Clinical Biochemistry

College of Nursing \Undergraduate Studies

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Article teachers

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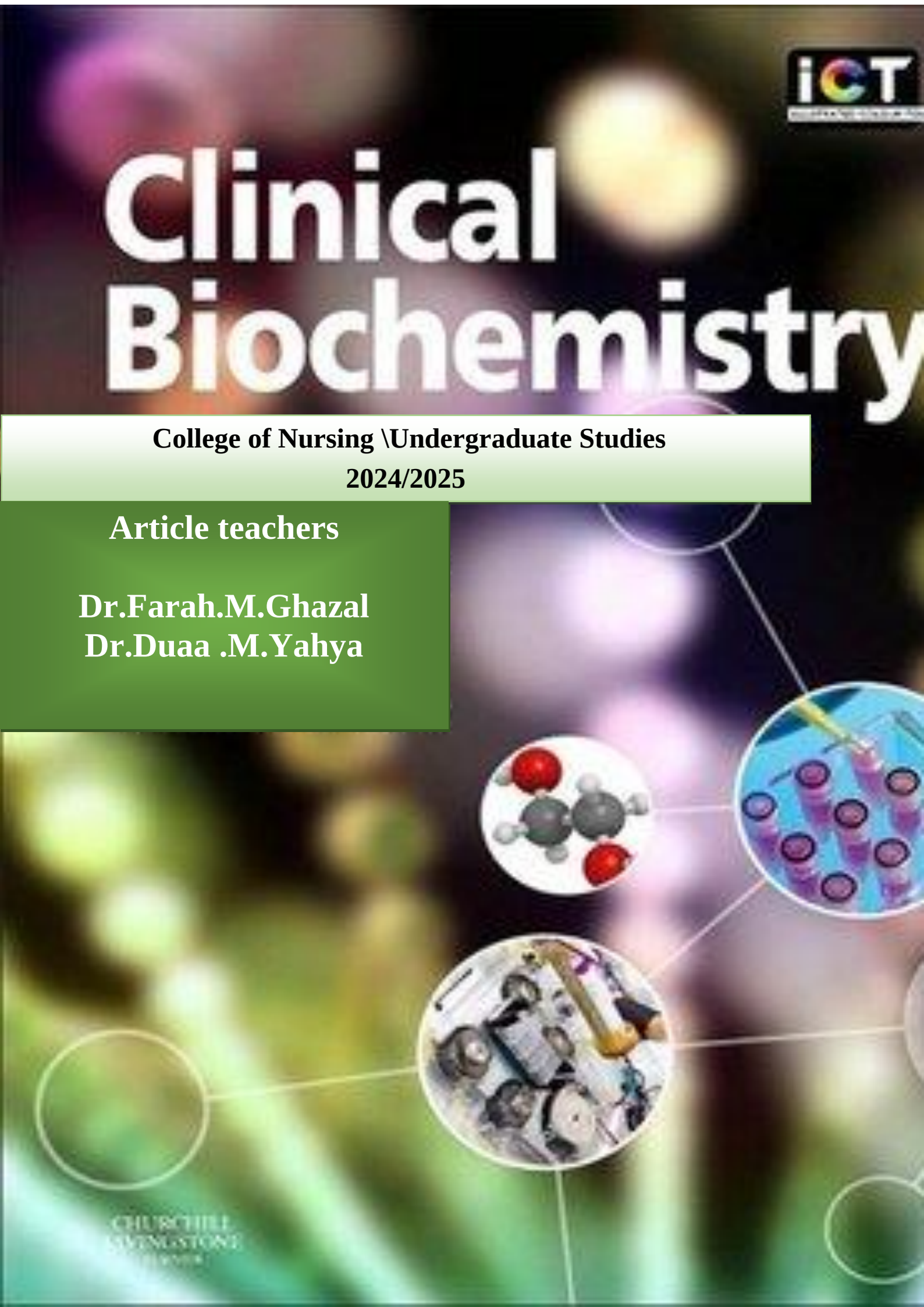


carbohydrates

Carbohydrates are compounds containing C,H and O. The general formula for a carbohydrate is Cx (H2O)y .All carbohydrates contain C= O and OH functional groups.There are some derivatives from this basic formula because carbohydrate derivatives can be formed by the addition of other chemical groups,such as phosphates,sulfates ,and amines . The classification of carbohydrates is based on four different properties:

1-The size of the base carbon chain

2-The location of the CO function group

3-The number of sugar units

4-The stereochemistry of the compound

1- The size of the base carbon chain :

Carbohydrates can be grouped into generic classifications based on the number of carbons in the molecule . for example , trioses contain three carbons , tetroses contain four, pentoses contain five ,and hexoses contain six .in actual practice,the smallest carbohydrate is glyceraldehyde,athree-carbon compound .

2-The location of the CO function group :

Carbohydrates are hydrates of aldehyde or ketone derivatives based on the location of the CO functional group . (fig. 1)

FIGI Fig (1): ways in glucose metabolism.

The two forms of carbohydrates are aldose and ketose (fig.2).The aldose form has aterminal carbonyl group (O=CH)called an aldehyde group ,whereas the ketose has a carbonyl group (O=C)in the middle linked to two other carbon atoms (called a ketone group).

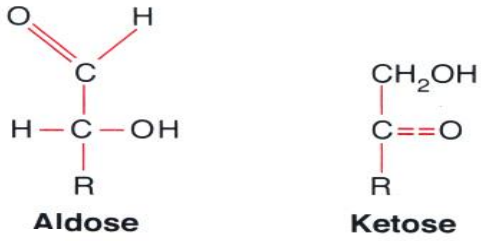


FIG Fig (2): orms of carbohydrates.

Several models are used to represent carbohydrates .The Fisher projection of a carbohydrate has the aldehyde or ketone at the top of the drawing . the compound can be represented as a straight chain or might be linked to show a representation of the cyclic hemiacetal form (fig 3).

