be displayed above by are shown above. Cleavage of the reactive benzyl or tert-butyl groups generates a common carbamic acid intermediate (HOCO-NHR) which spontaneously loses carbon dioxide, giving the corresponding amine. If the methyl ester at the C-terminus is left in place, this sequence of reactions may be repeated, using a different N-protected amino acid as the acylating reagent. Removal of the protective groups would then yield a specific tripeptide, determined by the nature of the reactants and order of the reactions.

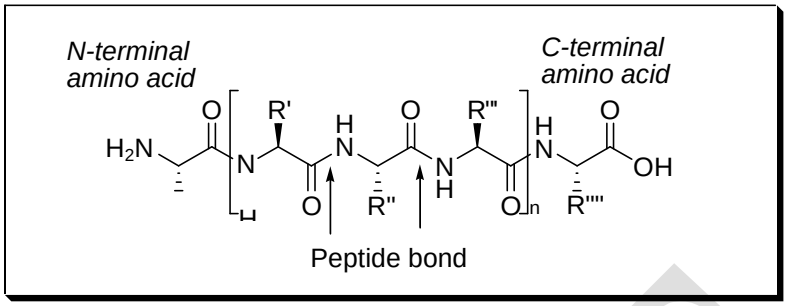


The synthesis of a peptide of significant length (e.g. ten residues) by this approach requires many steps, and the product must be carefully purified after each step to prevent unwanted cross-reactions. To facilitate the tedious and time consuming purifications, and reduce the material losses that occur in handling, a clever modification of this strategy has been developed. This procedure, known as the **Merrifield Synthesis** after its inventor R. Bruce Merrifield, involves attaching the C-terminus of the peptide chain to a polymeric solid, usually having the form of very small beads. Separation and purification is simply accomplished by filtering and washing the beads with appropriate solvents. The reagents for the next peptide bond addition are then added, and the purification steps repeated. The entire process can be automated, and peptide synthesis machines based on the Merrifield approach are commercially available. A series of equations illustrating the Merrifield synthesis may be viewed by on the following diagram. The final step, in which the completed peptide is released from the polymer support, is a simple benzyl ester cleavage.



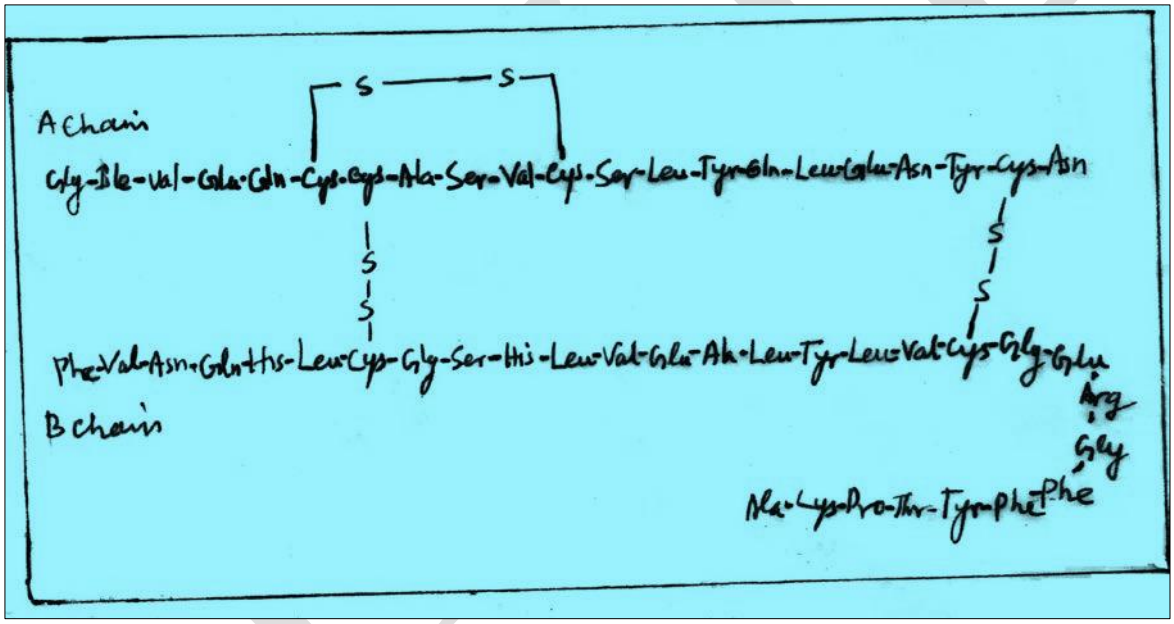

## *Peptides and Proteins*

These are naturally occurring polymers in living systems. The polymers with molecular weights less than 10000 are termed as peptides and those with higher molecular weights are termed as proteins. The acid-catalyzed hydrolysis of peptides and proteins affords the constituent α-amino acids.




## Primary Structure of Protein

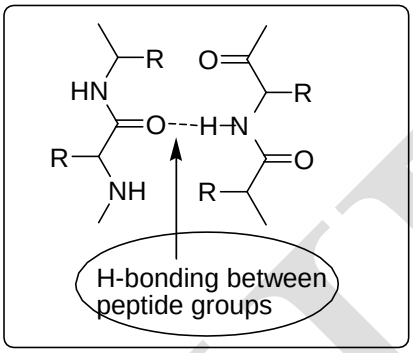
The primary structure of a protein describes the sequence of amino acids in the chain. Insulin is the first protein whose amino acid sequence was determined. Scheme 2 presents the primary structure of insulin.

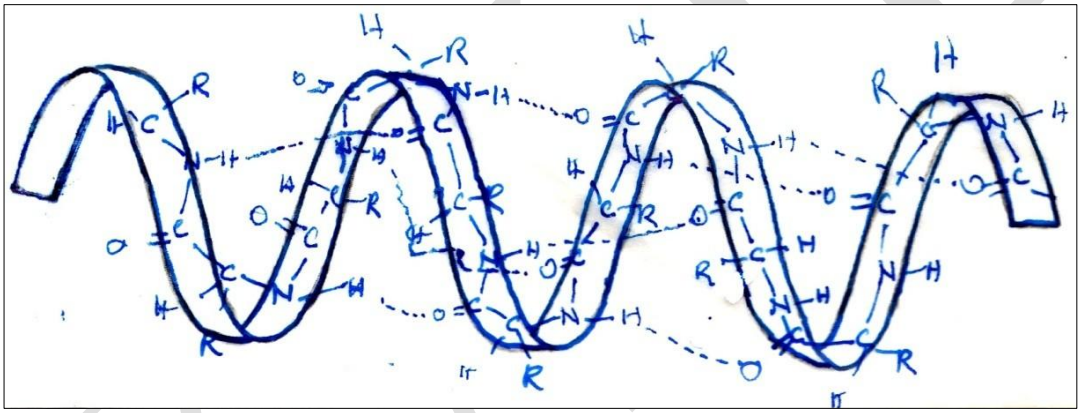



**Primary Structure of Insulin**

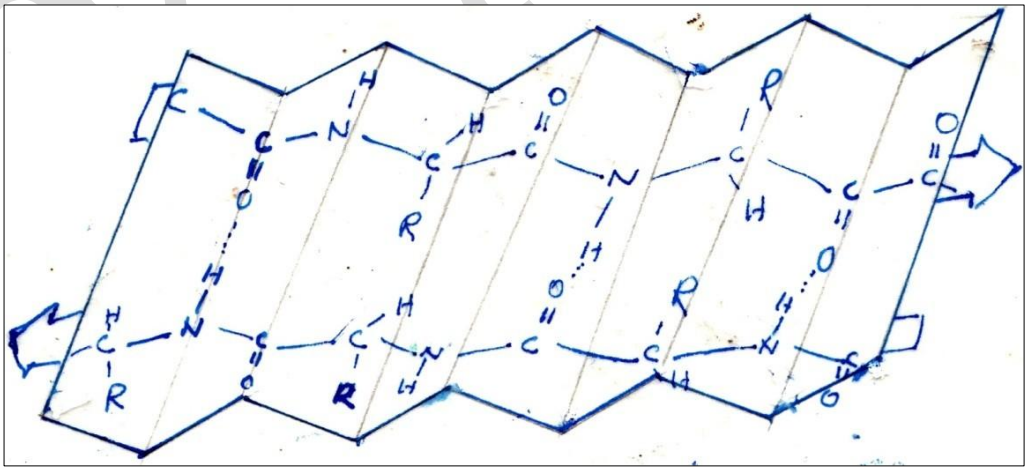
## Secondary Structure of Protein

The secondary structure describes how the segments of the backbone chain fold. These conformations are stabilized by H-bonding between the peptide groups- between NH of one amino acid residue and C=O group of another.



***(a) α-Helix***



**(b) β-Pleated Sheet**

**A segment of a protein in: (a) an α-helix; (b) β-pleated sheet.**

α-Helix:

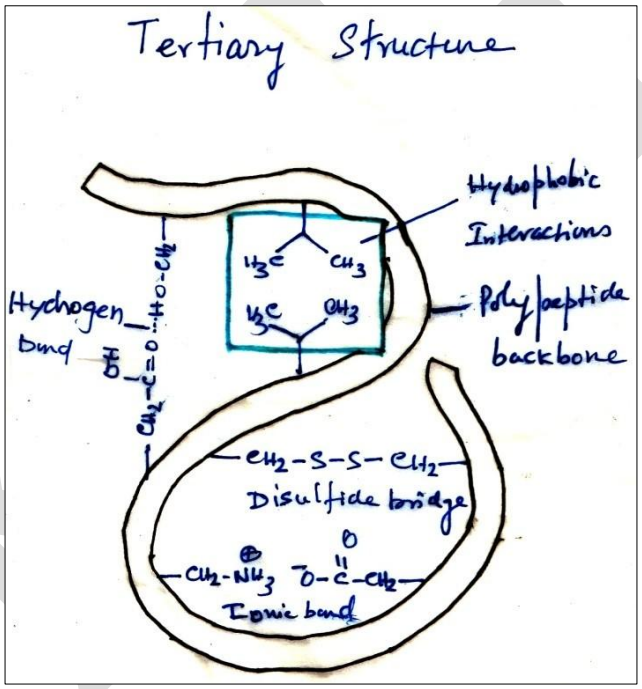
The first type of secondary structure is α-helix, where the backbone coils around the long axis of the protein molecule. The substituents on the α-carbon of the amino acids protrude outward from the helix to minimize the steric hindrance. The H attached to amide nitrogen makes H-bonding with the carbonyl oxygen of an amino acid.

***β-Pleated Sheet***

The second type of secondary structure is the β-pleated sheet, in which the backbone is extended in a zigzag structure resembling pleats. The H-bonding in a β-pleated sheet occurs between the adjacent peptide chains.

**Tertiary Structure of Protein**

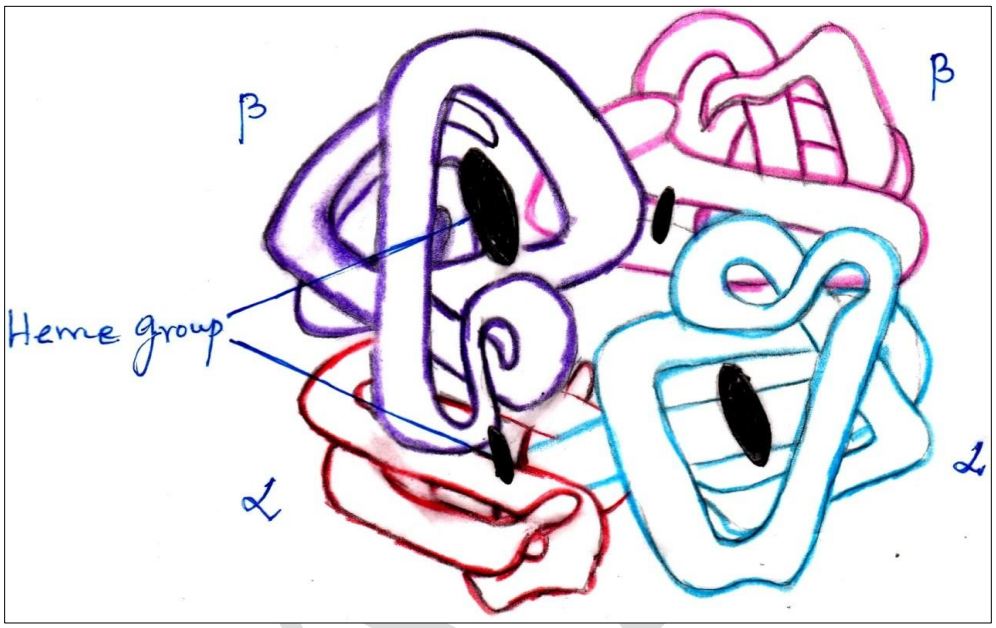
The tertiary structure of a protein describes the three-dimensional arrangement of all the atoms. In solution, proteins fold to maximize their stability through interactions include disulfide bonds, hydrogen bonds, electrostatic attractions and hydrophobic interactions.




**Stabilizing interactions for the tertiary structure of protein**

**Quaternary Structure of Protein**

Some proteins have more than one peptide chain and the individual chain is called a subunit. The subunits are held together by intractions such as hydrophobic intraction, H-bonding, and electrostatic attractions. The quarternary structure of a protein describes the way the subunits are arranged in space. Scheme 5 shows the structure of hemoglobin which is a tetrameric structural protein comprising two α and two β subunits.




**Quaternary Protein Structure: Three-Dimensional Arrangement of Subunit**

**SUGGESTING MATERIALS**

**Text Books:**

1. Morrison R.T & Boyd R.N., (1992), Organic Chemistry, Dorling Kindersley Pvt. Ltd., (Pearson Education)
2. Finar I.L (2002), Organic Chemistry- Volume 1, Dorling Kindersley Pvt. Ltd., (Pearson Education)
3. Finar I.L (2002), Organic Chemistry- Volume 2, Dorling Kindersley Pvt. Ltd., (Pearson Education).

**Reference Books:**

1. Nelson D.L & Cox M.M, (2012), Lehninger's Principles of Biochemistry, 7th Edition
2. Berg J.M, Tymoczko J.L & Stryer L. (2002), Biochemistry. W.H. Freeman

## Possible Questions

**Section A** **20x 1 = 20 marks**

**Answer all the questions**

1. At a pH below the isoelectric point, an amino acid exists as
a. **Cation** b. Anion c. Zwitter ion d. Undissociated molecule

2. An amino acid having a hydrohilic side chain is
a. Alanine b. Proline c. Methionine **d. Serine**

3. A protein rich in cysteine is
a. Collagen **b. Keratin** c. Heamoglobin d. Gelatin

4. Sanger's reagent contains
a. Phenylisothiocyanate b. Dansyl chloride **c. 1-Fluoro-2,4-dinitrobenzene** d. Ninhydrin

5. Primary structure of a protein is formed by
a. Hydrogen bonds **b. Peptide bonds** c. Disulphate bonds d. Ionic bond

6. α-Helix is formed by
a. **Hydrogen bonds** b. Hydrophobic bonds c. Electrostatic bonds d. Disulphide bonds

7. Glutelins are present in
a. **Milk** b. Eggs c. Meat d. Cereals

8. Two amino groups are present in
a. Lecuine b. Glutamate **c. Lysine** d. Threonine

9. All the following are branched chain amino acid except
a. Isoleucine **b. Alanine** c. Leucine d. Valine

10. Edmans reagent contains
a. **Phenylisothiocyanate** b. 1-Fluoro2,4-nitrobenzene c. Dansyl chloride d. tBOC azide

11. Edman's reaction can be used to
a. Determine the number of tyrosine residues in a protein
b. Determine the number of aromatic aminoacid residues in a protein
**c. Determine the amino acid sequence of a protein**
d. Hydrolyse the peptide bonds in a protein

12. The largest alpolipoprotein is
a. Apo E b. Apo B-48 **c. Apo B-100** d. Apo A- I

13. Apolipoprotein B-48 is synthesized in
a. Adipose tissue b. Liver **c. Intestine** d. Liver and intestine

14. Apolipoprotein A-1 acts as
a. **Enzyme activator** b. Ligand resistor c. Enzyme inhibitor d. Enzyme resistor
15. Apolipoprotein B-100 acts as
a. Enzyme activator **b. Ligand for receptor** c. Enzyme inhibitor d. Enzyme resistor

16. Apolipoprotein C II is an activator of
a. Lecithin cholesterola acyl transferase b. Phospholipase C
**c. Extrahepatic lipoprotein lipose** d. Hepatic lipoprotein lipase

17. Positive nitrogen balance is seen in
a. Starvation b. Wasting diseases **c. Growing age** d. Intestinal malabsorption

18. Glycine can be synthesized from
a. Serine b. Choline c. Betanine **d. tyrosin**

19. Non-Protein amino acids are
a. **Ornithine** b. β-alanine c. γ-amino butyric acid d. Glycine

20. Allosteric inhibitor of glutamate dehydrogenase is
a. **ATP** b. ADP c. AMP d. GMP

**Section-B (Answer all the questions) 5x2 = 10**

1. What is protein?
2. Define Zwitter ion
3. What is Isoelectric point
4. What is mean by Peptide linkage?
5. How the peptide linkage is formed?
6. Define Dipeptidase
7. Write a note on tBOC method for peptidase synthesis
8. How will you determine the amino acid by using DNFB method
9. What is aminoacid?
10. Write any four biological uses of proteins.

**Section- C (Answer all the questions) (5x6 = 30)**

1. Write a note on Zwitter ion and isoelectric point
2. Explain the Primary and secondary structure of Proteins
3. Give an account of tertiary and quatnary structure of proteins
4. Distinguish the structure of proteins?
5. How will you determine the peptide by DNFB and Edman method
6. How will you determine the C-terminal amino acid by using thiohydantion and carboxypeptidase method
7. Explain the synthesis of peptides based on N-production
8. Write any four methods for the peptides synthesis
9. What are the test available to determine the aminoacids
10. Explain the C-activating group and Merrifield synthesis of peptides

16CHU603B

Karpagam Academy of Higher Education

Coimbatore-21

(For the candidate admitted on 2016 onwards)

Department of Chemistry

VI- semester

Molecules of Life

| Unit-II Objective Questions for Online Examination (Each carry 1 Marks) | | | | | | |
|---|---|---|---|---|---|---|
| S.No. | Questions | Option A | Option B | Option C | Option D | Answer |
| 1 | At a pH below the isoelectric point, an amino acid exists as | Cation | Anion | Zwitter ion | Undissociated molecule | Cation |
| 2 | An amino acid having a hydrohilic side chain is | Alanine | Proline | Methionine | Serine | Serine |
| 3 | A protein rich in cysteine is | Collagen | Keratin | Haemoglobin | Gelatin | Keratin |
| 4 | Sanger's reagent contains | Phenylisothiocyanate | Dansyl chloride | 1-Fluoro-2,4-dinitrobenzene | Ninhydrin | 1-Fluoro-2,,4-dinirobenzene |
| 5 | Primary structure of a protein is formed by | Hydrogen bonds | Peptide bonds | Disulphate bonds | All of these | Peptide bonds |
| 6 | α-Helix is formed by | Hydrogen bonds | Hydrophobic bonds | Eletostatic bonds | Disulphide bonds | Hydrogen bonds |
| 7 | Glutelins are present in | Milk | Eggs | Meat | Cereals | Milk |
| 8 | Two amino groups are present in | Lecuine | Glutamate | Lysine | Threonine | Lysine |
| 9 | All the following are branched chain amino acid except | Isoleucine | Alanine | Leucine | Valine | Alanine |
| 10 | Edmans reagent contains | Phenylisothiocyanate | 1-Fluoro2,4-nitrobenzene | Dansyl chloride | tBOC azide | Phenylisothiocyanate |
| 11 | Edman's reaction can be used to | Determine the number of tyrosine residues in a protein | Determine the number of aromatic aminoacid residues in a protein | Determine the amino acid sequence of a protein | Hydrolyse the peptide bonds in a protein | Determine the amino acid sequence of a protein |
| 12 | The largest alpolipoprotein is | Apo E | Apo B-48 | Apo B-100 | Apo A- I | Apo B-100 |
| 13 | Apolipoprotein B-48 is synthesized in | Adipose tissue | Liver | Intestine | Liver and intestine | Intestine |
| 14 | Apolipoprotein A-1 acts as | Enzyme activator | Ligand resistor | Enzyme inhibitor | Enzyme resistor | Enzyme activator |
| 15 | Apolipoprotein B-100 acts as | Enzyme activator | Ligand for receptor | Enzyme inhibitor | Enzyme resistor | Ligand for acceptor |

| | | | | | | |
|---|---|---|---|---|---|---|
| 16 | Apolipoprotein C II is an activator of | Lecithin cholesterola acyl transferase | Phospholipase C | Extrahepatic lipoprotein lipose | Hepatic lipoprotein lipase | Extraheaptic lipoprotein lipase |
| 17 | Positive nitrogen balance is seen in | Starvation | Wasting diseases | Growing age | Intestinal malabsorption | Growing age |
| 18 | Glycine can be synthesized from | Serine | Choline | Betanine | tyrosin | All of these |
| 19 | Non-Protein amino acids are | Ornithine | β-alanine | γ-amino butyric acid | Glycine | Ornithine |
| 20 | Allosteric inhibitor of glutamate dehydrogenase is | ATP | ADP | AMP | GMP | ATP |
| 21 | Free amino is relesed during | Oxidative deamination of glutamide | Catabolism of pyruvate | anabolism of pyradines | Reductive deamination of galactose | Oxidative deamination of glutamide |
| 22 | Gluycine is not required for the formation of | Tauroidcholic acid | Creatine | Purines | Pyrimidines | Taurocholic acid |
| 23 | Pancreatic juice contains the precursors of all of the following except | Trypsin | Chymotrypsin | Carboxypeptidase | Aminopeptidase | Aminopeptidase |
| 24 | The most abundant immunoglobulin in plasma is | IgA | IgG | IgM | IgD | IgG |
| 25 | The largest immunoglobulin is | IgA | IgG | IgM | IgD | IgM |
| 26 | Allergic reactions are medited by | IgA | IgG | IgD | IgE | IgE |
| 27 | Antigens and haptens have the following similarity | They have high molecular weights | They can elicit immune response by themselves | They can elicit an immune response only in association with some other large molecule | Once an immune response develops , free antigen and free hapten can be recognized by the antibody | Once an immune response develops, free antigen and free antigen and free hapten can be recognized by the antibody |
| 28 | The molecular weight of the light chains is | 10,000-15,000 | 20,000-25,000 | 25,000-50,000 | 50,000-75,000 | 20,000-25,000 |
| 29 | The molecular weight of the heavy chains is | 20,000-25,000 | 25,000-50,000 | 50,000-70,000 | 70,000-1,00,000 | 50,000-70,000 |
| 30 | The half-life of IgG is | 2-3 days | 5-6 days | 8-10 days | 20-25 dys | 20-25 days |
| 31 | The components of compliment system are activated by | Microsomal hydroxylation | Phosphorylation | Glycosylation | Proteloysis | Proteloysis |
| 32 | Which amino acid is lipotropic factor? | Lysine | Leucine | Tryptophan | Methionine | Methionine |
| 33 | Which among the following a basic aminoacid | Aspargine | Arginine | Proline | Alanine | Arginine |

| | | | | | | |
|---|---|---|---|---|---|---|
| 34 | This amion acid cannot have optical isomers | Alanine | Histidine | Threonine | Glycine | Glycine |
| 35 | GABA(Gama amino butyric acid) is | Past-synaptic excitatory transmitter | Past-synaptic inhibitor trasmitter | activtor of glio-cell function | inhibitor of glio-cell function | Past-synaptic inhibitor tranmitter |
| 36 | Sulphur containing amino acid is | Glutathione | Chandroitin sulphate | Homocysteine | Tryptophan | Homocysteine |
| 37 | The amino acid which contains an indole group is | Histidine | Arginine | Glycine | Tryptophan | Tryptophan |
| 38 | Which among the following has an imidazole group? | Histidine | Trptophan | Proline | Hydroxy proline | Histidine |
| 39 | The neutral amino acid is | Lysine | Proline | Leucine | Histidine | Leucine |
| 40 | The sulphur containing amino acid | Homoserine | Serine | Methionine | Valine | Methionine |
| 41 | Egg is poor in | Essential amino acids | Carbohydrates | Avidin | Biotin | Carbohydrates |
| 42 | Cholestrol is present in all the following except | Milk | Fish | Egg white | Egg yolk | Egg white |
| 43 | Plasma calcium is lowered by | Parathormone | Calcitonin | Aldosterase | Deoxycorticosterone | Calcitonin |
| 44 | Gastrin stimulates | Gastric motility | Irritation | Allergy | Diahhreo | Gastric motility |
| 45 | All of the following are glyoproteins except | Collagen | Albumin | Transferrin | IgM | Albumin |
| 46 | Sialic acids are present in | Proteoglycans | Glycoproteins | Both (A) and (B) | None of these | Glycoproteins |
| 47 | Normal range of serum urea is | 0.6-1.5mg/dl | 9-11 mg/dl | 20-45 mg/dl | 60-100 mg/dl | 20-45 mg/gl |
| 48 | Sakaguchi reaction is answered by | Lysine | Ornithine | Arginine | Arinino succinic acid | Arginine |
| 49 | The pH of amino acid depends upon | Opticl rotation | Disociation constant | Diffusion coefficient | Chain length | Dissociation constant |
| 50 | Plasma proteins are isolated by | Salting out | Distilation | Flouimetry | Flotation | Salting out |
| 51 | Branched chain amino acids are | Cysteine and cystine | Tyrosine and tryptophan | Glycine and serine | Valine,Leucine and Isoleucine | Valine,Leucine and Isoleucine |
| 52 | Million's tst is for identification of | Tyrosine | Trptophan | Proline | Arginine | Tyrosine |
| 53 | The ionizable grups of amino acids are atleast | 1 | 2 | 3 | 4 | 2 |
| 54 | Amino acids are insoluble in | Acetic acid | Chloroform | Ethanol | Benzene | Benzene |
| 55 | The role of complement proteins | Defense | Helps immunity of the body | Helps digestive process | Help ion transfer | Defence |
| 56 | Albuminoids are similar to | Albumin | Aminoacids | Carbohydrates | Enzyme | Albumin |

| | | | | | | |
|---|---|---|---|---|---|---|
| 57 | One of the following amino acid is solely ketogenic | Lysine | Alanine | Valine | Glutamate | Lysine |
| 58 | 2-amino 3-OH propanoic acid is | Glycine | Alanine | Valine | Serine | Serine |
| 59 | $NH_3$ is detoxified in brain chiefly as | Urea | Uric acid | Creatinine | Glutamine | Glutamine |
| 60 | Cystenine has the formula | $CH_3SH$ | $H_2N\text{-}CH_2\text{-}COOH$ | $HS\text{-}CH_2\text{-}CH(NH_2)\text{-}COOH$ | $HOOC\text{-}CH_2\text{-}CH_2NH_2$ | $HS\text{-}CH_2\text{-}CH(NH_2)\text{-}COOH$ |

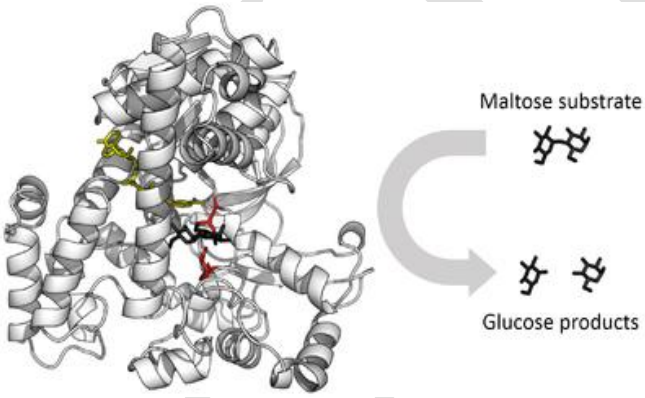
## Unit-III
## Syllabus

**ENZYMES AND CORRELATION WITH DRUG ACTION**

Mechanism of enzyme action, factors affecting enzyme action, Coenzymes and cofactors and their role in biological reactions, Specificity of enzyme action(Including stereospecificity), Enzyme inhibitors and their importance, phenomenon of inhibition(Competitive and Noncompetitive inhibition including allosteric inhibition). Drug action-receptor theory. Structure –activity relationships of drug molecules, binding role of –OH group,-$NH_2$ group, double bond and aromatic ring.

### Enzyme

*"Biocatalyst" redirects here. For the use of natural catalysts in organic chemistry.*




The enzyme glucosidase converts the sugar maltose to two glucosesugars. Active site residues in red, maltose substrate in black, and NADcofactor in yellow.

### Introduction

**Enzymes** are macromolecular biological catalysts. Enzymes accelerate chemical reactions. The molecules upon which enzymes may act are called substrates and the enzyme converts the substrates into different molecules known as products. Almost all metabolic processes in the cell need enzyme catalysis in order to occur at rates fast enough to sustain life. Metabolic pathways depend upon enzymes to catalyze individual steps. The study of enzymes is called *enzymology* and a new field of pseudoenzyme analysis has recently grown up, recognising that during evolution, some enzymes have lost the ability to carry out biological catalysis, which is often reflected in their amino acid sequences and unusual 'pseudocatalytic' properties.

Enzymes are known to catalyze more than 5,000 biochemical reaction types. Most enzymes are proteins, although a few are catalytic RNA molecules. The latter are called ribozymes. Enzymes' specificity comes from their unique three-dimensional structures.

Like all catalysts, enzymes increase the reaction rate by lowering its activation energy. Some enzymes can make their conversion of substrate to product occur many millions of times faster. An extreme example is orotidine 5'-phosphate decarboxylase, which allows a reaction that would otherwise take millions of years to occur in milliseconds. Chemically, enzymes are like any catalyst and are not consumed in chemical reactions, nor do they alter the equilibrium of a reaction. Enzymes differ from most other catalysts by being much more specific. Enzyme activity can be affected by other molecules: inhibitors are molecules that decrease enzyme activity, and activators are molecules that increase activity. Many therapeutic drugs and poisons are enzyme inhibitors. An enzyme's activity decreases markedly outside its optimal temperature and pH, and many enzymes are (permanently) denatured when exposed to excessive heat, losing their structure and catalytic properties.

Some enzymes are used commercially, for example, in the synthesis of antibiotics. Some household products use enzymes to speed up chemical reactions: enzymes in biological washing powders break down protein, starch or fat stains on clothes, and enzymes in meat tenderizer break down proteins into smaller molecules, making the meat easier to chew

**Etymology and history**

**Eduard Buchner**

By the late 17th and early 18th centuries, the digestion of meat by stomach secretions and the conversion of starch to sugars by plant extracts and saliva were known but the mechanisms by which these occurred had not been identified.

French chemist Anselme Payen was the first to discover an enzyme, diastase, in 1833.[9] A few decades later, when studying the fermentation of sugar to alcohol by yeast, Louis Pasteur concluded that this fermentation was caused by a vital force contained within the yeast cells called "ferments", which were thought to function only within living organisms. He wrote that "alcoholic fermentation is an act correlated with the life and organization of the yeast cells, not with the death or putrefaction of the cells."

In 1877, German physiologist Wilhelm Kühne (1837–1900) first used the term *enzyme*, which comes from Greek ἔνζυμον, "leavened" or "in yeast", to describe this process. The word *enzyme* was used later to refer to nonliving substances such as pepsin, and the word *ferment* was used to refer to chemical activity produced by living organisms. Eduard Buchner submitted his first paper on the study of yeast extracts in 1897. In a series of experiments at the University of Berlin, he found that sugar was fermented by yeast extracts even when there were no living yeast cells in the mixture. He named the enzyme that brought about the fermentation of sucrose "zymase".

In 1926, James B. Sumnershowed that the enzyme urease was a pure protein and crystallized it; he did likewise for the enzyme catalase in 1937. The conclusion that pure proteins can be enzymes was definitively demonstrated by John Howard Northrop and Wendell Meredith Stanley, who worked on the digestive enzymes pepsin (1930), trypsin and chymotrypsin. These three scientists were awarded the 1946 Nobel Prize in Chemistry.

The discovery that enzymes could be crystallized eventually allowed their structures to be solved by x-ray crystallography. This was first done for lysozyme, an enzyme found in tears, saliva and egg whites that digests the coating of some bacteria; the structure was solved by a group led by David Chilton Phillips and published in 1965. This high-resolution structure of lysozyme marked the beginning of the field of structural biology and the effort to understand how enzymes work at an atomic level of detail.

**Naming conventions**

An enzyme's name is often derived from its substrate or the chemical reaction it catalyzes, with the word ending in *-ase*.

Examples are lactase, alcohol dehydrogenase and DNA polymerase. Different enzymes that catalyze the same chemical reaction are called isozymes.

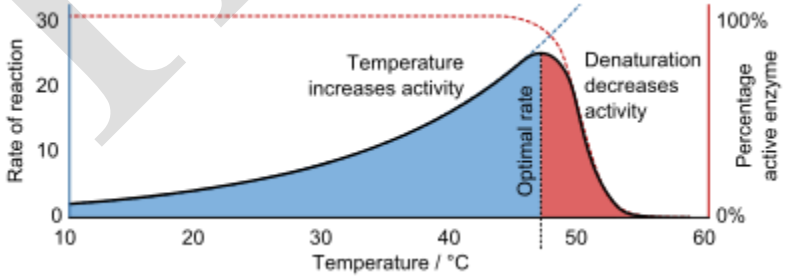
The International Union of Biochemistry and Molecular Biology have developed a nomenclature for enzymes, the EC numbers; each enzyme is described by a sequence of four numbers preceded by "EC", which stands for "Enzyme Commission". The first number broadly classifies the enzyme based on its mechanism.

The top-level classification is:

- EC 1, Oxidoreductases: catalyze oxidation/reduction reactions
- EC 2, Transferases: transfer a functional group (*e.g.* a methyl or phosphate group)
- EC 3, Hydrolases: catalyze the hydrolysis of various bonds
- EC 4, Lyases: cleave various bonds by means other than hydrolysis and oxidation
- EC 5, Isomerases: catalyze isomerization changes within a single molecule
- EC 6, Ligases: join two molecules with covalent bonds.

These sections are subdivided by other features such as the substrate, products, and chemical mechanism. An enzyme is fully specified by four numerical designations. For example, hexokinase (EC 2.7.1.1) is a transferase (EC 2) that adds a phosphate group (EC 2.7) to a hexose sugar, a molecule containing an alcohol group (EC 2.7.1).

**Structure**




Enzyme activity initially increases with temperature (Q10 coefficient) until the enzyme's structure unfolds (denaturation), leading to an optimal rate of reaction at an intermediate temperature.

Enzymes are generally globular proteins, acting alone or in larger complexes. The sequence of the amino acids specifies the structure which in turn determines the catalytic activity of the enzyme. Although structure determines function, a novel enzymatic activity cannot yet be predicted from structure alone. Enzyme structures unfold (denature) when heated or exposed to chemical denaturants and this disruption to the structure typically causes a loss of activity.[24] Enzyme denaturation is normally linked to temperatures above a species' normal level; as a result, enzymes from bacteria living in volcanic environments such as hot springs are prized by industrial users for their ability to function at high temperatures, allowing enzyme-catalysed reactions to be operated at a very high rate.

Enzymes are usually much larger than their substrates. Sizes range from just 62 amino acid residues, for the monomer of 4-oxalocrotonate tautomerase, to over 2,500 residues in the animal fatty acid synthase. Only a small portion of their structure (around 2–4 amino acids) is directly involved in catalysis: the catalytic site. This catalytic site is located next to one or more binding sites where residues orient the substrates. The catalytic site and binding site together comprise the enzyme's active site. The remaining majority of the enzyme structure serves to maintain the precise orientation and dynamics of the active site.

In some enzymes, no amino acids are directly involved in catalysis; instead, the enzyme contains sites to bind and orient catalytic cofactors. Enzyme structures may also contain allosteric sites where the binding of a small molecule causes a conformational change that increases or decreases activity.[29]

A small number of RNA-based biological catalysts called ribozymes exist, which again can act alone or in complex with proteins. The most common of these is the ribosome which is a complex of protein and catalytic RNA components.

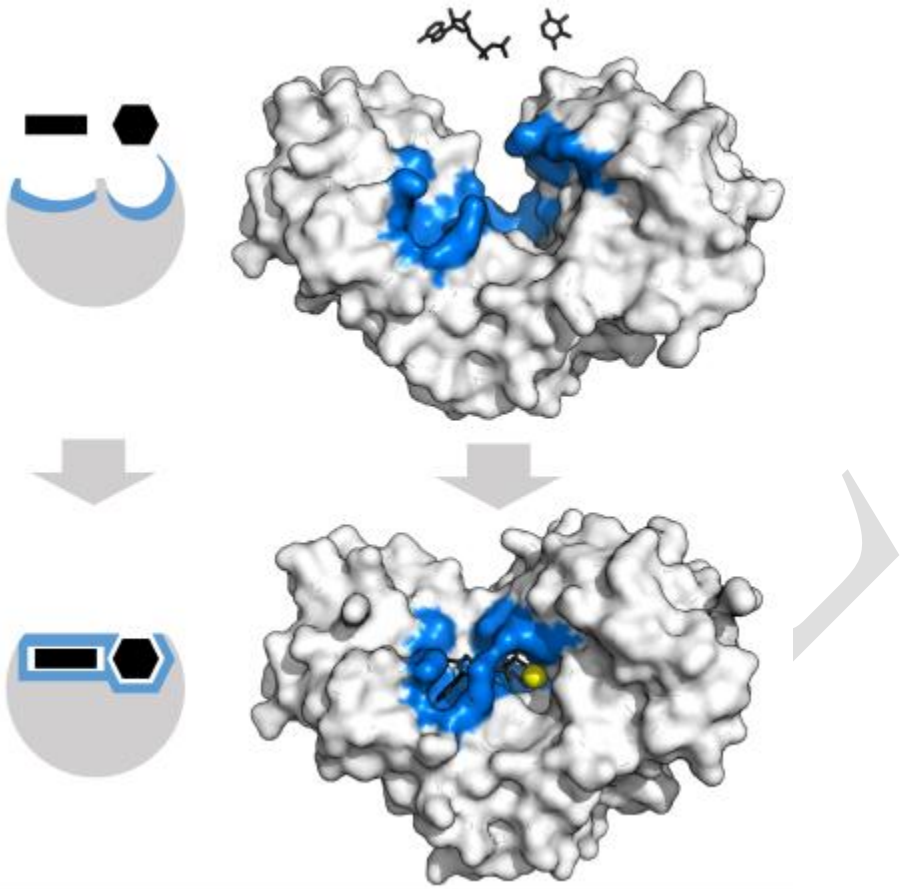
**Mechanism**

**Substrate binding**

Enzymes must bind their substrates before they can catalyse any chemical reaction. Enzymes are usually very specific as to what substrates they bind and then the chemical reaction catalysed. Specificity is achieved by binding pockets with complementary shape, charge and hydrophilic/hydrophobic characteristics to the substrates. Enzymes can therefore distinguish between very similar substrate molecules to be chemoselective, regioselective and stereospecific.

Some of the enzymes showing the highest specificity and accuracy are involved in the copying and expression of the genome. Some of these enzymes have "proof-reading" mechanisms. Here, an enzyme such as DNA polymerase catalyzes a reaction in a first step and then checks that the product is correct in a second step. This two-step process results in average error rates of less than 1 error in 100 million reactions in high-fidelity mammalian polymerases. Similar proofreading mechanisms are also found in RNA polymerase, aminoacyl tRNA synthetases and ribosomes.

Conversely, some enzymes display enzyme promiscuity, having broad specificity and acting on a range of different physiologically relevant substrates. Many enzymes possess small side activities which arose fortuitously (i.e. neutrally), which may be the starting point for the evolutionary selection of a new function.



Enzyme changes shape by induced fit upon substrate binding to form enzyme-substrate complex. Hexokinase has a large induced fit motion that closes over the substrates adenosine triphosphate and xylose. Binding sites in blue, substrates in black and $Mg^{2+}$ cofactor in yellow.

**"Lock and key" model**

To explain the observed specificity of enzymes, in 1894 Emil Fischer proposed that both the enzyme and the substrate possess specific complementary geometric shapes that fit exactly into one another. This is often referred to as "the lock and key" model. This early model explains enzyme specificity, but fails to explain the stabilization of the transition state that enzymes achieve.

**Induced fit model**

In 1958, Daniel Koshland suggested a modification to the lock and key model: since enzymes are rather flexible structures, the active site is continuously reshaped by interactions with the substrate as the substrate interacts with the enzyme. As a result, the substrate does not simply bind to a rigid active site; the amino acid side-chains that make up the active site are molded into the precise positions that enable the enzyme to perform its catalytic function. In some cases, such as glycosidases, the substrate molecule also changes shape slightly as it enters the active site. The

active site continues to change until the substrate is completely bound, at which point the final shape and charge distribution is determined. Induced fit may enhance the fidelity of molecular recognition in the presence of competition and noise via the conformational proofreading mechanism.

**Catalysis**

Enzymes can accelerate reactions in several ways, all of which lower the activation energy ($\Delta G^{\ddagger}$, Gibbs free energy)

1. By stabilizing the transition state:
   - Creating an environment with a charge distribution complementary to that of the transition state to lower its energy
2. By providing an alternative reaction pathway:
   - Temporarily reacting with the substrate, forming a covalent intermediate to provide a lower energy transition state
3. By destabilising the substrate ground state:
   - Distorting bound substrate(s) into their transition state form to reduce the energy required to reach the transition state
   - By orienting the substrates into a productive arrangement to reduce the reaction entropy change (the contribution of this mechanism to catalysis is relatively small)

Enzymes may use several of these mechanisms simultaneously. For example, proteases such as trypsin perform covalent catalysis using a catalytic triad, stabilise charge build-up on the transition states using an oxyanion hole, complete hydrolysis using an oriented water substrate.

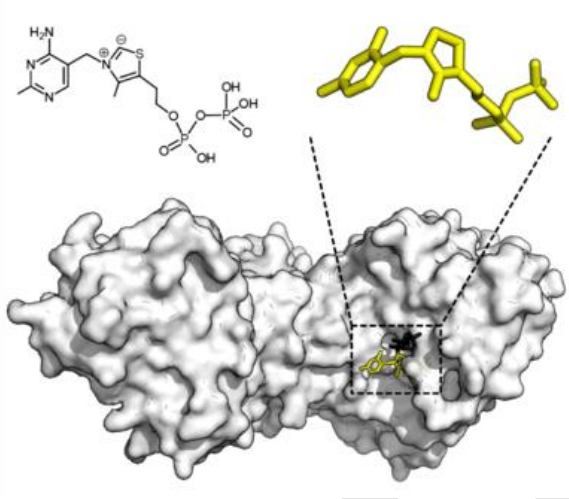
**Dynamics**

Enzymes are not rigid, static structures; instead they have complex internal dynamic motions – that is, movements of parts of the enzyme's structure such as individual amino acid residues, groups of residues forming a protein loop or unit of secondary structure, or even an entire protein domain. These motions give rise to a conformational ensemble of slightly different structures that interconvert with one another at equilibrium. Different states within this ensemble may be associated with different aspects of an enzyme's function. For example, different conformations of the enzyme dihydrofolate reductase are associated with the substrate binding, catalysis, cofactor release, and product release steps of the catalytic cycle.

**Allosteric modulation**

Allosteric sites are pockets on the enzyme, distinct from the active site, that bind to molecules in the cellular environment. These molecules then cause a change in the conformation or dynamics of the enzyme that is transduced to the active site and thus affects the reaction rate of the enzyme. In this way, allosteric interactions can either inhibit or activate enzymes. Allosteric interactions with metabolites upstream or downstream in an enzyme's metabolic pathway cause feedback regulation, altering the activity of the enzyme according to the flux through the rest of the pathway.

Cofactors



Chemical structure for thiamine pyrophosphate and protein structure of transketolase. Thiamine pyrophosphate cofactor in yellow and xylulose 5-phosphate substrate in black.

Some enzymes do not need additional components to show full activity. Others require non-protein molecules called cofactors to be bound for activity. Cofactors can be either inorganic (e.g., metal ions and iron-sulfur clusters) or organic compounds (e.g., flavin and heme). These cofactors serve many purposes; for instance, metal ions can help in stabilizing nucleophilic species within the active site. Organic cofactors can be either coenzymes, which are released from the enzyme's active site during the reaction, or prosthetic groups, which are tightly bound to an enzyme. Organic prosthetic groups can be covalently bound (e.g., biotin in enzymes such as pyruvate carboxylase).

An example of an enzyme that contains a cofactor is carbonic anhydrase, which is shown in the ribbon diagramabove with a zinc cofactor bound as part of its active site. These tightly bound ions or molecules are usually found in the active site and are involved in catalysis.

For example, flavin and heme cofactors are often involved in redox reactions.

Enzymes that require a cofactor but do not have one bound are called *apoenzymes* or *apoproteins*. An enzyme together with the cofactor(s) required for activity is called a *holoenzyme* (or haloenzyme). The term *holoenzyme*can also be applied to enzymes that contain multiple protein subunits, such as the DNA polymerases; here the holoenzyme is the complete complex containing all the subunits needed for activity.

**Coenzymes**

Coenzymes are small organic molecules that can be loosely or tightly bound to an enzyme. Coenzymes transport chemical groups from one enzyme to another.

Examples include NADH, NADPH and adenosine triphosphate (ATP).