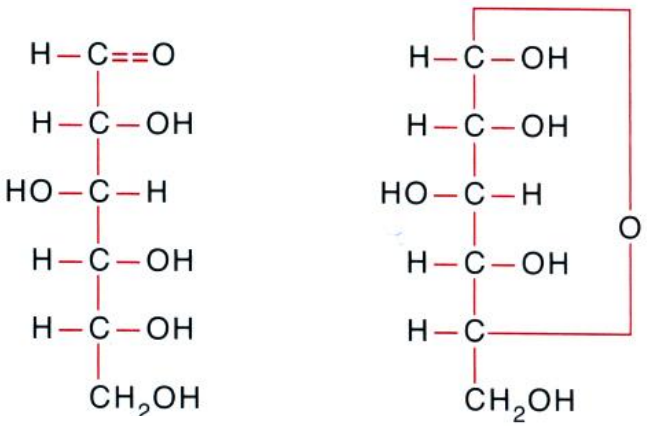


FIG **Fig (3):** projection of glucose. (**Left**) Open chain Fisher projections. (**Right**) Cyclic Fisher projection.

The Haworth projection represents the compound in the cyclic form.this structure is formed when the functional (carbonyl) group (ketone or aldehyde) reacts with an alcohol group on the same sugar to form a ring called a hemaketal or hemiacetal ring . (fig.4)

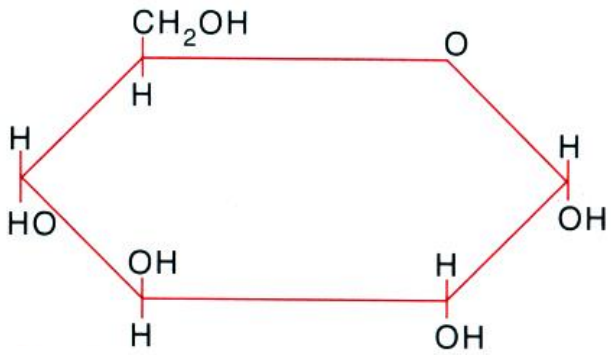


FIG Fig (4): rth projection of glucose.

3-The number sugar units :

Carbohydrates is based on number of sugar units in the chain : monosaccharides,disaccharides,oligosaccharides,and polysaccharides.when two carbohydrate molecules join,a water molecule is produced . when they split one molecule of water is used to form the individual compounds .this reaction is called hydrolysis .

Monosaccharides :

Monosaccharides are simple sugar that cannot be hydrolyzed to a simpler form .these sugars can contain three, four,five, and six or more carbon atoms (known as trioses,tetroses,pentoses,and hexoses,respectively).the most common include glucose, fructose, and galactose .

Disaccharides:

Disaccharides are formed when two monosaccharide units are joined by a glycosidic linkage .on hydrolysis disaccharides will be split into two monosaccharides by disaccharide enzymes (e.g. lactase) located on the microvilli of the intestine .the most common disaccharides are maltose (comprising 2-β-D-glucose in a 1→ 4 linkage),lactose, and sucrose .

- Sucrose : prevalent in sugar cane and sugar beet, is composed of glucose and fructose through an α-(1,2)β-glycosidic bond(Fig. 5) .

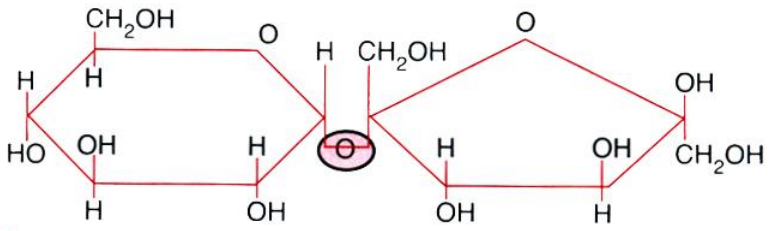
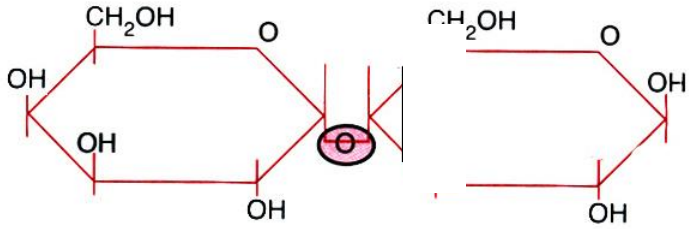


Fig (5): h projection of sucrose.

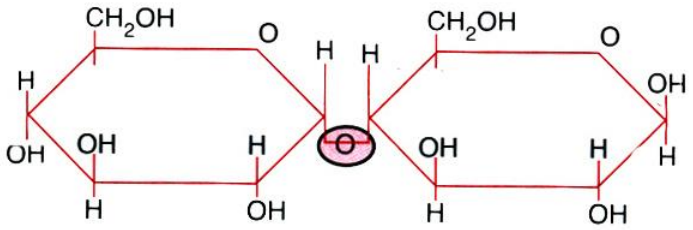
-Lactose : is found in the milk of mammals and consists of galactose and glucose in a β-(1,4)glycosidic bond (Fig.6).



Galactose Glucose

Fig (6) : Lactose

-Maltose :the major degradation product of starch ,is composed of 2 glucose monomers in an α-(1,4)glycosidic bond (Fig.7).