Some coenzymes, such as flavin mononucleotide(FMN), flavin adenine dinucleotide (FAD), thiamine pyrophosphate (TPP), and tetrahydrofolate (THF), are derived

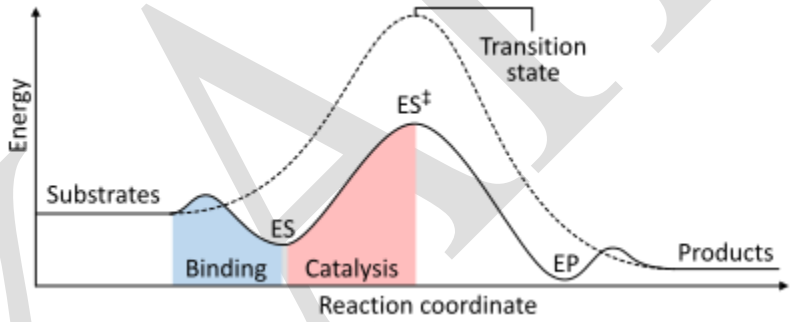
from vitamins. These coenzymes cannot be synthesized by the body *de novo* and closely related compounds (vitamins) must be acquired from the diet. The chemical groups carried include:

- the hydride ion ($H^-$), carried by NAD or $NADP^+$
- the phosphate group, carried by adenosine triphosphate
- the acetyl group, carried by coenzyme A
- formyl, methenyl or methyl groups, carried by folic acid and
- the methyl group, carried by S-adenosylmethionine

Since coenzymes are chemically changed as a consequence of enzyme action, it is useful to consider coenzymes to be a special class of substrates, or second substrates, which are common to many different enzymes. For example, about 1000 enzymes are known to use the coenzyme NADH.

Coenzymes are usually continuously regenerated and their concentrations maintained at a steady level inside the cell. For example, NADPH is regenerated through the pentose phosphate pathway and *S*-adenosylmethionine by methionine adenosyltransferase. This continuous regeneration means that small amounts of coenzymes can be used very intensively. For example, the human body turns over its own weight in ATP each day.

**Thermodynamics**




The energies of the stages of a chemical reaction. Uncatalysed (dashed line), substrates need a lot of activation energy to reach a transition state, which then decays into lower-energy products. When enzyme catalysed (solid line), the enzyme binds the substrates (ES), then stabilizes the transition state ($ES^‡$) to reduce the activation energy required to produce products (EP) which are finally released.

As with all catalysts, enzymes do not alter the position of the chemical equilibrium of the reaction. In the presence of an enzyme, the reaction runs in the same direction as it would without the enzyme, just more quickly.

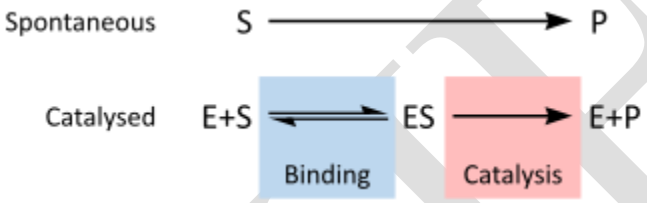
For example, carbonic anhydrase catalyzes its reaction in either direction depending on the concentration of its reactants:

The rate of a reaction is dependent on the activation energy needed to form the transition state which then decays into products. Enzymes increase reaction rates by lowering the energy of

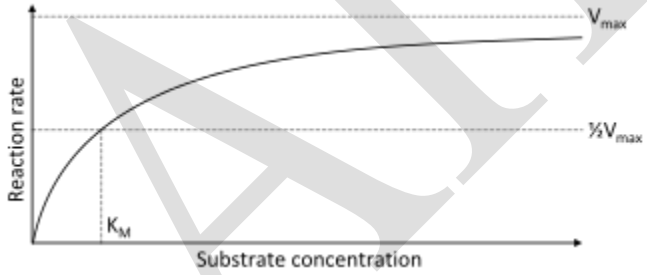
the transition state. First, binding forms a low energy enzyme-substrate complex (ES). Secondly the enzyme stabilises the transition state such that it requires less energy to achieve compared to the uncatalyzed reaction ($ES^{‡}$). Finally the enzyme-product complex (EP) dissociates to release the products.

Enzymes can couple two or more reactions, so that a thermodynamically favorable reaction can be used to "drive" a thermodynamically unfavourable one so that the combined energy of the products is lower than the substrates. For example, the hydrolysis of ATP is often used to drive other chemical reactions.

**Kinetics**




A chemical reaction mechanism with or without enzyme catalysis. The enzyme (E) binds substrate (S) to produce product (P).




Saturation curve for an enzyme reaction showing the relation between the substrate concentration and reaction rate.

Enzyme kinetics is the investigation of how enzymes bind substrates and turn them into products. The rate data used in kinetic analyses are commonly obtained from enzyme assays. In 1913 Leonor Michaelis and Maud Leonora Mentenproposed a quantitative theory of enzyme kinetics, which is referred to as Michaelis–Menten kinetics. The major contribution of Michaelis and Menten was to think of enzyme reactions in two stages. In the first, the substrate binds reversibly to the enzyme, forming the enzyme-substrate complex. This is sometimes called the Michaelis-Menten complex in their honor. The enzyme then catalyzes the chemical step in the reaction and releases the product. This work was further developed by G. E. Briggs and J. B. S. Haldane, who derived kinetic equations that are still widely used today.

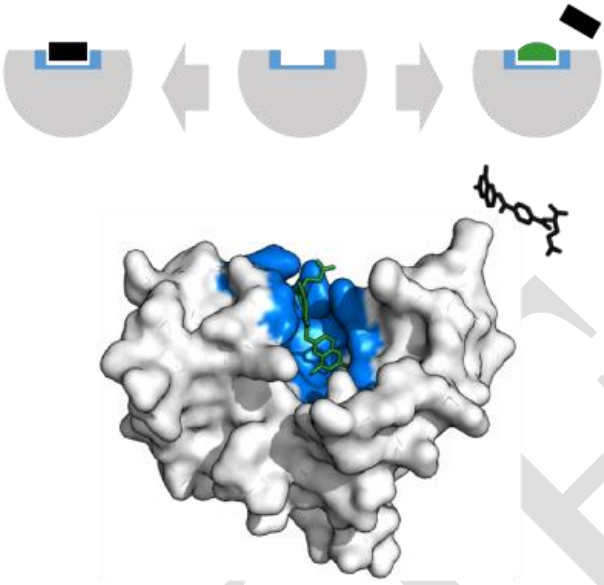
Enzyme rates depend on solution conditions and substrate concentration. To find the maximum speed of an enzymatic reaction, the substrate concentration is increased until a constant rate of product formation is seen. This is shown in the saturation curve on the right. Saturation happens

because, as substrate concentration increases, more and more of the free enzyme is converted into the substrate-bound ES complex. At the maximum reaction rate ($V_{max}$) of the enzyme, all the enzyme active sites are bound to substrate, and the amount of ES complex is the same as the total amount of enzyme.

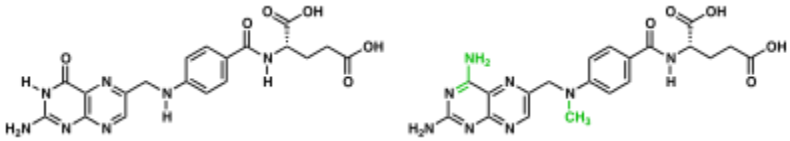
$V_{max}$ is only one of several important kinetic parameters. The amount of substrate needed to achieve a given rate of reaction is also important. This is given by the Michaelis-Menten constant ($K_m$), which is the substrate concentration required for an enzyme to reach one-half its maximum reaction rate; generally, each enzyme has a characteristic $K_M$ for a given substrate. Another useful constant is $k_{cat}$, also called the *turnover number*, which is the number of substrate molecules handled by one active site per second.

The efficiency of an enzyme can be expressed in terms of $k_{cat}/K_m$. This is also called the specificity constant and incorporates the rate constants for all steps in the reaction up to and including the first irreversible step. Because the specificity constant reflects both affinity and catalytic ability, it is useful for comparing different enzymes against each other, or the same enzyme with different substrates. The theoretical maximum for the specificity constant is called the diffusion limit and is about $10^8$ to $10^9$ ($M^{-1}$ $s^{-1}$). At this point every collision of the enzyme with its substrate will result in catalysis, and the rate of product formation is not limited by the reaction rate but by the diffusion rate. Enzymes with this property are called *catalytically perfect* or *kinetically perfect*. Example of such enzymes are triose-phosphate isomerase, carbonic anhydrase, acetylcholinesterase, catalase, fumarase, β-lactamase, and superoxide dismutase. The turnover of such enzymes can reach several million reactions per second.
Michaelis–Menten kinetics relies on the law of mass action, which is derived from the assumptions of free diffusion and thermodynamically driven random collision. Many biochemical or cellular processes deviate significantly from these conditions, because of macromolecular crowding and constrained molecular movement. More recent, complex extensions of the model attempt to correct for these effects.

**Inhibition**



An enzyme binding site that would normally bind substrate can alternatively bind a competitive inhibitor, preventing substrate access. Dihydrofolate reductase is inhibited by methotrexate which prevents binding of its substrate, folic acid. Binding site in blue, inhibitor in green, and substrate in black.



The coenzyme folic acid (left) and the anti-cancer drug methotrexate(right) are very similar in structure (differences show in green). As a result, methotrexate is a competitive inhibitor of many enzymes that use folates.

Enzyme reaction rates can be decreased by various types of enzyme inhibitors.

**Types of inhibition**

**Competitive**

A competitive inhibitor and substrate cannot bind to the enzyme at the same time. Often competitive inhibitors strongly resemble the real substrate of the enzyme. For example, the drug methotrexate is a competitive inhibitor of the enzyme dihydrofolate reductase, which catalyzes the reduction of dihydrofolate to tetrahydrofolate. The similarity between the structures of dihydrofolate and this drug are shown in the accompanying figure. This type of inhibition can be overcome with high substrate concentration. In some cases, the inhibitor can bind to a site other than the binding-site of the usual substrate and exert an allosteric effect to change the shape of the usual binding-site.

**Non-competitive**

A non-competitive inhibitor binds to a site other than where the substrate binds. The substrate still binds with its usual affinity and hence $K_m$ remains the same. However the inhibitor reduces the catalytic efficiency of the enzyme so that $V_{max}$ is reduced. In contrast to competitive inhibition, non-competitive inhibition cannot be overcome with high substrate concentration.

**Uncompetitive**

An uncompetitive inhibitor cannot bind to the free enzyme, only to the enzyme-substrate complex; hence, these types of inhibitors are most effective at high substrate concentration. In the presence of the inhibitor, the enzyme-substrate complex is inactive. This type of inhibition is rare.

**Mixed**

A mixed inhibitor binds to an allosteric site and the binding of the substrate and the inhibitor affect each other. The enzyme's function is reduced but not eliminated when bound to the inhibitor. This type of inhibitor does not follow the Michaelis-Menten equation.

**Irreversible**

An irreversible inhibitor permanently inactivates the enzyme, usually by forming a covalent bond to the protein. Penicillin and aspirin are common drugs that act in this manner.

**Functions of inhibitors**

In many organisms, inhibitors may act as part of a feedback mechanism. If an enzyme produces too much of one substance in the organism, that substance may act as an inhibitor for the enzyme at the beginning of the pathway that produces it, causing production of the substance to slow down or stop when there is sufficient amount. This is a form of negative feedback. Major metabolic pathways such as the citric acid cycle make use of this mechanism.

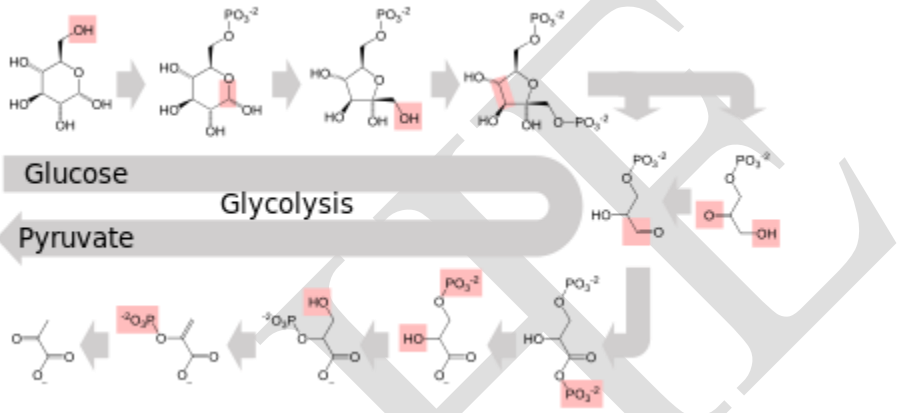
Since inhibitors modulate the function of enzymes they are often used as drugs. Many such drugs are reversible competitive inhibitors that resemble the enzyme's native substrate, similar to methotrexate above; other well-known examples include statins used to treat high cholesterol, and protease inhibitors used to treat retroviral infections such as HIV. A common example of an irreversible inhibitor that is used as a drug is aspirin, which inhibits the COX-1 and COX-2 enzymes that produce the inflammation messenger prostaglandin. Other enzyme inhibitors are poisons. For example, the poison cyanide is an irreversible enzyme inhibitor that combines with the copper and iron in the active site of the enzyme cytochrome c oxidase and blocks cellular respiration.

**Biological function**

Enzymes serve a wide variety of functions inside living organisms. They are indispensable for signal transduction and cell regulation, often via kinases and phosphatases. They also generate movement, with myosin hydrolyzing ATP to generate muscle contraction, and also transport cargo around the cell as part of the cytoskeleton. Other ATPases in the cell membrane are ion pumps involved in active transport. Enzymes are also involved in more exotic functions, such as luciferase generating light in fireflies. Viruses can also contain enzymes for infecting cells, such as the HIV integrase and reverse transcriptase, or for viral release from cells, like the influenza virus neuraminidase.

An important function of enzymes is in the digestive systems of animals. Enzymes such as amylases and proteases break down large molecules (starch or proteins, respectively) into smaller ones, so they can be absorbed by the intestines. Starch molecules, for example, are too large to be absorbed from the intestine, but enzymes hydrolyze the starch chains into smaller molecules such as maltose and eventually glucose, which can then be absorbed. Different enzymes digest different food substances. In ruminants, which have herbivorousdiets, microorganisms in the gut produce another enzyme, cellulase, to break down the cellulose cell walls of plant fiber.[83]

**Metabolism**




The metabolic pathway of glycolysis releases energy by converting glucose to pyruvate via a series of intermediate metabolites. Each chemical modification (red box) is performed by a different enzyme.

Several enzymes can work together in a specific order, creating metabolic pathways. In a metabolic pathway, one enzyme takes the product of another enzyme as a substrate. After the catalytic reaction, the product is then passed on to another enzyme. Sometimes more than one enzyme can catalyze the same reaction in parallel; this can allow more complex regulation: with, for example, a low constant activity provided by one enzyme but an inducible high activity from a second enzyme.

Enzymes determine what steps occur in these pathways. Without enzymes, metabolism would neither progress through the same steps and could not be regulated to serve the needs of the cell. Most central metabolic pathways are regulated at a few key steps, typically through enzymes whose activity involves the hydrolysis of ATP. Because this reaction releases so much energy, other reactions that are thermodynamically unfavorablecan be coupled to ATP hydrolysis, driving the overall series of linked metabolic reactions.

**Control of activity**

There are five main ways that enzyme activity is controlled in the cell.

**Regulation**

Enzymes can be either activated or inhibited by other molecules. For example, the end product(s) of a metabolic pathway are often inhibitors for one of the first enzymes of the pathway (usually the

first irreversible step, called committed step), thus regulating the amount of end product made by the pathways. Such a regulatory mechanism is called a negative feedback mechanism, because the amount of the end product produced is regulated by its own concentration. Negative feedback mechanism can effectively adjust the rate of synthesis of intermediate metabolites according to the demands of the cells. This helps with effective allocations of materials and energy economy, and it prevents the excess manufacture of end products. Like other homeostatic devices, the control of enzymatic action helps to maintain a stable internal environment in living organisms.

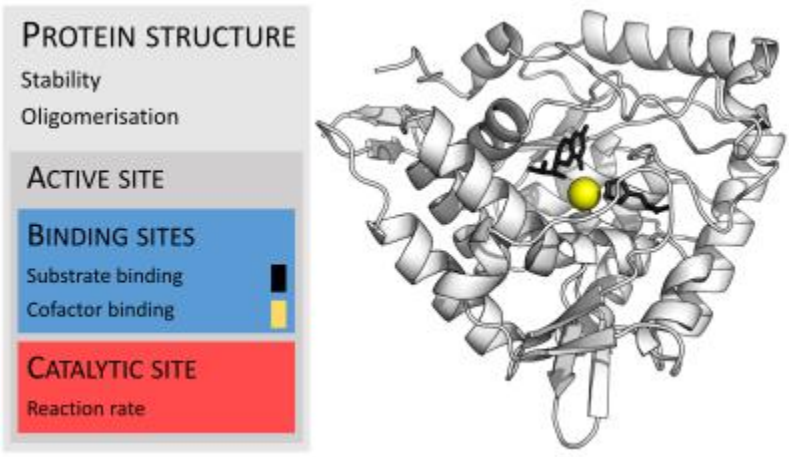
**Subcellular distribution**

Enzymes can be compartmentalized, with different metabolic pathways occurring in different cellular compartments. For example, fatty acids are synthesized by one set of enzymes in the cytosol, endoplasmic reticulum and Golgi and used by a different set of enzymes as a source of energy in the mitochondrion, through β-oxidation. In addition, trafficking of the enzyme to different compartments may change the degree of protonation (e.g., the neutral cytoplasm and the acidic lysosome) or oxidative state (e.g., oxidizing periplasm or reducing cytoplasm) which in turn affects enzyme activity. In contrast to partitioning into membrane bound organelles, enzyme subcellular localisation may also be altered through polymerisation of enzymes into macromolecular cytoplasmic filaments.

**Organ specialization**

In multicellular eukaryotes, cells in different organs and tissues have different patterns of gene expression and therefore have different sets of enzymes (known as isozymes) available for metabolic reactions. This provides a mechanism for regulating the overall metabolism of the organism. For example, hexokinase, the first enzyme in the glycolysispathway, has a specialized form called glucokinase expressed in the liver and pancreas that has a lower affinity for glucose yet is more sensitive to glucose concentration. This enzyme is involved in sensing blood sugar and regulating insulin production.

**Involvement in disease**



In phenylalanine hydroxylase over 300 different mutations throughout the structure cause phenylketonuria. Phenylalaninesubstrate and tetrahydrobiopterin coenzyme in black, and $Fe^{2+}$ cofactor in yellow.

Since the tight control of enzyme activity is essential for homeostasis, any malfunction (mutation, overproduction, underproduction or deletion) of a single critical enzyme can lead to a genetic disease. The malfunction of just one type of enzyme out of the thousands of types present in the human body can be fatal. An example of a fatal genetic disease due to enzyme insufficiency is Tay–Sachs disease, in which patients lack the enzyme hexosaminidase.

One example of enzyme deficiency is the most common type of phenylketonuria. Many different single amino acid mutations in the enzyme phenylalanine hydroxylase, which catalyzes the first step in the degradation of phenylalanine, result in build-up of phenylalanine and related products. Some mutations are in the active site, directly disrupting binding and catalysis, but many are far from the active site and reduce activity by destabilising the protein structure, or affecting correct oligomerisation. This can lead to intellectual disability if the disease is untreated. Another example is pseudocholinesterase deficiency, in which the body's ability to break down choline ester drugs is impaired. Oral administration of enzymes can be used to treat some functional enzyme deficiencies, such as pancreatic insufficiency and lactose intolerance.

Another way enzyme malfunctions can cause disease comes from germline mutations in genes coding for DNA repair enzymes. Defects in these enzymes cause cancer because cells are less able to repair mutations in their genomes. This causes a slow accumulation of mutations and results in the development of cancers. An example of such a hereditary cancer syndrome is xeroderma pigmentosum, which causes the development of skin cancers in response to even minimal exposure to ultraviolet light.

**Industrial applications**

Enzymes are used in the chemical industry and other industrial applications when extremely specific catalysts are required. Enzymes in general are limited in the number of reactions they have evolved to catalyze and also by their lack of stability in organic solvents and at high temperatures. As a consequence, protein engineering is an active area of research and involves attempts to create new enzymes with novel properties, either through rational design or *in vitro* evolution. These efforts have begun to be successful, and a few enzymes have now been designed "from scratch" to catalyze reactions that do not occur in nature.

| Application | Enzymes used | Uses |
|---|---|---|
| **Biofuel industry** | Cellulases | Break down cellulose into sugars that can be fermented to produce cellulosic ethanol. |

| | | |
|---|---|---|
| | Ligninases | Pretreatment of biomass for biofuel production. |
| **Biological detergent** | Proteases, amylases, lipases | Remove protein, starch, and fat or oil stains from laundry and dishware. |
| | Mannanases | Remove food stains from the common food additive guar gum. |
| **Brewing industry** | Amylase, glucanases, proteases | Split polysaccharides and proteins in the malt. |
| | Betaglucanases | Improve the wort and beer filtration characteristics. |
| | Amyloglucosidase and pullulanases | Make low-calorie beer and adjust fermentability. |
| | Acetolactate decarboxylase (ALDC) | Increase fermentation efficiency by reducing diacetylformation. |
| **Culinary uses** | Papain | Tenderize meat for cooking. |
| **Dairy industry** | Rennin | Hydrolyze protein in the manufacture of cheese. |
| | Lipases | Produce Camembert cheese and blue cheeses such as Roquefort. |
| **Food processing** | Amylases | Produce sugars from starch, such as in making high-fructose corn syrup. |
| | Proteases | Lower the protein level of flour, as in biscuit-making. |

| | | |
|---|---|---|
| | Trypsin | Manufacture hypoallergenic baby foods. |
| | Cellulases, pectinases | Clarify fruit juices. |
| **Molecular biology** | Nucleases, DNA ligase and polymerases | Use restriction digestion and the polymerase chain reaction to create recombinant DNA. |
| **Paper industry** | Xylanases, hemicellulases and lignin peroxidases | Remove lignin from kraft pulp. |
| **Personal care** | Proteases | Remove proteins on contact lenses to prevent infections. |
| **Starch industry** | Amylases | Convert starch into glucose and various syrups. |

Pharmacology: the study of the interaction of drugs within living systems Drug: any chemical that affects living tissue - Endogenous (internal substance) - Exogenous (externally substance) - Xenobiotic (foreign substance) –

Types:

o Natural
o Semi-synthetic
o Synthetic
o Genetically modified - Nomenclature: o Individual name: chemical formula
o Non-proprietary: generic o Proprietary: trade/brand - Class
o Therapeutic o Mode of action
**Structure Application**: identify and develop therapeutics Therapeutic: must be able to be administered and have an effect - Dose-response - Adverse effects - Evidence-based - Medical therapeutic: o Formulated to produce a therapeutic effect.

Administration stages: 1. Drug release 2. Movement of drug from site of administration to target site (distribution) 3. Interaction of drug with target to produce desired effect Study stages: -

Pharmacodynamics: how to drug causes its effects - Pharmacokinetics: how to body reacts to the drug (metabolism and distribution)

TWO Targets: -

Receptors
o GPCR (Adrenaline= alpha/beta adrenoceptors/acetylcholine= muscarinic/nicotinic cholinergic receptors)
o Nuclear/steroid receptors (oestrogen=oestrogen receptors)
o Ligand-gated ion channel receptors (tyrosine=tyrosine receptors/acetylcholine= nicotinic receptors)
o Kinase-linked receptors (cytokine= cytokine receptors) - Enzymes
o Ach esterase o Cyclo-oxygenase COX- NSAIDS - Ion channel
o Calcium/sodium channels- anaesthetics - Transporter/carrier molecules
o Noradrenaline o Na+
o Serotonin transporters- SSRIs Effects: for a drug to have an effect it must bind - Specific/non-specific to tissue - Drugs interact with specific molecular targets which determine the effect they produce - Drugs can only mimic the biological actions of the cell, modulating (blocking or enhancing) the effect of endogenous components. - No drug has complete specificity in its action and has varying degrees of selectivity - Effect depends on:
o Target (affinity and efficacy) o Number of targets interacted with
o Where the targets are ◊ how it gets there/what response occurs in same targets in different tissue Drugs often resemble the natural ligands structure and binding depends on: - Shape - Solubility: o Ionisation ▪ pKa of drug: depends on pH of target compartment o Size Not all drugs interact with specific targets: -
Osmotic effects Alters fluid balance between compartments ▪ GIT: osmotic laxatives (magnesium citrate) which act as antidiuretics causing water to be moved into the gut and retained to treat constipation

▪ Kidney: osmotic diuretics (mannitol): increased passing of urine by inhibiting water and sodium reabsorption. They increase pressure in renal tubules by causing retention of water in the proximal tubule and descending loop of Henle. Used to prevent reduction in urine production during renal failure. Reduces intracranial pressure during a cerebral oedema. - pH changes o Mylanta:

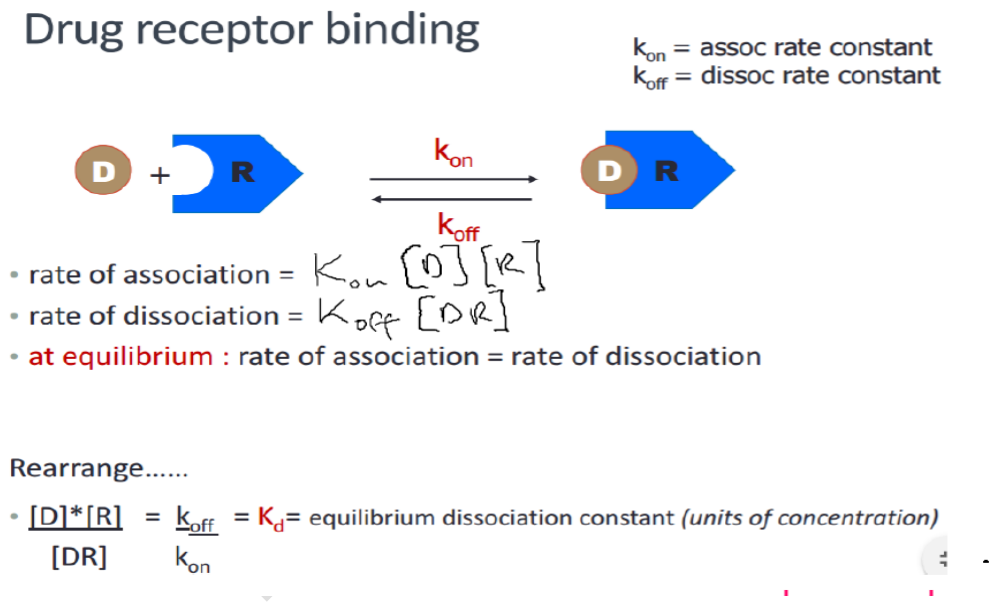
▪ Contains magnesium hydroxide: $Mg(OH)2 + 2HCl <=> MgCl2 + 2H2O$ ▪ Used for acid reflux by neutralising acid - Chelating agents (EDTA) - Anti-cancer drugs ACE Inhibitors: Uses: - Lowers BP - Heart failure◊ can remodel the cardiac muscle - Has a protective effect on the kidneys in diabetics - Coronary Artery Disease: reduced the risk of cardiac arrest (poor blood supply can

cause arrhythmia/tachycardia/bradycardia= heart stops) or fatal myocardial infarction (heart attack◊ blockage of the coronary artery and then the heart muscle dies)

Renin-angiotensin System: 1. Decrease in blood pressured causes release of renin from juxtaglomerular tubules of the kidneys 2. This triggers release of angiotensinogen from lungs 3. This becomes angiotensin I (no effect) 4. ACE found on endothelial cells, particular on the lining of the pulmonary system converts AI to AII by cleaving 2 amino acids from AI 5. Angiotensin II constricts blood vessels = increased BP 6. To stop increased BP, Captopril inhibits ACE. Bradykinin was also inactivated by Captopril

THREE Affinity:

ability to bind to a receptor - Electrostatic o Hydrogen bonds o Ionic forces o Van der Waals forces - Covalent Selectivity: preference for one receptor over another, though the drug will bind to both Efficacy: ability elicit a reaction once the drug binds Binding: - Reversible (non-covalent) o Drugs are only bound a receptor for a finite time = creates % drug bound o - Irreversible (covalent) o Sometimes irreversible binding is not wanted for a drug because the only way to overcome it is to synthesis more receptor.




Kd = amount of drug required to bind 50% of receptors. Inversely proportional to affinity
Affinity is measured by:
-Radioligands; ligands that have been tagged with a radioactive label. Radioligands are left to incubate in a receptor rich medium.
To separate the unbound ligands from the bound ones, filters are used (as bound radioligands are larger). A Geiger counter is used to measure bound radioligand concentration.

- Competition binding (IC50): concentration of compound X required to cause 50% binding inhibition (inversely proportional to affinity).

Uses unlabelled compound X and labelled ligand
It can also determine receptor density: Bmax

## SUGGESTING MATERIALS

**Text Books:**

1. Morrison R.T & Boyd R.N., (1992), Organic Chemistry, Dorling Kindersley Pvt. Ltd., (Pearson Education)
2. Finar I.L (2002), Organic Chemistry- Volume 1, Dorling Kindersley Pvt. Ltd., (Pearson Education)
3. Finar I.L (2002), Organic Chemistry- Volume 2, Dorling Kindersley Pvt. Ltd., (Pearson Education).

**Reference Books:**

1. Nelson D.L & Cox M.M, (2012), Lehninger's Principles of Biochemistry, 7th Edition
2. Berg J.M, Tymoczko J.L & Stryer L. (2002), Biochemistry. W.H. Freeman

## POSSIBLE QUESTIONS

### Section A **20x 1 = 20 marks**

1. Enzymes, which are produced in inactive form in the living cell are called
**a.** Papain b. Lysozymes c. Apoenzyme **d. Proenzyme**

2. Which one of the following is an example of ligases is
a. **Succinate thickinase** b. Alanine racemase c. Fumarase d. Aldolase

3. In which type of enzyme did not have inducer
a. Allosteric enzyme **b. Constitutive enzyme** c. Co-operative enzyme
c. Isoenzymic enzyme

4. In enzyme kinetics $V_{max}$ reflects
a. **The amount of an active enzyme** b. Substrate concentration
c. Half of the substrate concentration d. Enzyme substrate complex

5. When the activity inhibition occurred in competitive enzyme
a. Apparent $K_m$ is decreased **b. Apparent $K_m$ is increased**
c. $V_{max}$ is increased d. $V_{max}$ is decreased

6. In following which one is example of transferring co-enzyme
**a.** $NAD^-$ b. $NADP^+$ c. FAD **d. CoA**

7. The optimum $P^H$ of most of the enzyme is
a. Between 2 to 4 **b. Between 5 to 9** c. Between 8 to 12 d. Above 12

8. The co-enzyme which have not aromatic hetero ring in it
a. ATP b. Lipoic acid c. FMN **d. Biotin**

9. Serum acid phosphatase level increases in
a. **Metastatic carcinoma of prostate** b. Myocardial infarction
c. Wilson's disease d. Liver disease

10. The substrate for amylase is
a. Cane sugar **b. Starch** c. Lactose d. Ribose

11. In Conversion of Glucose to Glucose-6-Phosphate, the co-enzyme is
a. $Mg^{++}$ **b. ATP** c. ADP d. $Ca^{++}$

12. Cobamides contain a vitamin which is
**a.** Folic Acid b. Ascarbic acid c. Pantothemic acid **d. Vitamin B12**

13. Which of the following co-enzyme take part in tissue respiration
a. **Coenzyme Q** b. Coenzyme A c. $NADP^+$ d. Cobamide

14. Which of the following is a proteolytic enzyme
a. **Pepsin** b. Lipopic acid c. Coenzyme Q d. Biotin

15. The Induced fit model of enzyme action was proposed by
a. Fischer **b. Koshland** c. Mitchell d. Markert

16. Allosteric inhibition is also known as
a. Competitive inhibition b. Non-competitive inhibition **c. Feedback inhibition**
d. Irreversible inhibition

17. Alkaline Phosphate is present in
a. **Liver** b. Stomach c. Teeth d. Panceria

18. Inactive precursors of enzymes are known as
a. Apoenzymes b. Coenzymes **c. Proenzymes** d. Holoenzymes

19. End product of aerobic glycolysis is
a. Acetyl CoA b. Lactate **c. Pyruvate** d. $CO_2$ and $H_2O$

20. Malonate is an inhibitor of
a. Malate dehydrogenase b. alpha ketoglutarate dehydrogenase **c. Succinate dehydrogenase**
d. Isocitrate dehydrogenase

## Section-B (2 Marks)

1. What is enzyme?
2. Write any two uses of enzyme in biological activity
3. What is co-enzyme?
4. What is co-factor?
5. What is called as enzyme inhibition?
6. List out the types of enzyme inhibition
7. Write any four biological uses of enzyme
8. What is competitive inhibition
9. Write a short note on non-competitive inhibition?
10. Define: binding site

## Section-C (6 Marks)

1. Give an account of mechanism of enzyme
2. Explain the Phenomenon of enzyme inhibition
3. Write a Factors which are affecting the enzyme action and explain it

4. Briefly explain the Structural activity relationship of drug molecules with suitable example
5. Briefly explain the drug-receptor theory
6. How will you distinguish the types of enzyme inhibition
7. Explain the Relationship of drug molecule based on their structure
8. Give an account of enzyme action in living system
9. Distinguish the Competitive, Non-competitive and Allosteric inhibition of enzymes
10. Give an account of factors which are affect the enzyme action

**16CHU603B**
**Karpagam Academy of Higher Education**
**Coimbatore-21**

**(For the candidate admitted on 2016 onwards)**
**Department of Chemistry**
**VI- semester**
**Molecules of Life**

| **Unit-III (Multiple Choice Questions Each Carry 1 Mark).** | | | | | | |
|---|---|---|---|---|---|---|
| **S.No.** | **Question** | **Option A** | **Option B** | **Option C** | **Option D** | **Answer** |
| 1 | Enzymes, which are produced in inactive form in the living cell are called | Papain | Lysozymes | Apoenzyme | Proenzyme | Proenzyme |
| 2 | Which one of the following is an example of ligases is | Succinate thickinase | Alanine racemase | Fumarase | Aldolase | Succinate thickinase |
| 3 | In which type of enzyme did not have inducer | Allosteric enzyme | Constitutive enzyme | Co-operative enzyme | Isoenzymic enzyme | Constitutive enzyme |
| 4 | In enzyme kinetics $V_{max}$ reflects | The amount of an active enzyme | Substrate concentration | Half of the substrate concentration | Enzyme substrate complex | The amount of an active enzyme |
| 5 | When the activity inhibition occurred in competitive enzyme | Apparent $K_m$ is decreased | Apparent Km is increased | $V_{max}$ is increased | Vmax is decreased | Apparent Km is increased |
| 6 | In following which one is example of transferring co-enzyme | $NAD^-$ | NADP+ | FAD | CoA | CoA |
| 7 | The optimum $P^H$ of most of the enzyme is | Between 2 to 4 | Between 5 to 9 | Between 8 to 12 | Above 12 | Between 5 to 9 |
| 8 | The co-enzyme which have not aromatic hetero ring in it | ATP | Lipoic acid | FMN | Biotin | Biotin |
| 9 | Serum acid phosphatase level increases in | Metastatic carcinoma of prostate | Myocardial infarction | Wilson's disease | Liver disease | Metastatic carcinoma of prostate |
| 10 | The substrate for amylase is | Cane sugar | Starch | Lactose | Ribose | Starch |

| | | | | | | |
|---|---|---|---|---|---|---|
| 11 | The kinetic effect of purely competitive inhibition of enzyme | increases Km without affecting $V_{max}$ | Decreases $K_m$ without affecting $V_{max}$ | Increases $V_{max}$ without affecting $K_m$ | Decreases $V_{max}$ without affecting $K_m$ | increases Km without affecting $V_{max}$ |
| 12 | An example of hydrogen transferring coenzyme is | CoA | Biotin | $NAD^+$ | TPP | TPP |
| 13 | Enzyme involved in joining together two substrate is | Glutamin Synthetase | Aldolase | Gunanine deaminase | Arginase | Glutamin Synthetase |
| 14 | Coenzymes are | Heat stable, non-protein organic molecule | Soluble, collidal protein molecules | Structural analogue of enzymes | Different forms of enzyme | Heat stable, non-protein organic molecule |
| 15 | An example of lyases is | Glutamin Synthetase | Fumarase | Amylose | Chalinesterase | Fumarase |
| 16 | Example of an extracellular enzyme is | Lactate dehydrogenase | Cytochrome oxidase | Pancreatic lipase | Hexokinase | Pancreatic lipase |
| 17 | Cocarboxylase is | Thiomine pyrophosphase | Pyroxidal phosphate | Biotin | CoA | Biotin |
| 18 | A coenzyme containing aromatic hetero ring is | TPP | Lipoic acid | Coenzyme Q | Biotin | TPP |
| 19 | The pancreatic amylase activity increased in the presence of | Hcl | Bile salt | Thiocyanate ions | Calcium ions | Bile salt |
| 20 | The $P^H$ optima for sucrase is | 5.0-7.0 | 5.8-6.2 | 5.4-6.0 | 8.6 | 5.0-7.0 |
| 21 | Glucose absorption promoted by | Vitamin A | Vitamin C | Thiamin | Vitamin K | Thiamin |
| 22 | At low blood glucose concentration, liver will not take up glucose due to | Low Km of hexokinase | Low Km of glucokinase | Specificity of glucokinase | Blood brain barrier | Low Km of hexokinase |
| 23 | One of the enzymes regulating glycolysis is | Phosphofructokinase | phosphotriose isomerase | Phosphohexo isomerase | Glyceraldehyse-3-phosphate dehydrogenase | Phosphofructokinase |
| 24 | The $P^H$ optima for maltase is | 1.0-2.0 | 5.2-6.0 | 5.8-6.2 | 5.4-6.0 | 5.8-6.2 |
| 25 | Hexokinase is inhibited in an allosteric manner by | Glucose-6-phosphate | Glucose-1-Phosphate | Fructose-6-phosphate | Fructose-1,6-biphosphate | Glucose-6-phosphate |
| 26 | The net number of ATP formed per mole of glucose in anaerobic glycolysis is | 1 | 6 | 2 | 8 | 2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 27 | All the enzymes of glycolysis pathway are found in | Extramitochondrial soluble fraction of the cell | Mitochandria | Nucleus | Endoplasmic reticulum | Extramitochondrial soluble fraction of the cell |
| 28 | The enzymes of the citric acid cycle are located in | Mitochandrial matrix | Extramitochondrial soluble fraction of the cell | Endoplasmic reticulum | Nucleus | Mitochandrial matrix |
| 29 | Her's disease is characterizd by deficiency of | Muscle phosphorylase | Liver phosphorylase | Debranching enzyme | Glycogen synthase | Liver phosphorylase |
| 30 | The hydrogen acceptor used in pentose phosphate pathway is | ND | NADP | FAD | FMN | NADP |
| 31 | The sites for gluconeogenesis are | Liver and Kidney | Skin and Pancreas | Lungs and Bain | Intestine and Lens of eye | Liver and Kindey |
| 32 | The enzyme pyruvate carboxylase is present in | Cytosol | Mitochondria | Nucleus | Golgi bodies | Mitochondria |
| 33 | The enzyme glucose 6-phosphatase is present in | Liver | Muscule | Adipose tissue | Brain | Liver |
| 34 | the enzyme involved in esential pentasuria is | Reductase | Hydroxylase | Isomerase | Racemase | Reductase |
| 35 | Galactose is readily converted to glucose in | Liver | Intestine | Kidney | Adipose tissue | Liver |
| 36 | The $P^H$ optima for pancreatic analyse is | 4 | 7.1 | 7.9 | 8.6 | 8.6 |
| 37 | The best known cause of galactosemia is the deficiency of | Galactos 1-phosphate and uridyl transfer | Phosphoglucomutase | Galactokinase | Lactose synthse | Galactos 1-phosphate and |
| 38 | Conversion of fructose to sorbitol is catalysed by the enzyme | Sorbitol dehydrogenase | Aldose reductase | Fructokinase | Hexokinase | Sorbitol dehydrogenase |
| 39 | Insulin has no effect on the activity of the enzymes | Glycogen synthetase | Fructokinase | Pyruvate kinase | Pyruvate dehydrogenase | Fructokinase |
| 40 | The pH optima of gastric lipase is | 3.0-6.0 | 1.0-2.0 | 8 | 8.6 | 3.0-6.0 |
| 41 | The net gain of ATP/mol of palmitic acid on complete oxidation is | 88 | 105 | 129 | 135 | 129 |
| 42 | In β-oxidation, the coenzyme for acyl-CoA dehydrogenase is | FMN | NAD | NADP | FAD | FAD |
| 43 | In humans under normal conditions loss of ketone bodies via urine is usually less than | 1 mg/24hr | 4 mg/24hr | 8 mg/24hr | 10 mg/24hr | 1 mg/24hr |
| 44 | The starting material for ketogenesis is | Acyl-CoA | Acetyl-CoA | Acetoacetyl-CoA | Malonyl-CoA | Acetoacetyl-CoA |

| | | | | | | |
|---|---|---|---|---|---|---|
| 45 | Enzymes responsible for keton body formation are associated mainly with the | Mitochondria | Endoplasmic reticulum | nucleus | Golgi apparatus | Mitochondria |
| 46 | Ketone bodies serve as a fuel for | Extrahepatic tissues | Hepatic tissues | Erythrocytes | Mitochondria | Extrahepatic tissues |
| 47 | Which of the following is a substrate specific enzyme | Hexokinase | Thiokinase | Lactase | Amino-peptitase | Lactase |
| 48 | Co-enzymes combined with | Proenzymes | Apo enzymes | Holoenzymes | Anti-Enzymes | Apo enzymes |
| 49 | Co-enzymes are required in which of the following reactions | Oxidation-Reduction | Transfer | Oxidation | Reduction | Oxidation-Reduction |
| 50 | Which of the following co-enzyme takes part in H-transfer reactions | Tetrahydro folate | Coenzyme A | Coenzyme Q | Biotin | Coenzyme Q |
| 51 | In Conversion of Glucose to Glucose-6-Phosphate, the co-enzyme is | $Mg^{++}$ | ATP | ADP | $Ca^{++}$ | ATP |
| 52 | Cobamides contain a vitamin which is | Folic Acid | Ascarbic acid | Pantothemic acid | Vitamin B12 | Vitamin B12 |
| 53 | Which of the following co-enzyme take part in tissue respiration | Coenzyme Q | Coenzyme A | $NADP^{+}$ | Cobamide | Coenzyme Q |
| 54 | Which of the following is a proteolytic enzyme | Pepsin | Lipopic acid | Coenzyme Q | Biotin | Pepsin |
| 55 | The Induced fit model of enzyme action was proposed by | Fischer | Koshland | Mitchell | Markert | Koshland |
| 56 | Allosteric inhibition is also known as | Competitive inhibition | Non-competitive inhibition | Feedback inhibition | Irreversible inhibition | Feedback inhibition |
| 57 | Alkaline Phosphate is present in | Liver | Stomach | Teeth | Panceria | Liver |
| 58 | Inactive precursors of enzymes are known as | Apoenzymes | Coenzymes | Proenzymes | Holoenzymes | Proenzymes |
| 59 | End product of aerobic glycolysis is | Acetyl CoA | Lactate | Pyruvate | CO2 and H2O | Pyruvate |
| 60 | Malonate is an inhibitor of | Malate dehydrogenase | alpha ketoglutarate dehydrogenase | Succinate dehydrogenase | Isocitrate dehydrogenase | Succinate dehydrogenase |

## Unit-IV
## Syllabus

**NUCLEIC ACIDS** Components of Nucleic acids: Adenine, guanine, thymine and Cytosine (Structure only), other components of nucleic acids, Nucleosides and nucleotides **(nomenclature**), Structure of polynucleotides; Structure of DNA (Watson-Crick model) and RNA(**types of RNA**), Genetic Code, Biological roles of DNA and RNA: Replication, Transcription and Translation.

### Introduction

A most remarkable property of living cells is their ability to produce exact replicas of themselves. This is due to the cells containing fact that all the instructions needed for making the complete organism of which they are a part. Nucleic acids are the molecules within a cell that are responsible for these amazing capabilities.

The first isolation of nucleic acid we now refer to as DNA was accomplished by Swiss physiologist Johann Friedrich Miescher circa 1870 while studying the nuclei of white blood cells. In the 1920's nucleic acids were found to be major components of chromosomes, small gene-carrying bodies in the nuclei of complex cells. Elemental analysis of nucleic acids showed the presence of phosphorus, in addition to the usual C, H, N & O. We now know that nucleic acids are found throughout a cell, not just in the nucleus, the name nucleic acid is still used for such materials.

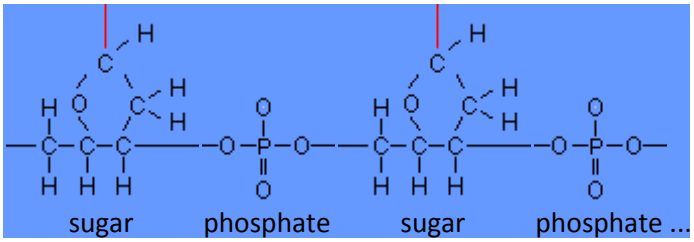
A nucleic acid is a polymer in which the monomer units are nucleotides. There are two Types of Nucleic Acids:

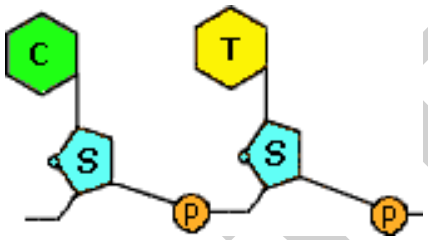
**DNA: Deoxyribonucleic Acid**: Found within cell nucleus for storing and transfering of genetic information that are passed from one cell to other during cell division

**RNA: Ribonucleic Acid**: Occurs in all parts of cell serving the primary function is to synthesize the proteins needed for cell functions.