Glucose Glucose

Fig (7) : Maltose

Polysaccharids:

Oligosaccharides are the chanining of 2 to 10 sugar units, whereas polysaccharides are formed by the linkage of many monosaccharide units . the most common polysaccharides are starch (glucose molecules)and glycogen(fig .8)

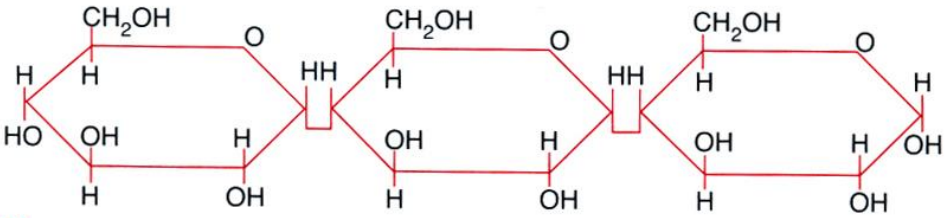


Fig (8): of monosaccharides.

Glycogen :

Glycogen is the major form of stored carbohydrate in animals .this molecule is a homopolymer of glucose in α-(1,4) linkage , it is also highly branched with α-(1,6)branch linkages occurring every (8-10)residues . glycogen is a very compact structure that result from the coiling of the polymer chains ,this compactness allows large amounts of carbon energy to be stored in small volume.

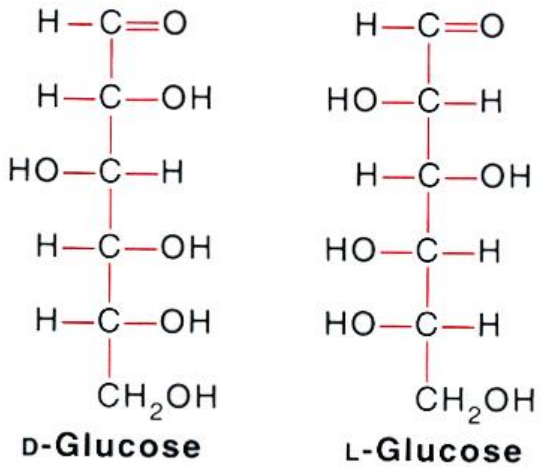
Starch :

Starch is the major form of stored carbohydrate in plant cells .its structure is identical to glycogen ,except for a much lower degree of branching about every (20-30) residues . unbrnched starch is called amylose , branched starch is called amylopectin .

4- The stereochemistry of the compound :

The central carbons of carbohydrate are asymmetric (chiral) – four different groups are attached to the carbon atoms . this allows for various spatial arrangements around each asymmetric carbon (also called stereogenic centers) forming molecules called

stereoisomers.A monosaccharide is assigned to to the D or the L series according to the configuration at the highest- numbered asymmetric carbon . If the hydroxyl group to the right in the Fisher projection ,the sugar belongs to the D series and if it projects to the left , then it belongs to the L series .Fig (9).



FIGI Fig (9) isomers of glucose.

Chemeical properties of carbohydrates :

Some carbohydrates are reducing substances, these carbohydrate must contain a ketone or an aldehyde group . All monosaccharides and many disaccharides are reducing agents because a free aldehyde or ketone (the open chain form)can be oxidized under the proper condition . As disaccharide remains areducing agent when the hemiacetal or ketal hydroxyl group is not linked to another molecule .

examples of reducing substances include glucose , maltose, fructose , lactose, and galactose . Nonreducing carbohydrates do not have an active ketone or aldehyde group. They will not reduce other compounds . the most common nonreducing sugar is sucrose – table sugar.

Carbohydrate can form glycosidic bonds with other carbohydrates and with noncarbohydrates . two sugar molecules can be joined in tandem forming a glycosidic bond between the hemiacetal group of one molecule and the hydroxyl group on the other molecule .

The Proteins

Definition of protein:

Protein are nitrogen organic components , they are complex molecules , protein are polymers that are composed of 20 different amino acids . each amuno acid consist of carbon , hydrogen , oxygen , nitrogen , some time sulpher and phosphorus , the percentage of them are C (53%) ,H(7%),O(23%),N(16%),S(1%).

Protein are primary structural componts of muscle ,connective tissue , bones , hormones , enzymes , and in all living organisms .

Amino acids :

Amino acids are the building blocks of proteins .amino acid contains at least one of both amino and carboxylic acid functional groups . the basic structure of an amino acid is depicted in fig. (1).

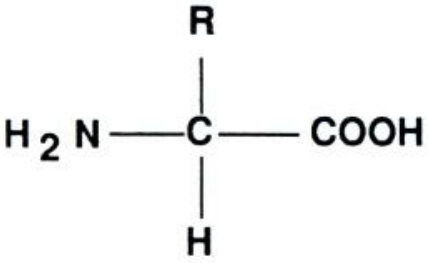


FIGURE 1. General structure of an α-amino acid.

The N-terminal end amino group (-NH2)and the C-terminal end carboxyl group (-COOH) bond to the α-carbon with the amino group of one amino acid linking with the carboxyl group of another , forming a peptide bond a peptide bond fig.(2)