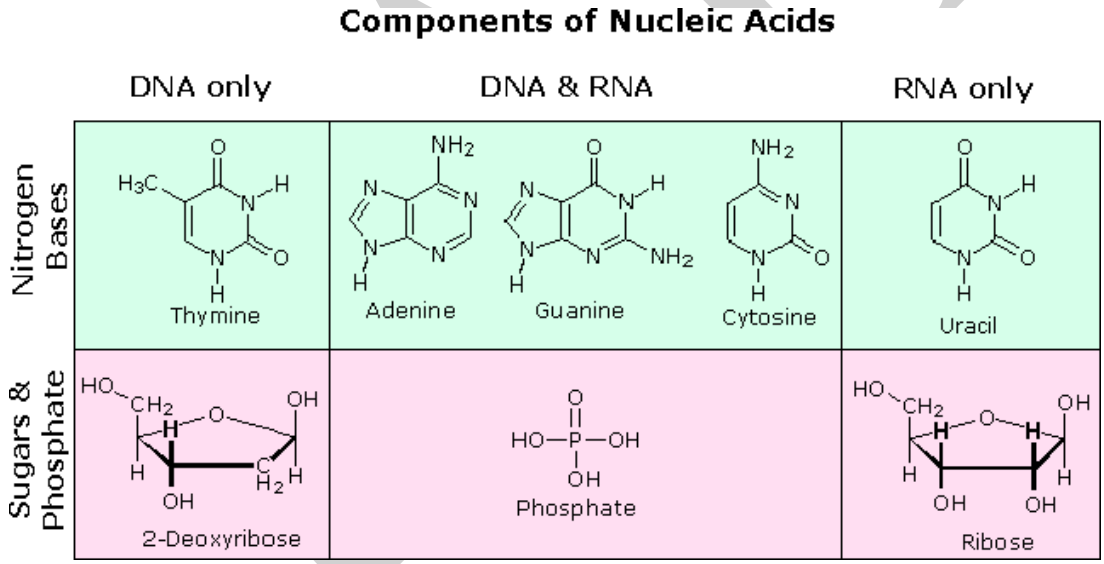
### Types of Nucleic Acids

The nucleic acids are very large molecules that have two main parts. The backbone of a nucleic acid is made of alternating sugar and phosphate molecules bonded together in a long chain, represented below:




Each of the sugar groups in the backbone is attached (via the bond shown in red) to a third type of molecule called a nucleotide base. There are only four different nucleotide bases can occur in a nucleic acid and are classified as pyrimidine or purine bases:




Though only four different nucleotide bases can occur in a nucleic acid, each nucleic acid contains millions of bases bonded to it. The order in which these nucleotide bases appear in the nucleic acid is the

coding for the information carried in the molecule. In other words, the nucleotide bases serve as a sort of genetic alphabet on which the structure of each protein in our bodies is encoded.

**DNA**

In most living organisms (except for viruses), genetic information is stored in the molecule deoxyribonucleic acid, or DNA. DNA is made and resides in the nucleus of living cells. DNA gets its name from the sugar molecule contained in its backbone(deoxyribose); however, it gets its significance from its unique structure. Four different nucleotide bases occur in DNA: adenine (A), cytosine (C), guanine (G), and thymine (T).

**Nucleotides: Building Blocks of Nucleic Acids**

| Names of DNA Nucleotide | | | |
|---|---|---|---|
| **Name** | **Base** | **Nucleoside** | **5'-Nucleotide** |
| **DAMP** | Adenine | 2'-Deoxyadenosine | 2'-Deoxyadenosine-5'-monophosphate |
| **DCMP** | Cytosine | 2'-Deoxycytidine | 2'-Deoxycytidine-5'-monophosphate |
| **DGMP** | Guanine | 2'-Deoxyguanosine | 2'-Deoxyguanosine-5'-monophosphate |
| **DTMP** | Thymine | 2'-Deoxythymidine | 2'-Deoxythymidine-5'-monophosphate |

**RNA** has the same nucleotide srtuctiure except the thymine base is replaces by uracil.

**Nucleotides: Nitrogenous base + pentose sugar + phosphate group(s)**

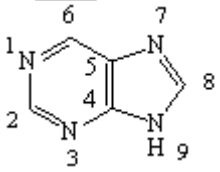
**(1) The Nitrogenous Bases:**

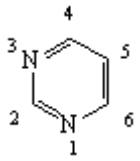
Planar, aromatic, heterocyclic

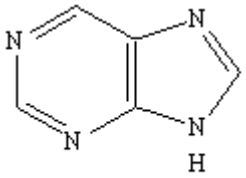
Structural derivatives of purine or pyrimidine

Note that numbers on the atoms are "unprimed"

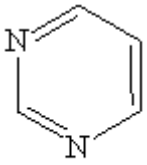
**The parent compounds are shown below:**



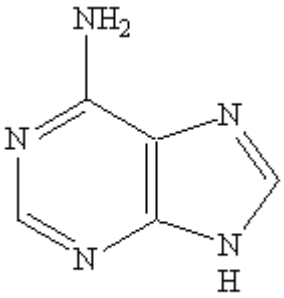


**Purine**

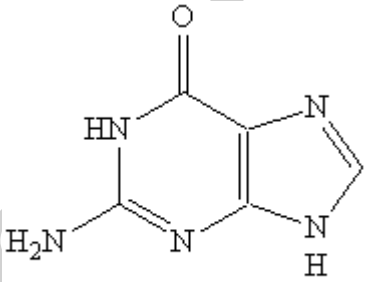


**Pyrimidine**

**The structures of the two most common purines are:**

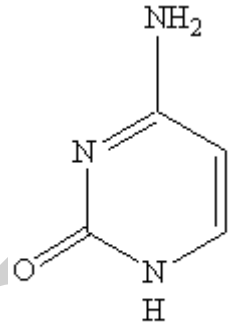


**Adenine (A)**

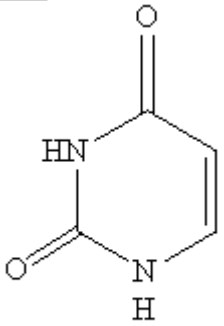


**Guanine (G)**

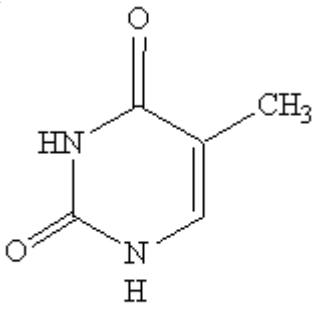
**The structures of the three most common pyrimidines are:**



**Cytosine (C)**



**Uracil (U)**

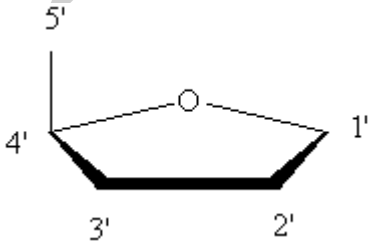


**Thymine (T)**
(5-methyluracil)

**(2) Sugars: D-ribose and 2'-deoxyribose**

Pentoses: 5-C sugars

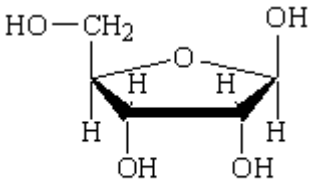
"Primes" refer to numbering of the atoms of the ribose



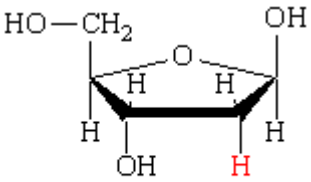
The "2'-deoxy-" notation means that there is no -OH group on the 2' carbon atom

Purines bond to the C1' of the sugar at their N9 atoms

Pyrimidines bond to the sugar C1' atom at their N1 atoms



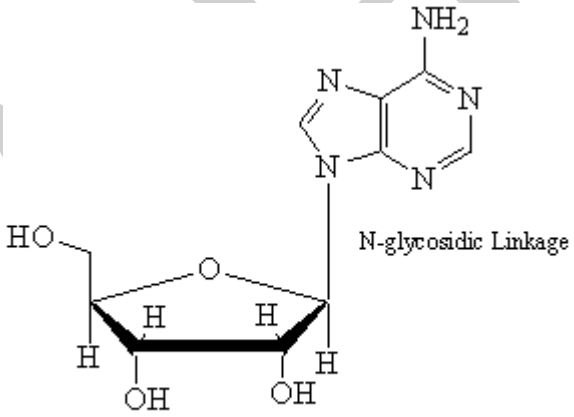

D-Ribose




2'-Deoxyribose

**A "nucleoside" results from the linking of one of these 2 sugars with one of the purine- or pyrimidine-derived bases through an N-glycosidic linkage.**

The chemical bond linking them is an "N- glycosidic bond"



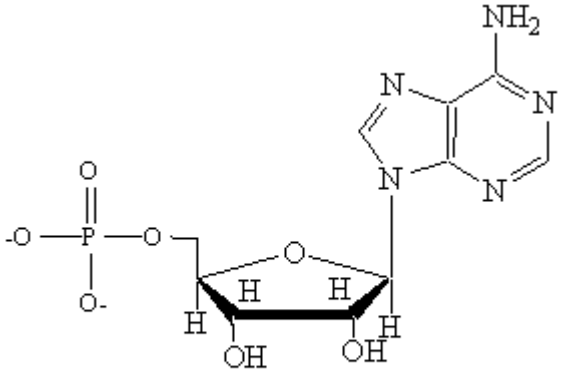

Adenosine

**(3) Phosphate Group(s)**

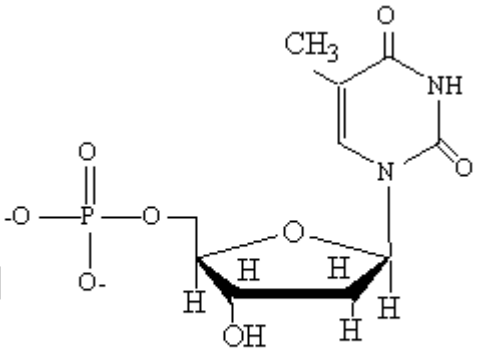
Mono-, di-, and triphosphates

Phosphate can be bonded to either C3' or C5' atoms of sugar

**A "nucleotide" is a 5'-phosphate ester of a nucleoside.**



**Adenosine Monophosphate (AMP)**
(a ribonucleotide)



**2'-Deoxythymidine Monophosphate**
(a deoxyribonucleotide)

RNA (ribonucleic acid) is a polymer of ribonucleotides

DNA (deoxyribonucleic acid) is a polymer of deoxynucleotides

Deoxy- and ribonucleotides contain adenine, guanine and cytosine

Ribonucleotides also contain uracil

Deoxynucleotides also contain thymine

**The Naming Conventions**

**There's a logic to the naming of the nucleosides and nucleotides, if you can remember a few rules.**

The purine NSs end in "-sine" : adenosine and guanosine

The pyrimidine NSs end in "-dine" : cytidine, uridine, deoxythymidine

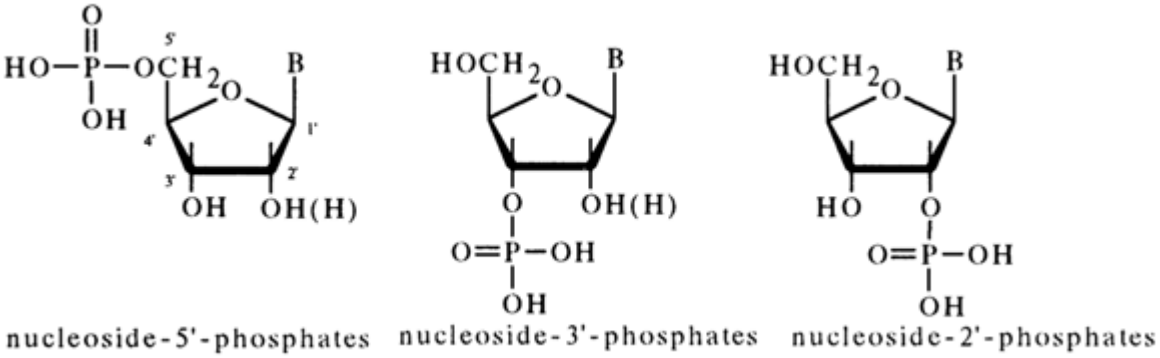
To name the NTs, use the NS name, followed by "mono-", "di-" or "triphosphate":

adenosine monophosphate, guanosine triphosphate, deoxythymidine monophosphate

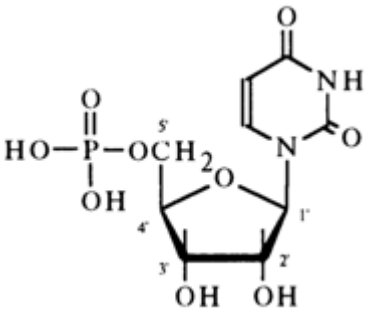
**Nucleotides have a number of roles. Most notably they are the monomers for nucleic acid polymers. Nucleoside triphosphates, like ATP and GTP, are energy carriers in metabolic pathways. Nucleotides are also components of some important coenzymes, like FAD, $NAD^+$ and Coenzyme A.**

**Nomenclature and Isomerism**

Depending on the positions occupied by the phosphate group in ribo- or deoxyribonucleoside, distinction is made between three types of (isomeric) nucleotides:

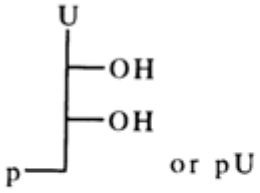



A nucleotide's name is usually based on that of the associated nucleoside. In the most common version, it consists of the nucleoside's name and position of the phosphate. For example, uridine 5'-phosphate:



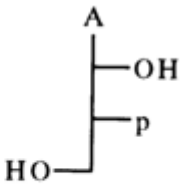
An alternative name of this nucleotide is 5-uridylic acid. In the case of pyrimidine nucleotides, the nomenclature consists of the name of the corresponding nucleoside (uridyl, cytidyl, etc.) plus the ending "ic" and the word "acid". For example: uridyl + ic acid = uridylic acid. Purine nucleotides have similar nomenclature with the difference that the basic component is the name of the corresponding base (guanyl, adenyl, etc.). For example: guanyl + ic acid = guanylic acid. The composite name is always preceded by the position of the phosphate in the nucleotide. Adenosine 3'-phosphate, for instance, may also be called 3'-adenylic acid.

Table lists the names of the major nucleotides isolated from natural nucleic acids (DNA and RNA). Also listed are abridged formulas and abbreviated symbols, which, in turn, are based on abridged formulas and abbreviated symbols for the corresponding nucleosides plus an abbreviated symbol of the phosphate group. According to the rules of IUPAC and IUB, the phosphate is designated as "p". The abridged formulas for the above nucleotides are as follows:




or pU

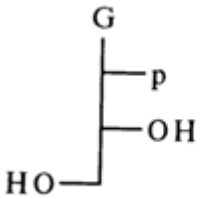
uridine 5'-phosphate
(5'-uridylic acid)




or Ap

adenosine 3'-phosphate
(3'-adenylic acid)

It can be seen that even more abbreviated symbols consisting of only two letters are used for nucleotides, the capital letter corresponding to the name of the nucleoside and the small letter (p) on the left indicating that there is a phosphate group at position 5'. If the phosphate group is linked to the carbohydrate moiety at position 3', the letter "p" is placed to the right of the capital letter (symbolyzing the nucleoside). The presence of a phosphate group at position 2', in guanosine 2'-phosphate, for example, is indicated as

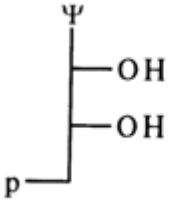



G2'p

follows:

In the case of deoxynucleotides, the letter "d" is added before the symbol.

The names and abbreviated symbols of nucleotides that are derivatives of minor nucleosides are based on the same principle. For instance, pseudouridine 5'-phosphate (5'-pseudouridylic acid) has the abbreviated symbol pY, while deoxyuridine 3'-phosphate (3'-deoxyuridylic acid) has the symbol dUp. Their abridged formulas are as follows:



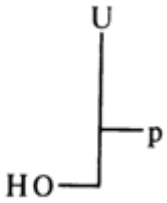
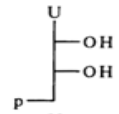
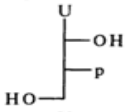
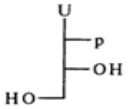
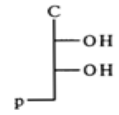
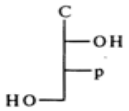
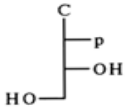
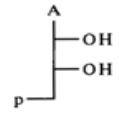
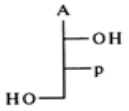
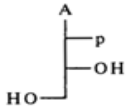
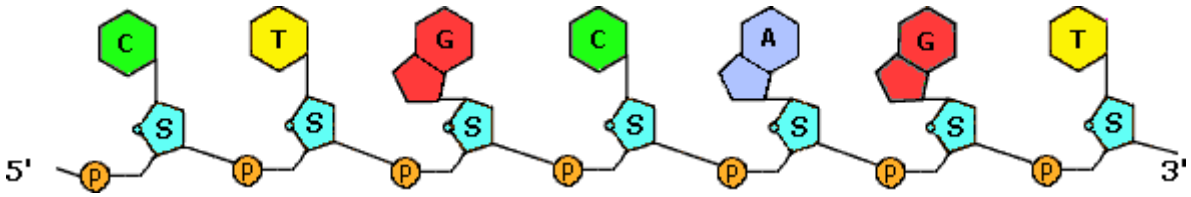



**Table 3-1.** Structure, Names and Symbols of the Major Nucleotides Isolated from RNA and DNA.

| Nucleoside in the nucleotide* | Nucleotide name | Abridged formula | Abbreviated symbol |
|---|---|---|---|
| Uridine | Uridine 5′-phosphate (5′-uridylic acid) |  | pU |
| | Uridine 3′-phosphate (3′-uridylic acid) |  | Up |
| | Uridine 2′-phosphate (2′-uridylic acid) |  | U2′p |
| Cytidine | Cytidine 5′-phosphate (5′-cytidylic acid) |  | pC |
| | Cytidine 3′-phosphate (3′-cytidylic acid) |  | Cp |
| | Cytidine 2′-phosphate (2′-cytidylic acid) |  | C2′p |
| Adenosine | Adenosine 5′-phosphate (5′-adenylic acid) |  | pA |
| | Adenosine 3′-phosphate (3′-adenylic acid) |  | Ap |
| | Adenosine 2′-phosphate (2′-adenylic acid) |  | A2′p |

**Primary Nucleic Acid Structure Polynucleotides**

In polynucleotides, nucleotides are joined to one another by covalent bonds between the phosphate of one and the sugar of another. These linkages are called **phosphodiester** linkages. This nucleic acids found in the cell have primary structures that arise from the end-to-endl polymerization of single nucleotide units. The links between each nucleotide are formed by esterification reactions between the sugar's C3′ hydroxyl group and the - phosphate of an incoming nucleoside triphosphate (NTP) to form a phosphoester linkage.



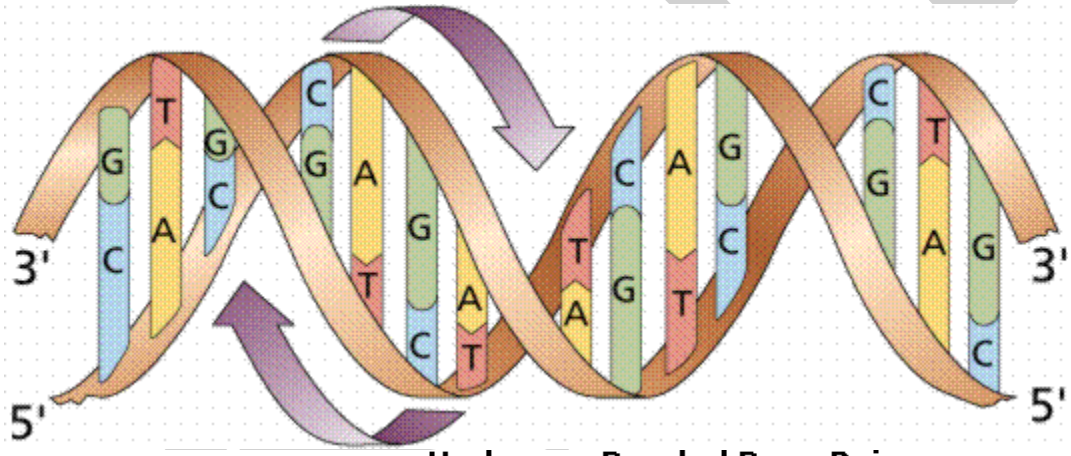

The sugar is ribose in the case of RNA, deoxyribose in DNA. This polymerization process leaves a free hydroxyl on the incoming nucleotide (on the 3′ C of the sugar) to serve for the next reaction in chain elongation.

**The DNA Double Helix**

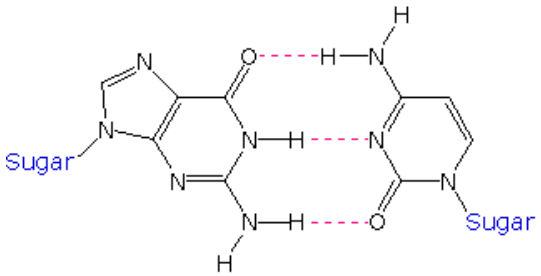
The 1962 Nobel Prize in Physiology or Medicine was awarded to Crick, Watson and Wilkins for the discovery of the molecular structure of DNA – the double helix.

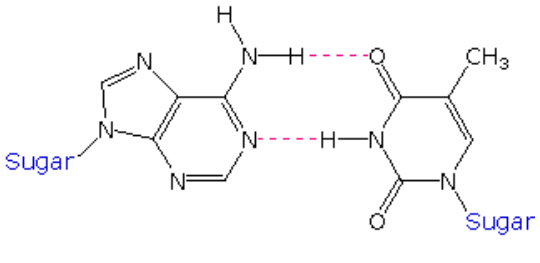
**Chemical Structure of the DNA double strands**

DNA (deoxyribonucleic acid) is a double-stranded molecule that is twisted into a helix like a spiral staircase. Each strand is comprised of a sugar- phosphate backbone and numerous base chemicals attached in pairs.




**Hydrogen Bonded Base Pairs**




The four bases that make up the stairs in the spiraling staircase are adenine (A), thymine (T), cytosine

(C) and guanine (G). These stairs act as the "letters" in the genetic alphabet, combining into complex sequences to form the words, sentences and paragraphs that act as instructions to guide the formation and functioning of the host cell. Maybe even more appropriately, the A, T, C and G in the genetic code of the DNA molecule can be compared to the "0" and "1" in the binary code of computer software. Like software to a computer, the DNA code is a genetic language that communicates information to the organic cell.

**Genetic code**

The DNA code, like a floppy disk of binary code, is quite simple in its basic paired structure. However, it's the sequencing and functioning of that code that's enormously complex. Through recent technologies like x-ray crystallography, we now know that the cell is not a "blob of protoplasm", but rather a microscopic marvel that is more complex than the space shuttle. The cell is very complicated, using vast numbers of phenomenally precise DNA instructions to control its every function.

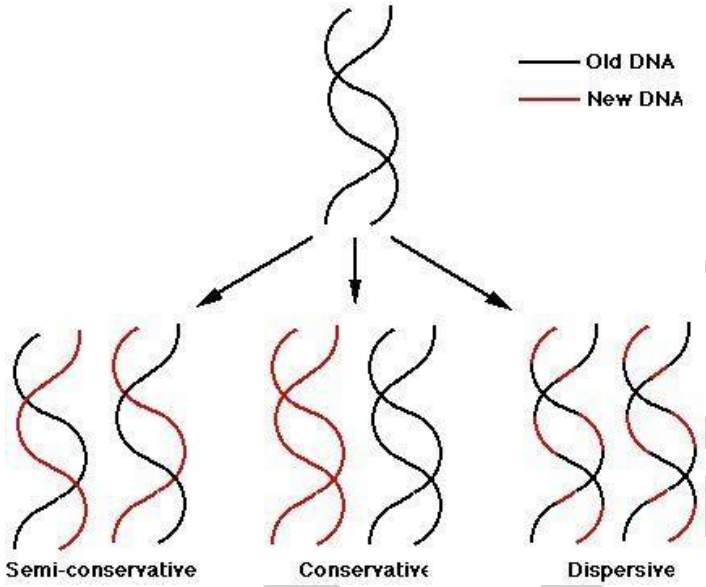
**Replication of DNA Molecules**

Before a cell divides, its DNA is replicated (duplicated.) Because the two strands of a DNA molecule have complementary base pairs, the nucleotide sequence of each strand automatically supplies the information needed to produce its partner. If the two strands of a DNA molecule are separated, each can be used as a pattern or template to produce a complementary strand. Each template and its new complement together then form a new DNA double helix, identical to the original.

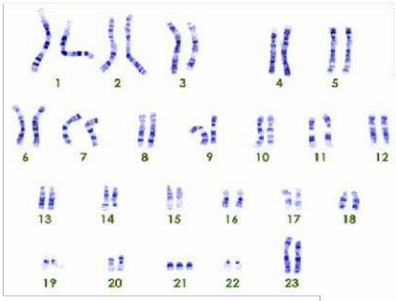
Before replication can occur, the length of the DNA double helix about to be copied must be unwound. In addition, the two strands must be separated, much like the two sides of a zipper, by breaking the weak hydrogen bonds that link the paired bases. Once the DNA strands have been unwound, they must be held apart to expose the bases so that new nucleotide partners can hydrogen-bond to them.

The enzyme DNA polymerase then moves along the exposed DNA strand, joining newly arrived nucleotides into a new DNA strand that is complementary to the template.

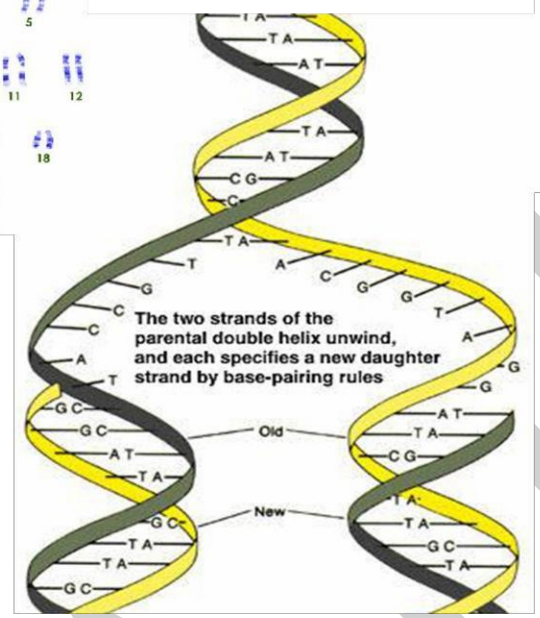
Each cell contains a family of more than thirty enzymes to insure the accurate replication of DNA.

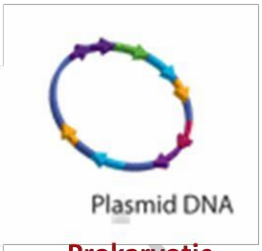

Old DNA
New DNA
Semi-conservative
Conservative
Dispersive

# Replications



Human Chromosomes
**Eukaryotic**



Plasmid DNA
**Prokaryotic**

**Overview of Protein Synthesis**

**DNA code**: containing specific base code is used to create a specific polypepetide-the protein containing a certain sequence of amino acids.

The genetic code present in the DNA and later transcribed into mRNA consists of **64 triplets of nucleotides**. These triplets are called **codons**.With three exceptions, each codon encodes for one of the **20 amino** acids used in the synthesis of proteins. That produces some redundancy in the code: most of the amino acids being encoded by more than one codon.

**RNA polymerase:** RNA polymerases are enzyme complexes that synthesize mRNA molecules using DNA as a template, in the process known as transcription.

Protein snthesis can be divided into two parts:

**1. Transcription**

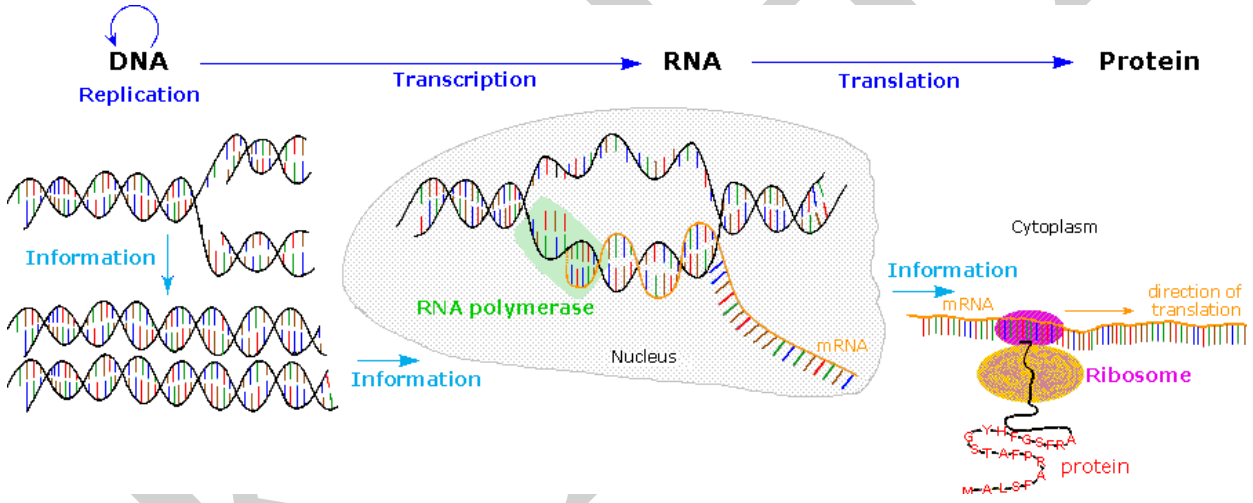
Before the synthesis of a protein begins, the corresponding RNA molecule is produced by **RNA**

**transcription**. One strand of the DNA double helix is used as a template by the **RNA polymerase** to synthesize a **messenger RNA** (mRNA). This **mRNA** migrates from the nucleus to the cytoplasm. During this step, mRNA goes through different types of maturation including one called **splicing** when the non-coding sequences are eliminated. The coding mRNA sequence can be described as a unit of three nucleotides called a **codon**.

**2. Translation**

The **ribosome** binds to the **mRNA** at the start codon (AUG) that is recognized only by the initiator **tRNA**. The ribosome proceeds to the elongation phase of protein synthesis. During this stage, complexes, composed of an amino acid linked to tRNA, sequentially bind to the appropriate codon in mRNA by forming complementary base pairs with the **tRNA anticodon**. The ribosome moves from codon to codon along the mRNA. Amino acids are added one by one, translated into polypeptidic sequences dictated by DNA and represented by mRNA. At the end, a release factor binds to the stop codon, terminating translation and releasing the complete **polypeptide** from the ribosome.

One specific amino acid can correspond to more than one codon. The genetic code is said to be degenerate.




**Ribonucleic Acids**

One of the two main types of nucleic acid (the other being DNA), which functions in cellular protein synthesis in all living cells. Like DNA, it consists of strands of repeating nucleotides joined in chainlike fashion, but the **strands are single** and it has the nucleotide **uracil (U)** where DNA has **thymine (T)**.

**Messenger RNA**

Whereas most types of RNA are the final products of their genes, mRNA is an intermediate in information transfer. It carries information from DNA to the ribosome in a genetic code that the protein-synthesizing machinery translates into protein. Specifically, mRNA sequence is recognized in a

sequential fashion as a series of nucleotide triplets by tRNAs via base pairing to the three-nucleotide anticodons in the tRNAs. There are specific triplet codons that specify the beginning and end of the protein-coding sequence. Thus, the function of mRNA involves the reading of its primary nucleotide sequence, rather than the activity of its overall structure. Messenger RNAs are typically shorter-lived than the more stable structural RNAs, such as tRNA and rRNA. See Genetic code

**Small nuclear RNA**

Small RNAs, generally less than 300 nucleotides long and rich in uridine (U), are localized in the nucleoplasm (snRNAs) and nucleolus (snoRNAs) of eukaryotic cells. There they take part in RNA processing, such as intron removal during eukaryotic mRNA splicing and posttranscriptional modification that occurs during production of mature rRNA. See Intron

**Catalytic RNA**

RNA enzymes, or ribozymes, are able to catalyze specific cleavage or joining reactions either in themselves or in other molecules of nucleic acid. See Catalysis, Ribozyme

**Transcription: RNA Synthesis**

Transcription is the process of creating an equivalent RNA copy of a sequence of DNA in double helix. Both RNA and DNA have base pairs of nucleotides as a complementary language that can be converted back and forth from DNA to RNA in the presence of the correct enzymes, RNA polymerase. During transcription, a DNA sequence is read by RNA polymerase, which produces a complementary, antiparallel RNA strand. As opposed to DNA replication, transcription results in an RNA complement that includes uracil (U) in all instances where thymine (T) would have occurred in a DNA complement.

Transcription is the first step leading to gene expression. The stretch of DNA transcribed into an RNA molecule is called a transcription unit and encodes at least one gene. If the gene transcribed encodes for a protein, the result of transcription is messenger RNA (mRNA), which will then be used to create that protein via the process of translation. Alternatively, the transcribed gene may encode for either ribosomal RNA (rRNA) or transfer RNA (tRNA), other components of the protein-assembly process, or other ribozymes.

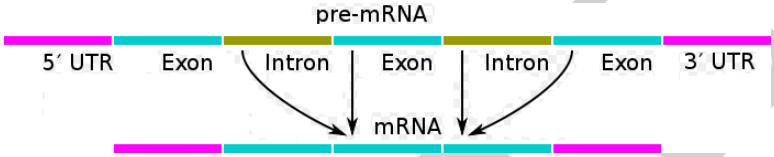
A DNA transcription unit encoding for a protein contains not only the sequence that will eventually be directly translated into the protein (the coding sequence) but also regulatory sequences that direct and regulate the synthesis of that protein. The regulatory sequence before (upstream from) the coding sequence is called the five prime untranslated region (5'UTR), and the sequence following (downstream from) the coding sequence is called the three prime untranslated region (3'UTR).

Transcription has some proofreading mechanisms, but they are fewer and less effective than the controls for copying DNA; therefore, transcription has a lower copying fidelity than DNA replication.

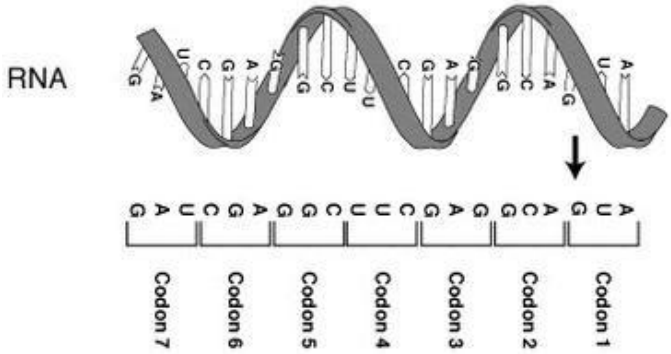
As in DNA replication, DNA is read from 3' → 5' during transcription. Meanwhile, the complementary RNA is created from the 5' → 3' direction. Although DNA is arranged as two antiparallel strands in a double helix, only one of the two DNA strands, called the template strand, is used for transcription. This is because RNA is only single-stranded, as opposed to double-stranded DNA. The other DNA strand is called the coding strand, because its sequence is the same as the newly

created RNA transcript (except for the substitution of uracil for thymine). The use of only the 3' → 5' strand eliminates the need for the Okazaki fragments seen in DNA replication.Transcription is divided into 5 stages: pre-initiation, initiation, promoter clearance, elongation and termination.

**Splicing of mRNA:** Splicing is a modification of an RNA after transcription, in which **introns** (nonessential part opf the code)are removed and **exons**(essential part opf the code) are joined. Also tThe **UTR**s, non-coding parts of exons at the ends of the mRNA is also removed.




**Codon:** The code is defined as a mapping of three-nucleotide base sequences and the amino acids. A




triplet codon in a nucleic acid sequence usually specifies a single amino acid (though in some cases the same codon triplet in different locations can code unambiguously for two different amino acids

**The Genetic Code**

**DNA code**: containing specific base code to create a specific polypepetide- the protein containing a certain sequence of amino acids.

The genetic code consists of **64 triplets of nucleotides**. These triplets are called **codons**.With three exceptions, each codon encodes for one of the 20 amino acids used in the synthesis of proteins. That produces some redundancy in the code: most of the amino acids being encoded by more than one codon.

One codon, **AUG** serves two related functions:

- it signals the start of translation
- it codes for the incorporation of the amino acid methionine (Met) into the growing polypeptide chain

The genetic code can be expressed as either **RNA codons** or **DNA codons**. RNA codons occur in messenger RNA (**mRNA**) and are the codons that are actually "read" during the synthesis of polypeptides during **translation**. But each mRNA molecule acquires its sequence of nucleotides by **transcription** from the corresponding gene. Because DNA sequencing has become so rapid and because most genes are now being discovered at the level of DNA before they are discovered as mRNA or as a protein product, it is extremely useful to have a table of codons expressed as DNA. So here are both.

Note that for each table, the left-hand column gives the first nucleotide of the codon, the 4 middle columns give the second nucleotide, and the last column gives the third nucleotide.

**The RNA Codons**

| | Second nucleotide | | | | |
|---|---|---|---|---|---|
| | **U** | **C** | **A** | **G** | |
| **U** | UUU **Phenylalanine** (Phe) | UCU **Serine** (Ser) | UAU **Tyrosine** (Tyr) | UGU **Cysteine** (Cys) | **U** |
| | UUC Phe | UCC Ser | UAC Tyr | UGC Cys | **C** |
| | UUA **Leucine** (Leu) | UCA Ser | UAA **STOP** | UGA **STOP** | **A** |
| | UUG Leu | UCG Ser | UAG **STOP** | UGG **Tryptophan** (Trp) | **G** |
| **C** | CUU **Leucine** (Leu) | CCU **Proline** (Pro) | CAU **Histidine** (His) | CGU **Arginine** (Arg) | **U** |
| | CUC Leu | CCC Pro | CAC His | CGC Arg | **C** |
| | CUA Leu | CCA Pro | CAA **Glutamine** (Gln) | CGA Arg | **A** |
| | CUG Leu | CCG Pro | CAG Gln | CGG Arg | **G** |

| | | | | | |
|---|---|---|---|---|---|
| | AUU **Isoleucine** (Ile) | ACU **Threonine** (Thr) | AAU **Asparagine** (Asn) | AGU **Serine** (Ser) | **U** |
| **A** | AUC Ile | ACC Thr | AAC Asn | AGC Ser | **C** |
| | AUA Ile | ACA Thr | AAA **Lysine** (Lys) | AGA **Arginine** (Arg) | **A** |
| | AUG **Methionine** (Met) or **START** | ACG Thr | AAG Lys | AGG Arg | **G** |
| | GUU **Valine** Val | GCU **Alanine** (Ala) | GAU **Aspartic acid** (Asp) | GGU **Glycine** (Gly) | **U** |
| **G** | GUC (Val) | GCC Ala | GAC Asp | GGC Gly | **C** |
| | GUA Val | GCA Ala | GAA **Glutamic acid** (Glu) | GGA Gly | **A** |
| | GUG Val | GCG Ala | GAG Glu | GGG Gly | **G** |

**Genome:**

The **genome** is the entirety of an organism's hereditary information. It is encoded either in DNA or, for many types of virus, in RNA.

**The Human Genome Project** - the entire human genome is currently being decoded by labs around the world. The project, which started in 1990, aims to have the complete 3.2 billion base pair genome completed is a high quality form in 2003, at a final cost of over 3 billion dollars. Recently (1998) a private company, Celera Genomics, has amassed enough high speed automated DNA sequencers and computing power (second only to the Pentagon)

**Anticodons and tRNA Molecules**

These small RNAs (70–90 nucleotides) that act as adapters to translate the nucleotide sequence of mRNA into protein sequence. They do this by carrying the appropriate amino acid to the ribosome

during the process of protein synthesis. Each cell contains at least one type of tRNA specific for each of the 20 amino acids, and usually several types. The base sequence in the mRNA directs the appropriate amino acid-carrying tRNAs to the ribosome to ensure that the correct protein sequence is made.

**Translation: Protein Synthesis**

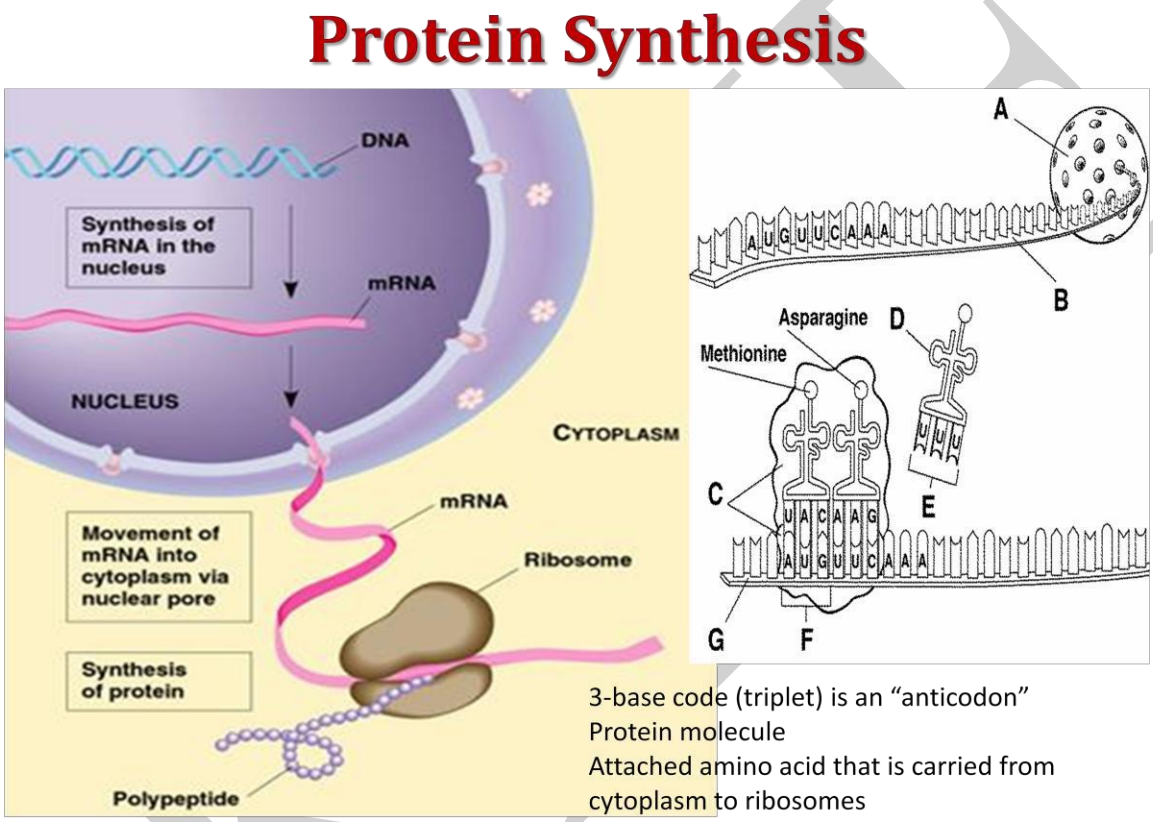
This process involves following components:

**mRNA:** Messenger RNA which is a single stranded copy of a DNA double helix base par sequence with uracil in the places where thyamine was.

**Ribosome**

Ribosomes are the components of cells that make proteins from amino acids. Ribosomes then read the information in the mRNA and use the codond to produce proteins.

**tRNA:** The genetic code is read during translation using transfer-RNA, tRNAs that have 3-base anticodons complementary to codons in mRNA.




**The Steps of Translation**

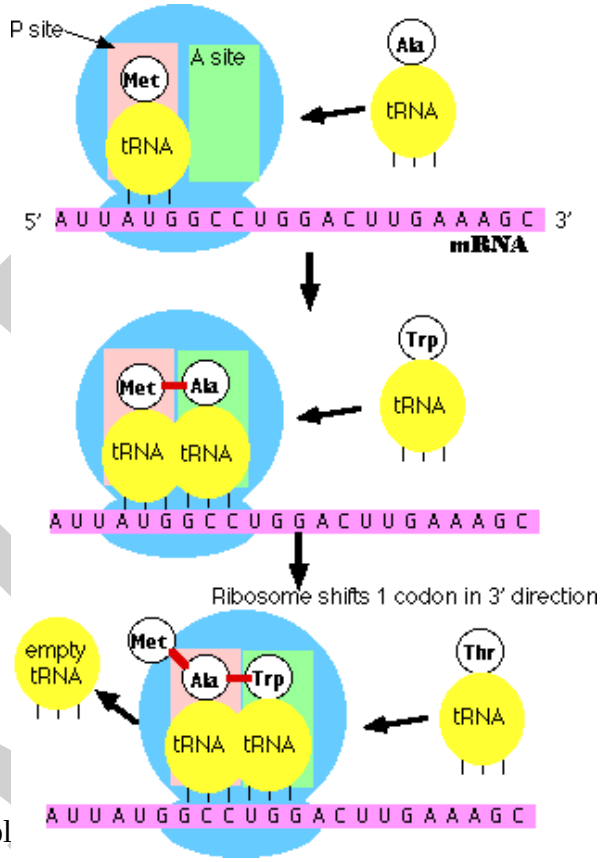
**Initiation**

- The **small subunit** of the ribosome binds to a site "upstream" (on the 5' side) of the start of the message.
- It proceeds downstream (5' -> 3') until it encounters the start codon **AUG**. (The region between the cap and the AUG is known as the 5'- untranslated region [**5'-UTR**].)
- Here it is joined by the **large subunit** and a special **initiator tRNA**.
- The initiator tRNA binds to the **P site** (shown in pink) on the ribosome.