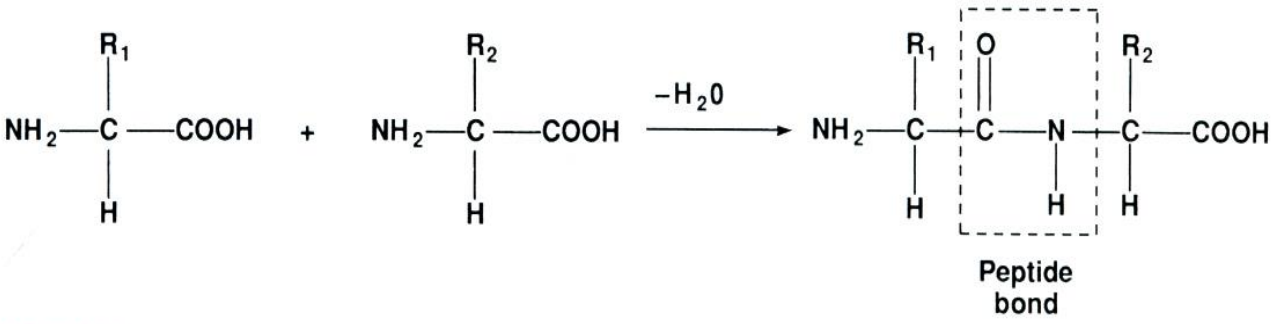
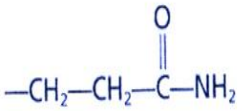
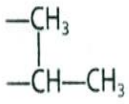
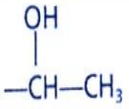
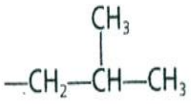
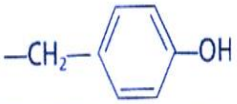
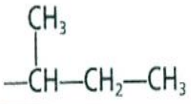
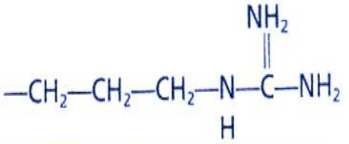
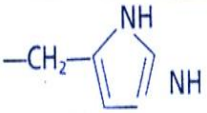
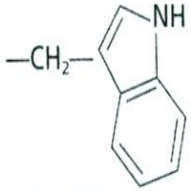
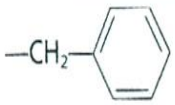
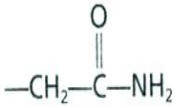
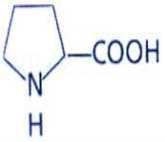


FIGURE 2. Formation of a dipeptide.

A chain of amino acids is known as a polypeptide , and a large polypeptide constitutes a protein .in human serum , proteins average about 100-150 amino acids in the polypeptide chains. Amino acids differ from one another by the chemical composition of their R group (side chains). The R group found on the 20 different amino acids used in building proteins are shown in table(1).

TABLE 1 AMINO ACIDS REQUIRED IN THE SYNTHESIS OF PROTEINS

AMINO ACID	R	AMINO ACID	R
Glycine (Gly)	—H	Glutamine (Gln)	
Alanine (Ala)	—CH_3	Serine (Ser)	
Valine (Val)*		Threonine (Thr)*	
Leucine (Leu)*		Tyrosine (Tyr)	
Isoleucine (Ile)*		Lysine (Lys)*	—CH_2—CH_2—CH_2—CH_2—NH_2
Cysteine (Cys)	—CH_2—SH	Arginine (Arg)	
Methionine (Met)*	—CH_2—CH_2—S—CH_3	Histidine (His)	
Tryptophan (Trp)*		Aspartate (Asp)	—CH_2—COOH
Phenylalanine (Phe)*		Glutamate (Glu)	—CH_2—CH_2—COOH
Asparagine (Asn)		Proline (Pro)*†	

The R group is the group attached to the α carbon.

*Nutritionally esssential.

†Exception to attachment of R group is proline.

- Essential amino acids :

About half of the 20 amino acids needed by humans can not be synthesized at a rapid enough rate to support growth,they must be supplied in food . these nutritionally essential amino acids must be supplied by diet in the form of proteins . the essential amino acids are ,(arginine , histidine , isoleucine,leucine,lysine, methionine , phenylalanine,threonine ,tryptophan , and valine).

-Semiessential amino acids:

It is required for the young but not for adults and can be synthesized in high enough amounts that the body needs as: (cystine , tyrosine),tyrosine is produced from phenylalanine , so if the diet is deficient in phenylalanine ,tyrosine will be required as well.

-Non essential amino acids :

The 10 amino acids that the body can produce are (alanine , asparagines ,aspartic , cycteine , glutamic acid , glutamine , glycine , proline, serine , tyrosine)

- Classification by Protein Functions:

1-Enzymes :proteins that catalyze chemical reaction . examples ,the transaminases , dehydrogenases , and phosphatases .

2-Hormones : proteins that are chemical messengers that control the actions of specific cells or organs . examples, insulin, testosterone , growth hormone .

3-Transport proteins : proteins that transport of ions , small molecules , or macromolecules , such as hormones , vitamins , minerals , and lipids , across a biologic membrane .examples of transport proteins , hemoglobin , albumin , and transferring .

4- Immunoglobulins(antibodies): proteins produced by B-cell (lymphocytes)in the bone marrow . examples are, IgG , IgM, and IgA.

5- Structural proteins : fibrous are the structures of cells and tissues such as muscle , tendons , and bone matrix . collagen , elastin , and keratin are examples of structural proteins .

6- Storage proteins :proteins that serve as reserves of metal ions and amino acids that can be released and used .the most storage protein is ferritin, which stores iron to be later used in the manufacture of hemoglobin .

7-Energy source : plasma proteins serve as a reserve source of energy for tissues and muscle.

8- Osmotic force : plasma proteins function in the distribution of water throughout the compartments of the body.

-Classification by protein structure :

1-Simple proteins : simple proteins may be globular or fibrous in shape .

a- Globular proteins are globelike , symmetrical proteins that are soluble in water ,globular proteins are transporters .examples of globular proteins are, albumin , hemoglobin , and the immunoglobulins IgG ,IgA,and IgM.

b-Fibrous proteins form long protein filaments or subunits , are asymmetrical and usually inert , and are generally water insoluble . fibrous proteins are structural ,such as connective tissues , tendons , bone and muscle examples of fibrous proteins include ,keratins and collagen.

2-Conjugated proteins :conjugated proteins consist of a protein and a nonprotein (prosthetic) group,The prosthetic group is the non amino part of a conjugated protein, the prosthetic group may be lipid , carbohydrate , metals and others ,example of conjugated proteins are the metalloproteins , glycoproteins , lipoproteins and nucleoproteins .

- **Metalloproteins** have a metal ion attached to the protein such as ferritin contains iron and ceruloplasmin which contains copper .
- **Lipoproteins** have lipids such as cholesterol and triglyceride linked to proteins ,such as high density lipoproteins (HDL)and very low density lipoproteins (VLDL) .
- **Glycoproteins** are used to describe carbohydrate with joined to proteins , generally those molecules with 10%-40% carbohydrate are called glycoproteins .example of glycoproteins are , haptoglobin and α1-antitrypsin.
- **Nucleoproteins** are those proteins that are combined with nucleic acids ,DNA or RNA.chromatin is an example of nucleoprotein that is the complex of DNAand protein that makes up chromosomes .

-Plasma proteins:

The major plasma proteins are divided into two group :albumin and globulins . there are four major types of globulins,α1,α2,β,and γ fractions ,each with specific properties and actions . Atypical blood panel will provide four different measurements – total protein , albumin , globulins , and the albumin /globulin ratio.

-Albumin :

Albumin is synthesized in the liver from 585 amino acids at the rate of 9-12 gm/day with no reserve or storage .

Function of albumin :

1- Albumin is responsible for nearly 80% of the osmotic pressure intravascular fluid .
2- Albumin transports thyroid hormone, fat-soluble , iron , fatty acids , un conjugated bilirubin , calcium ,and drugs ,
3-Source of endogenous amino acids.

Normal range of serum albumin is : (3.8-4.4)gm/dl

Decreased concentrations of albumin may be caused by the following :

1- An inadequate source of amino acids that occurs in malnutrition and malabsorption.
2- Liver disease , resulting in decreased synthesis by the hepatocytes.
3- protein-losing lead to disease of intestinal tract as in diarrhea.
4- Kidney loss to the urine in renal disease .
5- Skin loss in the absence of the skin barrier such as in burns .
6- Hypothyroidism .
7- Dilution by excess drinking too much water or excess administration of intravenous fluids
8- Acute disease states .

Increased serum albumin levels are seen only with:

1-Dehydration
2-After excessive albumin infusion.

Lipids

Lipids are water-insoluble organic biomolecules that can be extracted from cells and tissues by nonpolar solvents e.g : chloroform ,ether , or benzene.

Fatty acids:

Fatty acids fill two major roles in the body :

1-As the components of membrane lipids .

2-As the major components of stored fat in the form of triacylglycerols .

All fatty acids are a long hydrocarbon chain and a terminal carboxyl group , fatty acids that contain no carbon-carbon double bonds are termed **saturated fatty acids** as palmitic acid , those that contain one or more double bonds are **unsaturated fatty acids** as oleic acid , fatty acids differ from each other primarily in chain length and in the number and position of their unsaturated bonds .

Table (1) gives the structures and symbols of some important saturated and unsaturated fatty acids . the most common among the saturated fatty acids are pallmitic acid (C16) and stearic acid (C18)and among the unsaturated fatty acids oleic acid (C18).

Table (1) : Physiologically Relevant Fatty Acids

Numerical Symbol	Common Name	Structure
14:0	Myristic acid	$CH_3(CH_2)_{12}COOH$
16:0	Palmitic acid	$CH_3(CH_2)_{14}COOH$
$16:1^{\Delta 9}$	Palmitoleic acid	$CH_3(CH_2)_5C{=}C(CH_2)_7COOH$

18:0	Stearic acid	$CH_3(CH_2)_{16}COOH$
$18:1^{\Delta 9}$	Oleic acid	$CH_3(CH_2)_7C{=}C(CH_2)_7COOH$
$18:2^{\Delta 9,12}$	Linoleic acid	$CH_3(CH_2)_4C{=}CCH_2C{=}C(CH_2)_7COOH$
$18:3^{\Delta 9,12,15}$	Linolenic acid	$CH_3CH_2C{=}CCH_2C{=}CCH_2C{=}C(CH_2)_7COOH$
$20:4^{\Delta 5,8,11,14}$	Arachidonic acid	$CH_3(CH_2)_3(CH_2C{=}C)_4(CH_2)_3COOH$

Essential Fatty acids :

Fatty acids required in the diet of mammals are called essential fatty acids , the most abundant essential fatty acids , **linoleic** and **γ-linolenic** acids cannot be synthesized by mammals but must be obtained from plant sources , in which they are very abundant , linoleic acid is a necessary precursor in mammals for the biosynthesis of **arachidonic** acid which is not found in plants .

Essential fatty acids are necessary precursors in the biosynthesis of a group of fatty acid derivatives called **prostaglandins** .

Classification of lipids :

1-Simple Lipids.
2-Conjugated lipids.
3-Derived lipids .

1-Simple lipids divided into:

A-Neutral lipids :

Neutral lipids are composed of esters of fatty acids with alcohol (glycerol) to produced **Glycerides** , **triacylglycerides** are esters of glycerol with three fatty acid molecules , **glycerides** with one or two fatty acid groups called **monoglycerides** and **Diglycerides** respectively Fig(1) , Glycerides mixtures are referred to as fats or oils . fats ,which are solid at room temperature contain a large proportion of saturated fatty

acids .oils. are liquid at room temperature because of their relatively high unsaturated fatty acid content .