- In eukaryotes, initiator tRNA carries **methionine** (Met). (Bacteria use a modified methionine designated **fMet**.)

**Elongation**

- An **aminoacyl-tRNA** (a tRNA covalently bound to its amino acid) able to base pair with the next codon on the mRNA arrives at the **A site** (green) associated with:
  - an **elongation factor** (called EF-Tu in bacteria)
  - **GTP** (the source of the needed energy)
- The preceding amino acid (Met at the start of translation) is covalently linked to the incoming amino acid with a peptide bond (shown in red).
- The initiator tRNA is released from the P site.
- The ribosome moves one codon downstream.
- This shifts the more recently-arrived tRNA, with its attached peptide, to the P site and opens the A site for the arrival of a new aminoacyl-tRNA.
- This last step is promoted by another protein **elongation factor** (called EF-G in bacteria) and the energy of another mol




Note: the initiator tRNA is the only member of the tRNA family that can bind directly to the P site. The P site is so-named because, with the exception of initiator tRNA, it binds only to a **p**eptidyl-tRNA molecule; that is, a tRNA with the growing peptide attached.

The A site is so-named because it binds only to the incoming **a**minoacyl- tRNA; that is the tRNA bringing the next amino acid. So, for example, the tRNA that brings Met into the interior of the polypeptide can bind only to the A site.

**Termination**

- The end of translation occurs when the ribosome reaches one or more **STOP** codons (**UAA**, **UAG**, **UGA**). (The nucleotides from this point to the poly(A) tail make up the 3'-untranslated region [**3'-UTR**] of the mRNA.)
- There are no tRNA molecules with anticodons for STOP codons.
- However, protein release factors recognize these codons when they arrive at the A site.
- Binding of these proteins —along with a molecule of **GTP** — releases the polypeptide from the ribosome.
- The ribosome splits into its subunits, which can later be reassembled for another round of protein synthesis.

**Mutations**

A mutation is a permanent change in the DNA sequence of a gene or the genetic code. Mutations in a gene's DNA sequence can alter the amino acid sequence of the protein encoded by the gene.

How does this happen? Like words in a sentence, the DNA sequence of each gene determines the amino acid sequence for the protein it encodes. The DNA sequence is interpreted in groups of three nucleotide bases, called codons. Each codon specifies a single amino acid in a protein.

Mutations can lead to changes in the structure of an encoded protein or to a decrease or complete loss in its expression. Because a change in the DNA sequence affects all copies of the encoded protein, mutations can be particularly damaging to a cell or organism. In contrast, any alterations in the sequences of RNA or protein molecules that occur during their synthesis are less serious because many copies of each RNA and protein are synthesized.

Geneticists often distinguish between the **genotype** and **phenotype** of an organism. Strictly speaking, the entire set of genes carried by an individual is its genotype, whereas the function and physical appearance of an individual is referred to as its phenotype.

**Chemistry at a Glance: Protein Synthesis**

## 22.2 Nucleic Acids and Viruses

All viruses have genes made from either **DNA** or **RNA,** long molecules that carry genetic information; all have a protein coat that protects these genes;

and some have an envelope of fat that surrounds them when they are outside a cell. **Viroids** do not have a protein coat and **prions** contain no RNA or DNA. Viruses vary from simple helical and icosahedral shapes, to more complex structures. Most viruses are about one hundred times smaller than an average bacterium. The origins of viruses in the evolutionary history of life are unclear: some may have evolved from **plasmids**—pieces of DNA that can move between cells—while others may have evolved from bacteria. In evolution, viruses are an important means of **horizontal gene transfer**, which increases genetic diversity.

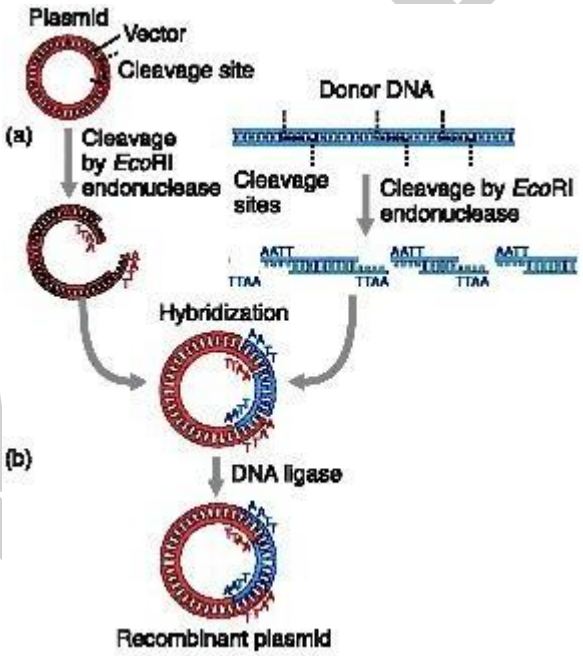
**Recombinant DNA and Genetic Engineering**

**Isolate Gene of Interest**

The gene for producing a protein is isolated from a cell. The gene is on the DNA in a chromosome. Special DNA cutting proteins are used to cut out certain sections of DNA. The gene can be isolated and then copied so that many genes are available to work with.

**Prepare Target DNA**

In 1973, two scientists named Boyer and Cohen developed a way to put DNA from one organism into the DNA of bacteria. This process is called recombinant DNA technology. First, a circular piece of DNA called a plasmid is removed from a bacterial cell. Special proteins are used to cut the plasmid ring to open it up.




**Insert DNA into Plasmid**

The host DNA that produces the wanted protein is inserted into the opened plasmid DNA ring. Then special cell proteins help close the plasmid ring.

**Insert Plasmid back into cell**

The circular plasmid DNA that now contains the host gene is inserted back into a bacteria cell. The plasmid is a natural part of the bacteria cell. The bacteria cell now has a gene in it that is from a different organism, even from a human. This is what is called recombinant DNA technology

**Plasmid multiplies**

The plasmid that was inserted into the bacteria cell can multiply to make several copies of the wanted gene. Now the gene can be turned on in the cell to make proteins.

**Target Cells Reproduce**

Many recombined plasmids are inserted into many bacteria cells. While they live, the bacteria's cell processes turn on the inserted gene and the protein is produced in the cell. When the bacterial cells reproduce by dividing, the inserted gene is also reproduced in the newly created cells.

**Cells Produce Proteins**

The protein that is produced can be purified and used for a medicine, industrial, agricultural, or other uses. Check out the Uses section to see how **GE** is used.

**The Polymerase Chain Reaction**

The polymerase chain reaction is a technique for quickly "cloning" a particular piece of DNA in the test tube (rather than in living cells like E. coli). Thanks to this procedure, one can make virtually unlimited copies of a single DNA molecule even though it is initially present in a mixture containing many different DNA molecules.

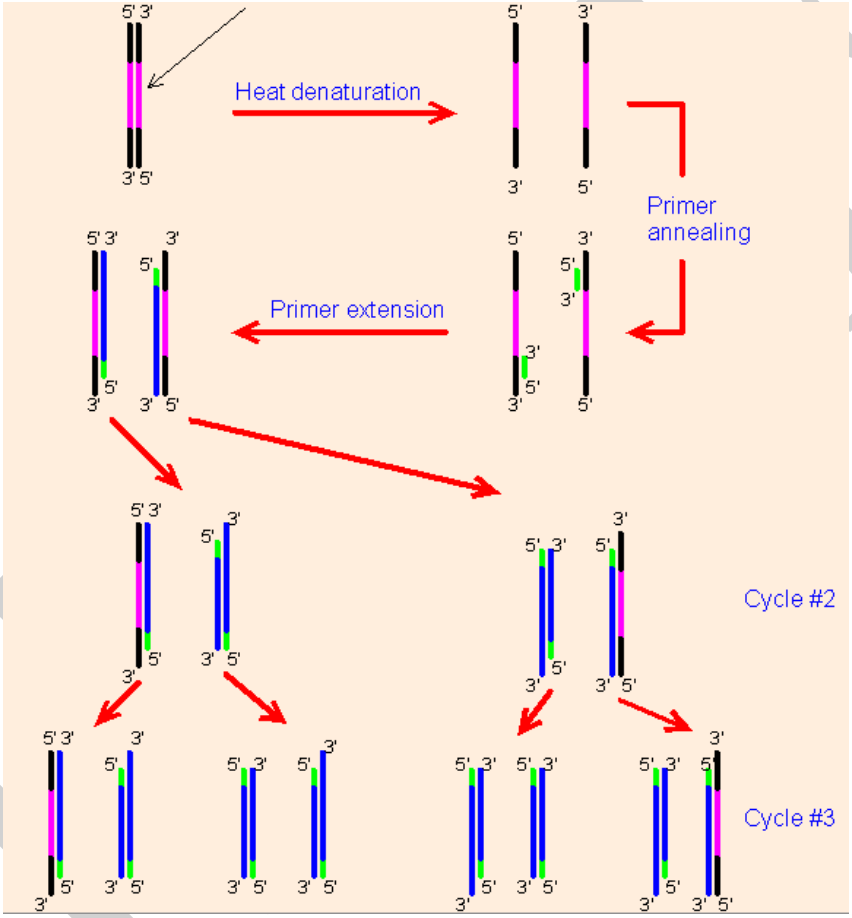
The technique was made possible by the discovery of **Taq polymerase**, the **DNA polymerase** that is used by the bacterium **Thermus auquaticus** that was discovered in hot springs. This DNA polymerase is stable at the high temperatures need to perform the amplification, whereas other DNA polymerases become denatured.

Since this technique involves amplification of DNA, the most obvious application of the method is in the detection of minuscule amounts of specific DNAs. This important in the detection of low level **bacterial infections** or rapid changes in transcription at the single cell level, as well as the detection of a **specific individual's DNA in forensic science** (like in the O.J. trial). It can also be used in DNA sequencing, **screening for genetic disorders**, site specific **mutation of DNA**, or **cloning or subcloning** of **cDNAs**.

There are three basic steps in PCR. First, the target genetic material must be denatured-that is, the strands of its helix must be unwound and separated-

by heating to 90-96°C. The second step is hybridization or annealing, in which the primers bind to their complementary bases on the now single- stranded DNA. The third is DNA synthesis by a polymerase. Starting from the primer, the polymerase can read a template strand and match it with complementary nucleotides very quickly. The result is two new helixes in place of the first, each composed of one of the original strands plus its newly assembled complementary strand.

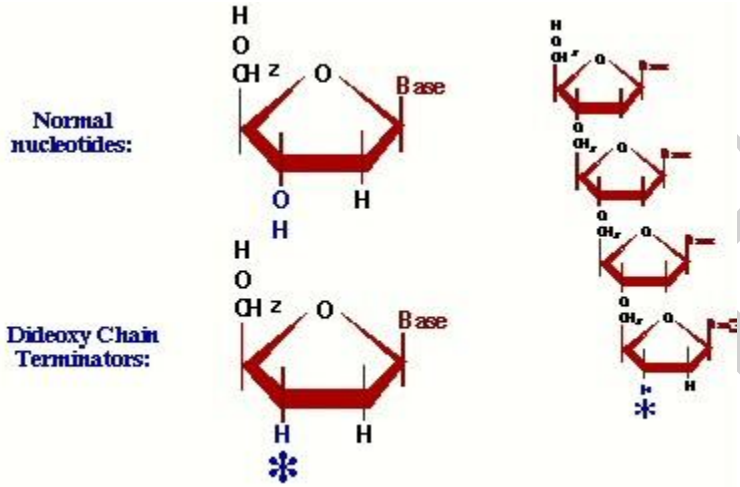
All PCR really requires in the way of equipment is a reaction tube, reagents, and a source of heat. But different temperatures are optimal for each of the three steps, so machines now control these temperature variations automatically.




**DNA Sequencing**

DNA sequencing is the determination of the precise sequence of nucleotides in a sample of DNA.

The most popular method for doing this is called the **dideoxy method** or Sanger method (named after its inventor, Frederick Sanger, who was awarded the 1980 Nobel prize in chemistry [his second] for this achievment).




**Replicating a DNA strand in the presence of dideoxy-T**

MOST of the time when a 'T' is required to make the new strand, the enzyme will get a good one and there's no problem. MOST of the time after adding a T, the enzyme will go ahead and add more nucleotides. However, 5% of the time, the enzyme will get a dideoxy-T, and that strand can never again be elongated. It eventually breaks away from the enzyme, a dead end product.

Sooner or later ALL of the copies will get terminated by a T, but each time the enzyme makes a new strand, the place it gets stopped will be random. In millions of starts, there will be strands stopping at every possible T along the way.

**SUGGESTING MATERIALS**
**Text Books:**

1. Morrison R.T & Boyd R.N., (1992), Organic Chemistry, Dorling Kindersley Pvt. Ltd., (Pearson Education)
2. Finar I.L (2002), Organic Chemistry- Volume 1, Dorling Kindersley Pvt. Ltd., (Pearson Education)
3. Finar I.L (2002), Organic Chemistry- Volume 2, Dorling Kindersley Pvt. Ltd., (Pearson Education).

**Reference Books:**

1. Nelson D.L & Cox M.M, (2012), Lehninger's Principles of Biochemistry, 7th Edition
2. Berg J.M, Tymoczko J.L & Stryer L. (2002), Biochemistry. W.H. Freeman

**Possible Questions**

**Section A** **20x 1 = 20 marks**

**Answer all the questions**

1. A nucleotide consists of
a. A nitrogenous base like Choline
**b. Purine + Pyrimidine base + Sugar + P**
c. Purine or pyrimidine Base + Sugar
d. Purine or Pyrimidine base + Phosphorous

2. A purine nucleotide is
a. **AMP** b. UMP c. CNP d. DNP

3. A Pyrimidine nucleotide is
a. GMP b. AMP **c. CMP** d. IMP

4. Adenine is
a. **6-Amino purine** b. 2-Amino-6-oxy purine c. 2-Oxy-4-amino pyrimidine
d. 2,4-dioxy pyrimidine

5. 2,4-Dioxy Pyrimidine is
a. Thymine b. Cystosine **c. Uracil** d. Guanine

6. The Chemical name for Guanine is
a. 2,4-dioxy-5-methyl Pyrimidine b**. 2-Amino-6-oxy purine**
c. 2-Oxy-4-amino Pyrimidine d. 2,4-dioxy pyrimidine

7. Nucleodites and Nucleic acids concentration are often also expressed in terms of
a. ng b. mg c. meq **d. OD at 260nm**

8. The pyrimidine nucleotide acting as the high energy intermediate is
a. ATP b. UTP **c. UDPG** d. CMP

9. A Carbon of the pentose in ester linkage with the phosphate in a nucleotide structure is
**a.** C b. C-3 c. C-4 **d. C-5**

10. Uracil and Ribose form
a. **Uridine** bCytidine c. Guanosine d. Adenosine

11. The most abundant free nucleotide in Mammalian cells is
a. **ATP** b. NAD c. GTP d. FAD

12. The nucleic acid base found in mRNA but not in DNA is
a. Adenine b. Cytosine c. Guanine **d. Uracil**

13. The size of small stable RNA ranges from
a. 0-40 nucleotides b. 40-80 nucleotides **c. 90-300 nucleotide**s
d. more than 320 nucleotides

14. The number of small stable RNAs per cell ranges from
a. 10-50000 b. 50,000-1,00,000 **c. 1,00,000-10,00,000** d. more than 10 lakhs

15. Molecular weight of heterogenous nuclear RNA(hnRNA) is
a. **More than $10^7$** b. $10^5$to $10^6$ c. $10^4$to $10^5$ d. Less than $10^4$

16. The nitrogen base present in the RNA molecule is
a. Thymine **b. Uracil** c. Xanthine d. Hypoxanthine

17. RNA does not contain
a. Uracil b. Adenine **c. Thymine** d. Ribose

18. The sugar moiety present in RNA is
a. Ribulose b. Arabinose **c. Ribose** d. Deoxyribose

19. Thymine is present in
a. **tRNA** b. RibosomaRNA c. Mammalian mRNA d. Prokryotic mRNA

20. The approximate number of nucleotides in tRNA molecule is
a. 25 b. 50 **c. 75** d. 100

## Section B

**5x 2 = 10 marks**

**Answer all the questions**

1. Define nucleic acid
2. What are DNA and RNA?
3. Write the components present in nucleic acid
4. Draw the structure of adnine and thymine
5. Give the structure of Guanine and Cytosine
6. What is nucleotides
7. What is called as nucleosides

8. List out the types of RNA
9. Define Replication
10. What is translation in nucleic acids

**Section C** **5x 6 = 30 marks**

**Answer all the questions**

1. Explain the components present in the nucleic acid?
2. Give an account of structure of components in nucleic acids
3. Briefly explain the Watson Crick model of DNA?
4. How to classify the RNA explain it briefly
5. What are the biological role of nucleic acid
6. Write a note on
   i) Replication ii) Translation iii) Transmission
7. Explain briefly biological importance of DNA and RNA?
8. What is DNA and explain its basic model of its structure

**16CHU603B**
**Karpagam Academy of Higher Education**
**Coimbatore-21**

**(For the candidate admitted on 2016 onwards)**
**Department of Chemistry**
**VI- semester**
**Molecules of Life**

**Unit-IV (Multiple Choice Questions Each Carry 1**

| S.No. | Question | Option A | Option B | Option C | Option D | Answer |
|---|---|---|---|---|---|---|
| 1 | Nucleoside consists of | Nitrogenous base | Purine or pyrimidine Base + Sugar | Purine or Pyrimidine base + Phosphorous | Purine + Pyrimidine base + Sugar + P | Purine or pyrimidine Base + Sugar |
| 2 | A nucleotide consists of | A nitrogenous base like Choline | Purine + Pyrimidine base + Sugar + P | Purine or pyrimidine Base + Sugar | Purine or Pyrimidine base + Phosphorous | Purine + Pyrimidine base + Sugar + P |
| 3 | A purine nucleotide is | AMP | UMP | CNP | DNP | AMP |
| 4 | A Pyrimidine nucleotide is | GMP | AMP | CMP | IMP | CMP |
| 5 | Adenine is | 6-Amino purine | 2-Amino-6-oxy purine | 2-Oxy-4-amino pyrimidine | 2,4-dioxy pyrimidine | 6-Amino purine |
| 6 | 2,4-Dioxy Pyrimidine is | Thymine | Cystosine | Uracil | Guanine | Uracil |
| 7 | The Chemical name for Guanine is | 2,4-dioxy-5-methyl pyrimidine | 2-Amino-6-oxy purine | 2-Oxy-4-amino pyrimidine | 2,4-dioxy pyrimidine | 2-Amino-6-oxy purine |
| 8 | Nucleodites and Nucleic acids concentration are often also expressed in terms of | ng | mg | meq | OD at 260nm | OD at 260nm |
| 9 | The pyrimidine nucleotide acting as the high energy intermediate is | ATP | UTP | UDPG | CMP | UDPG |
| 10 | A Carbon of the pentose in ester linkage with the phosphate in a nucleotide structure is | C | C-3 | C-4 | C-5 | C-5 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 11 | Uracil and Ribose form | Uridine | Cytidine | Guanosine | Adenosine | Uridine |
| 12 | The most abundant free nucleotide in Mammalian cells is | ATP | NAD | GTP | FAD | ATP |
| 13 | The nucleic acid base found in mRNA but not in DNA is | Adenine | Cytosine | Guanine | Uracil | Uracil |
| 14 | The size of small stable RNA ranges from | 0-40 nucleotides | 40-80 nucleotides | 90-300 nucleotides | more than 320 nucleotides | 90-300 nucleotides |
| 15 | The number of small stable RNAs per cell ranges from | 10-50000 | 50,000-1,00,000 | 1,00,000-10,00,000 | more than 10 lakhs | 1,00,000-10,00,000 |
| 16 | Molecular weight of heterogenous nuclear RNA(hnRNA) is | More than $10^7$ | $10^5$to $10^6$ | $10^4$to $10^5$ | Less than $10^4$ | More than $10^7$ |
| 17 | The nitrogen base present in the RNA molecule is | Thymine | Uracil | Xanthine | Hypoxanthine | Uracil |
| 18 | RNA does not contain | Uracil | Adenine | Thymine | Ribose | Thymine |
| 19 | The sugar moiety present in RNA is | Ribulose | Arabinose | Ribose | Deoxyribose | Ribose |
| 20 | Thymine is present in | tRNA | RibosomaRNA | Mammalian mRNA | Prokryotic mRNA | tRNA |
| 21 | The approximate number of nucleotides in tRNA molecule is | 25 | 50 | 75 | 100 | 75 |
| 22 | The structure of tRNA appears like a | Helix | Hair pin | Clover leaf | Coil | Clover leaf |
| 23 | Double helical structure model of the DNA was proposed by | Pouling and Corey | Peter Mitchell | Watsan and Crick | King and Wooten | Watsan and Crick |
| 24 | DNA does not contain | Thymine | Adenine | Uracil | Deoxyribose | Uracil |
| 25 | The sugar moiety present in DNA is | Deoxyribose | Ribose | Lyxose | Ribulose | Deoxyribose |
| 26 | DNA rich in A-T pairs have | 1 Hydrogen bond | 2 Hydrogen bond | 3 Hydrogen bond | 4 Hydrogen bond | 2 Hydrogen bond |
| 27 | DNA rich in G-C pairs have | 1 Hydrogen bond | 2 Hydrogen bond | 3 Hydrogen bond | 4 Hydrogen bond | 3 Hydrogen bond |
| 28 | The Width (helical diameter) of the double helix in B-form DNA in nm is | 1 | 2 | 3 | 4 | 2 |
| 29 | The distance spanned by one turn of B from DNA is | 1.0 nm | 2.0 nm | 3.0 nm | 3.4 nm | 3.4 nm |
| 30 | In a DNA molecule the guanosine content is 40%, the adenine will be | 10% | 20% | 30% | 40% | 10% |

| | | | | | | |
|---|---|---|---|---|---|---|
| 31 | An increased melting temperature of Duplex DNA results from a high content of | Adenine + Guanine | Thymine + Cytosine | Cystosine + Guanine | Cytosine + Adenine | Cystosine + Guanine |
| 32 | A synthetic nucleotide analogue used in the chemotherapy of cancer and viral infections is | Arbinosyl cytosine | 4-Hydrooxypyrazolpyrimidine | 6-Mercaptopurine | 6-Thioguanine | Arbinosyl cytosine |
| 33 | Which of the following aminoacid produce a vascoconsister on de carboxylation | Histidine | Thyrosine | Tyronine | Arginine | Thyrosine |
| 34 | The degradation of RNA by pancreatic ribonucleus produces | Nucleoside-2-Phosphates | Nucleoside-5-phosphates | Oligonucleosides | Nucleoside-3-Phosphate and Oligonucleotide | Nucleoside-3-Phosphate and Oligonucleotide |
| 35 | Interstitinal nucleosideases act on nucleosides and produce | Purine base only | Phosphate only | Sugar only | Purine or pyrimidine bases and sugar | Purine or pyrimidine bases and sugar |
| 36 | 6-Mercaptopurine inhibits the conversion of | IMP-XMP | Ribose-5phosphate to PRPP | PRPP to 5phospo to β dribosylamine | Glycinamide ribosyl 5-phosphate to formylg lycinamide ribosyl-5-phosphate | IMP-XMP |
| 37 | Purine biosynthesis is inhibited by | Aminopterin | Tetracyclin | Methotrexate | Chloramphenicol | Aminopterin |
| 38 | Pyrimidine and Purine nucleoside biosynthesis share a common precursor | PRPP | Glycine | Fumarate | Alanine | PRPP |
| 39 | The two nitrogen of pyrimidine ring are contributed by | Ammonia and glycine | Asparate and Carbomyl posphate | Glutamine and Ammonia | Aspartate and ammonia | Asparate and Carbomyl posphate |
| 40 | The first true pyrimidine ribonuleotide synthesised is | UMP | FMN | NAD | CTP | UMP |
| 41 | UDP and UTP are formed by phosphorylation from | AMP | ADP | ATP | GTP | ATP |
| 42 | A substrate of enzymes of pyirmidine nucleotide biosynthesis is | Allopurinol | Tetracyclin | Chloramphenicol | Puromycin | Allopurinol |
| 43 | In humans end product of purine catabolism is | Uric acid | Urea | Allantoin | Xanthine | Uric acid |
| 44 | In humans purine are catabolised and uric acid due to lack of the enzyme | Urease | Uricase | Xanthine oxidase | Guanase | Uricase |

| | | | | | | |
|---|---|---|---|---|---|---|
| 45 | The major catabolic product of pyrimidines in human is | β-Alanine | Urea | Uric acid | Guanine | β-Alanine |
| 46 | Genetic information flows from | DNA to DNA | DNA to RNA | RNA to ellular proteins | DNA to cellular proteins | DNA to RNA |
| 47 | Genetic code is | Collection of codon | Collection of amino acids | Collectio of purine nucelotide | Collection of pyrimidine nucleotide | Collection of amnoacids |
| 48 | Genetic code is | Overlapping | Non overlapping | Not universal | Ambiguous | Non overlapping |
| 49 | 5'-Terminus of m-RNA molecule is capped with | Guanosine triphophate | 7-methylguanosin etriphosphate | Adenoisne triphosphate | Adenosine diphosate | 7-metylguanosinetrip hophate |
| 50 | The first codon to be translated on m-RNA is | AUG | GGU | GGA | AAA | AUG |
| 51 | Initiation of protein synthesis requires | ATP | AMP | GDP | GTP | GTP |
| 52 | Translation results in a prouct known as | Protein | t-RNA | m-RNA | r-RNA | Protein |
| 53 | The Mushroom poison amanitin is an inhabitor of | Protein synthesis | mRNA synthesis | DNA synthesis | Adenosine synthesis | mRNA synthesis |
| 54 | The gene which is transcribed during repression is | Structural | Regulator | Promotor | Operator | Regulator |
| 55 | Restriction endonucleases | Cut RNA chains at specific locations | Excise introns from hnRNA | Remove Okazaki fragments | Act as defensive enzymes to protect the host bacterial DNA from DNA of foreign organisms | Act as defensive enzymes to protect the host bacterial DNA from DNA of foreign organisms |
| 56 | Reverse Transcripatase is capable of synthesizing | RNA to DNA | DNA to RNA | RNA to RNA | DNA to DNA | RNA to DNA |
| 57 | A retro Viru is | Polio Virus | HIV | Herpes Virus | Tobacco Mosaic Virus | HIV |
| 58 | Presence of arginine can be detected by | Sakaguchi reaction | Million-Nasse reaction | Hopkins-Cole reaction | Gas Chromotography | Sakaguchi reaction |
| 59 | Mitochondrial DNA is present in | Bacteria | Viruses | Eukaryotes | Fungus | Eukaryotes |
| 60 | Transfer RNA transfers | Information from DNA to Ribosomes | Information from mRNA to cytosol | Amino acids from cytosol to ribosomes | Proteins from Ribosomes to cytosols | Amino acids from cytosol to ribosomes |

## Unit-V

## Syllabus

**LIPIDS**

Introduction to lipids, classification. Oils and fats: Common fatty acids present in oils and fats, Omega fatty acids, Trans fats, Hydrogenation, Saponification value, Iodine number. Biological importance of triglycerides, phospholipids, glycolipids, and steroids (cholesterol).

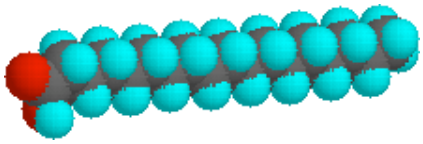
**Concept of energy in Biosystems**

Calorific value of food. Standard caloric content of carbohydrates, proteins and fats. Oxidation of foodstuff (organic molecules) as a source of energy for cells. Introduction to Metabolism (catabolism, anabolism), ATP: the universal currency of cellular energy, ATP hydrolysis and free energy change. Conversion of food into energy. Outline of catabolic pathways of Carbohydrate-Glycolysis, Fermentation, Krebs Cycle. Overview of catabolic pathways of Fats and Proteins. Interrelationships in the metabolic pathways of Proteins, Fats and Carbohydrates.

### Lipids

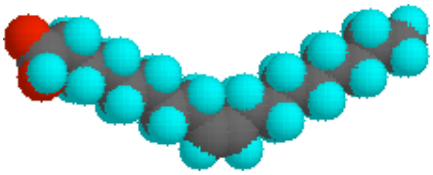
**Lipids** are organic compounds that contain hydrocarbons which are the foundation for the structure and function of living cells. Lipids are non polar so they are soluble in nonpolar environments thus not being water soluble because water is polar.

Fatty Acids



Stearic acid
An 18-carbon fatty acid

with no double bonds



Oleic acid
An 18-carbon fatty acids

with one double bond

**Fatty acids** are "carboxylic acids (or organic acid), often with a long aliphatic tails (long chains), either saturated or unsaturated." When a fatty acid is saturated it is an indication that there are no carbon-carbon double bonds and if the fatty acid is saturated it is an indication that it has at least one carbon-carbon double bond. As the following data indicate, the saturated acids have higher melting points than unsaturated acids of corresponding size. If a fatty acid has more than one double bond then this is an indication that it is a **polyunsaturated fatty acid**. The fatty acids most frequently found in nature are shown in the table below. "Most naturally occurring fatty acids contain an even number of carbon atoms and are unbranched."

**FATTY ACIDS**

| Saturated | | | Unsaturated | | |
|---|---|---|---|---|---|
| Formula | Common Name | Melting Point | Formula | Common Name | Melting Point |
| $CH_3(CH_2)_{10}CO_2H$ | lauric acid | 45 °C | $CH_3(CH_2)_5CH=CH(CH_2)_7CO_2H$ | palmitoleic acid | 0 °C |
| $CH_3(CH_2)_{12}CO_2H$ | myristic acid | 55 °C | $CH_3(CH_2)_7CH=CH(CH_2)_7CO_2H$ | oleic acid | 13 °C |
| $CH_3(CH_2)_{14}CO_2H$ | palmitic acid | 63 °C | $CH_3(CH_2)_4CH=CHCH_2CH=CH(CH_2)_7CO_2H$ | linoleic acid | -5 °C |
| $CH_3(CH_2)_{16}CO_2H$ | stearic acid | 69 °C | $CH_3CH_2CH=CHCH_2CH=CHCH_2CH=CH(CH_2)_7CO_2H$ | linolenic acid | -11 °C |
| $CH_3(CH_2)_{18}CO_2H$ | arachidic acid | 76 °C | $CH_3(CH_2)_4(CH=CHCH_2)_4(CH_2)_2CO_2H$ | arachidonic acid | -49 °C |

Saturated fatty acids have higher melting points due to their ability to pack their molecules together thus leading to a straight rod-like shape. Unsaturated fatty acids on the other hand have cis-double bond(s) that create a kink in their structure which doesn't allow them to group their molecules in straight rod-like shape.

## Classification of Lipids

Lipids are divided into:

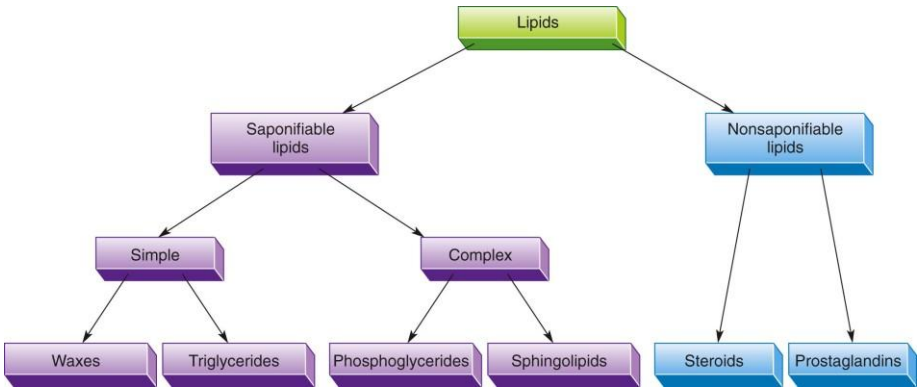
Saponifiable lipids — contain esters, which can undergo saponification (hydrolysis under basic conditions) (waxes, triglycerides, phospho- glycerides, sphingolipids)

Nonsaponifiable lipids — do not contain ester groups, and cannot be saponified (steroids, prostaglandins)

Saponifiable lipids can also be divided into groups:

Simple lipids — contain two types of components (a fatty acid and an alcohol)

Complex lipids — contain more than two components (fatty acids, an alcohol, and other components)



**Fats and Oils**

**Triacylglycerols** are the products of a reaction in which three OH groups of glycerol are esterfied with fatty acids. "A **simple triacylglycerol** is a triacylglycerol with three of the same fatty acid components. A **mixed triacylglycerol** is a triacylglycerol that contains two or three different fatty acid components and are more common than simple triacylglycerols" (Bruice, Pg. 1078). **Fat** is the name given to a class of triglycerides that appear as solid or semisolid at room temperature, fats are mainly present in animals. **Oil** is the name given to class triglycerides that appear as a liquid at room temperature, oils are mainly present in plants and sometimes in fish.

The fact that saturated fatty acid tails can bunch up closely together, its allows the triacylglycerols relatively high melting points, which in turn allows them to appear as solids at room temperature.

The opposite goes for unsaturated fatty acids, their tails cannot pack as closely together so in turn they have relatively low melting points which causes them to appear as liquids at room temperature.

Fats usually consist of *saturated* fatty acids while oils usually consist of *unsaturated* fatty acids.By a process known as catalytic hydrogenation some or all of the double bonds of the polyunsaturated oils can be reduced which will allow them to be solids at room temperature. (Bruice, Pg. 1079)

$RCH{=}CHCH_2CH{=}CHCH_2CH{=}CH\text{-}\ \ RCH_2CH_2CH_2CH{=}CHCH_2CH_2CH_2\text{-}$

Margarine and shortening originate from vegetable oils (i.e. soybean oil and safflower oil) that have been hydrogenated. This process is called "hardening of oils." When fats are consumed the body hydrolysis's the dietary fat in the intestine which regenerates the glycerol and fatty acids (Bruice, Pg. 1079). "**Soaps** are sodium or potassium salts of fatty acids. Thus, soaps are obtained when fats or oils are hydrolyzed under basic conditions" (Bruice, Pg. 700).

"The surfactant molecules reversibly assemble into polymolecular aggregates called

**micelles**

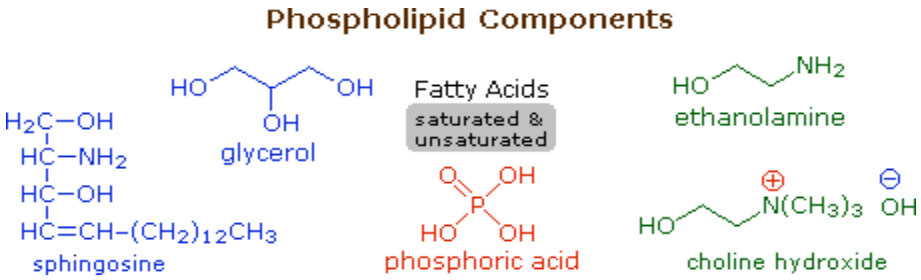
The fact that soaps have hydrophobic and hydrophilic regions allows them to wet all of the areas of an object so it can be cleaned; the job of the micelles is removing the dirt in areas that are not water soluble.

Problem- the contents of our supply of water includes calcium and magnesium, which allows for the derivation of the words "hard water." "These divalent cations cause aggregation of the micelles, which then deposit as a dirty scum."[4]

Solution- the use of detergents because of their greater solubility.

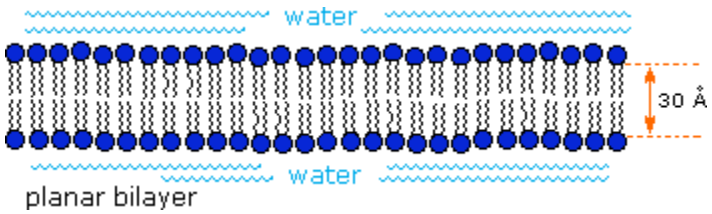
Membranes: **Membranes** are lipid bilayers that act as a boundary to various cellular structures; however they also allow for careful transfer of ions and organic molecules into and out of the cell.

**Phospholipids:** Membranes are chiefly made of phospholipids which are **Phosphoacylgycerols**. Triacylglycerols and phosphoaclyglycerols are similar however the terminal OH group of the phosphoaclyglycerol is esterfied with phosphoric acid instead of a fatty acid which leads to the formation of **phosphatidic acid**. The name **phospholipid** comes from fact that phosphoaclyglycerols are lipids that contain a phosphate group.




**Hydrophobic effect**: "Hydrophobic lipid tails avoid water but associate with each other, resulting in phospholipid bilayer.

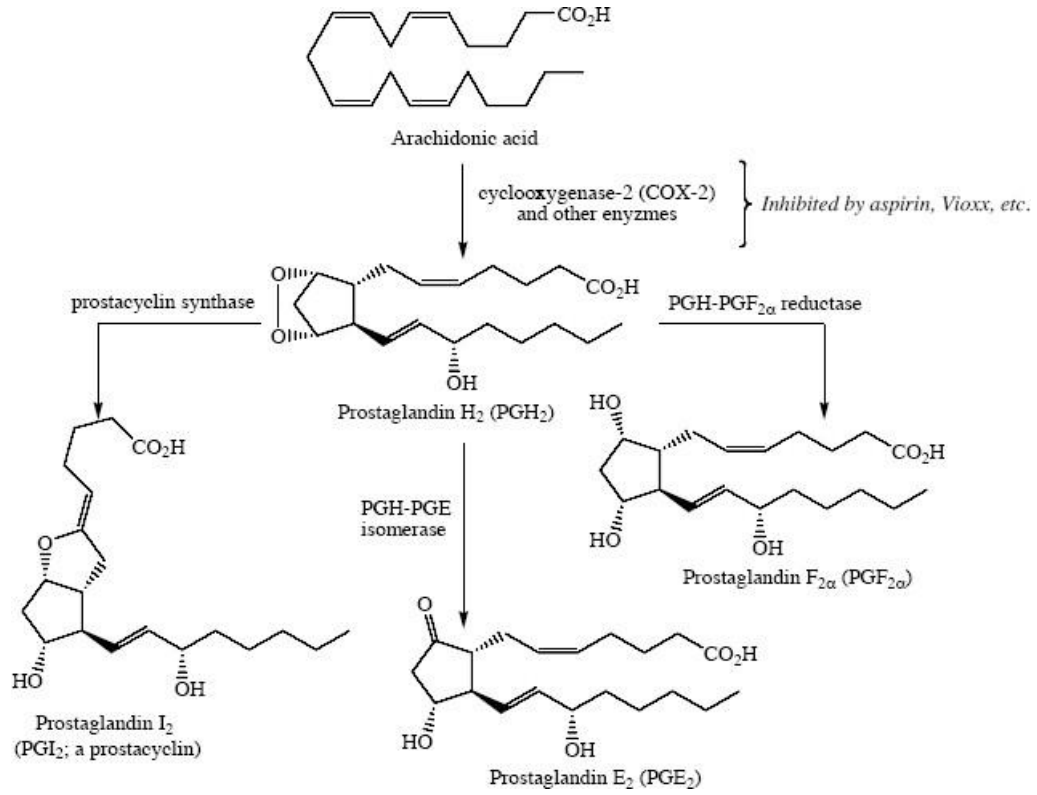
The blue circles are the hydrophilic heads and the black zig zag lines are the hydrophobic tails. Main biological function: Their role as a cell membrane




**Prostaglandins**

**Prostaglandin** is "any member of a group of lipid compounds that are derived enzymatically from fatty acids and have important functions in the animal body. Every prostaglandin contains 20 carbon atoms, including a 5-carbon ring."[5] Prostaglandins are responsible for an array of

physiological effects, such as inflammation, blood pressure (PGE2, see below for structure), blood clotting (PGI2, see below for structure), fever, pain, the induction of labor (PGF2alpha, see below for structure), and sleep-wake cycle.




Prostaglandins are named by following the PGX formula, where X designates the functional groups of the five-membered ring. PGAs, PGBs, and PGCs all contain a carbonyl group and a double bond in the five-membered ring. The location of the double bond determines whether a prostaglandin is PGA, PGB, OR PGC. PGDs and PGEs are beta-hydroxy ketones, PGFs are 1,3 diols. The subscript indicates the total number of double bonds in the side chains, and the "alpha" and "beta" indicates a cis diol and trans diol respectively.

**Hydrogenation**

In hydrogenation reactions, alkenes are converted into alkanes with hydrogen gas (H2) and a catalyst (Pt, Ni, or some other metal). This process is used to convert unsaturated vegetable oils, which are liquids at room temp., to saturated fats, which are solids at room temp.

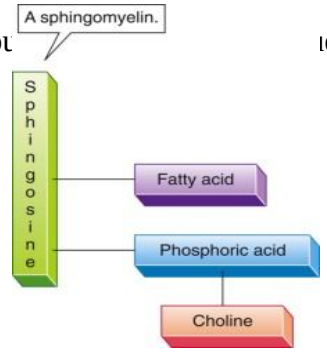
Sphingolipids

Sphingolipids are complex lipids that contain sphingosine instead of glycerol.

**Sphingomyelin**

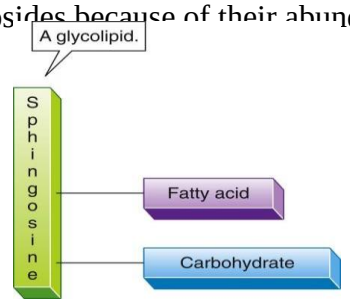
In the sphingomyelins, a choline is attached to sphingosine through a phosphate group, along with a single fatty acid attached to the sphingosine N via an amide linkage.

Sphingomyelins are fou ıe, and in the myelin sheath that protects nerves.



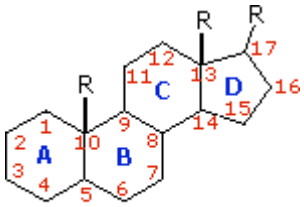

**Glycolipids**

Glycolipids are sphingolipids that contain carbo- hydrates (usually monosaccharides). They are also referred to as cerebrosides because of their abundance in brain tissue.



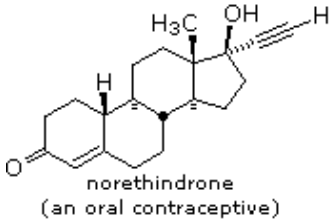
**Steroids**

The chemical messengers in our bodies are known as **Hormones** which are organic compounds synthesized in glands and delivered by the bloodstream to certain tissues in order to stimulate or inhibit a desired process. **Steroids** are a type of hormone which are usually recognized by their tetracyclic skeleton, consisting of three fused six-membered and one five-membered ring, as shown in the diagram below. The four rings are designated A, B, C & D as noted in blue, and the numbers in red represent the carbons.

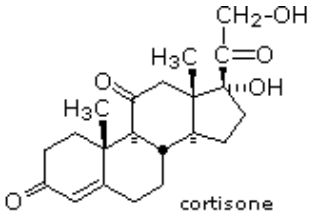



The Steroid
Carbon Skeleton

All steroids are products from the acetyl CoA biosynthetic pathway (see Pg. 95 of summer 2006 Thinkbook or Pg. 1101 in the Bruice 4th edition for the biosynthesis pathway diagram) which yields cholesterol. [7] Cholesterol is the most common steroid encountered by animals. Some important steroids are shown below.

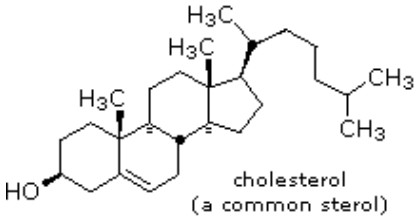



norethindrone
(an oral contraceptive)

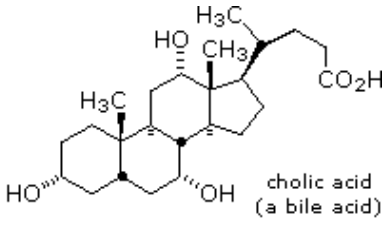



cortisone
(an anti-inflammatory hormone)

Medicinally Useful Steroids

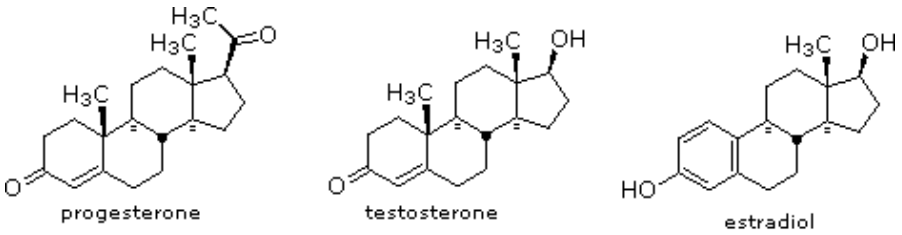



cholesterol
(a common sterol)




cholic acid
(a bile acid)

Typical Animal Steroids

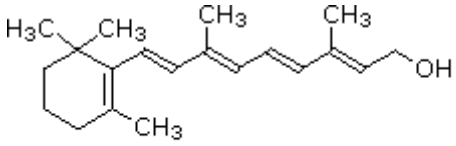



Steroid Sex Hormones

Lipophilic Vitamins

**Vitamin**: "An organic compound, other than fat, protein or carbohydrates, required for the normal growth maintenance of animals." (Pg. 97 of the summer 2006 Thinkbook by Dr. S. Hardinger). Vitamins A, D, E, and K are in the lipid family.