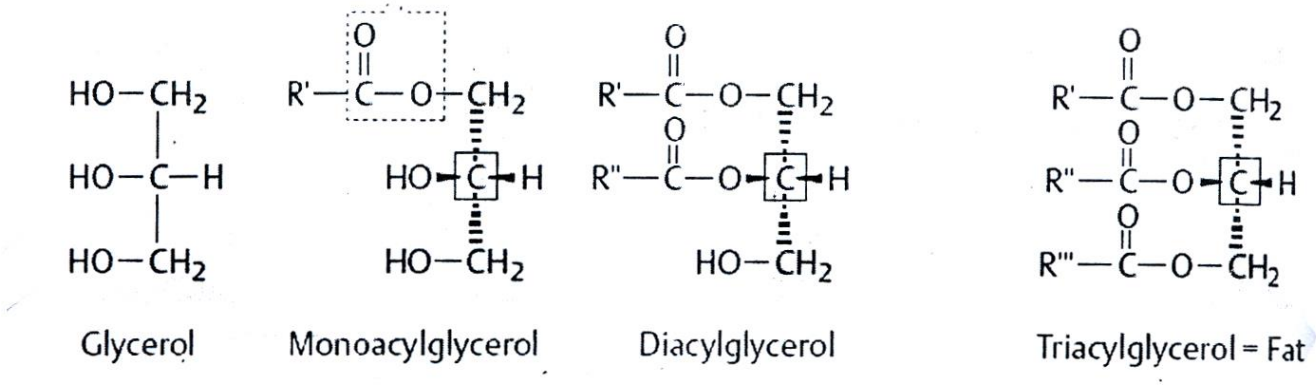


Fig (1) : Neutral lipids

B-Waxes:

Waxes are complex mixtures of nonpolar lipids . they sere as protective coatings on leaves , stems ,and fruit of plant ,the skin and fur of animals . esters composed of long –chain fatty acids and long chain alcohols are prominent constituents of most waxes ex: Beeswax (myricylplamitate).

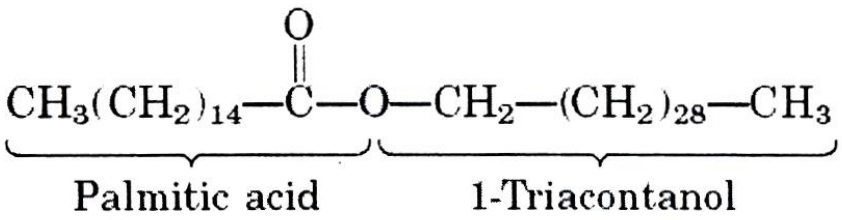


Fig (2) : Beeswax (Myricylplamitate)

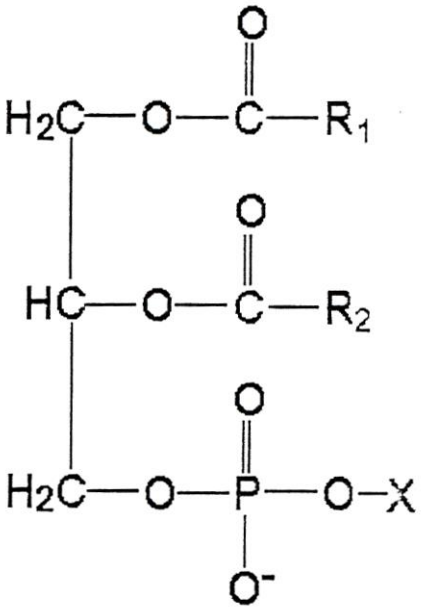
2-Conjugated lipids divided into :

A-Phospholipids:

The basic structure of phospholipids is very similar to that of the triacylglycerides except that C-3 of the glycerol backbone is esterifid to phosphoric acid . the building block of the phospholipids is **phosphatidic acid** which results when the X substitution in the basic structure shown in the Fig (3).

Substitutions include:

- **Ethanolamine** (phosphatidyl ethanolamine also called cephalins).
- **Choline** (phosphatidylcholine also called lecithins).
- **Serine** (phosphatidylserine).
- **Sphingolipids**.
- **Plasmalogen**.



X : CH_2CH_2-NH_3^+ Ethanol amine

X : $CH_2CH_2N^+(CH_3)_3$ Choline

X : CH_2CH_2-COO^- Serine

NH_3

Fig (3) : Phosphatidic acid

B-Glycolipids:

Glycolipids are composed of carbohydrates and fatty acids such as :

- Cerebrosides .

- Gangliosides.

C-Sulfolipids:

D-Lipoproteins:

Function of lipoproteins are transport the lipids in the blood such as:

- Chylomicrones.

- Very low density lipoproteins (VLDL).

- Low density lipoproteins .

- High density lipoproteins.

3-Derives lipids:

Derives are composed from :

-Saturated and unsaturated fatty acid .

- Steroid .

-Sterols .

- Fatty aldehyde .

- Keton bodies .

- Terpens .

Functions of Lipids:

1- as structure components of biological membranes .

2-as storage and transport forms of metabolic fuel.

3-as protective coating on the surface of many organisms .

4-They provide energy reserves in the form of triacylglycerols .

5-Both lipid and lipid derivatives serve as vitamins and hormones .

Steroids :

Steroids are derivatives of saturated tatracyclic hydrocarbon perhydrocyclophenanthrene Fig (4) .

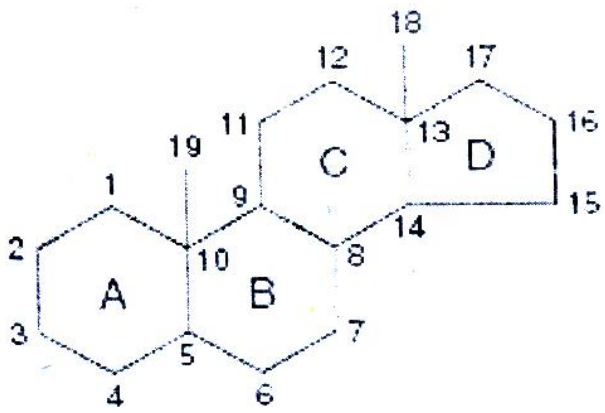


Fig (4) : perhydrocyclophenanthrene

First important steroid product is **Lanosterol** which in animal tissues is the precursor of cholesterol .cholesterol and lanosterol are members of a large subgroup of steroids called **sterols** .

Cholesterol is the precursor of many other steroids ,including the bile acids , male sex hormones , the estrogens ,or female sex hormones , the progestational hormone progesterone and the adrenocortical hormones.

Blood lipids includes :

1. Cholesterol.
2. Triglyceride.
3. Lipoprotein.

Concentration of the total lipids is about **500 mg /dl**

Cholesterol :

The cholesterol is asteroid compound contaning tetracyclic hydrocarbons cholesterols 9(the ring A,B,C,D) chole : means bile sterol , sterol : means solid alcohol cholesterol , cholesterol : means **bile solid alcohol** Fig (5).

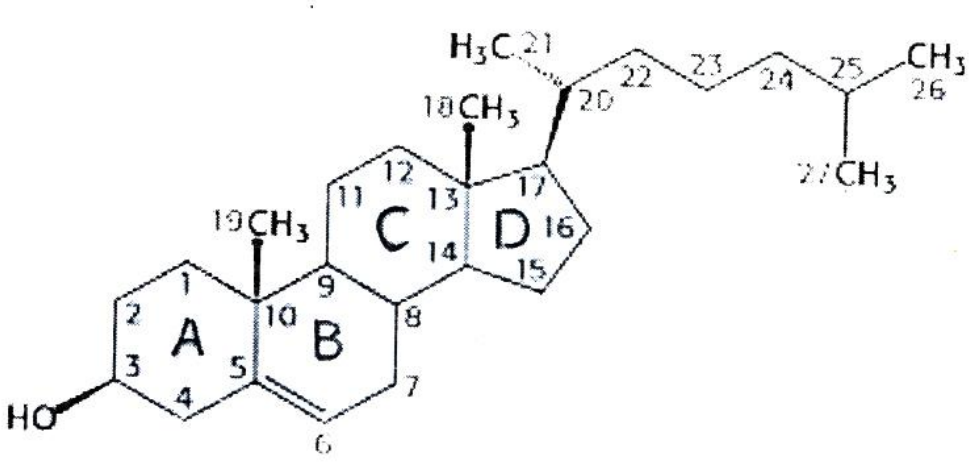


Fig (5) : Cholesterol

Molecular structure of cholesterol is (C27H45OH)
Normal level of cholesterol in the blood **150 -250 mg /dl**

Cholesterol is present in most human tissues the largest amount of it is present into :

1. Brain
2. Nerve tissue
3. Bile
4. Blood
5. Liver

Cholesterol has been found in blood in two forms :

1. Free cholesterol **1/3 of total cholesterol**
2. Cholesterol ester **2/3 of total cholesterol**

There are two sources of cholesterol in the body :

1. **Exogenous**: diet ex; (egg yolk , meat , animal fats , dairy products) absorption of cholesterol from diet in small intestine
2. **Endogenous** from :
   a- Liver (cholesterol produce from acetyl COA that is product from the metabolism of carbohydrates , amino acids , fats) .
   b- Skin

Chemistry of Enzymes

Enzymes are specific biologic proteins that catalyze biochemical reaction without changed in composition ,the other substances in the reaction are converted to products . the catalyzed reactions are essential to physiologic functions , such as nerve conduction , muscle contraction , nutrient degradation ,energy use .plasma or serum enzyme level are useful in the diagnosis of particular diseases or physiologic abnormalities .

In addition to the basic enzyme structure , a nonprotein molecule ,called a cofactor , may be necessary for enzyme activity . Inorganic cofactors ,such as chloride or magnesium ions , are called activators . A coenzyme is an organic cofactor , such as nicotinamide adenine dinucleotide (NAD). When bound to the enzyme is called a **prosthetic group** .

The enzyme that lacks with an essential cofactors is called an **apoenzymes** , Intact enzymes with their bound cofactors are referred to as **holoenzymes** .

Inhibitors :

Enzymatic reaction may not progress normally if a particular substance , an inhibitor , interferes with the reaction .

Classification of Enzyme inhibitors into three types:

1- Competitive inhibitor :

Competitive inhibitors physically bind to the active site of an enzyme and compete with the substrate for the active site, the inhibition is reversible because the substrate is more likely than the inhibitor to bind the active site and the inhibition is reversed by increasing the concentration of substrate . Fig.(1)

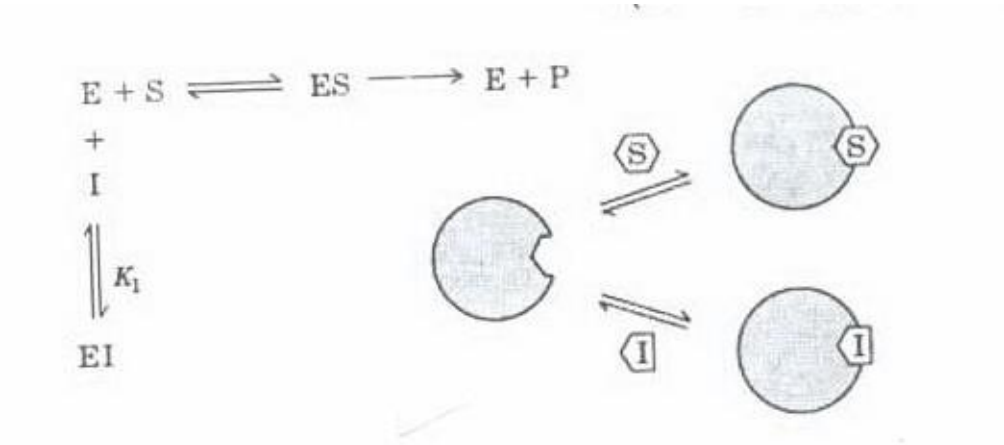


Fig.(1) Competitive inhibitor

2-Noncompetitive Inhibitor :

A noncompetitive inhibtor binds an enzyme at a place other than the active site , because the inhibitor binds the enzyme in dependently from the substrate , increasing substrate concentration does not reverse the inhibition . noncompetitive inhibitor divided into two types :

A- Reversible noncompetitive inhibitor .