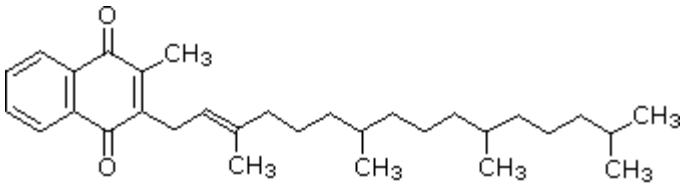
Beta-Carotene is sliced to create two molecules of vitamin A. Vitamin A, which is also known as



**vitamin A**
$C_{20}H_{30}O$ part of the visual pigment

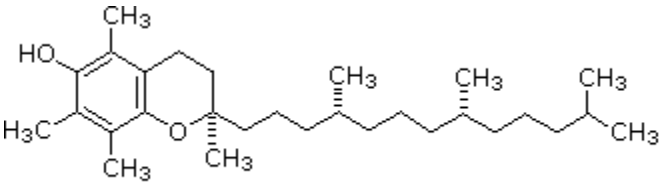
retinol, serves its main purpose in contributing to vision. It works together with the light-harvesting portion of rhodopsin (vision protein)

Vitamin K plays a key role in allowing blood to clot properly. The letter K is derived from *koagulation*, which is German for "clotting."



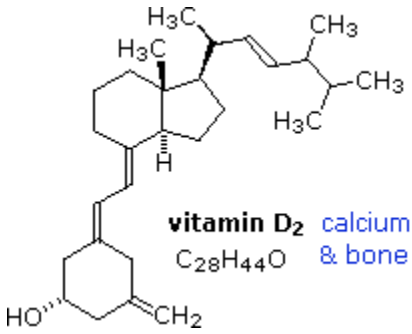
**vitamin $K_1$** a blood clotting factor
$C_{31}H_{46}O_2$

Vitamin E is a water-soluble compound that holds radicals in nonpolar membranes. Some of these are which we encounter everyday in our daily food consumption are known as *preservatives* or *antioxidants*. They are used to preserve food by preventing unwanted radical reactions. "It also prevents oxidative cellular damage from radicals".




$C_{29}H_{50}O_2$ **vitamin E** an antioxidant

Vitamin D is a hormone foundation such that its main purpose is to help maintain normal levels of calcium and phosphorus in the blood. Vitamin D also contributes in keeping a strong and sturdy skeleton.




**vitamin $D_2$** calcium metabolism
$C_{28}H_{44}O$ & bone growth

**Introduction To Metabolism. Specific And General Pathways Of Carbohydrates, Lipids And Proteins Metabolism**

Metabolism is the set of life-sustaining chemical transformations within the cells of living organisms. These enzyme-catalyzed reactions allow organisms to grow and reproduce, maintain their structures, and respond to their environments. The word metabolism can also refer to all chemical reactions that occur in living organisms, including digestion and the transport of substances into and between different cells, in which case the set of reactions within the cells is called intermediary metabolism or intermediate metabolism.

Metabolism is a term that is used to describe all chemical reactions involved in maintaining the living state of the cells and the organism. Metabolism can be conveniently divided into two categories:

Catabolism - the breakdown of molecules to obtain energy
Anabolism - the synthesis of all compounds needed by the cells

**Anabolism** is the set of constructive metabolic processes where the energy released by catabolism is used to synthesize complex molecules. In general, the complex molecules that make up cellular structures are constructed step-by-step from small and simple precursors. Anabolism involves three basic stages. Firstly, the production of precursors such as aminoacids, monosaccharides,isoprenoids and nucleotides, secondly, their activation into reactive forms using energy from ATP, and thirdly, the assembly of these precursors into complex molecules such as proteins, polysaccharides, lipids and nucleic acids.

Metabolism refers to the highly integrated network of chemical reactions by which living cells grow and sustain themselves. This network is composed of two major types of pathways: anabolism and catabolism. Anabolism uses energy stored in the form of adenosine triphosphate (ATP) to build larger molecules from smaller molecules. Catabolic reactions degrade larger molecules in order to produce ATP and raw materials for anabolic reactions.

Together, these two general metabolic networks have three major functions:

(1) to extract energy from nutrients or solar energy;

(2) to synthesize the building blocks that make up the large molecules of life: proteins, fats, carbohydrates, nucleic acids, and combinations of these substances;

(3) to synthesize and degrade molecules required for special functions in the cell.

The series of products created by the sequential enzymatic steps of anabolismor catabolism are called metabolic intermediates, or metabolites. Each steprepresents a small change in the molecule, usually the removal, transfer, oraddition of a specific atom, molecule, or group of atoms that serves as a functional group, such as the amino groups ($-NH_2$) of proteins.

Most such metabolic pathways are linear, that is, they begin with a specificsubstrate and end with a specific product. However, some pathways, such as the Krebs cycle, are cyclic. Often, metabolic pathways also have branches thatfeed into or out of them. The specific sequences of intermediates in the pathways of cell metabolism are called intermediary metabolism.

Among the many hundreds of chemical reactions there are only a few that are central to the activity of the cell, and these pathways are identical in mostforms of life.

Catabolic reactions are used to capture and save energy from nutrients, as well as to degrade larger molecules into smaller, molecular raw materials for reuse by the cell. The energy is stored in the form of energy-rich ATP, whichpowers the reactions of anabolism. The useful energy of ATP is stored in theform of a high-energy bond between the second and third phosphate groups of ATP. The cell makes ATP by adding a phosphate group to the molecule adenosinediphosphate (ADP). Therefore, ATP is the major chemical link between the energy-yielding reactions of catabolism, and the energy-requiring reactions of anabolism.

In some cases, energy is also conserved as energy-rich hydrogen atoms in thecoenzyme nicotinamide adenine dinucleotide phosphate in the reduced form of NADPH. The NADPH can then be used as a source of high-energy hydrogen atoms during certain biosynthetic reactions of anabolism.

Some reactions can be either catabolic or anabolic, depending on the circumstances. Such reactions are called amphibolic reactions. Many of the reactions interconverting the "simple molecules" fall in this category.

Catabolic and anabolic pathways are interrelated in three ways:

Matter (catabolic pathways furnish the precursor compounds for anabolism. Energy (catabolic pathways furnish the energy to "drive" anabolism). Electrons (catabolic pathways furnish the reducing power for anabolism).

Linear pathways convert one compound through a series of intermediates to another compound. An example would be glycolysis, where glucose is converted to pyruvate.

Branched pathways may either be divergent (an intermediate can enter several linear pathways to different end products) or convergent (several precursors can give rise to a common intermediate). Biosynthesis of purines and of some amino acids are examples of divergent pathways. There is usually some regulation at the branch point. The conversion of various carbohydrates into the glycolytic pathway would be an example of convergent pathways.

In a cyclic pathway, intermediates are regenerated, and so some intermediates act in a catalytic fashion. In this illustration, the cyclic pathway carries out the net conversion of X to Z. The Tricarboxylic Acid Cycle is an example of a cyclic pathway.

Metabolism is closely linked to nutrition and the availability of nutrients. Bioenergetics is a term which describes the biochemical or metabolic pathways by which the cell ultimately obtains energy. Energy formation is one of the vital components of metabolism.

The speed of metabolism, the metabolic rate, influences how much food an organism will require, and also affects how it is able to obtain that food.

Nutrition is the key to metabolism. The pathways of metabolism rely upon nutrients that they breakdown in order to produce energy. This energy in turn is required by the body to synthesize new proteins, nucleic acids (DNA, RNA) etc.

Nutrients in relation to metabolism encompass bodily requirement for various substances, individual functions in body, amount needed, level below which poor health results etc.

Essential nutrients supply energy (calories) and supply the necessary chemicals which the body itself cannot synthesize. Food provides a variety of substances that are essential for the building, upkeep, and repair of body tissues, and for the efficient functioning of the body.

Pyruvate is an intermediate in several metabolic pathways, but the majority is converted to acetyl-CoA and fed into the citric acid cycle. Although some more ATP is generated in the citric acid cycle, the most important product is NADH, which is made from $NAD^+$ as the acetyl-CoA is oxidized. This oxidation releases carbon dioxide as a waste product. In anaerobic conditions, glycolysis produces lactate, through the enzyme lactate dehydrogenase re-oxidizing NADH to NAD+ for re-use in glycolysis. An alternative route for glucose breakdown is the pentose phosphate pathway, which reduces the coenzyme NADPH and produces pentose sugars such asribose, the sugar component of nucleic acids.

Fats are catabolised by hydrolysis to free fatty acids and glycerol. The glycerol enters glycolysis and the fatty acids are broken down bybeta oxidation to release acetyl-CoA, which then is fed into the citric acid cycle. Fatty acids release more energy upon oxidation than carbohydrates because carbohydrates contain more oxygen in their structures.

Amino acids are either used to synthesize proteins and other biomolecules, or oxidized to urea and carbon dioxide as a source of energy. The oxidation pathway starts with the removal of the amino group by a transaminase. The amino group is fed into the urea cycle, leaving a deaminated carbon skeleton in the form of a keto acid. Several of these keto acids are intermediates in the citric acid cycle, for example the deamination of glutamate forms α-ketoglutarate. The glucogenic amino acids can also be converted into glucose, through gluconeogenesis .

**Stages of catabolism**

Catabolism can be broken down into 3 main stages.

**Stage 1 – Stage of Digestion**

The large organic molecules like proteins, lipids and polysaccharides are digested into their smaller components outside cells. This stage acts on starch, cellulose or proteins that cannot be directly absorbed by the cells and need to be broken into their smaller units before they can be used in cell metabolism.

Digestive enzymes include glycoside hydrolases that digest polysaccharides into monosaccharides or simple sugars.

The primary enzyme involved in protein digestion is pepsin which catalyzes the nonspecific hydrolysis of peptide bonds at an optimal pH of 2. In the lumen of the small intestine, the pancreas secretes zymogens of trypsin, chymotrypsin, elastase etc. These proteolytic enzymes break the proteins down into free amino acids as well as dipeptides and tripeptides. The free amino

acids as well as the di and tripeptides are absorbed by the intestinal mucosa cells which subsequently are released into the blood stream where they are absorbed by other tissues.

The amino acids and sugars are then pumped into cells by specific active transport proteins.

**Stage 2 – Release of energy**

Once broken down these molecules are taken up by cells and converted to yet smaller molecules, usually acetyl coenzyme A (acetyl-CoA), which releases some energy.

**Stage 3** - The acetyl group on the CoA is oxidised to water and carbon dioxide in the citric acid cycle and electron transport chain, releasing the energy that is stored by reducing the coenzyme nicotinamide adenine dinucleotide (NAD+) into NADH.

- Metabolic pathways are often regulated by feedback inhibition.
- Some metabolic pathways flow in a 'cycle' wherein each component of the cycle is a substrate for the subsequent reaction in the cycle, such as in the Krebs Cycle (see below).
- Anabolic and catabolic pathways in eukaryotes often occur independently of each other, separated either physically by compartmentalization within organelles or separated biochemically by the requirement of different enzymes and co-factors.

**Catabolism**is characterized by convergence of three major routs toward a final common pathway.

Different proteins, fats and carbohydrates enter the same pathway – tricarboxylic acid cycle.

**Anabolism** can also be divided into stages, however the anabolic pathways are characterized by divergence.

Monosaccharide synthesis begin with $CO_2$, oxaloacetate, pyruvate or lactate. Amino acids are synthesized from acetyl CoA, pyruvate or keto acids of Krebs cycle. .

Fatty acids are constructed from acetyl CoA.

On the next stage monosaccharides, amino acids and fatty acids are used for the synthesis of polysaccharides, proteins andfats.

Compartmentation of metabolic processes permits:

- separate pools of metabolites within a cell
- simultaneous operation of opposing metabolic paths
- high local concentrations of metabolites

Example: fatty acid synthesis enzymes (cytosol), fatty acid breakdown enzymes (mitochondria).

**Glycolysis** enzymes are located in the **cytosol** of cells. Pyruvate enters the **mitochondrion** to be metabolized further.

Pyruvate dehydrogenase complex is a bridge between glycolysis and aerobic metabolism – citric acid cycle.

**Pyruvate Dehydrogenase** catalyzes oxidative decarboxylation of pyruvate, to form acetyl-CoA. The overall reaction is shown below.

Pyruvate Dehydrogenase is a **large complex** containing many copies of each of three enzymes, $\mathbf{E_1}$, $\mathbf{E_2}$, and $\mathbf{E_3}$.

**Prosthetic groups are listed below**

| Enzyme | Abbreviated | Prosthetic Group |
|---|---|---|
| Pyruvate Dehydrogenase | E1 | Thiamine pyrophosphate (TPP) |
| Dihydrolipoyl Transacetylase | E2 | Lipoamide |
| Dihydrolipoyl Dehydrogenase | E3 | FAD |

In the overall reaction, the acetic acid generated is transferred to **coenzyme A**.

The final electron acceptor is $\mathbf{NAD^+}$.

The reaction proceeds as follows:

The keto carbon of pyruvate reacts with the carbanion of TPP on E1 to yield an addition compound. The electron-pulling positively charged nitrogen of the thiazole ring promotes loss of $CO_2$. What remains is hydroxyethyl-TPP.

The hydroxyethyl carbanion on TPP of E1 reacts with the disulfide of lipoamide on E2. What was the keto carbon of pyruvate is oxidized to a carboxylic acid, as the disulfide of lipoamide is reduced to a dithiol. The acetate formed by oxidation of the hydroxyethyl moiety is linked to one of the thiols of the reduced lipoamide as a thioester (~).

The acetate is transferred from the thiol of lipoamide to the thiol of coenzyme A, yielding acetyl CoA.

The reduced lipoamide swings over to the E3 active site. Dihydrolipoamide is reoxidized to the disulfide, as 2 e- + 2 H+ are transferred to a disulfide on E3 (disulfide interchange).

The dithiol on E3 is reoxidized as 2 e- + 2 H+ are transferred to FAD. The resulting FADH2 is reoxidized by electron transfer to NAD+, to yield NADH + H+.

Acetyl CoA, a product of the Pyruvate Dehydrogenase reaction, is a central compound in metabolism. The "high energy" thioester linkage makes it an excellent donor of the acetate moiety.

For example, acetyl CoA functions as:

- input to the Krebs Cycle, where the acetate moiety is further degraded to $CO_2$.
- donor of acetate for synthesis of fatty acids, ketone bodies, and cholesterol.

**Regulation** of Pyruvate Dehydrogenase complex.

Pyruvate dehydrogenase is a major regulatory point for entry of materials into the citric acid cycle.. The enzyme is regulated allosterically and by covalent modification**.**

E2 - inhibited by acetyl-CoA, activated by CoA-SH

E3 - inhibited by NADH, activated by $NAD^+$.

ATP is an allosteric inhibitor of the complex, and AMP is an activator. The activity of this key reaction is coordinated with the energy charge, the $[NAD^+]/[NADH]$ ratio, and the ratio of acetylated to free coenzyme A.

**Krebs Cycle**

The Krebs cycle, also known as the tricarboxylic acid cycle (TCA), was first recognized in 1937 by the man for whom it is named, German biochemist Hans Adolph Krebs.

The Krebs cycle refers to a complex series of chemical reactions that produce carbon dioxide and Adenosine triphosphate (ATP), a compound rich in energy. The cycle occurs by essentially linking two carbon coenzyme with carbon compounds; the created compound then goes through a series of changes that produce energy. This cycle occurs in all cells that utilize oxygen as part of their respiration process; this includes those cells of creatures from the higher animal kingdom such as humans. Carbon dioxide is important for various reasons, the main one being that it stimulates breathing, while ATP provides cells with the energy required for the synthesis of proteins from amino acids and the replication of deoxyribonucleic acid (DNA); both are vital for energy supply and for life to continue. In short, the Krebs cycle constitutes the discovery of the major source of energy in all living organisms.

**Functions**

Within the Krebs cycle, energy in the form of ATP is usually derived from the breakdown of glucose, although fats and proteins can also be utilized as energy sources. Since glucose can pass through cell membranes, it transports energy from one part of the body to another. The Krebs cycle affects all types of life and is, as such, the metabolic pathway within the cells. This pathway chemically converts carbohydrates, fats, and proteins into carbon dioxide, and converts water into serviceable energy.

The Krebs cycle is the second stage of aerobic respiration, the first being glycolysis and last being the electron transport chain; the cycle is a series of stages that every living cell must undergo in order to produce energy. The enzymes that cause each step of the process to occur are all located in the cell's "power plant"; in animals, this power plant is the mitochondria; in plants, it is the chloroplasts; and in microorganisms, it can be found in the cell membrane. The Krebs cycle is also known as the citric acid cycle, because citric acid is the very first product generated by this sequence of chemical conversions, and it is also regenerated at the end of the cycle.

The pyruvate molecules produced during glycolysis contains a lot of energy in the bonds between their molecules. In order to use that energy, the cell must convert it into the form of ATP. To do so, pyruvate molecules are processed through the Kreb Cycle, also known as the citric acid cycle.

1. Prior to entering the Krebs Cycle, pyruvate must be converted into acetyl CoA. This is achieved by removing a CO2 molecule from pyruvate and then removing an electron to reduce an NAD+ into NADH. An enzyme called coenzyme A is combined with the remaini ow:

2. Citrate is formed when the acetyl group from acetyl CoA combines with oxaloacetate from the previous Krebs cycle.

3. Citrate is converted into its isomer isocitrate.

4. Isocitrate is oxidized to form the 5-carbon α-ketoglutarate. This step releases one molecule of CO2 and reduces NAD+ to NADH2+.

5. The α-ketoglutarate is oxidized to succinyl CoA, yielding CO2 and NADH2+.

The □-Ketoglutarate Dehydrogenase Complex is

Similar to pyruvate dehydrogenase complex

Same coenzymes, identical mechanisms

E1 - a-ketoglutarate dehydrogenase (with TPP)

E2 – dihydrolipoyl succinyltransferase (with flexible lipoamide prosthetic group)

E3 - dihydrolipoyl dehydrogenase (with FAD)

6. Succinyl CoA releases coenzyme A and phosphorylates ADP into ATP.

In the succinyl CoA synthetase reaction, the thioester bond between HS-CoA and the succinyl group is hydrolyzed.

Since it is a rich in energy bond, the energy released is enough for synthesizing GTP from GDP + (P).

This GTP is equivalent, from the energetic point of view, to ATP. In fact, GTP can transfer the (P) group to ADP to form ATP:

GTP + ADP ————à GDP + ATP

Since ATP can be produced from this reaction, without participation of the respiratory chain, this process is called Substrate Level Phosphorylation (SLP) in contrast to the Oxidative Phosphorylation (ATP synthesis using the energy released in the Electron Transport Chain).

A few other reactions in metabolism are also coupled with ATP synthesis without participation of the respiratory chain. They are considered also SLP reactions.

7. Succinate is oxidized to fumarate, converting FAD to FADH2.

The Succinate Dehydrogenase Complex of several polypeptides, an FAD prosthetic group and iron-sulfur clusters, embedded in the inner mitochondrial membrane. Electrons are transferred

from succinate to FAD and then to ubiquinone (Q) in electron transport chain. Dehydrogenation is stereospecific; only the trans isomer is formed

8. Fumarate is hydrolized to form malate.

9. Malate is oxidized to oxaloacetate, reducing $NAD^+$ to $NADH^{2+}$.

We are now back at the beginning of the Krebs Cycle. Because glycolysis produces two pyruvate molecules from one glucose, each glucose is processes through the kreb cycle twice. For each molecule of glucose, six $NADH^{2+}$,two $FADH_2$, and two ATP.

**Overview**

The sum of all reactions in the citric acid cycle is:

$$\text{Acetyl-CoA} + 3\ NAD^+ + FAD + GDP + P_i + 2\ H_2O \rightarrow \text{CoA-SH} + 3\ NADH + 3\ H^+ + FADH_2 + GTP + 2\ CO_2$$

(the above reaction is equilibrated if $P_i$ represents the $H_2PO_4^-$ ion, GDP the $GDP^{2-}$ ion and GTP the $GTP^{3-}$ ion).

Two carbons are oxidized to $CO_2$, and the energy from these reactions is stored in GTP, NADH and $FADH_2$. NADH and $FADH_2$ are coenzymes (molecules that enable or enhance enzymes) that store energy and are utilized in oxidative phosphorylation.

The oxidation of acetyl-CoA to $CO_2$by the TCA cycle is the central process in energy metabolism. However, the TCA cycle also functions in biosynthetic pathways in which intermediates leave the cycle to be converted primarily to glucose, fatty acids, or non-essential amino acids. If TCA cycle anions are removed from the cycle they must be replaced to permit its continued function. This process is termed *anaplerosis*. Pyruvate carboxylase, which generates oxalacetate directly in the mitochondria, is the major anaplerotic enzyme. Conversely, 4- and 5-carbon intermediates enter the TCA cycle during the catabolism of amino acids. Because the TCA cycle cannot fully oxidize 4- and 5-carbon compounds, these intermediates must be removed from the cycle by a process termed *cataplerosis*.

**Nutrition labels**

Many governments require food manufacturers to label the energy content of their products, to help consumers control their energy intake.[8]In the European Union, manufacturers of packaged food must label the nutritional energy of their products in both kilocalories and kilojoules, when required. In the United States, the equivalent mandatory labels display only "Calories" (kilocalories),[9] often as a substitute for the name of the quantity being measured, food energy; an additional kilojoules figure is optional and is rarely used. In Australia and New Zealand, the food energy must be stated in kilojoules (and optionally in kilocalories as well), and other nutritional energy information is similarly conveyed in kilojoules. The energy available from the respiration

of food is usually given on labels for 100 g, for a typical serving size (according to the manufacturer), and/or for the entire pack contents.

The amount of food energy associated with a particular food could be measured by completely burning the dried food in a bomb calorimeter, a method known as direct calorimetry. However, the values given on food labels are not determined in this way. The reason for this is that direct calorimetry also burns the dietary fiber, and so does not allow for fecal losses; thus direct calorimetry would give systematic overestimates of the amount of fuel that actually enters the blood through digestion. What are used instead are standardized chemical tests or an analysis of the recipe using reference tables for common ingredients to estimate the product's digestible constituents (protein, carbohydrate, fat, etc.). These results are then converted into an equivalent energy value based on the following standardized table of energy densities. However "energy density" is a misleading term for it once again assumes that energy is IN the particular food, whereas it simply means that "high density" food needs more oxygen during respiration, leading to greater transfer of energy.

Note that the following standardized table of energy densities is an approximation and the value in kJ/g does not convert exactly to kcal/g using a conversion factor.

The use of such a simple system has been criticized for not taking into consideration other factors pertaining to the influence of different foods on obesity.

| **Food component** | **Energy density** | |
|---|---|---|
| | **kJ/g** | **kcal/g** |
| Fat | 37 | 9 |
| Ethanol (drinking alcohol) | 29 | 7 |
| Proteins | 17 | 4 |
| Carbohydrates | 17 | 4 |
| Organic acids | 13 | 3 |
| Polyols (sugar alcohols, sweeteners) | 10 | 2.4 |
| Fiber | 8 | 2 |

All the other nutrients in food are noncaloric and are thus not counted.

**Recommended daily intake**

Increased mental activity has been linked with moderately increased brain energy consumption. Older people and those with sedentary lifestyles require less energy; children and physically active people require more.

According to the Food and Agriculture Organization of the United Nations, the average minimum energy requirement per person per day is about 7,500 kJ (1,800 kcal).

Recommendations in the United States are 2,600 and 2,000 kcal (10,900 and 8,400 kJ) for men and women (respectively) between 31 and 35, at a physical activity level equivalent to walking about 2 to 5 km (1 ½ to 3 mi) per day at 5 to 6 km/h (3 to 4 mph) in addition to the light physical activity associated with typical day-to-day life.[19] French guidance suggests roughly the same levels.

For young children, estimated caloric needs range from 1,000 to 2,000 kilocalories per day. The recommended caloric intake for older children and adolescents, on the other hand, varies greatly from 1,400 to 3,200 kilocalories per day. Boys in general require higher caloric intake than girls.

Recognizing that people of different age and gender groups have varying daily activity levels, Australia's National Health and Medical Research Council recommends no single daily energy intake but instead prescribes an appropriate recommendation for each age and gender group. Not withstanding, nutrition labels on Australian food products typically recommend the average daily energy intake of 2,100 kcal (8,800 kJ).

**Energy usage in the human body**

The human body uses the energy released by respiration for a wide range of purposes: about 20% of the energy is used for brain metabolism, and much of the rest is used for the basal metabolic requirements of other organs and tissues. In cold environments, metabolism may increase simply to produce heat to maintain body temperature. Among the diverse uses for energy, one is the production of mechanical energy by skeletal muscle to maintain posture and produce motion.

The conversion efficiency of energy from respiration into mechanical (physical) power depends on the type of food and on the type of physical energy usage (e.g., which muscles are used, whether the muscle is used aerobically or anaerobically). In general, the efficiency of muscles is rather low: only 18 to 26% of the energy available from respiration is converted into mechanical energy. This low efficiency is the result of about 40% efficiency of generating ATP from the respiration of food, losses in converting energy from ATP into mechanical work inside the muscle, and mechanical losses inside the body. The latter two losses are dependent on the type of exercise and the type of muscle fibers being used (fast-twitch or slow-twitch). For an overall efficiency of 20%, one watt of mechanical power is equivalent to 4.3 kcal (18 kJ) per hour. For example, a manufacturer of rowing equipment shows calories released from 'burning' food as four times the actual mechanical work, plus 300 kcal (1,300 kJ) per hour, which amounts to about 20% efficiency at 250 watts of mechanical output. It can take up to 20 hours of little physical output (e.g., walking) to "burn off" 4,000 kcal (17,000 kJ) more than a body would otherwise consume. For reference, each kilogram of body fat is roughly equivalent to 32,300 kilojoules or 7,700 kilocalories of food energy (i.e., 3,500 kilocalories per pound).

Changes in body temperature – either hotter or cooler – increase the metabolic rate, thus burning more energy. Prolonged exposure to extremely warm or very cold environments increases the basal

metabolic rate (BMR). People who live in these types of settings often have BMRs 5–20% higher than those in other climates.

**Connections Of Carbohydrate, Protein, And Lipid Metabolic Pathways**

You have learned about the catabolism of glucose, which provides energy to living cells. But living things consume more than glucose for food. How does a turkey sandwich end up as ATP in your cells? This happens because all of the catabolic pathways for carbohydrates, proteins, and lipids eventually connect into glycolysis and the citric acid cycle pathways (see Figure 7.6.2). Metabolic pathways should be thought of as porous—that is, substances enter from other pathways, and intermediates leave for other pathways. These pathways are not closed systems. Many of the substrates, intermediates, and products in a particular pathway are reactants in other pathways.

**Connections of Other Sugars To Glucose Metabolism**

Glycogen, a polymer of glucose, is an energy storage molecule in animals. When there is adequate ATP present, excess glucose is shunted into glycogen for storage. Glycogen is made and stored in both liver and muscle. The glycogen will be hydrolyzed into glucose monomers (G-1-P) if blood sugar levels drop. The presence of glycogen as a source of glucose allows ATP to be produced for a longer period of time during exercise. Glycogen is broken down into G-1-P and converted into G-6-P in both muscle and liver cells, and this product enters the glycolytic pathway.

Sucrose is a disaccharide with a molecule of glucose and a molecule of fructose bonded together with a glycosidic linkage. Fructose is one of the three dietary monosaccharides, along with glucose and galactose (which is part of the milk sugar, the disaccharide lactose), which are absorbed directly into the bloodstream during digestion. The catabolism of both fructose and galactose produces the same number of ATP molecules as glucose.

**Connections of Proteins To Glucose Metabolism**

Proteins are hydrolyzed by a variety of enzymes in cells. Most of the time, the amino acids are recycled into the synthesis of new proteins. If there are excess amino acids, however, or if the body is in a state of starvation, some amino acids will be shunted into the pathways of glucose catabolism. Each amino acid must have its amino group removed prior to entry into these pathways. The amino group is converted into ammonia. In mammals, the liver synthesizes urea from two ammonia molecules and a carbon dioxide molecule. Thus, urea is the principal waste product in mammals produced from the nitrogen originating in amino acids, and it leaves the body in urine.

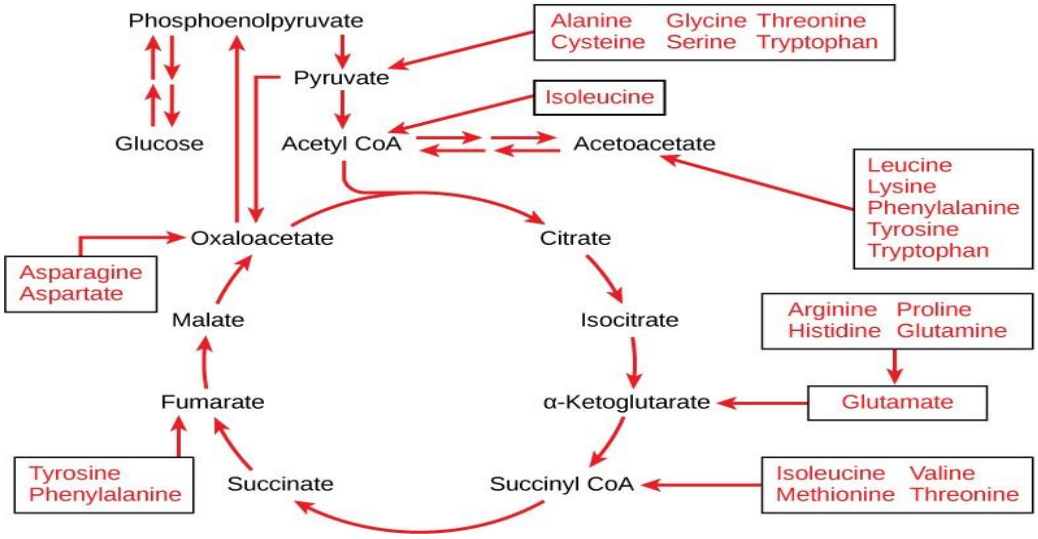



***Figure:*** *The carbon skeletons of certain amino acids (indicated in boxes) derived from proteins can feed into the citric acid cycle. (credit: modification of work by Mikael Häggström)*

**Connections of Lipid And Glucose Metabolisms**

The lipids that are connected to the glucose pathways are cholesterol and triglycerides. Cholesterol is a lipid that contributes to cell membrane flexibility and is a precursor of steroid hormones. The synthesis of cholesterol starts with acetyl groups and proceeds in only one direction. The process cannot be reversed.

Triglycerides are a form of long-term energy storage in animals. Triglycerides are made of glycerol and three fatty acids. Animals can make most of the fatty acids they need. Triglycerides can be both made and broken down through parts of the glucose catabolism pathways. Glycerol can be phosphorylated to glycerol-3-phosphate, which continues through glycolysis. Fatty acids are catabolized in a process called beta-oxidation that takes place in the matrix of the mitochondria and converts their fatty acid chains into two carbon units of acetyl groups. The acetyl groups are picked up by CoA to form acetyl CoA that proceeds into the citric acid cycle.

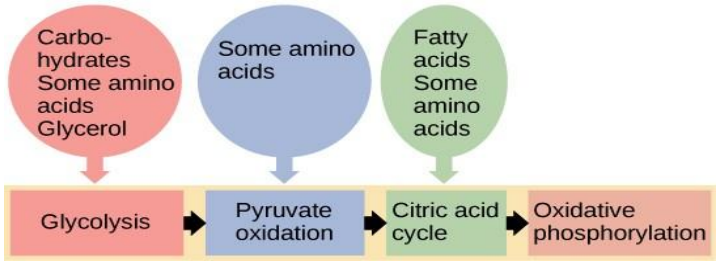



***Figure:*** *Glycogen from the liver and muscles, hydrolyzed into glucose-1-phosphate, together with fats and proteins, can feed into the catabolic pathways for carbohydrates.*

**SUGGESTING MATERIALS**

**Text Books:**

1. Morrison R.T & Boyd R.N., (1992), Organic Chemistry, Dorling Kindersley Pvt. Ltd., (Pearson Education)
2. Finar I.L (2002), Organic Chemistry- Volume 1, Dorling Kindersley Pvt. Ltd., (Pearson Education)
3. Finar I.L (2002), Organic Chemistry- Volume 2, Dorling Kindersley Pvt. Ltd., (Pearson Education).

**Reference Books:**

1. Nelson D.L & Cox M.M, (2012), Lehninger's Principles of Biochemistry, 7th Edition
2. Berg J.M, Tymoczko J.L & Stryer L. (2002), Biochemistry. W.H. Freeman

**Possible Questions**

**Section A** **20x 1 = 20 marks**

**Answer all the questions**

1. The number of double bonds in arachidonic acid is
a. 1 b. 2 **c. 4** d. 6

2. In humans, a dietary essential fatty acid is
a. Palmitic acid b. Stearic acid c. Oleic acid **d. Linoleic acid**

3. A lipid containing alcoholic amine residue is
a. Phosphatidic acid b. Gangloide c. Glucocerebroside d**. Sphingomyelin**

4. In mammals, the major fat in adipose tissues is
a. Phospholipid b. Cholesterol c. Sphingolipids **d. Tricylglycerol**

5. Glycosphigolipids are a combination of
**a. Ceramide with one or more sugar residues**
b. Glycerol with galactose
c. Sphingosine with galactose
d. Sphingosine with phosphoric acid

6. In neutral fats, the unsaponificable matter includes
a. **Hydrocarbons** b. Triacylglycerol c. Phospholipids d. Cholesterol

7. Higher alcohol present in waxes is
a. Benzyl b. Methyl c. Ethyl **d. Cetyl**

8. Kerasin consists of
a. Nervonic acid **b. Lignoceric acid** c. Cervonic acid d. Clupanodonic acid

9. Pospholipid acting as surfactant is
a. Cephalin b. Phosphatidyl inosital **c. Lecithin** d. Phosphatidyl serine

10. An oil which contains cyclic fatty acids and once used in the treatment of leprosy is
**a.** Elaidic oil b. Rapeseed oil c. Lanoline **d. Chaulmoogric oil**

11. The number of ml of N/10 KOH required to neutraliz the fatty acids in the distillate from 5gm of fat is called
a. **Reichert-Meissel number** b. Polenske number c. Acetyl number
d. Non volatile fatty acid number

12. Molecular formula of cholesterol is
a. **$C_{27}H_{45}OH$** b. $C_{29}H_{47}OH$ c. $C_{29}H_{46}OH$ d. $C_{23}H_{41}OH$

13. The Cholesterol molecule is
a. Benzene derivatives b. Quinoline derivatives **c. Steroid**
d. Straight chain acid

14. Salkowski test is performed to detect
a. Glyecerol **b. Cholesterol** c. Fatty acid d. Vitamin D

15. Free fatty acid are trasported in the blood
**a. Combined with albumin**
b. Combined with fatty acid binding protein
c. Combined with β lipoprotein
d. In unbound free salts

16. Long chain fatty acids are first activated to acetyl-CoA in
a. **Cytosol** b. Microsomes c. Nucleus d. Mitochandria

17. The enzyme of β-oxidants are found in
a. **Mitchandria** b. Cytosol c. Golgi apparatus d. Nucleus

18. An important finding in Neiman-Pick disease is
a. Leukopenia b. Cordiac enlargement c. Corneal opacity **d. Heptosplenomegaly**

19. Fucosidosis is characterized by
a. **Muscle spasticity** b. Liver enlargement c. Skin rash d. Kidney failure

20. Absence of phenylalanine hytroxylase causes
a. Neonatal tyrosinemia b. Phenylketonuria c. Primary hyperoxaluria **d. Albinism**

## Section B

**5x 2 = 10 marks**

**Answer all the questions**

1. Define iodine number
2. What is Oil?
3. What is fat?
4. Write the hydrogenation process of oil?
5. What are Glyco and Phospho lipids?
6. Write a short note on omega fatty acid
7. Define Saponification process
8. Tabulate the calorific value of Carbohydrates, Fats and proteins of human system
9. What is metabolism?
10. List out the types of lipids?
11. What are Catabolism and anabolism?
12. What is Krebs cycle

**Section C** **5x 6 = 30 marks**

**Answer all the questions**

1. Write a note on
   i) Saponification value ii) Iodine number iii) Hydrogenation of oil
2. What is lipids and briefly classify it
3. Outline the Krebs cycle and explain it briefly
4. Explain the metabolism process of carbohydrates
5. Give an account of interrelation of metabolism of carbohydrates, fats and proteins
6. Briefly explain the biological role of phospholipids and glycolipids
7. How will you calculate the Saponification and Iodine number of Oil
8. How to classify the fats and explain them briefly
9. Explain the biological conversion of ATP from organic food stuff
10. Outline the pathway of fat and protein hydrolysis

**16CHU603B**
**Karpagam Academy of Higher Education**
**Coimbatore-21**

**(For the candidate admitted on 2016 onwards)**
**Department of Chemistry**
**VI- semester**
**Molecules of Life**

**Unit-V (Multiple Choice Questions Each Carry 1 Mark).**

| S.No. | Question | Option A | Option B | Option C | Option D | Answer |
|---|---|---|---|---|---|---|
| 1 | An example of hydroxy fatty acid is | Ricinoleic acid | Crotonic acid | Butyric acid | Oleic acid | Ricinoleic acid |
| 2 | An example of saturated fatty acids | Palmitic acid | Oleic acid | Linoleic acid | Euric acid | Palmitic acid |
| 3 | A fatty acid which us not synthesized in the body and has to be supplied in the diet is | Palmic acid | Lauric acid | Linoieric acid | Palmiloeic acid | Linoieric acid |
| 4 | The fatty acid present in cerebrosides in | Lignoceric acid | Valeric acid | Caprylic acid | Behenic acid | Lignoceric acid |
| 5 | The number of double bonds in arachidonic acid is | 1 | 2 | 4 | 6 | 4 |
| 6 | In humans, a dietary essential fatty acid is | Palmitic acid | Stearic acid | Oleic acid | Linoleic acid | Linoleic acid |
| 7 | A lipid containing alcoholic amine residue is | Phosphatidic acid | Gangloide | Glucocerebroside | Sphingomyelin | Sphingomyelin |
| 8 | In mammals, the major fat in adipose tissues is | Phospholipid | Cholesterol | Sphingolipids | Tricylglycerol | Tricylglycerol |
| 9 | Glycosphigolipids are a combination of | Ceramide with one or more sugar residues | Glycerol with galactose | Sphingosine with galactose | Sphingosine with phosphoric acid | Ceramide with one or more sugar residues |
| 10 | In neutral fats, the unsaponificable matter includes | Hydrocarbons | Triacylglycerol | Phospholipids | Cholsesteol | Hydrocarbons |
| 11 | Higher alcohol present in waxes is | Benzyl | Methyl | Ethyl | Cetyl | Cetyl |
| 12 | Kerasin consists of | Nervonic acid | Lignoceric acid | Cervonic acid | Clupanodonic acid | Lignoceric acid |

| | | | | | | |
|---|---|---|---|---|---|---|
| 13 | Pospholipid acting as surfactant is | Cephalin | Phosphatidyl inosital | Lecithin | Phosphatidyl serine | Lecithin |
| 14 | An oil which contains cyclic fatty acids and once used in the treatment of leprosy is | Elaidic oil | Rapeseed oil | Lanoline | Chaulmoogric oil | Chaulmoogric oil |
| 15 | The number of ml of N/10 KOH required to neutraliz the fatty acids in the distillate from 5gm of fat is called | Reichert-Meissel number | Polenske number | Acetyl number | Non volatile fatty acid number | Reichert-Meissel number |
| 16 | Molecular formula of choleserol is | $C_{27}H_{45}OH$ | $C_{29}H_{47}OH$ | $C_{29}H_{46}OH$ | $C_{23}H_{41}OH$ | $C_{27}H_{45}OH$ |
| 17 | The Cholesterol molecule is | Benzene derivatives | Quinoline derivatives | Steroid | Straight chain acid | Steroid |
| 18 | Salkowski test is performed to detect | Glyecerol | Cholesterol | Fatty acid | Vitamin D | Cholesterol |
| 19 | Free fatty acid are trasported in the blood | Combined with albumin | Combined with fatty acid binding protein | Combined with β lipoprotein | In unbound free salts | Combined with albumin |
| 20 | Long chain fatty acids are first activated to acetyl-CoA in | Cytosol | Microsomes | Nucleus | Mitochandria | Cytosol |
| 21 | The enzyme of β-oxidants are found in | Mitchandria | Cytosol | Golgi apparatus | Nucleus | Mitchandria |
| 22 | An important finding in Neiman-Pick disease is | Leukopenia | Cordiac enlargement | Corneal opacity | Heptosplenomegaly | Heptosplenomegaly |
| 23 | Fucosidosis is characterized by | Muscle spasticity | Liver enlargement | Skin rash | Kidney failure | Muscle spasticity |
| 24 | A Significant features of Tangier disease is | Impairment of chylomicrom formation | Hypotriocyl glycerolmia | Absence of Apo-C-II | Absence of Apo-C-I | Absence of Apo-C-II |
| 25 | Absence of phenylalanine hytroxylase causes | Neonatal tyrosinemia | phenylketonuria | primary hyperoxaluria | Albinism | Albinism |
| 26 | Tyrosinosis is due to defect in the enzyme | Fumarylccetoocetate hydrolase | P-Hydroxy phenyl pyruvate hydroxylase | Tyrosine transamanise | Tyrasine hydroxylase | Fumarylccetoocetate hydrolase |
| 27 | The percentage of linoleic acid in safflower oil is | 73 | 57 | 40 | 15 | 73 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 28 | The percentage of polyunsaturated fatty acids in butter is | 60 | 6 | 8 | 3 | 3 |
| 29 | The normal range of total serum bilirubin is | 0.2-1.2 mg/100ml | 1.5-1.8 mg/100ml | 2.0-4.0 mg/100ml | Above 7.0 mg/100ml | 0.2-1.2 mg/100ml |
| 30 | Immediate direct Vanden Bergh reaction indicates | Hemolytic jaundice | Hepatic jaundice | Obstructive jaundice | Megalobastic anemia | Hepatic jaundice |
| 31 | The normal level of prothrombin time is about | 2 sec | 4 sec | 14 sec | 10-16 sec | 14 sec |
| 32 | The normal range of filtration factor in an adult is | 0.10-0.15 | 0.16-0.21 | 0.25-0.30 | 0.35-0.40 | 0.16-0.21 |
| 33 | The major storage form of lipids is | Esterified cholesterol | Glycerophospholipids | Triglycerides | Sphingolipids | Triglycerides |
| 34 | Cerebonic acid ispresent in | Triglycerides | Cerebrosides | Esterified cholesterol | Sphingomyelin | Cerebrosides |
| 35 | The nitrogenous base in lecithin is | Ethanolamine | Choline | Serine | Betaine | Choline |
| 36 | Lipid stores are mainly present in | Liver | Brain | Muscles | Adipose tissue | Adipose tissue |
| 37 | alpha-oxidation of fatty acids occurs mainly in | Liver | Brain | Muscles | Adipose tissue | Brain |
| 38 | Activation of fatty acids requires all the following except | ATP | Coenzyme A | Thiokinase | Carnitine | Carnitine |
| 39 | Net ATP generation on complete oxidation of stearic acid is | 129 | 131 | 146 | 148 | 146 |
| 40 | Plasma becomes milky | Due to high level of HDL | Due to high level of LDL | During fasting | After a meal | After a meal |
| 41 | Invisible fat is present in | Milk | Coconut oil | Groundnut oil | Hydrogenated oil | Milk |
| 42 | Visible fat present in | Milk | Pulses | Coconut oil | Egg yolk | Coconut oil |
| 43 | Fat content of eggs is about | 7% | 10% | 13% | 16% | 13% |
| 44 | Predominant fatty acids in meat are | Saturated | Monounsaturated | Polyunsaturated | Disaturated | Saturated |
| 45 | Which of the following has the highest cholesteral content | Meat | Fish | Butter | Milk | Butter |
| 46 | The starch content of wheat is about | 50% | 60% | 70% | 80% | 70% |

| | | | | | | |
|---|---|---|---|---|---|---|
| 47 | A significant source of starch among vegetables is | Radish | Spinach | Potato | Cauliflower | Potato |
| 48 | An enzyme which is excreted in urine is | Lactase dehydrogenase | Amylase | Ornithine transcarbamoylase | Glycases | Ornithine transcarbamoylase |
| 49 | Lecithins combine with protein to form | Phosphoprotein | Mucoprotein | Lipoprotein | Glycoprotein | Lipoprotein |
| 50 | Lipoproteins may be identified more accurately by means of | Electrophoresis | Ultra centrifugation | Centrifugation | Immunoelectrophoresis | Immunoelectrophoresis |
| 51 | The iodine number of essential fatty acids of vegetable oils | High | Very high | Very low | Low | Low |
| 52 | Lecithins are soluble in ordinary solvents except | Benzene | Ethanol | Mathanol | Acetone | Acetone |
| 53 | Saponification number indicates | Unsaturation in fat | Average MW of fatty acid | Acetyl number | Acid number | Average MW of fatty acid |
| 54 | Calorific value of lipids per gram is | 5Kcal | 8Kcal | 9Kcal | 12Kcal | 9Kcal |
| 55 | Carbohydrate moiety in cerebrosides is | Glucose | Sucrose | Galactose | Maltose | Sucrose |
| 56 | A fatty  acid not synthesised in man is | Oleic | Palmitic | Linoleic | Stearic | Linoleic |
| 57 | Maximum energy produced by | Fats | Carbohydrates | Proteins | Nucleic acids | Fats |
| 58 | Carboxypeptidase, an enzyme of pancreatic juice contains | Mn | Zn | Mg | Ca | Zn |
| 59 | Accumulation of trytaphan in blood is known as | Pompe's disease | Wilson's disease | Wolman's disease | Hartnup's disease | Hartnup's disease |
| 60 | How much moles of ATP required to produce one molecule of urea | 2 | 4 | 3 | 5 | 3 |

Reg. No.: ---------- [16CHU603B]

**KARPAGAM ACADEMY OF HIGHER EDUCATION**
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**COIMBATORE-641 021**

**B.Sc., Degree Examination**
**(For the candidates admitted from 2016 & onwards)**

**III- B.Sc., Chemistry**
**I$^{st}$ Internal Test**
**Molecules of Life**

Time: 2 Hours Maximum: 50 marks
Date:

**Section-A** **20X1=20**

**Answer all the questions**

1. The general formula of monosaccharides is
   a. $C_nH_{2n}O_n$ b. $C_{2n}H_nO_n$ c. $C_nH_2O_n$ d. $C_nH_{2n}O_{2n}$

2. The aldose sugar is
   a. Ribulose b. Glycerose c. Erythrulose d. Dihydroxyacetone

3. The most important epimer of glucose is
   a. Fructose b. Arabinose c. Xylose d. Galactose

4. alpha-D-glucose and beta-D-glucose are
   a. Stereoisomers b. Epimers c. Anomers d. Keto-aldol pair

5. The Change in specific rotation values of sugars is called as
   a. Optical isomerism b. Mutarotation c. Epimerisation d. Isomerisation

6. Compounds having same structural formula but differing in spatial configuration are known as
   a. Stereoisomers b. Anomers c. Isomers d. Epimers

7. ADH test is based on the measurement of
   a. Specific gravity of urine b. Concentration of urea in urine
   c. Concentration of urea in blood d. Volume of urine in ml/minute

8. The specific gravity of urine normally in the ranges from
   a. 0.900-0.999 b. 1.003-1.030 c. 1.000-1.001 d. 1.101-1.120

9. Number of stereoisomers present in glucose is
   a. 4 b. 8 c. 16 d. 12

10. The following which one gave malose on hydrolysis
    a. Sucrose b. Starch c. Glucose d. Galactose

11. All proteins contains the
    a. Same 20 amino acids b. Different amino acids
    c. 300 amino acids occurring in nature d. Only a few amino acids

12. $P^H$ (Isoelectric point) of alanine is
    a. 6.02 b. 6.6 c. 6.8 d. 7.2

13. Which one of the following amino acid contain Sulphur in it structure
    a. Methionine b. Leucine c. Valine d. Asparagine

14. Pick out the aromatic amino acid
    a. Lysine b. Tyrosine c. Taurine d. Arginine

15. The function of plasma albumin are
    a. Osmosis b. Transport c. Immunity d. Transmission

16. Which one of the following amino acid essential to man
    a. Aspartate b. Tyrosine c. Methionine d. Serine

17. A protein rich in cysteine is
    a. Collagen b. Keratine c. Hemoglobin d. Gelatin

18. Sanger's reagent contains
    a. Phenylisothiocyanate b. Dansyl chloride c. 1-fluoro-2,4-dinitrobenzene
    d. Ninhydrin

19. Edmans reagent contains
    a. Phenylisothiocyanate b. 1-fluoro-2,4-dinitrobenzene c. Dansyl chloride
    d. tBOC,azide

20. A Zwitter ion also called as
    a. Positive ion b. negative ion c. Dipolar ion d. Larger anion

**Section B** **3x2 = 6**

**Answer all the questions**

21. What is reducing and non-reducing sugar?

22. Define mutarotation?

23. What is "Isoelectric point" of proteins?

**Section C** **3x8 = 24**

**Answer all the questions**

24. a. Explain the Fischer proof for determine the configuration of D(+)- Glucose?

Or

b. Write a note on classification of carbohydrates? Explain with suitable examples?

25. a. Briefly explain the Haworth projection for cyclic structure of Glucose?

Or

b. Write a note on structure of maltose, lactose and sucrose and its properties?

26. a. Distinguish the primary, secondary, tertiary and quatnary structure of proteins?

Or

b. Explain the DNFB and Edman method to determine the N-terminal amino acid?

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***Answer Key***

**Section-A** **20X1=20**

**Answer all the questions**

1. **b. $C_{2n}H_nO_n$**
2. **b. Glycerose**
3. **d. Galactose**
4. **c. Anomers**
5. **b. Mutarotation**
6. **a. Stereoisomers**
7. **a. Specific gravity of urine**
8. **b. 1.003-1.030**
9. **c. 16**
10. **b. Starch**
11. **a. Same 20 amino acids**
12. **a. 6.02**
13. **a. Methionine**
14. **b. Tyrosine**
15. **a. Osmosis**
16. **c. Methionine**
17. **b. Keratine**
18. **c. 1-fluoro-2,4-dinitrobenzene**
19. **a. Phenylisothiocyanate**
20. **c. Dipolar ion**

**Section B** **3x2 = 6**

**Answer all the questions**

21. **What is reducing and non-reducing sugar?**

**Ans:** The carbohydrates may also be classified as either reducing or non-reducing sugars. Cyclic acetals or ketals are not in equilibrium with their open chain carbonyl group containing forms in neutral or basic aqueous solutions. They cannot be oxidized by reagents such as Tollen's reagent ($Ag^+$, $NH_3$, $OH^-$) or $Br_2$. So, these are referred as non- reducing sugars. Whereas hemiacetals or

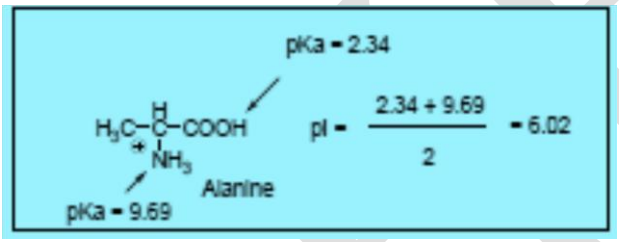
hemiketals are in equilibrium with the open- chain sugars in aqueous solution. These compounds can reduce an oxidizing agent (eg. $Br_2$), thus, they are classified as a reducing sugar.

22. **Define mutarotation?**

**Ans:** a solution of D-(+)-glucose (mp 146 °C) specific rotation gradually decreases from an initial value of + 112.2° to + 52.7°, while The D-(+)- glucose (mp 150 °C) specific rotation gradually increases from an initial value of + 18.7° to + 52.7°. The three forms of glucose reach equilibrium concentrations with the specific rotation of +52.7. This change ("mutation") in the specific rotation toward equilibrium is called ***mutarotation.***

23. **What is "Isoelectric point" of proteins?**

**Ans:** The isoelectric point (pI) of an amino acid is the $P^H$ where it has no net charge. For example, the pI of an amino acid that does not possess an ionizable side chain is midway between its two pKa values.




**Section C** **3x8 = 24**

**Answer all the questions**

24. **a. Explain the Fischer proof for determine the configuration of D(+)- Glucose?**

**Ans: The Fischer proof of the structure of (+)-glucose**

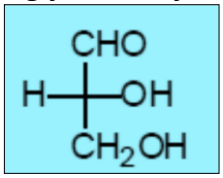
Started in 1888, 12 years after the proposal that carbon was tetrahedral, and thus had stereoisomers.

Tools:

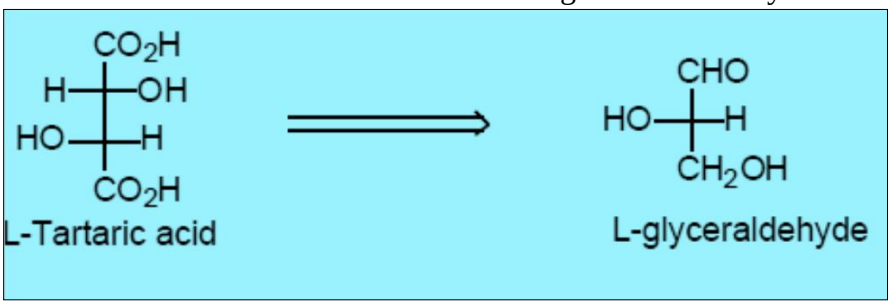
- melting points
- optical rotation (determine whether a molecule is optically active)
- chemical reactions

Fischer knew:

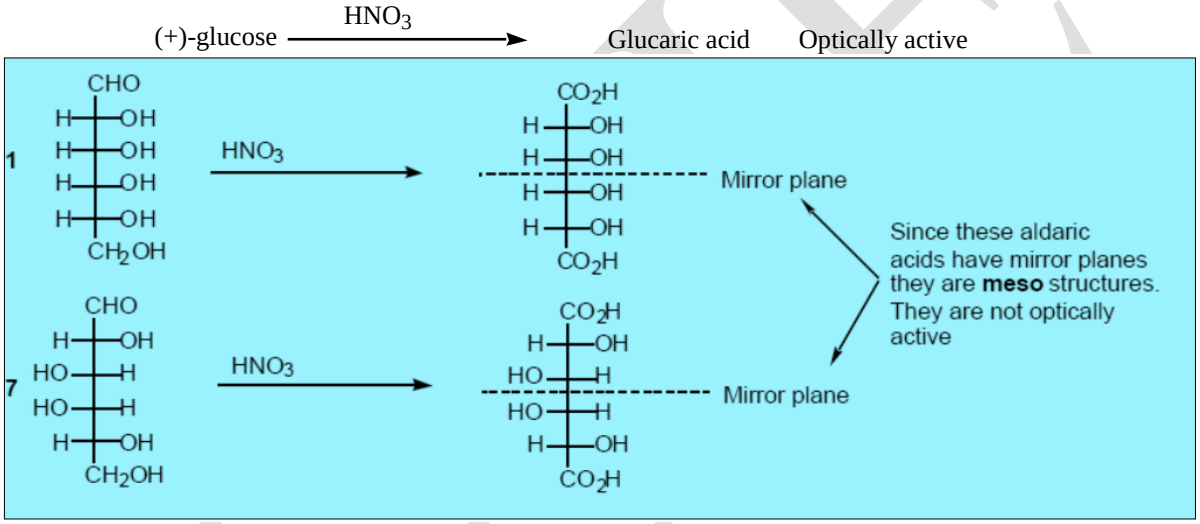
- (+)-glucose is an aldohexose.
- Therefore, there are 4 stereocenters and $2^4$ = 16 stereoisomers (8 D-sugars and 8 L-sugars)
- At this time could not determine the actual configuration (D or L) of sugars
- Fischer arbitrarily assigned D-glyceraldehyde the following structure.



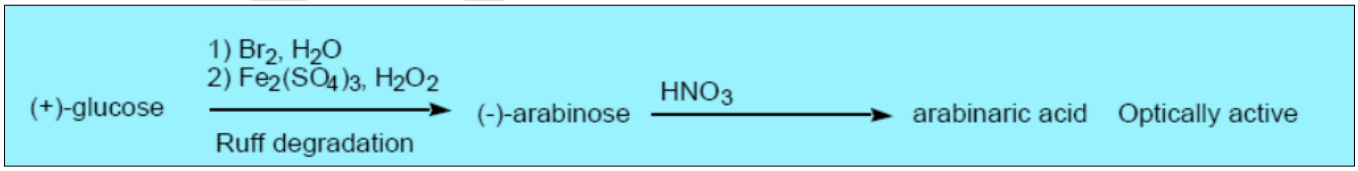
- In 1951 Fischer was shown to have guessed correctly.

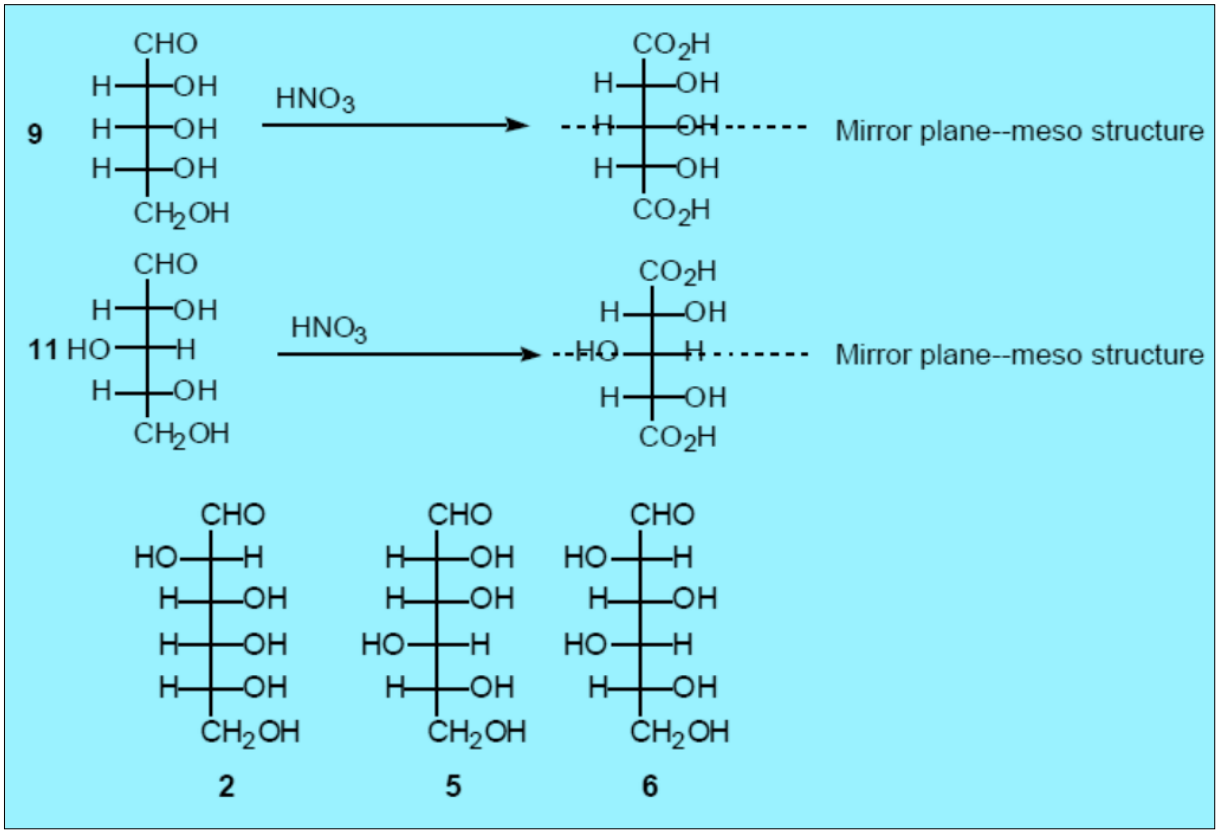



1) Oxidation of (+)-glucose with nitric acid gives an aldaric acid, glucaric acid, that is optically active. Therefore (+)-glucose cannot have structures **1** or **7**, which would give optically inactive aldaric acids.

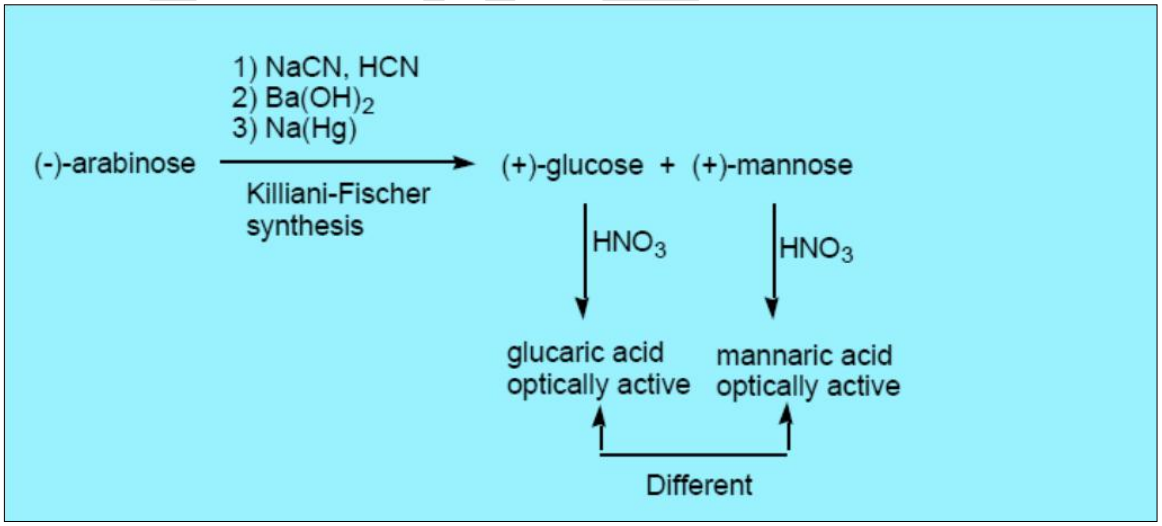


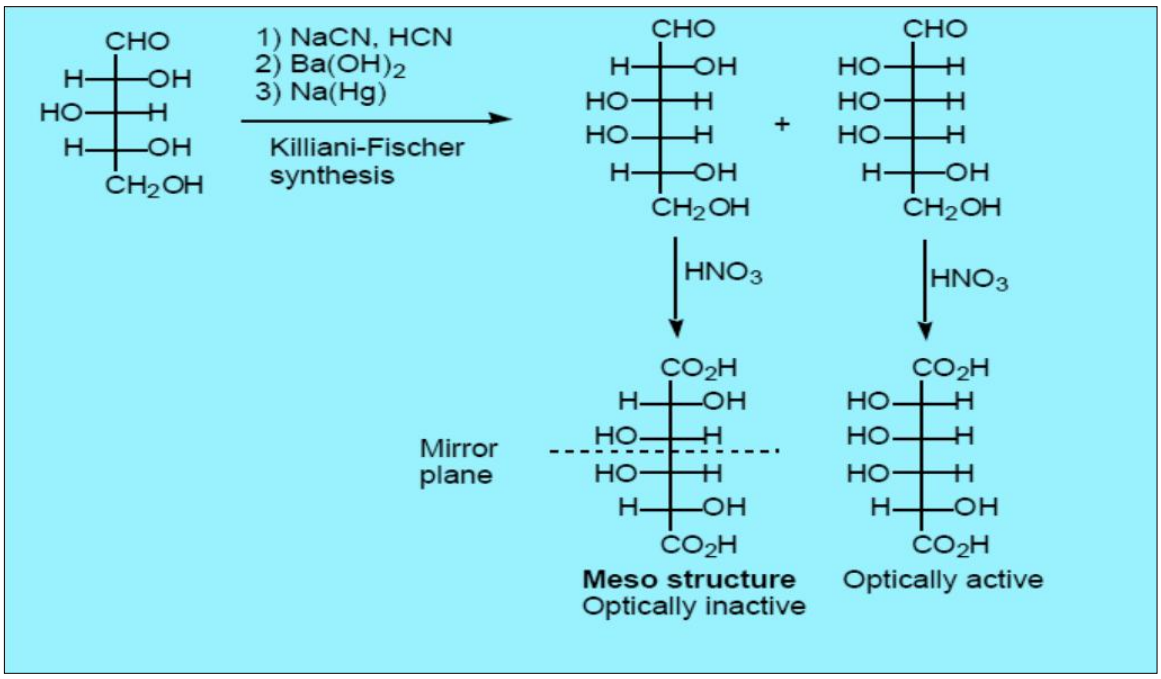

2) Ruff degradation of (+)-glucose gives (-)-arabinose. Oxidation of (-)-arabinose with nitric acid gives arabanaric acid, which is optically active. Therefore, (-)-arabinose cannot have structures **9** or **11**, which would give optically inactive aldaric acids. If arabinose cannot be **9** or **11**, (+)-glucose cannot be **2** (**1** was already eliminated), **5** or **6**, which would give **9** or **11** in a Ruff degradation.



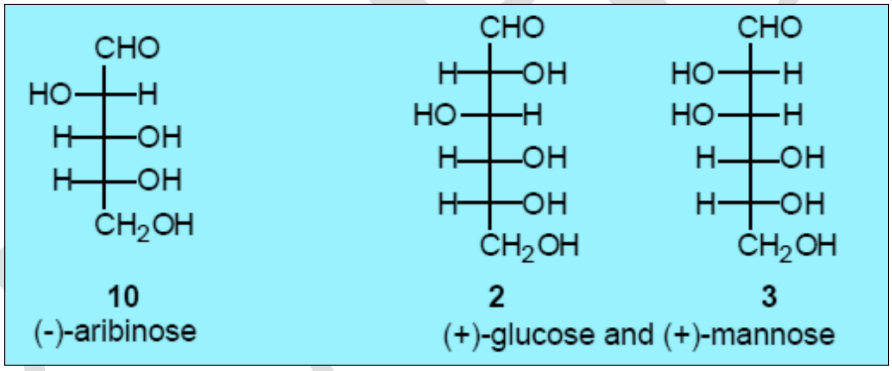



3) Killiani-Fischer chain extension of (-)-arabinose gives (+)-glucose and (+)-mannose. Both of which give optically active aldaric acids when oxidized with nitric acid. Therefore, (-)-arabinose cannot be structure **12**. **12** would give **7** and **8** in a Killiani- Fischer chain extension. **8** would give an optically active aldaric acid, but **7** would give an optically inactive aldaric acid.

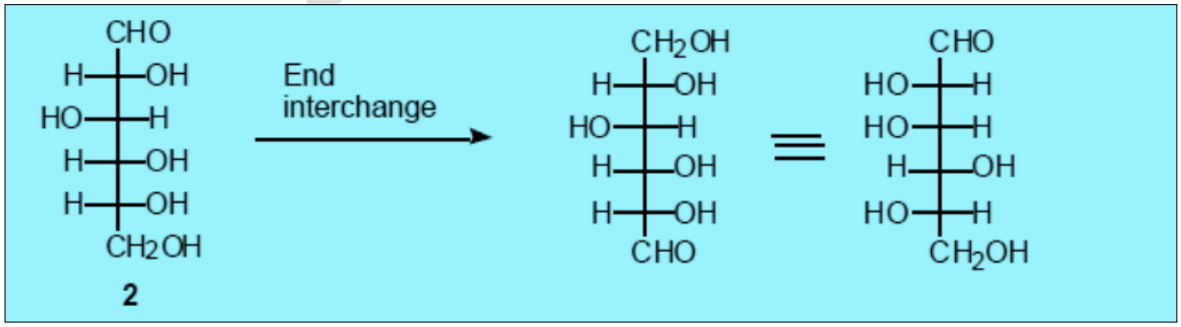


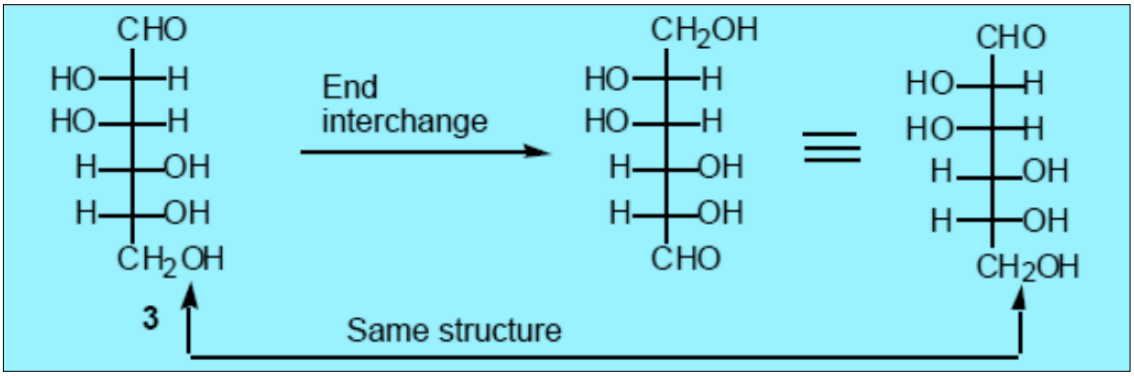


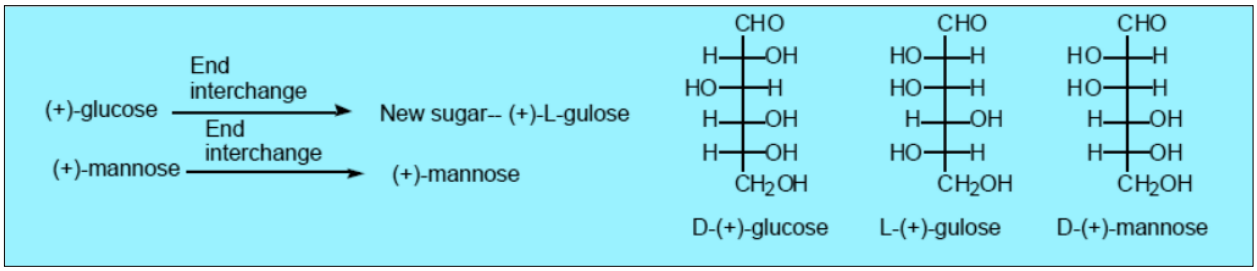

4) The structure of arabinose is **10**. Therefore the structures of (+)-glucose and (+)- mannose are **2** and **3**



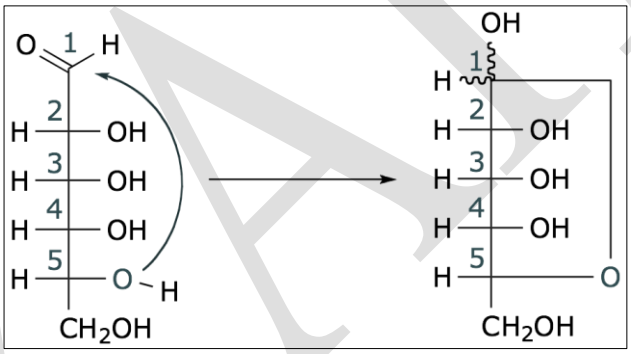

Fischer had previously developed a method to interchange the ends of a sugar (the aldehyde is converted to a $CH_2OH$ and the $CH_2OH$ is converted to an aldehyde, but we won't worry about how this is done). Fischer reasoned that if ends of **2** were interchanged, a new L-aldohexose would be obtained. On the other hand, if the ends of **3** were interchanged, the product would be the same (structure **3**). When the ends of (+)-glucose were interchanged a new sugar was obtained, which Fischer named L-gulose. When the ends of (+)-mannose were interchanged, the product was (+)-mannose. **Therefore the structure of (+) glucose is structure 2, and strucutre 3 is (+)-mannose.**






Aldoses contain an aldehyde group and hydroxyl groups, and they undergo intramolecular reactions to form cyclic hemiacetals. These five-membered and six-membered cyclic hemiacetals are often more stable than the open-chain form of the sugar.



In D-allose, nucleophilic attack on the carbonyl carbon of the aldehyde group by the hydroxyl group on carbon five (C-5) gives a six-membered ring cyclic hemiacetal. The new bond that forms between the oxygen atom on C-5 and the hemiacetal carbon atom C-1 is usually shown by using a box in the Fischer projection. This cyclic structure is called the pyranose ring form of the sugar.

When the cyclic hemiacetal forms, the C-1 carbon atom becomes a new stereogenic center and can have either an *R*- or an *S*-configuration. To illustrate the ambiguity in the configuration at this new stereogenic center, squiggly lines are used in the Fischer projection to connect the hydrogen and the hydroxyl group to C-1.

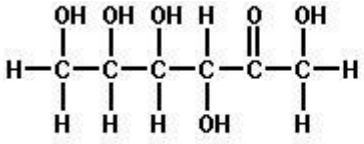
A Fischer projection can illustrate the structure of the cyclic hemiacetal form of a sugar, but it lacks something aesthetically as far as representing the six-membered ring in the structure. In addition, this type of Fischer projection gives little information about the orientation of the groups on C-2 through C-5 in the cyclic form of the sugar.

Or

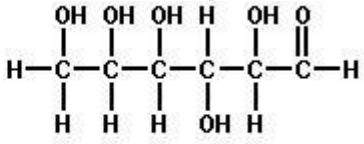
**b. <u>Write a note on classification of carbohydrates? Explain with suitable examples?</u>**

**Ans: <u>Classification and nomenclature</u>**

Although a number of classification schemes have been devised for carbohydrates, the division into four major groups—monosaccharides, disaccharides, oligosaccharides, and polysaccharides—used here is among the most common. Most monosaccharides, or simple sugars, are found in grapes, other fruits, and honey. Although they can contain from three to nine carbon atoms, the most common representatives consist of five or six joined together to form a chainlike molecule. Three of the most important simple sugars—glucose (also known as dextrose, grape sugar, and corn sugar), fructose (fruit sugar), and galactose—have the same molecular formula, ($C_6H_{12}O_6$), but, because their atoms have different structural arrangements, the sugars have different characteristics; i.e., they are isomers.



Fructose

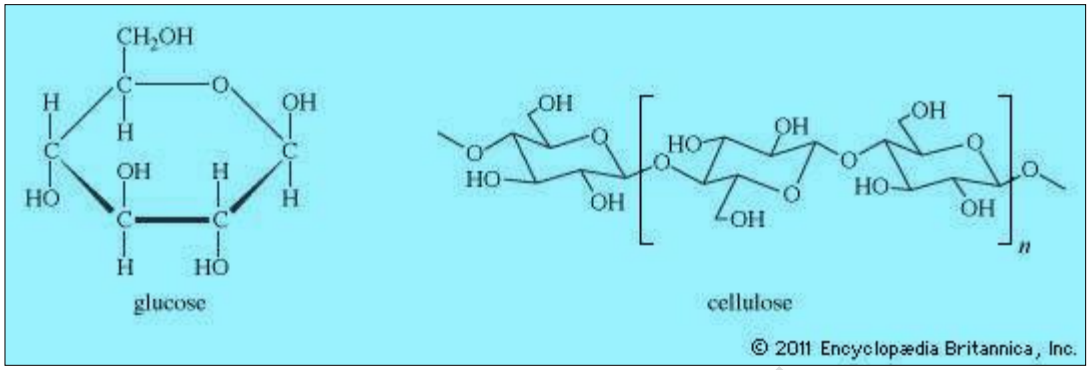


Glucose

Slight changes in structural arrangements are detectable by living things and influence the biological significance of isomeric compounds. It is known, for example, that the degree of sweetness of various sugars differs according to the arrangement of the hydroxyl groups (—OH) that compose part of the molecular structure. A direct correlation that may exist between taste and any specific structural arrangement, however, has not yet been established; that is, it is not yet possible to predict the taste of a sugar by knowing its specific structural arrangement. The energy in the chemical bonds of glucose indirectly supplies most living things with a major part of the energy that is necessary for them to carry on their activities. Galactose, which is rarely found as a simple sugar, is usually combined with other simple sugars in order to form larger molecules.

Two molecules of a simple sugar that are linked to each other form a disaccharide, or double sugar. The disaccharide sucrose, or table sugar, consists of one molecule of glucose and one molecule of fructose; the most familiar sources of sucrose are sugar beets and cane sugar. Milk sugar, or lactose, and maltose are also disaccharides. Before the energy in disaccharides can be utilized by living things, the molecules must be broken down into their respective monosaccharides. Oligosaccharides, which consist of three to six monosaccharide units, are rather infrequently found in natural sources, although a few plant derivatives have been identified.

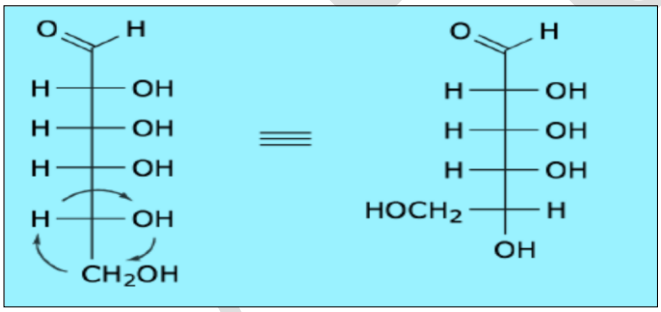
Polysaccharides (the term means many sugars) represent most of the structural and energy-reserve carbohydrates found in nature. Large molecules that may consist of as many as 10,000 monosaccharide units linked together, polysaccharides vary considerably in size, in structural complexity, and in sugar content; several hundred distinct types have thus far been identified. Cellulose, the principal structural component of plants, is a complex polysaccharide comprising many glucose units linked together; it is the most common polysaccharide. The starch found in plants and the glycogen found in animals also are complex glucose polysaccharides. Starch (from the Old English word *stercan*, meaning “to stiffen”) is found mostly in seeds, roots, and stems, where it is stored as an available energy source for plants. Plant starch may be processed into foods such as bread, or it may be consumed directly—as in potatoes, for instance. Glycogen, which consists of branching chains of glucose molecules, is formed in the liver and muscles of higher animals and is stored as an energy source.




25. **a. Briefly explain the Haworth projection for cyclic structure of Glucose?**

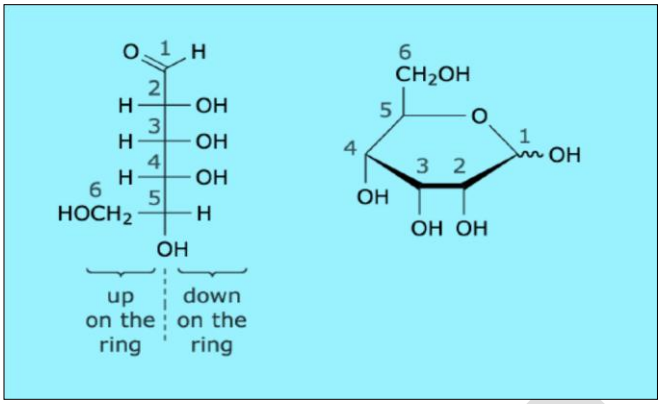
**Ans: Drawing a Haworth Structure from a Fischer Projection**

The most important thing to keep straight in drawing the correct Haworth structure of a sugar is that the stereochemistry at C-2 through C-5, because a change in the configuration at any of these stereogenic centers changes the identity of the sugar. As we saw in the analysis above, a conformational change is needed to get the C-5 hydroxyl group in the proper orientation far attack on the carbonyl group. We can illustrate this conformational change on the Fischer projection of the sugar as a rotation about the C4–C5 bond, swapping the positions of the H, the OH, and the $CH_2OH$ groups on C-5. The second Fischer projection below is simply a different conformation of the same sugar as the first one.

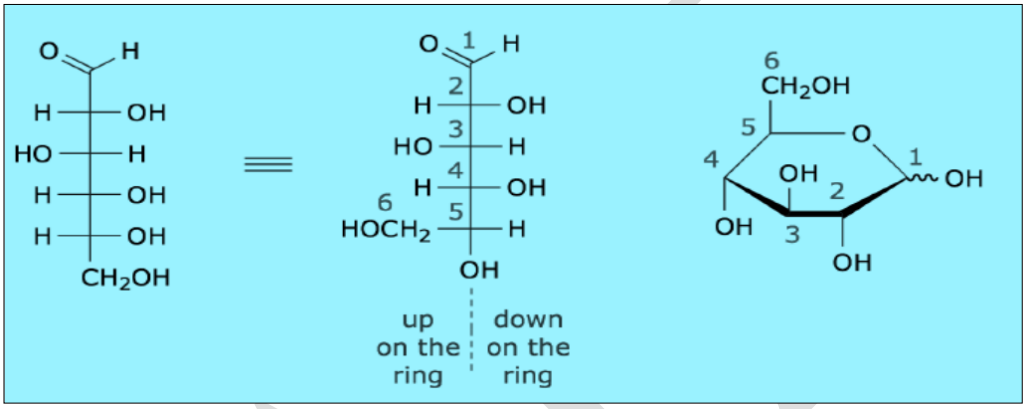


The second Fischer projection has the proper conformation for cyclic hemiacetal formation. Recall that to view this cyclization we turned the structure $90^o$ to the right. This turn takes all of the groups that are on the right-hand side of the backbone in the Fischer projection and orients them into the plane, while all of the groups on the left-hand side of the backbone are now oriented out of the plane. Since the orientations of these groups are retained when the cyclic

hemiacetal forms, any group on the right-hand side in the Fischer projection will be on the bottom face of the Haworth structure, while all of the groups on the left-hand side of the Fischer projection will be on the top face of the Haworth structure. Numbering the carbon atoms in the Fischer projection and on the Haworth structure makes it easy to put the groups on the ring carbons in the proper orientation.

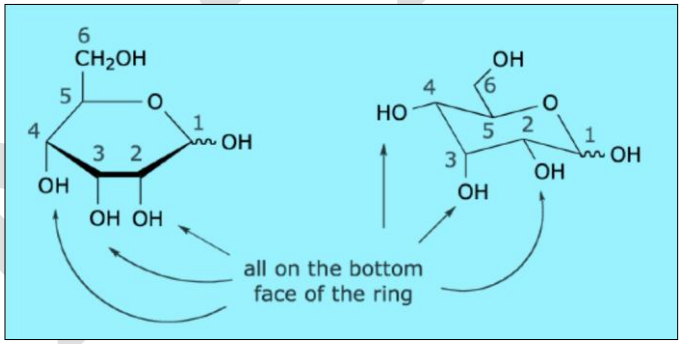



As a second example, D-glucose has the following Fischer projection and Haworth structure:



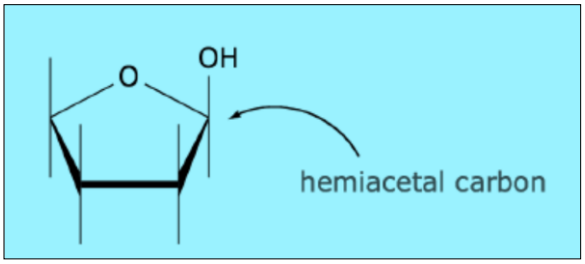

**Drawing a Sugar's Chair Conformation from a Haworth Structure or Fischer Projection**

If you have either the Haworth structure or the Fischer projection of the sugar, drawing the chair conformation of the sugar is easy as long as you remember the orientations of the axial and equatorial bonds on each carbon atom of the chair conformation. For example, given the Haworth structure, the chair conformation for D-allose is:

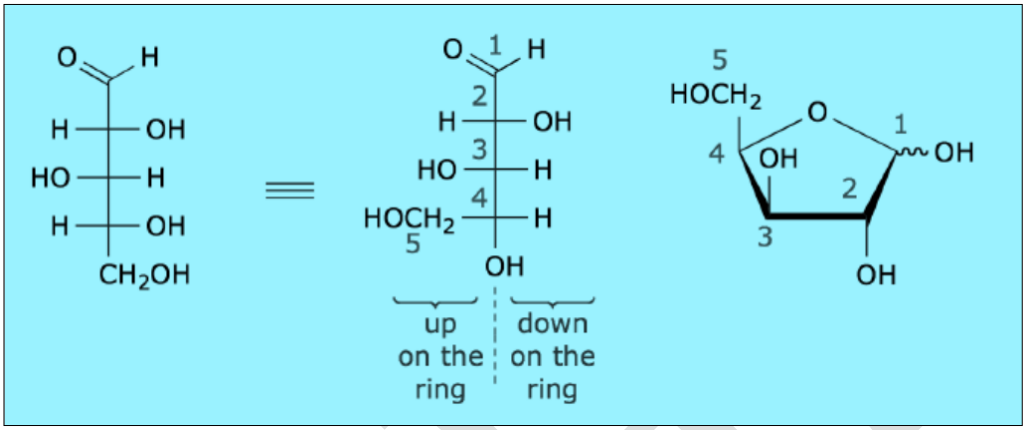



**Furanose Ring systems**

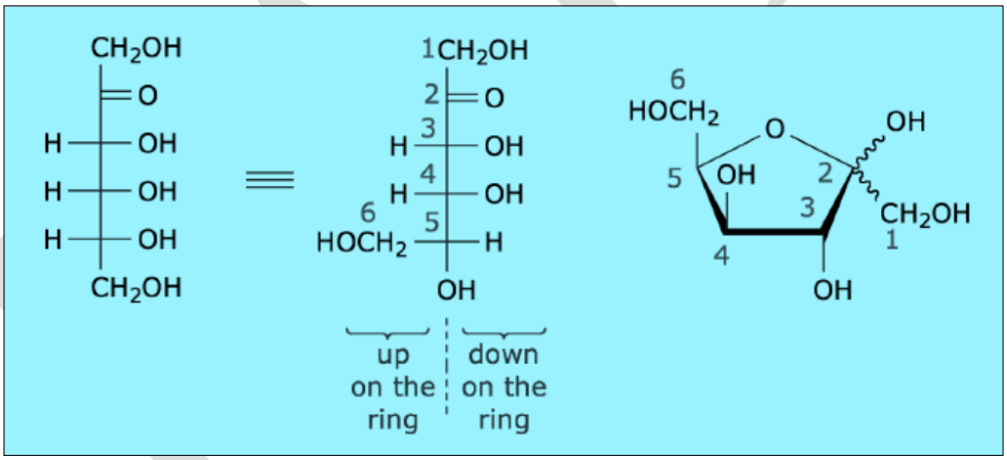
Many sugars (ketohexoses, aldopentoses, and in some cases even aldohexoses) form five-membered ring cyclic hemiacetals, which are called furanose ring forms. These cyclic hemiacetal structures form through exactly the same process was previously outlined for the formation of the pyranose rings of aldohexoses. In the furanose systems, a pentagon is used to represent the cyclic hemiacetal, with the oxygen atom at the apex of the pentagon.




The Fischer projection and the Haworth structure for the aldopentose D-xylose are given below.



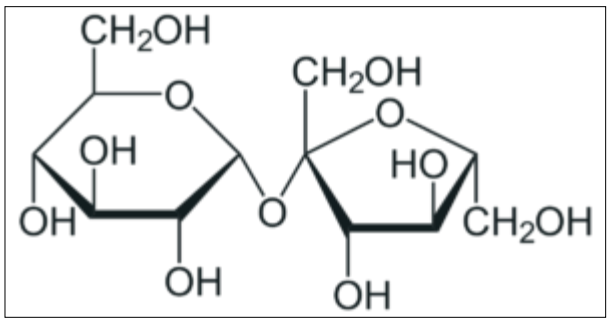

The Fischer projection and the Haworth structure for furanose ring form of the ketohexose D-sorbose are shown below. Note that in the cyclic hemiacetal form of this keto-sugar, the anomeric carbon is C-2, not C-1 as it was in the previous examples.




Or

**a. <u>Write a note on structure of maltose, lactose and sucrose and its properties?</u>**

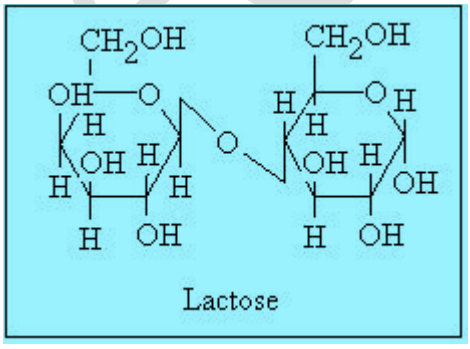
**Ans: Sucrose**




This is the most important disaccharide. It is popularly known as *table sugar*. Sucrose is found in all photosynthetic plants. It is commercially obtained from sugarcane and sugar beets via an industrial process. Let us take a look at some chemical properties of sucrose

- The molecular formula of sucrose is **$C_{12}H_{22}O_{11}$.**
- If sucrose goes through acid catalysed hydrolysis it will give one mole of D-Glucose and one mole of D-Fructose.
- The chemical structure of sucrose comprises of α form of glucose and β form of fructose
- The glycosidic linkage is α linkage because the molecule formation is in α orientation
- Sucrose is a non-reducing sugar. As you can see from the structure it is combined (linked) at the hemiacetal oxygen and does not have a free hemiacetal hydroxide
- Since has no free hemiacetal hydroxide it does not show mutarotation (α to β conversion). Sucrose also does not form osazones for the same reason.
- We can prove the structural formula of sucrose by hydrolysing it with α-glycosidase enzymes which only hydrolyses α glucose. This test is positive for sucrose.

**Lactose**

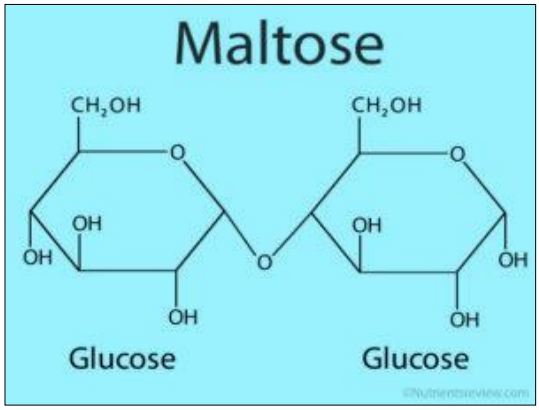



This is a disaccharide you may already be familiar with. Lactose is the primary ingredient found in the milk of all mammals. Unlike the majority of saccharides, lactose is not sweet to taste. Lactose consists of one galactose carbohydrate and one glucose carbohydrate. These are bound together by a 1-4 glycosidic bond in a beta orientation.

If you look at the structure of lactose you will see that there is one significant difference between galactose and glucose. Galactose's fourth carbon has a different orientation in galactose than in sucrose. If it was not so the resulting molecule would have just been sucrose (glucose+glucose) instead of lactose.

Also from the structure, we can notice that lactose is a reacting sugar since it has one free hemiacetal hydroxide. So when we react Lactose with bromine water it will give monocarboxylic acid.

**Maltose**



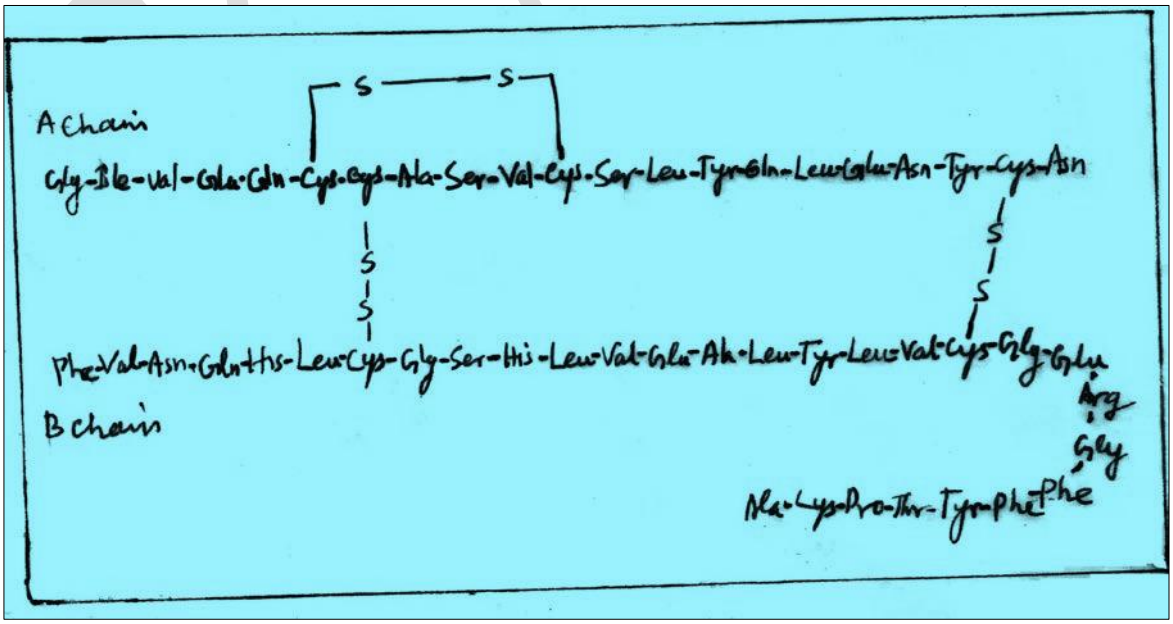

Maltose is another disaccharide commonly found. It has two monosaccharide glucose molecules bound together, The link is between the first carbon atom of glucose and the fourth carbon of another glucose molecule. This, as you know, is the one-four glycosidic linkage. Let us look at a few of its properties

- On acid catalysed hydrolysis one mole of maltose gives two moles of D-glucose.
- Maltose has a free hemiacetal hydroxide, hence it undergoes mutarotation. It exists as both α-Maltose and also β-Maltose
- For the same reasons it also gives a positive test with Benedicts and Tollens reagent.

26. **a. Distinguish the primary, secondary, tertiary and quatnary structure of proteins?**

**Ans: Primary Structure of Protein**

The primary structure of a protein describes the sequence of amino acids in the chain. Insulin is the first protein whose amino acid sequence was determined. Scheme 2 presents the primary structure of insulin.

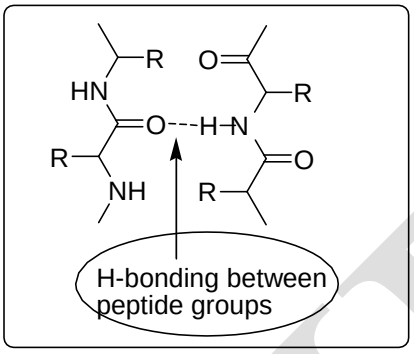


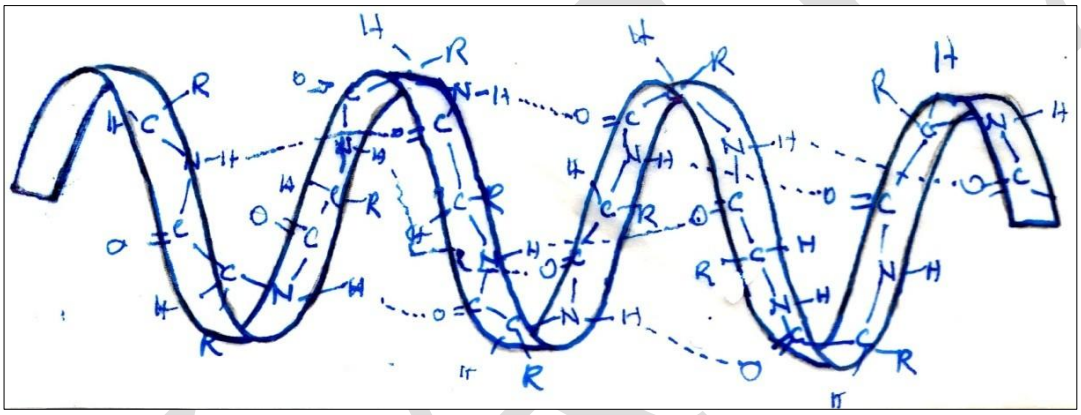

**Primary Structure of Insulin**

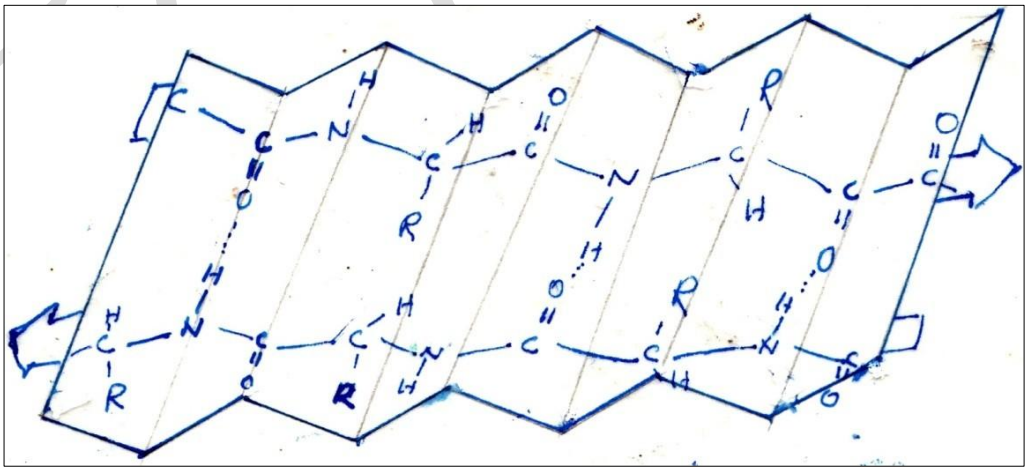
**Secondary Structure of Protein**

The secondary structure describes how the segments of the backbone chain fold. These conformations are stabilized by H-bonding between the peptide groups- between NH of one amino acid residue and C=O group of another.

***(a) α-Helix***





**(b) β-Pleated Sheet**

**A segment of a protein in: (a) an α-helix; (b) β-pleated sheet.**

α-Helix:

The first type of secondary structure is α-helix, where the backbone coils around the long

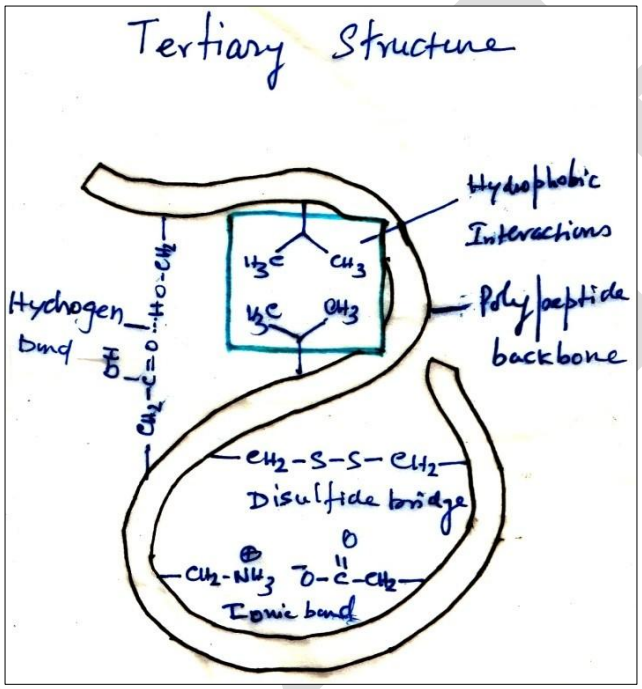
axis of the protein molecule. The substituents on the α-carbon of the amino acids protrude outward from the helix to minimize the steric hindrance. The H attached to amide nitrogen makes H-bonding with the carbonyl oxygen of an amino acid.

***β-Pleated Sheet***

The second type of secondary structure is the β-pleated sheet, in which the backbone is extended in a zigzag structure resembling pleats. The H-bonding in a β-pleated sheet occurs between the adjacent peptide chains.

## Tertiary Structure of Protein

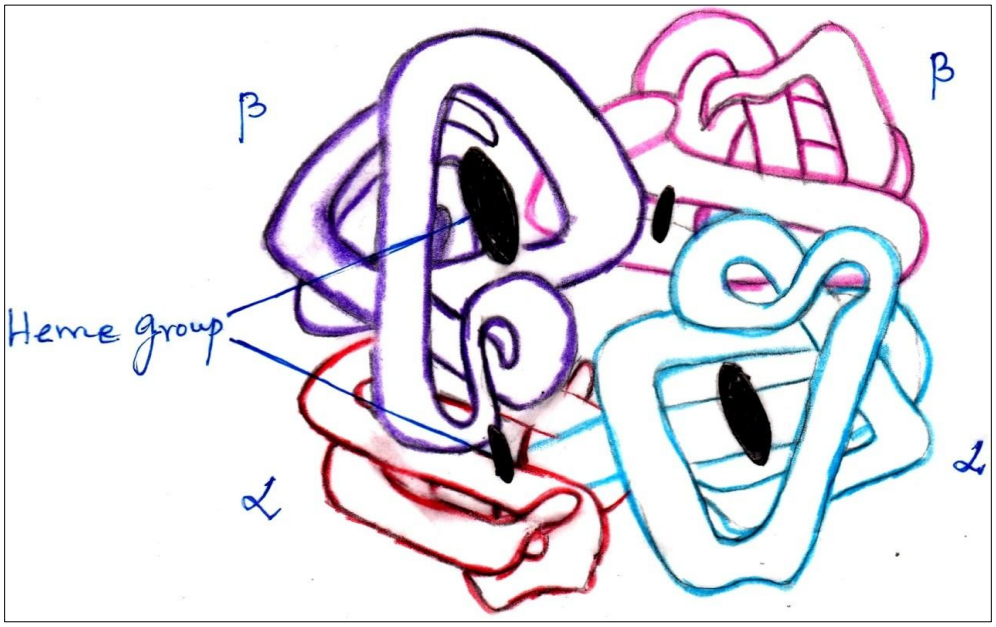
The tertiary structure of a protein describes the three-dimensional arrangement of all the atoms. In solution, proteins fold to maximize their stability through interactions include disulfide bonds, hydrogen bonds, electrostatic attractions and hydrophobic interactions.




**Stabilizing interactions for the tertiary structure of protein**

**Quaternary Structure of Protein**

Some proteins have more than one peptide chain and the individual chain is called a subunit. The subunits are held together by intractions such as hydrophobic intraction, H- bonding, and electrostatic attractions. The quarternary structure of a protein describes the way the subunits are arranged in space. Scheme 5 shows the structure of hemoglobin which is a tetrameric structural protein comprising two α and two β subunits.




**Quaternary Protein Structure: Three-Dimensional Arrangement of Subunit**

Or

**b. <u>Explain the DNFB and Edman method to determine the N-terminal amino acid?</u>**

**Ans:** In order to synthesize a peptide from its component amino acids, two obstacles must be overcome. The first of these is statistical in nature, and is illustrated by considering the dipeptide Ala-Gly as a proposed target. If we ignore the chemistry involved, a mixture of equal molar amounts of alanine and glycine would generate four different dipeptides. These are: **Ala-Ala, Gly-Gly, Ala-Gly & Gly-Ala**. In the case of tripeptides, the number of possible products from these two amino acids rises to eight. Clearly, some kind of selectivity must be exercised if complex mixtures are to be avoided.

The second difficulty arises from the fact that carboxylic acids and 1º or 2º-amines do not form amide bonds on mixing, but will generally react by proton transfer to give salts (the intermolecular equivalent of zwitterion formation).

From the perspective of an organic chemist, peptide synthesis requires selective acylation of a free amine. To accomplish the desired amide bond formation, we must first deactivate all

extraneous amine functions so they do not compete for the acylation reagent. Then we must selectively activate the designated carboxyl function so that it will acylate the one remaining free amine. Fortunately, chemical reactions that permit us to accomplish these selections are well known.

First, the basicity and nucleophilicity of amines are substantially reduced by amide formation. Consequently, the acylation of amino acids by treatment with acyl chlorides or anhydrides at pH > 10, as described earlier, serves to protect their amino groups from further reaction.

Second, acyl halide or anhydride-like activation of a specific carboxyl reactant must occur as a prelude to peptide (amide) bond formation. This is possible, provided competing reactions involving other carboxyl functions that might be present are precluded by preliminary ester formation. Remember, esters are weaker acylating reagents than either anhydrides or acyl halides, as noted earlier.

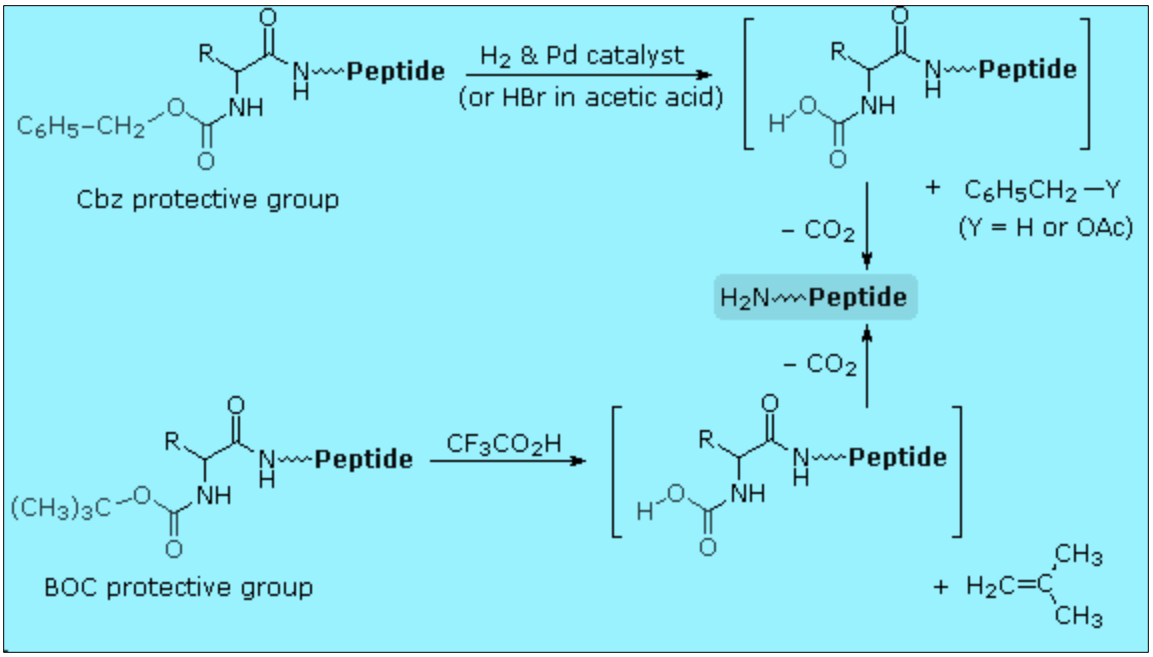
Finally, dicyclohexylcarbodiimide (DCC) effects the dehydration of a carboxylic acid and amine mixture to the corresponding amide under relatively mild conditions. The structure of this reagent and the mechanism of its action have been described. Its application to peptide synthesis will become apparent in the following discussion.

The strategy for peptide synthesis, as outlined here, should now be apparent. The following example shows a selective synthesis of the dipeptide Ala-Gly.

An important issue remains to be addressed. Since the N-protective group is an amide, removal of this function might require conditions that would also cleave the just formed peptide bond. Furthermore, the harsh conditions often required for amide hydrolysis might cause extensive racemization of the amino acids in the resulting peptide. This problem strikes at the heart of our strategy, so it is important to give careful thought to the design of specific N-protective groups. In particular, three qualities are desired:

1. The protective amide should be easy to attach to amino acids.
2. The protected amino group should not react under peptide forming conditions.
3. The protective amide group should be easy to remove under mild conditions.

A number of protective groups that satisfy these conditions have been devised; and two of the most widely used, **carbobenzoxy** (Cbz) and **t-butoxycarbonyl** (BOC or t-BOC), are described here.




The reagents for introducing these N-protective groups are the acyl chlorides or anhydrides shown in the left portion of the above diagram. Reaction with a free amine function of an amino acid occurs rapidly to give the "protected" amino acid derivative shown in the center. This can then be used to form a peptide (amide) bond to a second amino acid. Once the desired peptide bond is created the protective group can be removed under relatively mild non-hydrolytic conditions. Equations showing the protective group removal will be displayed above by are shown above. Cleavage of the reactive benzyl or tert-butyl groups generates a common carbamic acid intermediate (HOCO-NHR) which spontaneously loses carbon dioxide, giving the corresponding amine. If the methyl ester at the C-terminus is left in place, this sequence of reactions may be repeated, using a different N-protected amino acid as the acylating reagent. Removal of the protective groups would then yield a specific tripeptide, determined by the nature of the reactants and order of the reactions.

Reg. No.: ---------- [16CHU603B]

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**COIMBATORE-641 021**

**B.Sc., Degree Examination**
**(For the candidates admitted from 2016 & onwards)**

**III- B.Sc., Chemistry**
**II$^{nd}$ Internal Test**
**Molecules of Life**

Time: 2 Hours Maximum: 50 marks
Date: 5.2.2019

**Section-A** **20X1=20**

**Answer all the questions**

1. Apolipoprotein B-100 acts as
a. Enzyme activator b. Ligand for receptor c. Enzyme inhibitor d. Enzyme resistor

2. Free amino is relesed during
a. Oxidative deamination of glutamide b. Catabolism of pyruvate
c. Anabolism of pyradines d. Reductive deamination of galactose

3. Gluycine is not required for the formation of
a. Tauroidcholic acid b. Creatine c. Purines d. Pyrimidines

4. Pancreatic juice contains the precursors of all of the following except
a. Trypsin b. Chymotrypsin c. Carboxypeptidase d. Aminopeptidase

5. The most abundant immunoglobulin in plasma is
a. IgA b. IgG c. IgM d. IgD

6. Allosteric inhibitor of glutamate dehydrogenase is
a. ATP b. ADP c. AMP d. GMP

7. The components of compliment system are activated by
a. Microsomal hydroxylation b. Phosphorylation c. Glycosylation d. Proteloysis

8. Which amino acid is lipotropic factor?
a. Lysine b. Leucine c. Tryptophan d. Methionine

9. Which among the following has an imidazole group?
a. Histidine b. Trptophan c. Proline d. Hydroxy proline

10. The neutral amino acid is
a. Lysine b. Proline c. Leucine d. Histidine

11. Enzymes, which are produced in inactive form in the living cell are called
a. Papain b. Lysozymes c. Apoenzyme d. Proenzyme

12. Which one of the following is an example of ligases is
a. Succinate thickinase b. Alanine racemase c. Fumarase d. Aldolase

13. In which type of enzyme did not have inducer
a. Allosteric enzyme b. Constitutive enzyme c. Co-operative enzyme
d. Isoenzymic enzyme

14. In enzyme kinetics $V_{max}$ reflects
a. The amount of an active enzyme b. Substrate concentration
c. Half of the substrate concentration d. Enzyme substrate complex

15. When the activity inhibition occurred in competitive enzyme
a. Apparent $K_m$ is decreased b. Apparent $K_m$ is increased
c. $V_{max}$ is increased d. $V_{max}$ is decreased

16. In following which one is example of transferring co-enzyme
a. $NAD^-$ b. $NADP^+$ c. FAD d. CoA

17. The optimum $P^H$ of most of the enzyme is
a. Between 2 to 4 b. Between 5 to 9 c. Between 8 to 12 d. Above 12

18. The co-enzyme which have not aromatic hetero ring in it
a. ATP b. Lipoic acid c. FMN d. Biotin

19. Serum acid phosphatase level increases in
a. Metastatic carcinoma of prostate b. Myocardial infarction
c. Wilson's disease d. Liver disease

20. The substrate for amylase is
a. Cane sugar b. Starch c. Lactose d. Ribose

**Section B** **3x2 = 6**

**Answer all the questions**

21. Define: Enzyme

22. What is Coenzyme and co-factor?

23. Write any two points about importance of enzyme inhibition?

**Section C** **3x8 = 24**

**Answer all the questions**

24. a. Briefly explain the peptidase synthesis.

Or

b. Write a note on enzyme, coenzyme and co-factors and its role biological reactions.

25. a. Explain the mechanism of enzyme action?

Or

b. Write a note on Drug-receptor theory?

26. a. Distinguish the Competitive, Non competitive and Allosteric inhibition of enzyme.

Or

b. Explain Structural Activity relationship of drug molecules?

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e. Anabolism of pyradines d. Reductive deamination of galactose

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33. The components of compliment system are activated by
a. Microsomal hydroxylation b. Phosphorylation c. Glycosylation d. **Proteloysis**

34. Which amino acid is lipotropic factor?
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36. The neutral amino acid is
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39. In which type of enzyme did not have inducer
a. Allosteric enzyme **b. Constitutive enzyme** c. Co-operative enzyme
f. Isoenzymic enzyme

40. In enzyme kinetics $V_{max}$ reflects
a. **The amount of an active enzyme** b. Substrate concentration
d. Half of the substrate concentration d. Enzyme substrate complex

41. When the activity inhibition occurred in competitive enzyme
a. Apparent $K_m$ is decreased **b. Apparent $K_m$ is increased**
d. $V_{max}$ is increased d. $V_{max}$ is decreased

42. In following which one is example of transferring co-enzyme
**a.** $NAD^-$ b. $NADP^+$ c. FAD **d. CoA**

43. The optimum $P^H$ of most of the enzyme is
a. Between 2 to 4 **b. Between 5 to 9** c. Between 8 to 12 d. Above 12

44. The co-enzyme which have not aromatic hetero ring in it
a. ATP b. Lipoic acid c. FMN **d. Biotin**

45. Serum acid phosphatase level increases in
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d. Wilson's disease d. Liver disease

46. The substrate for amylase is
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**Section B** **3x2 = 6**

**Answer all the questions**

47. Define: Enzyme

48. What is Coenzyme and co-factor?

49. Write any two points about importance of enzyme inhibition?

**Section C** **3x8 = 24**

**Answer all the questions**

50. a. Briefly explain the peptidase synthesis.

Or

c. Write a note on enzyme, coenzyme and co-factors and its role biological reactions.

51. a. Explain the mechanism of enzyme action?

Or

c. Write a note on Drug-receptor theory?

52. a. Distinguish the Competitive, Non competitive and Allosteric inhibition of enzyme.

Or

b. Explain Structural Activity relationship of drug molecules?

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**Answer Key**

**Section-A** **20X1=20**

**Answer all the questions**

1. **b. Ligand for receptor**
2. **a. Oxidative deamination of glutamide**
3. **a. Tauroidcholic** acid
4. **d. Aminopeptidase**
5. **b. IgG**
6. **a. ATP**
7. **d. Proteloysis**
8. **d. Methionine**
9. **a. Histidine**
10. **c. Leucine**
11. **d. Proenzyme**
12. **a. Succinate thickinase**
13. **b. Constitutive enzyme**
14. **a. The amount of an active enzyme**
15. **b. Apparent $K_m$ is increased**
16. **d. CoA**
17. **b. Between 5 to 9**
18. **d. Biotin**
19. **a. Metastatic carcinoma of prostate**
20. **b. Starch**

**Section B** **3x2 = 6**

**Answer all the questions**

21. Define: Enzyme

**Ans:** **Enzymes** are macromolecular biological catalysts. Enzymes accelerate chemical reactions. The molecules upon which enzymes may act are called substrates and the

enzyme converts the substrates into different molecules known as products. Almost all metabolic processes in the cell need enzyme catalysis in order to occur at rates fast enough to sustain life.

22. What is Coenzyme and co-factor?

**Ans:** Some enzymes do not need additional components to show full activity. Others require non-protein molecules called cofactors to be bound for activity. Cofactors can be either inorganic (e.g., metal ions and iron-sulfur clusters) or organic compounds (e.g., flavin and heme). These cofactors serve many purposes; for instance, metal ions can help in stabilizing nucleophilic species within the active site.

Coenzymes are small organic molecules that can be loosely or tightly bound to an enzyme. Coenzymes transport chemical groups from one enzyme to another.

Examples include NADH, NADPH and adenosine triphosphate (ATP).

23. Write any two points about importance of enzyme inhibition?

**Ans:** If an enzyme produces too much of one substance in the organism, that substance may act as an inhibitor for the enzyme at the beginning of the pathway that produces it, causing production of the substance to slow down or stop when there is sufficient amount.

Since inhibitors modulate the function of enzymes they are often used as drugs. Many such drugs are reversible competitive inhibitors that resemble the enzyme's native substrate, similar to methotrexate.

**Section C** **3x8 = 24**

**Answer all the questions**

24. a. Briefly explain the peptidase synthesis.

**Ans: Peptide Synthesis**

In order to synthesize a peptide from its component amino acids, two obstacles must be overcome. The first of these is statistical in nature, and is illustrated by considering the dipeptide Ala-Gly as a proposed target. If we ignore the chemistry involved, a mixture of equal molar amounts of alanine and glycine would generate four different dipeptides. These are: **Ala-Ala, Gly-Gly, Ala-Gly & Gly-Ala**. In the case of tripeptides, the number of possible products from these two amino acids rises to eight. Clearly, some kind of selectivity must be exercised if complex mixtures are to be avoided.

The second difficulty arises from the fact that carboxylic acids and 1º or 2º-amines do not form amide bonds on mixing, but will generally react by proton transfer to give salts (the intermolecular equivalent of zwitterion formation).

From the perspective of an organic chemist, peptide synthesis requires selective acylation of a free amine. To accomplish the desired amide bond formation, we must first deactivate all extraneous amine functions so they do not compete for the acylation reagent. Then we must selectively activate the designated carboxyl function so that it will acylate the one remaining free amine. Fortunately, chemical reactions that permit us to accomplish these selections are well known.

First, the basicity and nucleophilicity of amines are substantially reduced by amide formation. Consequently, the acylation of amino acids by treatment with acyl chlorides or anhydrides at pH > 10, as described earlier, serves to protect their amino groups from further reaction.

Second, acyl halide or anhydride-like activation of a specific carboxyl reactant must occur as a prelude to peptide (amide) bond formation. This is possible, provided competing reactions involving other carboxyl functions that might be present are precluded by preliminary ester formation. Remember, esters are weaker acylating reagents than either anhydrides or acyl halides, as noted earlier.

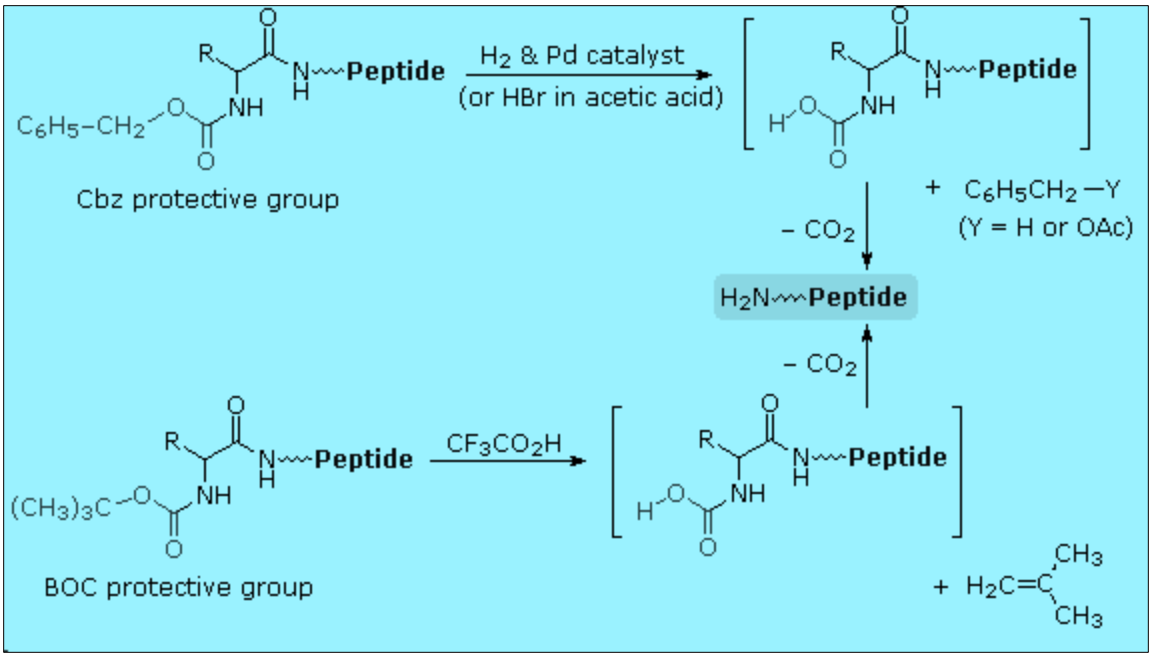
Finally, dicyclohexylcarbodiimide (DCC) effects the dehydration of a carboxylic acid and amine mixture to the corresponding amide under relatively mild conditions. The structure of this reagent and the mechanism of its action have been described. Its application to peptide synthesis will become apparent in the following discussion.

The strategy for peptide synthesis, as outlined here, should now be apparent. The following example shows a selective synthesis of the dipeptide Ala-Gly.

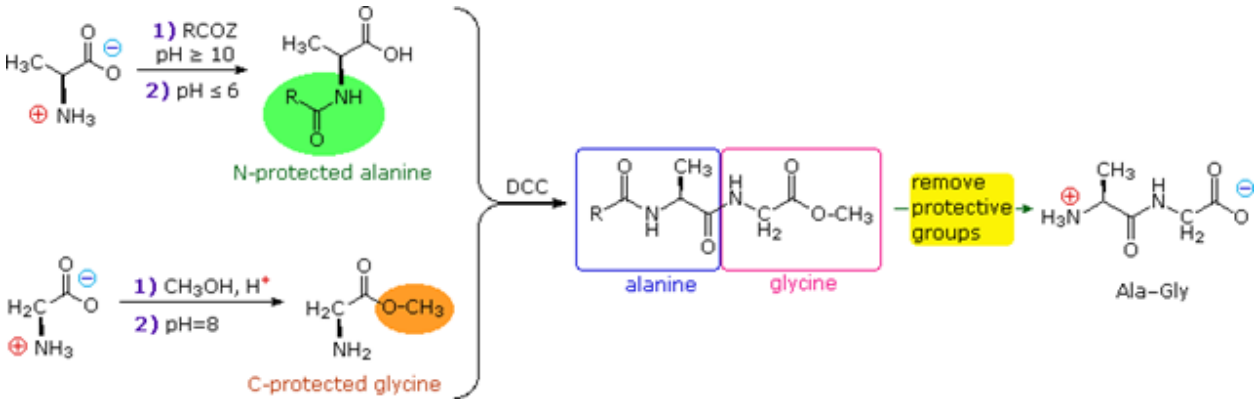
An important issue remains to be addressed. Since the N-protective group is an amide, removal of this function might require conditions that would also cleave the just formed peptide bond. Furthermore, the harsh conditions often required for amide hydrolysis might cause extensive racemization of the amino acids in the resulting peptide. This problem strikes at the heart of our strategy, so it is important to give careful thought to the design of specific N-protective groups. In particular, three qualities are desired:

1. The protective amide should be easy to attach to amino acids.
2. The protected amino group should not react under peptide forming conditions.
3. The protective amide group should be easy to remove under mild conditions.

A number of protective groups that satisfy these conditions have been devised; and two of the most widely used, **carbobenzoxy** (Cbz) and **t-butoxycarbonyl** (BOC or t-BOC), are described here.

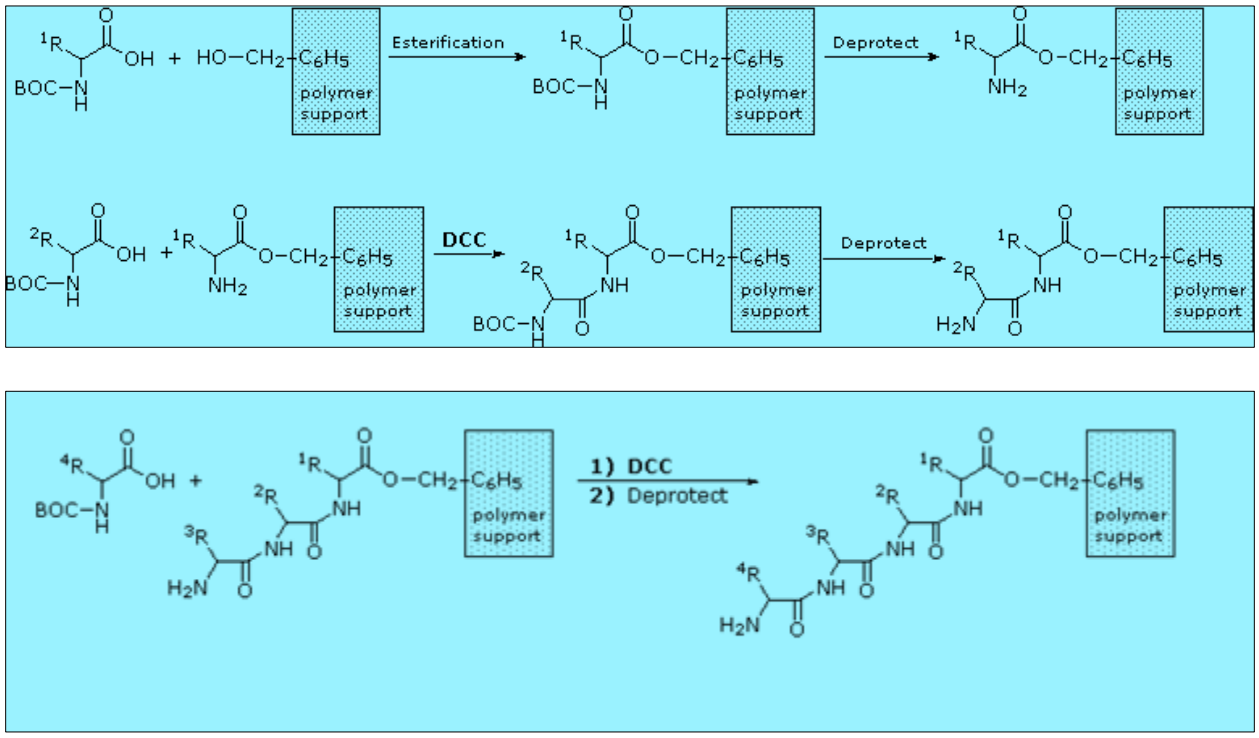



The reagents for introducing these N-protective groups are the acyl chlorides or anhydrides shown in the left portion of the above diagram. Reaction with a free amine function of an amino acid occurs rapidly to give the "protected" amino acid derivative shown in the center. This can then be used to form a peptide (amide) bond to a second amino acid. Once the desired peptide bond is created the protective group can be removed under relatively mild non-hydrolytic conditions. Equations showing the protective group removal will be displayed above by are shown above. Cleavage of the reactive benzyl or tert-butyl groups generates a common carbamic acid intermediate (HOCO-NHR) which spontaneously loses carbon dioxide, giving the corresponding amine. If the methyl ester at the C-terminus is left in place, this sequence of reactions may be repeated, using a different N-protected amino acid as the acylating reagent. Removal of the protective groups would then yield a specific tripeptide, determined by the nature of the reactants and order of the reactions.




The synthesis of a peptide of significant length (e.g. ten residues) by this approach requires many steps, and the product must be carefully purified after each step to prevent unwanted cross-reactions. To facilitate the tedious and time consuming purifications, and reduce the material

losses that occur in handling, a clever modification of this strategy has been developed. This procedure, known as the **Merrifield Synthesis** after its inventor R. Bruce Merrifield, involves attaching the C-terminus of the peptide chain to a polymeric solid, usually having the form of very small beads. Separation and purification is simply accomplished by filtering and washing the beads with appropriate solvents. The reagents for the next peptide bond addition are then added, and the purification steps repeated. The entire process can be automated, and peptide synthesis machines based on the Merrifield approach are commercially available. A series of equations illustrating the Merrifield synthesis may be viewed by on the following diagram. The final step, in which the completed peptide is released from the polymer support, is a simple benzyl ester cleavage.




Or

b. Write a note on enzyme, coenzyme and co-factors and its role biological reactions.

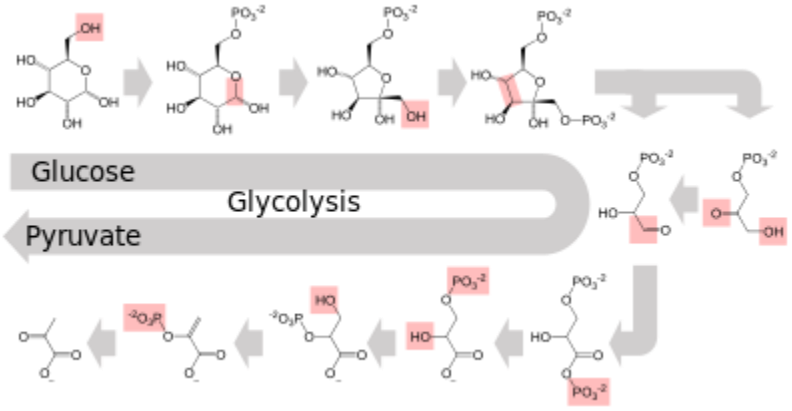
**Ans: Biological function**

Enzymes serve a wide variety of functions inside living organisms. They are indispensable for signal transduction and cell regulation, often via kinases and phosphatases. They also generate movement, with myosin hydrolyzing ATP to generate muscle contraction, and also transport cargo around the cell as part of the cytoskeleton. Other ATPases in the cell membrane are ion pumps involved in active transport. Enzymes are also involved in more exotic functions, such as luciferase generating light in fireflies. Viruses can also contain enzymes for infecting cells, such as the HIV integrase and reverse transcriptase, or for viral release from cells, like the influenza virus neuraminidase.

An important function of enzymes is in the digestive systems of animals. Enzymes such as amylases and proteases break down large molecules (starch or proteins, respectively) into

smaller ones, so they can be absorbed by the intestines. Starch molecules, for example, are too large to be absorbed from the intestine, but enzymes hydrolyze the starch chains into smaller molecules such as maltose and eventually glucose, which can then be absorbed. Different enzymes digest different food substances. In ruminants, which have herbivorousdiets, microorganisms in the gut produce another enzyme, cellulase, to break down the cellulose cell walls of plant fiber.[83]

**Metabolism**




The metabolic pathway of glycolysis releases energy by converting glucose to pyruvate via a series of intermediate metabolites. Each chemical modification (red box) is performed by a different enzyme.

Several enzymes can work together in a specific order, creating metabolic pathways. In a metabolic pathway, one enzyme takes the product of another enzyme as a substrate. After the catalytic reaction, the product is then passed on to another enzyme. Sometimes more than one enzyme can catalyze the same reaction in parallel; this can allow more complex regulation: with, for example, a low constant activity provided by one enzyme but an inducible high activity from a second enzyme.

Enzymes determine what steps occur in these pathways. Without enzymes, metabolism would neither progress through the same steps and could not be regulated to serve the needs of the cell. Most central metabolic pathways are regulated at a few key steps, typically through enzymes whose activity involves the hydrolysis of ATP. Because this reaction releases so much energy, other reactions that are thermodynamically unfavorablecan be coupled to ATP hydrolysis, driving the overall series of linked metabolic reactions.

flavin and heme cofactors are often involved in redox reactions.

Coenzymes are usually continuously regenerated and their concentrations maintained at a steady level inside the cell. For example, NADPH is regenerated through the pentose phosphate pathway and *S*-adenosylmethionine by methionine adenosyltransferase. This continuous regeneration means that small amounts of coenzymes can be used very intensively. For example, the human body turns over its own weight in ATP each day

25. a. Explain the mechanism of enzyme action?

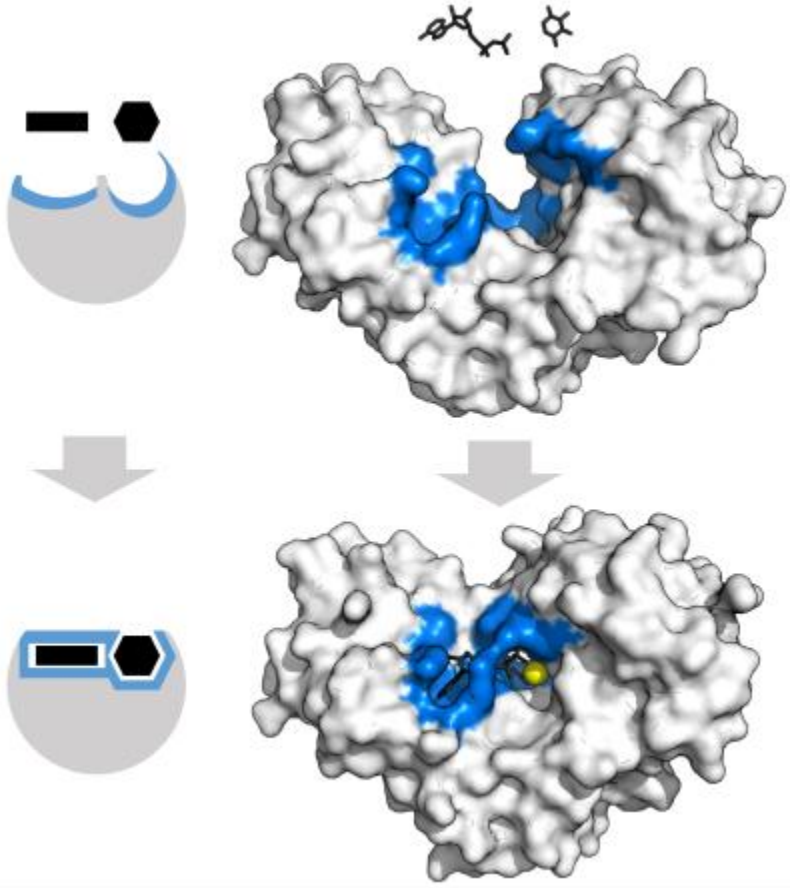
**Ans: Mechanism**

**Substrate binding**

Enzymes must bind their substrates before they can catalyse any chemical reaction. Enzymes are usually very specific as to what substrates they bind and then the chemical reaction catalysed. Specificity is achieved by binding pockets with complementary shape, charge and hydrophilic/hydrophobic characteristics to the substrates. Enzymes can therefore distinguish between very similar substrate molecules to be chemoselective, regioselective and stereospecific.

Some of the enzymes showing the highest specificity and accuracy are involved in the copying and expression of the genome. Some of these enzymes have "proof-reading" mechanisms. Here, an enzyme such as DNA polymerase catalyzes a reaction in a first step and then checks that the product is correct in a second step. This two-step process results in average error rates of less than 1 error in 100 million reactions in high-fidelity mammalian polymerases. Similar proofreading mechanisms are also found in RNA polymerase, aminoacyl tRNA synthetases and ribosomes.

Conversely, some enzymes display enzyme promiscuity, having broad specificity and acting on a range of different physiologically relevant substrates. Many enzymes possess small side activities which arose fortuitously (i.e. neutrally), which may be the starting point for the evolutionary selection of a new function.



Enzyme changes shape by induced fit upon substrate binding to form enzyme-substrate complex. Hexokinase has a large induced fit motion that closes over the substrates adenosine triphosphate and xylose. Binding sites in blue, substrates in black and $Mg^{2+}$ cofactor in yellow.

**"Lock and key" model**

To explain the observed specificity of enzymes, in 1894 Emil Fischer proposed that both the enzyme and the substrate possess specific complementary geometric shapes that fit exactly into one another. This is often referred to as "the lock and key" model. This early model explains enzyme specificity, but fails to explain the stabilization of the transition state that enzymes achieve.

**Induced fit model**

In 1958, Daniel Koshland suggested a modification to the lock and key model: since enzymes are rather flexible structures, the active site is continuously reshaped by interactions with the substrate as the substrate interacts with the enzyme. As a result, the substrate does not simply bind to a rigid active site; the amino acid side-chains that make up the active site are molded into the precise positions that enable the enzyme to perform its catalytic function. In some cases, such as glycosidases, the substrate molecule also changes shape slightly as it enters the active site. The active site continues to change until the substrate is completely bound, at which point the final shape and charge distribution is determined. Induced fit may enhance the fidelity of molecular recognition in the presence of competition and noise via the conformational proofreading mechanism.

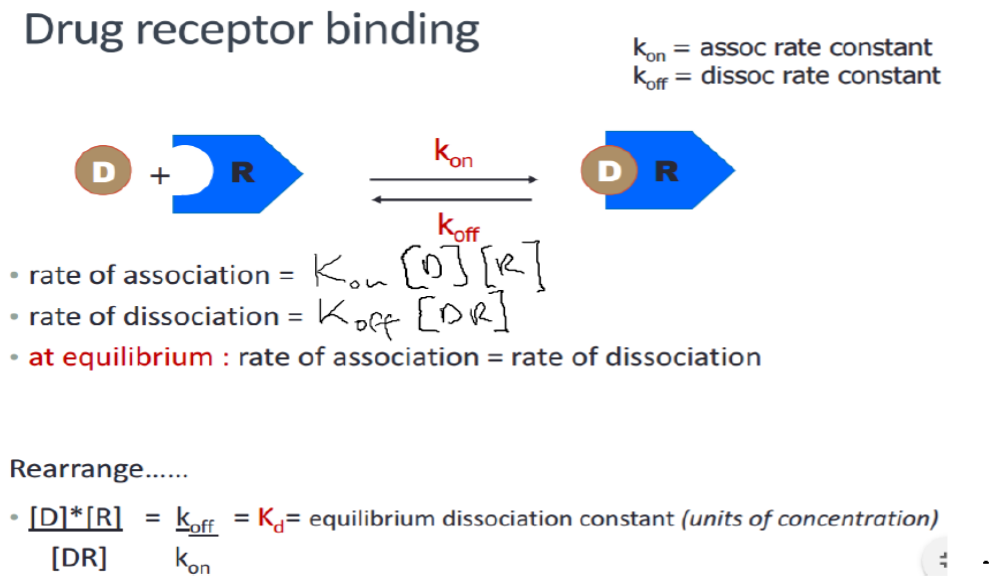
Or

b. Write a note on Drug-receptor theory?

**Ans:** 1. Decrease in blood pressured causes release of renin from juxtaglomerular tubules of the kidneys 2. This triggers release of angiotensinogen from lungs 3. This becomes angiotensin I (no effect) 4. ACE found on endothelial cells, particular on the lining of the pulmonary system converts AI to AII by cleaving 2 amino acids from AI 5. Angiotensin II constricts blood vessels = increased BP 6. To stop increased BP, Captopril inhibits ACE. Bradykinin was also inactivated by Captopril

THREE Affinity:

ability to bind to a receptor - Electrostatic o Hydrogen bonds o Ionic forces o Van der Waals forces - Covalent Selectivity: preference for one receptor over another, though the drug will bind to both Efficacy: ability elicit a reaction once the drug binds Binding: - Reversible (non-covalent) o Drugs are only bound a receptor for a finite time = creates % drug bound o - Irreversible (covalent) o Sometimes irreversible binding is not wanted for a drug because the only way to overcome it is to synthesis more receptor.




Kd = amount of drug required to bind 50% of receptors. Inversely proportional to affinity
Affinity is measured by:
-Radioligands; ligands that have been tagged with a radioactive label. Radioligands are left to incubate in a receptor rich medium.

To separate the unbound ligands from the bound ones, filters are used (as bound radioligands are larger). A Geiger counter is used to measure bound radioligand concentration.

- Competition binding (IC50): concentration of compound X required to cause 50% binding inhibition (inversely proportional to affinity).

Uses unlabelled compound X and labelled ligand
It can also determine receptor density: Bmax

26. a. Distinguish the Competitive, Non competitive and Allosteric inhibition of enzyme.

**Ans: Types of inhibition**

**Competitive**

A competitive inhibitor and substrate cannot bind to the enzyme at the same time. Often competitive inhibitors strongly resemble the real substrate of the enzyme. For example, the drug methotrexate is a competitive inhibitor of the enzyme dihydrofolate reductase, which catalyzes the reduction of dihydrofolate to tetrahydrofolate. The similarity between the structures of dihydrofolate and this drug are shown in the accompanying figure. This type of inhibition can be overcome with high substrate concentration. In some cases, the inhibitor can bind to a site other than the binding-site of the usual substrate and exert an allosteric effect to change the shape of the usual binding-site.

**Non-competitive**

A non-competitive inhibitor binds to a site other than where the substrate binds. The substrate still binds with its usual affinity and hence $K_m$ remains the same. However the inhibitor reduces the catalytic efficiency of the enzyme so that $V_{max}$ is reduced. In contrast to competitive inhibition, non-competitive inhibition cannot be overcome with high substrate concentration.

**Uncompetitive**

An uncompetitive inhibitor cannot bind to the free enzyme, only to the enzyme-substrate complex; hence, these types of inhibitors are most effective at high substrate concentration. In the presence of the inhibitor, the enzyme-substrate complex is inactive. This type of inhibition is rare.

Or

b. Explain Structural Activity relationship of drug molecules?

**Ans:**

The **structure–activity relationship** (**SAR**) is the relationship between the chemical structure of a molecule and its biological activity. This idea was first presented by Crum-Brown and Fraser in 1865. The analysis of SAR enables the determination of the chemical group responsible for evoking a target biological effect in the organism. This allows modification of the effect or the potency of a bioactive compound (typically a drug) by changing its chemical structure. Medicinal chemists use the techniques of chemical synthesis to insert new chemical groups into the biomedical compound and test the modifications for their biological effects.

This method was refined to build mathematical relationships between the chemical structure and the biological activity, known as quantitative structure–activity relationships (QSAR). A related term is structure affinity relationship (SAFIR).

Structure-biodegradability relationship

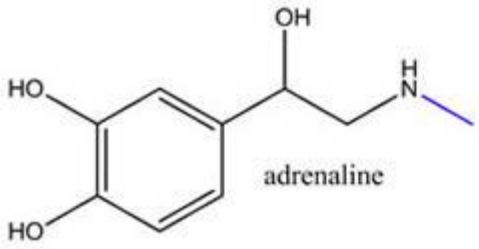
The large number of synthetic organic chemicals currently in production presents a huge challenge for timely collection of detailed environmental data on each compound. The concept of structure biodegradability relationships (SBR) has been applied to explain variability in persistence among organic chemicals in the environment. Early attempts generally consisted of examining the degradation of a homologous series of structurally related compounds under identical conditions with a complex "universal" inoculum, typically derived from numerous sources. This approach revealed that the nature and positions of substituents affected the apparent biodegradability of several chemical classes, with resulting general themes, such as halogens generally conferring persistence under aerobic conditions. Subsequently, more quantitative approaches have been developed using principles of QSAR and often accounting for the role of sorption (bioavailability) in chemical fate

SAR depends on the recognition of which structural characteristics correlate with chemical and biological reactivity. Thus the ability to draw conclusions about an unknown compound depends upon both the structural features that can be characterized as well as the database of molecules against which they are compared. When combined with appropriate professional judgment, SAR can be a powerful tool to understanding functional implications when similarities are found. For example, in the case of risk assessment of uncharacterized compounds, data from the most sensitive toxicological endpoints should be included in the analysis, such as carcinogenicity or cardiotoxicity.

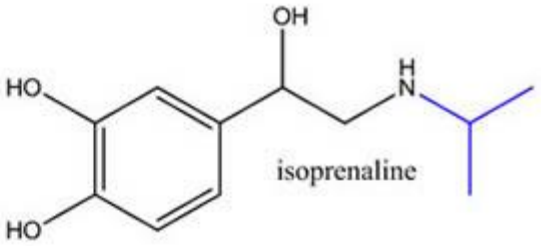
## *Structural modifications*

**1) Alkyl substituent modifications**

Modifying the steric bulk or the chain length of alkyl substituents can alter selectivity and/or activity. Isoprenaline is an N-isopropyl derivative of adrenaline. Adrenaline is also known as epinephrine. The compound isoprenaline has greater selectivity for the ß-adrenoceptors over the a-adrenoceptors. The selectivity is attributed to the bulky isopropyl group which can fit in a hydrophobic pocket present in the ß-adrenoceptors. The structural differences between the molecules are highlighted in blue.



adrenaline

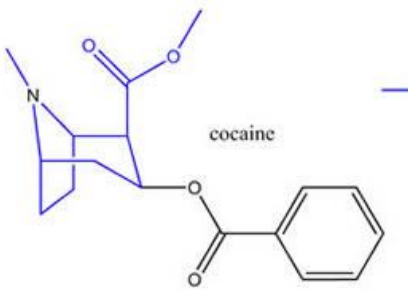


isoprenaline

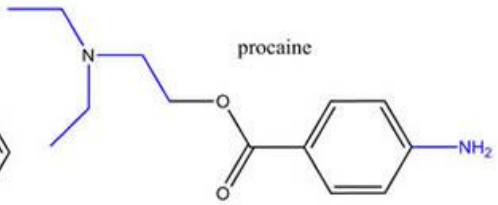
**2) Structural simplifications**

As mentioned before in an earlier article, lead compounds from natural sources typically have complex chemical structures. Through knowledge of structure-activity relationships, it is possible to identify non-pharmacophoric molecular fragments (ie. the auxophore). Removing complex auxophoric molecular fragments would simplify the lead's structure. Biological activity is generally retained after simplification, though this is not always the case.

Simplification strategies allow for the synthesis of structurally simpler analogues. This was performed in the development of the local anaesthetic, procaine. The lead compound that was used in the development of procaine was the tropane alkaloid, cocaine. Cocaine has been historically used as a local anaesthetic.



cocaine

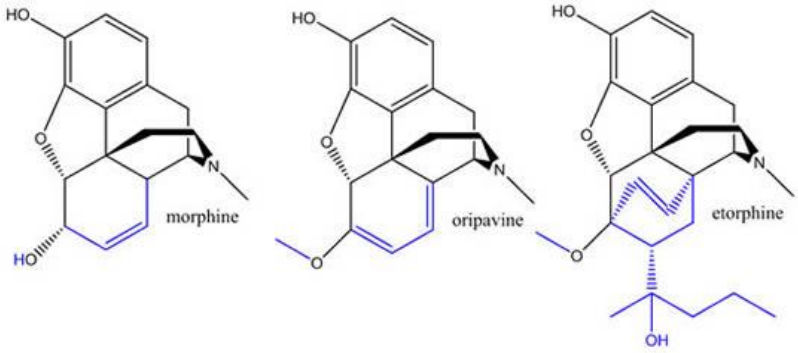


procaine

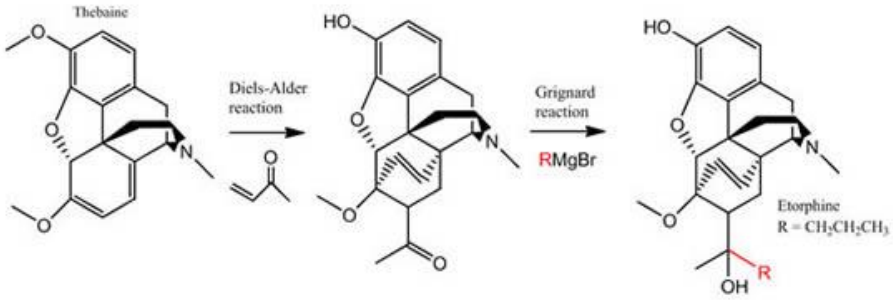
**3) Rigidification**

There is typically free rotation about unhindered single bonds. Bond rotation gives molecules access to many conformations other than the bioactive conformation. Rigidification restricts the conformations molecules can adopt. The rationale behind rigidification is to keep a molecule in its bioactive conformation while eliminating alternative conformations that may interact with other targets. By keeping molecules in a certain conformation, activity may be improved, binding site interactions may be enhanced, and/or side effects could be minimised.

Rigidification can be achieved by locking bonds within a ring. Oripavine is an opioid analgesic whose potency is comparable to morphine. The oripavine derivative, etorphine uses an extra ring thereby rigidifying its structure. Etorphine is an analgesic that is several thousand times stronger than morphine. The increased potency of etorphine compared to morphine is due to the combination of improved blood-brain barrier penetration because of greater lipophilicity and enhanced binding site interactions. Etorphine is used in veterinary medicine to immobilise large animals.

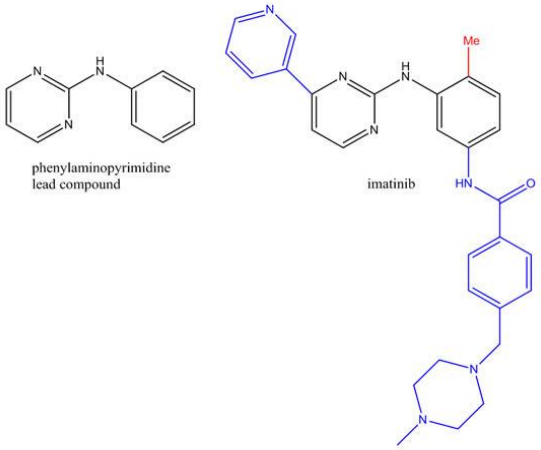



Etorphine can be derived from another related opiate alkaloid, thebaine. Thebaine is structurally similar to other opiate alkaloids but possesses no analgesic activity. Like oripavine, thebaine contains a diene. For simplicity, other reaction details have been omitted. A ketone and the extra ring are introduced through a Diels-Alder reaction with 3-buten-2-one. The resulting compound is more rigid than thebaine due to the extra ring. Various groups can be delivered to the ketone through a Grignard reaction in a stereospecific fashion.




**4) Conformational blocker**

A similar approach was done in the next example. Free rotation can also be restricted by using conformational blockers. The rationally designed tyrosine kinase inhibitor, imatinib uses a conformational blocker. The lead compound of imatinib was identified from the screening of chemical libraries. Imatinib uses a methyl group in the ortho position as a conformational blocker (highlighted in red). This hinders rotation about the aryl-N bond. The pyridine-pyrimidine rings are oriented away from the methyl conformational blocker. The use of the conformational blocker is thought to be responsible for enhanced tyrosine kinase activity. Imatinib is employed to treat multiple cancers, but most notably $Ph^+$ chronic myelogenous leukemia (CML).




This concludes the article on structure-activity relationships. Analogues may be synthesised in such a way that they fulfil the pharmacophoric requirements and have optimised binding site interactions. However, these analogues may have poor pharmacokinetic profiles. Further structural modifications may be needed in order to rectify the problem of poor pharmacokinetic properties. Solutions to these problems will be the focus of the next article. The next article will also introduce the concepts of prodrugs and bioisosterism.

Reg. No.: ---------- [16CHU603B]

**KARPAGAM ACADEMY OF HIGHER EDUCATION**
**Deemed to be University**
**(Established Under Section 3 of UGC Act 1956)**
**COIMBATORE-641 021**

**B.Sc., Degree Examination**
**(For the candidates admitted from 2016 & onwards)**

**III- B.Sc., Chemistry**
**III$^{rd}$ Internal Test**
**Molecules of Life**

Time: 2 Hours Maximum: 50 marks
Date: .3.2019

**Section-A** **20X1=20**

**Answer all the questions**

1. A purine nucleotide is
a. **AMP** b. UMP c. CNP d. DNP

2. Adenine is
a. **6-Amino purine** b. 2-Amino-6-oxy purine c. 2-Oxy-4-amino Pyrimidine
d. 2,4-dioxy Pyrimidine

3. The fatty acid present in cerebrosides in
a. **Lignoceric acid** b. Valeric acid c. Caprylic acid d. Behenic acid

4. The number of double bonds in arachidonic acid is
a. 1 b. 2 **c. 4** d. 6

5. In humans, a dietary essential fatty acid is
a. Palmitic acid b. Stearic acid c. Oleic acid **d. Linoleic acid**

6. A lipid containing alcoholic amine residue is
a. Phosphatidic acid b. Gangloide c. Glucocerebroside **d. Sphingomyelin**

7. An example of lyases is
a. Glutamin Synthetase **b. Fumarase** c. Amylose d. Chalinesterase

8. Uracil and Ribose form
a. **Uridine** b. Cytidine c. Guanosine d. Adenosine

9. The most abundant free nucleotide in Mammalian cells is
a. **ATP** b. NAD c. GTP d. FAD

10. The nucleic acid base found in mRNA but not in DNA is
a. Adenine b. Cytosine c. Guanine **d. Uracil**

11. The size of small stable RNA ranges from
a. 0-40 nucleotides b. 40-80 nucleotides **c. 90-300 nucleotides**
d. More than 320 nucleotides

12. Higher alcohol present in waxes is
a. Benzyl b. Methyl c. Ethyl **d. Cetyl**

13. Pospholipid acting as surfactant is
a. Cephalin b. Phosphatidyl inosital **c. Lecithin** d. Phosphatidyl serine

14. Molecular weight of heterogenous nuclear RNA(hnRNA) is
a. **More than 107** b. 105to 106 c. 104to 105 d. Less than 104

15. RNA does not contain
a. Uracil b. Adenine **c. Thymine** d. Ribose

16. The sugar moiety present in RNA is
a. Ribulose b. Arabinose **c. Ribose** d. Deoxyribose

17. Molecular formula of cholesterol is
a. **$C_{27}H_{45}OH$** b. $C_{29}H_{47}OH$ c. $C_{29}H_{46}OH$ d. $C_{23}H_{41}OH$

18. The Cholesterol molecule is
a. Benzene derivatives b. Quinoline derivatives **c. Steroid** d. Straight chain acid

19. Salkowski test is performed to detect
a. Glyecerol **b. Cholesterol** c. Fatty acid d. Vitamin D

20. Free fatty acid are trasported in the blood
a. **Combined with albumin** b. Combined with fatty acid binding protein
c. Combined with β lipoprotein d. In unbound free salts

**Section B** **3x2 = 6**

**Answer all the questions**

21. Write a structure of adenine and guanine?

22. Define Iodine number of oils

23. What is nucleotide and nucleoside?

**Section C** **3x8 = 24**

**Answer all the questions**

24. a. Write a note on Replication and translation process in human body

(Or)

b. Which one is basic model of DNA and briefly explains it?

25. a. Write a note on

i. Replication ii. Transcription iii. Translation

(Or)

b. Explain the components present in the nucleic acid?

26. a**.** Draw a outline of Krebs cycle and explain it briefly

(Or)

b. Briefly explain Iodine number value and saponification value of oil.

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***Answer Key***

**Section-A** **20X1=20**

**Answer all the questions**

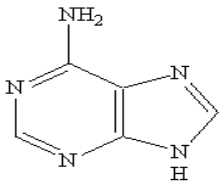
1. **a. AMP**
2. **a. 6-Amino purine**
3. **a. Lignoceric acid**
4. **c. 4**
5. **d. Linoleic acid**
6. **d. Sphingomyelin**
7. **b. Fumarase**
8. **a. Uridine**
9. **a. ATP**
10. **d. Uracil**
11. **c. 90-300 nucleotides**
12. **d. Cetyl**
13. **c. Lecithin**
14. **a. More than 107**
15. **c. Thymine**
16. **c. Ribose**
17. **a. $C_{27}H_{45}OH$**
18. **c. Steroid**
19. **b. Cholesterol**
20. **a. Combined with albumin**

**Section B** **3x2 = 6**

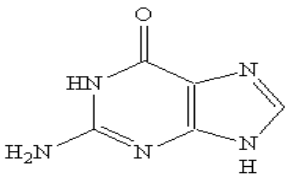
**Answer all the questions**

21. Write a structure of adenine and guanine?

**Ans: The structures of the two most common purines are:**



Adenine (A)



Guanine (G)

22. Define Iodine number of oils

**Ans: Iodine value**, also called **Iodine Number**, in analytical chemistry, measure of the degree of unsaturation of an **oil**, fat, or wax; the **amount** of **iodine**, in grams, that is taken up by 100 grams of the **oil**, fat, or wax.

23. What is nucleotide and nucleoside?

**Ans:** A "nucleotide" is a 5'-phosphate ester of a nucleoside.

A "nucleoside" results from the linking of one of these 2 sugars with one of the purine- or pyrimidine-derived bases through an N-glycosidic linkage.

**Section C** **3x8 = 24**

**Answer all the questions**

24. a. Write a note on Replication and translation process in human body

**Ans:**

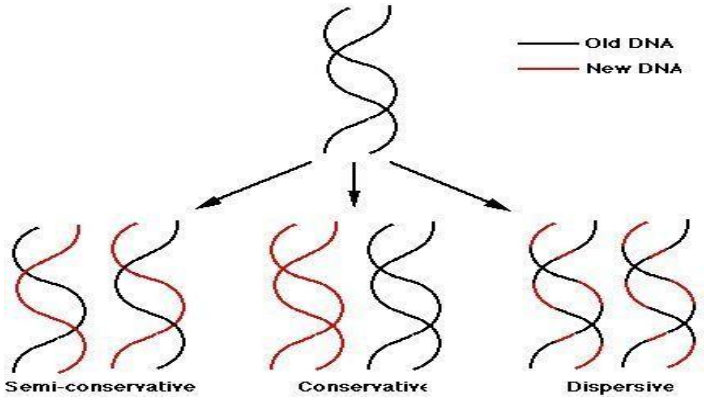
**1. Replication of DNA Molecules**

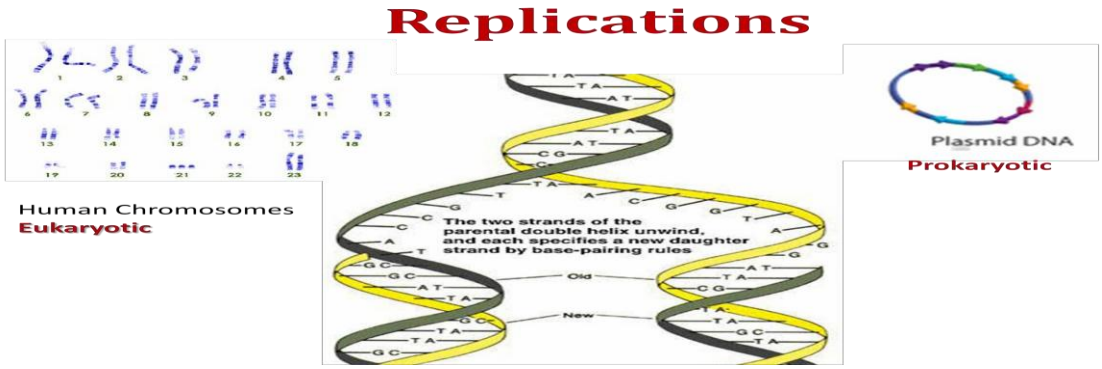
Before a cell divides, its DNA is replicated (duplicated.) Because the two strands of a DNA molecule have complementary base pairs, the nucleotide sequence of each strand automatically supplies the information needed to produce its partner. If the two strands of a DNA molecule are separated, each can be used as a pattern or template to produce a complementary strand. Each template and its new complement together then form a new DNA double helix, identical to the original.

Before replication can occur, the length of the DNA double helix about to be copied must be unwound. In addition, the two strands must be separated, much like the two sides of a zipper, by breaking the weak hydrogen bonds that link the paired bases. Once the DNA strands have been unwound, they must be held apart to expose the bases so that new nucleotide partners can hydrogen-bond to them.

The enzyme DNA polymerase then moves along the exposed DNA strand, joining newly arrived nucleotides into a new DNA strand that is complementary to the template.

Each cell contains a family of more than thirty enzymes to insure the accurate replication of DNA.

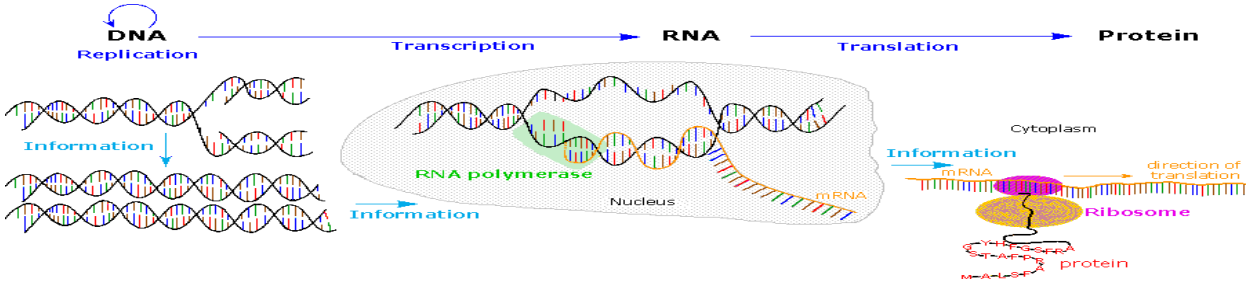



## 2. Translation

The **ribosome** binds to the **mRNA** at the start codon (AUG) that is recognized only by the initiator **tRNA**. The ribosome proceeds to the elongation phase of protein synthesis. During this stage, complexes, composed of an amino acid linked to tRNA, sequentially bind to the appropriate codon in mRNA by forming complementary base pairs with the **tRNA anticodon**. The ribosome moves from codon to codon along the mRNA. Amino acids are added one by one, translated into polypeptidic sequences dictated by DNA and represented by mRNA. At the end, a release factor binds to the stop codon, terminating translation and releasing the complete **polypeptide** from the ribosome.

One specific amino acid can correspond to more than one codon. The genetic code is said to be degenerate.



(Or)

b. Which one is basic model of DNA and briefly explains it?

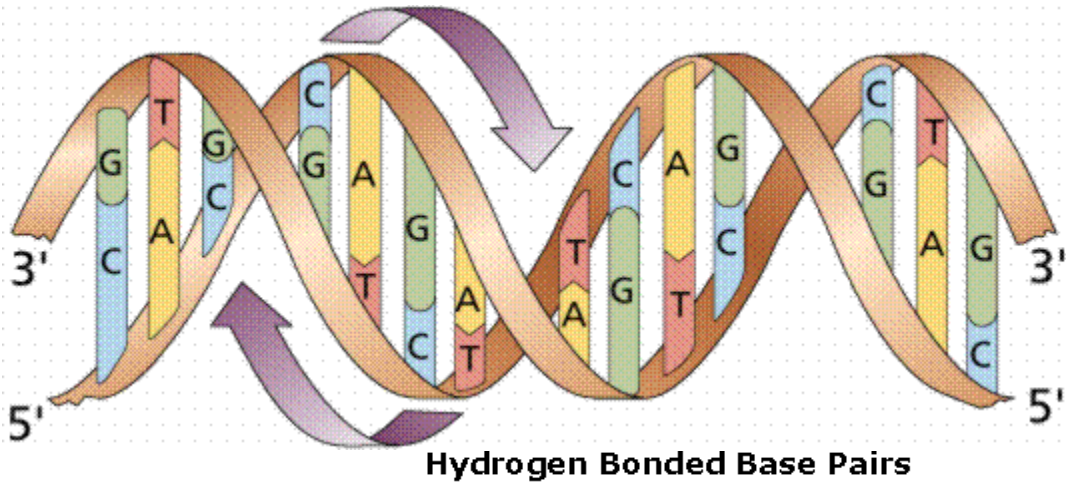
**Ans:**

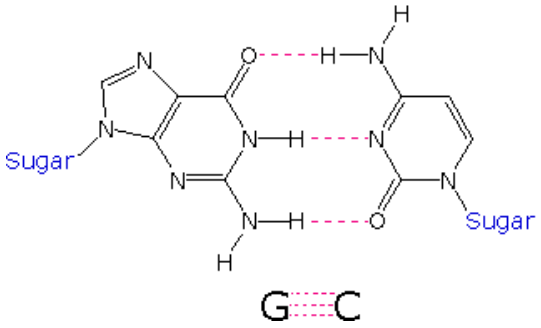
**The DNA Double Helix**

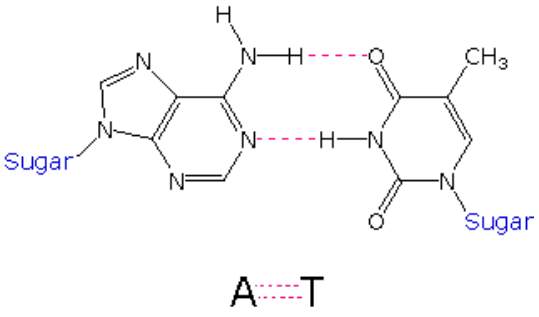
The 1962 Nobel Prize in Physiology or Medicine was awarded to Crick, Watson and Wilkins for the discovery of the molecular structure of DNA – the double helix.

**Chemical Structure of the DNA double strands**

DNA (deoxyribonucleic acid) is a double-stranded molecule that is twisted into a helix like a spiral staircase. Each strand is comprised of a sugar- phosphate backbone and numerous base chemicals attached in pairs.




The four bases that make up the stairs in the spiraling staircase are adenine (A), thymine (T), cytosine (C) and guanine (G). These stairs act as the "letters" in the genetic alphabet, combining into complex sequences to form the words, sentences and paragraphs that act as instructions to guide the formation and functioning of the host cell. Maybe even more appropriately, the A, T, C and G in the genetic code of the DNA molecule can be compared to the "0" and "1" in the binary code of computer software. Like software to a computer, the DNA code is a genetic language that communicates information to the organic cell.

**Genetic code**

The DNA code, like a floppy disk of binary code, is quite simple in its basic paired structure. However, it's the sequencing and functioning of that code that's enormously complex. Through recent technologies like x-ray crystallography, we now know that the cell is not a "blob of protoplasm", but rather a microscopic marvel that is more complex than the space shuttle. The cell is very complicated, using vast numbers of phenomenally precise DNA instructions to control its every function.

25. a. Write a note on

i. Replication ii. Transcription iii. Translation

Ans: **Replication of DNA Molecules**

Before a cell divides, its DNA is replicated (duplicated.) Because the two strands of a DNA molecule have complementary base pairs, the nucleotide sequence of each strand automatically supplies the information needed to produce its partner. If the two strands of a DNA molecule are separated, each can be used as a pattern or template to produce a complementary strand. Each template and its new complement together then form a new DNA double helix, identical to the original.

**1. Transcription**

Before the synthesis of a protein begins, the corresponding RNA molecule is produced by **RNA transcription**. One strand of the DNA double helix is used as a template by the **RNA polymerase** to synthesize a **messenger RNA** (mRNA). This **mRNA** migrates from the nucleus to the cytoplasm. During this step, mRNA goes through different types of maturation including one called **splicing** when the non-coding sequences are eliminated. The coding mRNA sequence can be described as a unit of three nucleotides called a **codon**.

**2. Translation**

The **ribosome** binds to the **mRNA** at the start codon (AUG) that is recognized only by the initiator **tRNA**. The ribosome proceeds to the elongation phase of protein synthesis. During this stage, complexes, composed of an amino acid linked to tRNA, sequentially bind to the appropriate codon in mRNA by forming complementary base pairs with the **tRNA anticodon**. The ribosome moves from codon to codon along the mRNA. Amino acids are added one by one, translated into polypeptidic sequences dictated by DNA and represented by mRNA. At the end, a release factor binds to the stop codon, terminating translation and releasing the complete **polypeptide** from the ribosome.

(Or)

b. Explain the components present in the nucleic acid?

**Ans:**

Each of the sugar groups in the backbone is attached (via the bond shown in red) to a third type of molecule called a nucleotide base. There are only four different nucleotide bases can occur in a nucleic acid and are classified as pyrimidine or purine bases:

Though only four different nucleotide bases can occur in a nucleic acid, each nucleic acid

contains millions of bases bonded to it. The order in which these nucleotide bases appear in the nucleic acid is the coding for the information carried in the molecule. In other words, the nucleotide bases serve as a sort of genetic alphabet on which the structure of each protein in our bodies is encoded.

**DNA**

In most living organisms (except for viruses), genetic information is stored in the molecule deoxyribonucleic acid, or DNA. DNA is made and resides in the nucleus of living cells. DNA gets its name from the sugar molecule contained in its backbone(deoxyribose); however, it gets its significance from its unique structure. Four different nucleotide bases occur in DNA: adenine (A), cytosine (C), guanine (G), and thymine (T).

**Nucleotides: Building Blocks of Nucleic Acids**

| Names of DNA Nucleotide | | | |
|---|---|---|---|
| **Name** | **Base** | **Nucleoside** | **5'-Nucleotide** |
| **DAMP** | Adenine | 2'-Deoxyadenosine | 2'-Deoxyadenosine-5'-monophosphate |
| **DCMP** | Cytosine | 2'-Deoxycytidine | 2'-Deoxycytidine-5'-monophosphate |
| **DGMP** | Guanine | 2'-Deoxyguanosine | 2'-Deoxyguanosine-5'-monophosphate |
| **DTMP** | Thymine | 2'-Deoxythymidine | 2'-Deoxythymidine-5'-monophosphate |

**RNA** has the same nucleotide srtuctiure except the thymine base is replaces by uracil.

**Nucleotides: Nitrogenous base + pentose sugar + phosphate group(s)**

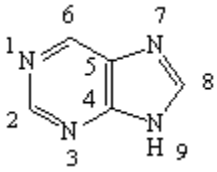
**(1) The Nitrogenous Bases:**

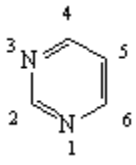
Planar, aromatic, heterocyclic

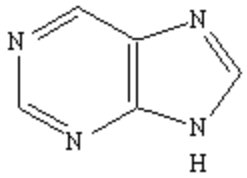
Structural derivatives of purine or pyrimidine

Note that numbers on the atoms are "unprimed"

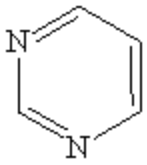
**The parent compounds are shown below:**



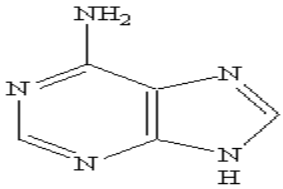


Purine

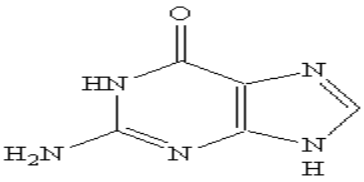


Pyrimidine

**The structures of the two most common purines are:**

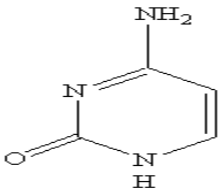


Adenine (A)

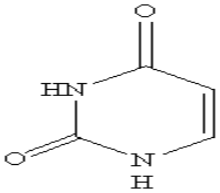


Guanine (G)

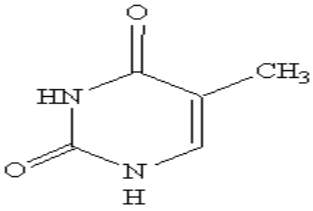
**The structures of the three most common pyrimidines are:**



Cytosine (C)



Uracil (U)

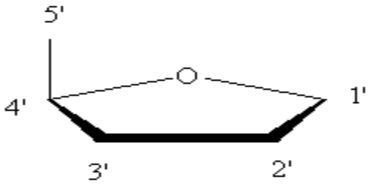


Thymine (T)
(5-methyluracil)

**(2) Sugars: D-ribose and 2'-deoxyribose**

Pentoses: 5-C sugars

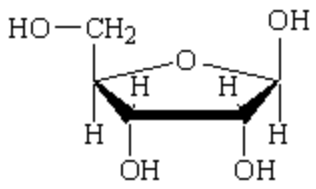
"Primes" refer to numbering of the atoms of the ribose



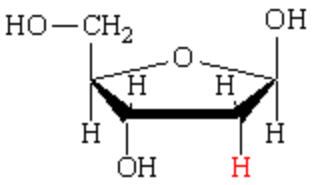
The "2'-deoxy-" notation means that there is no -OH group on the 2' carbon atom

Purines bond to the C1' of the sugar at their N9 atoms

Pyrimidines bond to the sugar C1' atom at their N1 atoms



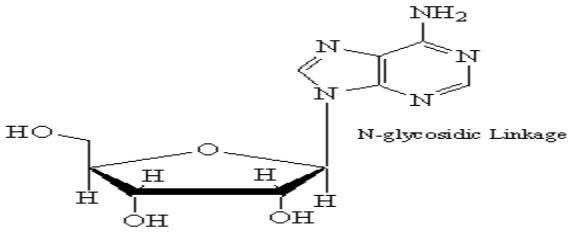

D-Ribose




2'-Deoxyribose

**A "nucleoside" results from the linking of one of these 2 sugars with one of the purine- or pyrimidine-derived bases through an N-glycosidic linkage.**

The chemical bond linking them is an "N- glycosidic bond"



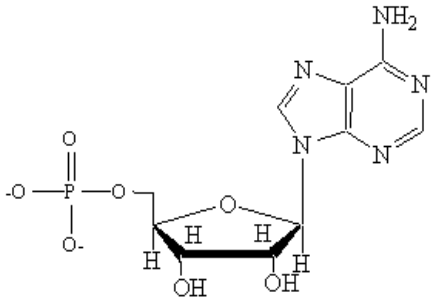

Adenosine

**(3) Phosphate Group(s)**

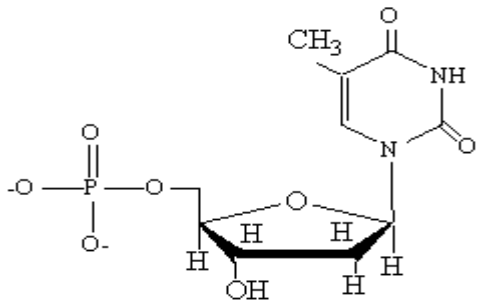
Mono-, di-, and triphosphates

Phosphate can be bonded to either C3' or C5' atoms of sugar

**A "nucleotide" is a 5'-phosphate ester of a nucleoside.**




Adenosine Monophosphate (AMP)
(a ribonucleotide)




2'-Deoxythymidine Monophosphate
(a deoxyribonucleotide)

26. a. Draw a outline of Krebs cycle and explain it briefly

**Ans:**

**Krebs Cycle**

The Krebs cycle, also known as the tricarboxylic acid cycle (TCA), was first recognized in 1937 by the man for whom it is named, German biochemist Hans Adolph Krebs.

The Krebs cycle refers to a complex series of chemical reactions that produce carbon dioxide and Adenosine triphosphate (ATP), a compound rich in energy. The cycle occurs by essentially linking two carbon coenzyme with carbon compounds; the created compound then goes through a series of changes that produce energy. This cycle occurs in all cells that utilize oxygen as part of their respiration process; this includes those cells of creatures from the higher animal kingdom such as humans. Carbon dioxide is important for various reasons, the main one being that it stimulates breathing, while ATP provides cells with the energy required for the synthesis of proteins from amino acids and the replication of deoxyribonucleic acid (DNA); both are vital for energy supply and for life to continue. In short, the Krebs cycle constitutes the discovery of the major source of energy in all living organisms.

**Functions**

Within the Krebs cycle, energy in the form of ATP is usually derived from the breakdown of glucose, although fats and proteins can also be utilized as energy sources. Since glucose can pass through cell membranes, it transports energy from one part of the body to another. The Krebs cycle affects all types of life and is, as such, the metabolic pathway within the cells. This pathway chemically converts carbohydrates, fats, and proteins into carbon dioxide, and converts water into serviceable energy.

The Krebs cycle is the second stage of aerobic respiration, the first being glycolysis and last being the electron transport chain; the cycle is a series of stages that every living cell must undergo in order to produce energy. The enzymes that cause each step of the process to occur are all located in the cell's "power plant"; in animals, this power plant is the mitochondria; in plants, it is the chloroplasts; and in microorganisms, it can be found in the cell membrane. The Krebs cycle is also known as the citric acid cycle, because citric acid is the very first product generated by this sequence of chemical conversions, and it is also regenerated at the end of the cycle.

The pyruvate molecules produced during glycolysis contains a lot of energy in the bonds between their molecules. In order to use that energy, the cell must convert it into the form of ATP. To do so, pyruvate molecules are processed through the Kreb Cycle, also known as the citric acid cycle.

1. Prior to entering the Krebs Cycle, pyruvate must be converted into acetyl CoA. This is achieved by removing a CO2 molecule from pyruvate and then removing an electron to reduce an NAD+ into NADH. An enzyme called coenzyme A is combined with the remaini ow:

2. Citrate is formed when the acetyl group from acetyl CoA combines with oxaloacetate from the previous Krebs cycle.

3. Citrate is converted into its isomer isocitrate.

4. Isocitrate is oxidized to form the 5-carbon α-ketoglutarate. This step releases one molecule of CO2 and reduces NAD+ to NADH2+.

5. The α-ketoglutarate is oxidized to succinyl CoA, yielding CO2 and NADH2+.

The □-Ketoglutarate Dehydrogenase Complex is

Similar to pyruvate dehydrogenase complex

Same coenzymes, identical mechanisms

E1 - a-ketoglutarate dehydrogenase (with TPP)

E2 – dihydrolipoyl succinyltransferase (with flexible lipoamide prosthetic group)

E3 - dihydrolipoyl dehydrogenase (with FAD)

6. Succinyl CoA releases coenzyme A and phosphorylates ADP into ATP.

In the succinyl CoA synthetase reaction, the thioester bond between HS-CoA and the succinyl group is hydrolyzed.

Since it is a rich in energy bond, the energy released is enough for synthesizing GTP from GDP + (P).

This GTP is equivalent, from the energetic point of view, to ATP. In fact, GTP can transfer the (P) group to ADP to form ATP:

GTP + ADP ————à GDP + ATP

Since ATP can be produced from this reaction, without participation of the respiratory chain, this process is called Substrate Level Phosphorylation (SLP) in contrast to the Oxidative Phosphorylation (ATP synthesis using the energy released in the Electron Transport Chain).

A few other reactions in metabolism are also coupled with ATP synthesis without participation of the respiratory chain. They are considered also SLP reactions.

7. Succinate is oxidized to fumarate, converting FAD to FADH2.

The Succinate Dehydrogenase Complex of several polypeptides, an FAD prosthetic group and iron-sulfur clusters, embedded in the inner mitochondrial membrane. Electrons are transferred from succinate to FAD and then to ubiquinone (Q) in electron transport chain. Dehydrogenation is stereospecific; only the trans isomer is formed

8. Fumarate is hydrolized to form malate.

9. Malate is oxidized to oxaloacetate, reducing $NAD^+$ to $NADH^{2+}$.

We are now back at the beginning of the Krebs Cycle. Because glycolysis produces two pyruvate molecules from one glucose, each glucose is processes through the kreb cycle twice. For each molecule of glucose, six $NADH^{2+}$,two $FADH_2$, and two ATP.

**Overview**

The sum of all reactions in the citric acid cycle is:

$$\text{Acetyl-CoA} + 3\ NAD^+ + FAD + GDP + P_i + 2\ H_2O \rightarrow \text{CoA-SH} + 3\ NADH + 3\ H^+ + FADH_2 + GTP + 2\ CO_2$$

(the above reaction is equilibrated if $P_i$ represents the $H_2PO_4^-$ ion, GDP the $GDP^{2-}$ ion and GTP the $GTP^{3-}$ ion).

(Or)

b. Briefly explain Iodine number value and saponification value of oil.

**Ans:**

**Iodine value**, also called **Iodine Number**, in analytical chemistry, measure of the degree of unsaturation of an oil, fat, or wax; the amount of iodine, in grams, that is taken up by 100 grams of the oil, fat, or wax. Saturated oils, fats, and waxes take up no iodine; therefore their iodine value is zero; but unsaturated oils, fats, and waxes take up iodine. (Unsaturated compounds contain molecules with double or triple bonds, which are very reactive toward iodine.) The more iodine is attached, the higher is the iodine value, and the more reactive, less stable, softer, and more susceptible to oxidation and rancidification is the oil, fat, or wax. In performing the test, a known excess of iodine, usually in the form of iodine monochloride, is allowed to react with a known weight of the oil, fat, or wax, and then the amount of iodine remaining unreacted is determined by titration.

Drying oils used in the paint and varnish industry have relatively high iodine values (about 190). Semidrying oils, such as soybean oil, have intermediate iodine values (about 130). Nondrying oils, such as olive oil, used for soapmaking and in food products, have relatively low iodine values (about 80).

| Fat | Iodine Number |
|---|---|
| Tung oil | 163 – 173 |
| Cod liver oil | 145 – 180 |
| Grape seed oil | 124 – 144[2] |
| Palm oil | 50.0 – 55.0 |
| Butter | 26 – 40 |
| Olive oil | 80 – 88 |

**Saponification value** number represents the number of milligrams of potassium hydroxide required to saponify 1g of fat under the conditions specified. It is a measure of the average molecular weight (or chain length) of all the fatty acids present. As most of the mass of a fat/tri-ester is in the 3 fatty acids, the saponification value allows for comparison of the average fatty acid chain length. The long chain fatty acids found in fats have a low saponification value because they have a relatively fewer number of carboxylic functional groups per unit mass of the fat as compared to short chain fatty acids. If more moles of base are required to saponify N grams of fat then there are more moles of the fat and the chain lengths are relatively small, given the following relation:

Number of moles = mass of oil / average molecular mass

The calculated molar mass is not applicable to fats and oils containing high amounts of unsaponifiable material, free fatty acids (>0.1%), or mono- and diacylglycerols (>0.1%).

Handmade soap makers who aim for bar soap use NaOH (sodium hydroxide, lye). Because saponification values are listed in KOH (potassium hydroxide) the value must be converted from potassium to sodium to make bar soap; potassium soaps make a paste, gel or liquid soap. To convert KOH values to NaOH values, divide the KOH values by the ratio of the molecular weights of KOH and NaOH (1.403).

Standard methods for analysis are for example: ASTM D5558 for vegetable and animal fats, ASTM D 94 (for petroleum) and DIN 51559.

The percentage of unsaponifiable material varies with the substance:

- low percentage (<1%) : refined oils, refined shea butter, olive oil
- high percentage (6–17%): unrefined shea butter
- very high percentage (≥50%): beeswax
- unsaponifiable (~100%) mineral oil, paraffin wax