B- Irreversible noncompetitive inhibitor .

A- Reversible noncompetitive inhibitor:

The inhibitor binds to the enzyme in reversible reactions and composed two complex EI and ESI. **Fig.(2)**

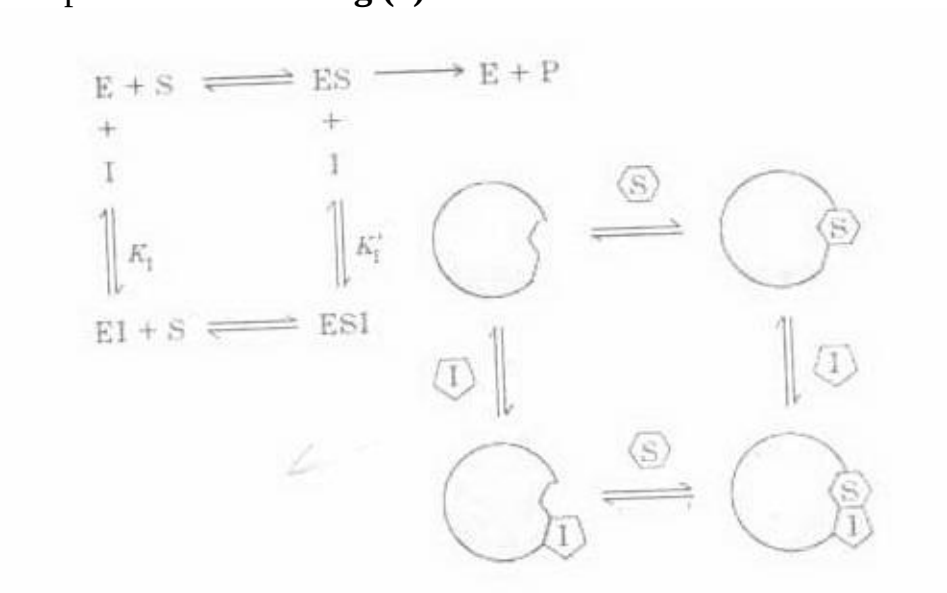


Fig.(2) Reversible noncompetitive inhibitor

B- Irreversible noncompetitive inhibitor :

The inhibitor destroys part of the enzyme involved in catalytic activity ,usually the inhibitor bound covalently to the enzyme and poison enzyme . **Fig.(3)**

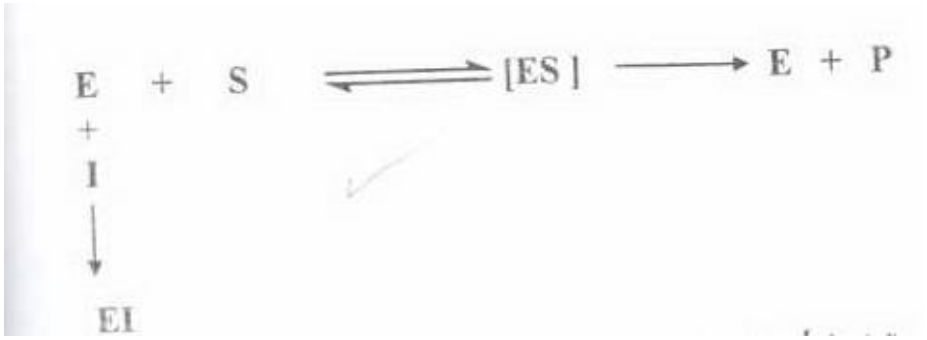


Fig.(3) Irreversible noncompetitive inhibitor

3-Uncompetitive inhibitor :

Uncompetitive inhibition is another kind of inhibition in which the inhibitor binds to the ES complex –increasing substrate concentration results in more ES complexes to which the inhibitor binds , thereby ,increases the inhibition .the enzyme –substrate –inhibitor complex does not yield product. **Fig.(4)**

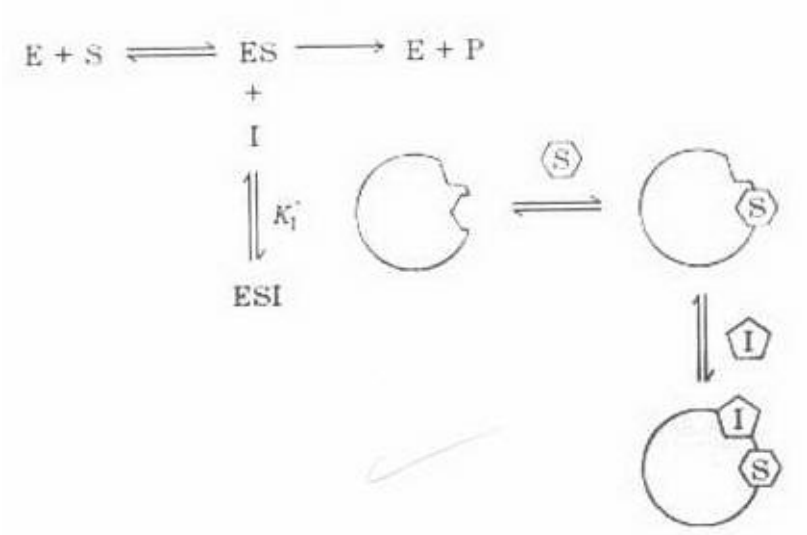


Fig.(4) Uncompetitive inhibitor

Factors that Influence Enzymatic Reactions :

1-Substrate Concentration :

The substrate binds to free at a low –substrate concentration ,the reaction rate increases as more substrate is added . the reaction is following first –order kinetics because the reaction rate is directly proportional to substrate concentration when the substrate concentration is high enough to saturate

all available enzyme and the reaction velocity reaches its maximum , the reaction is in zero –order kinetics , and the reaction rate depends only on enzyme concentration . **Fig.(5)**

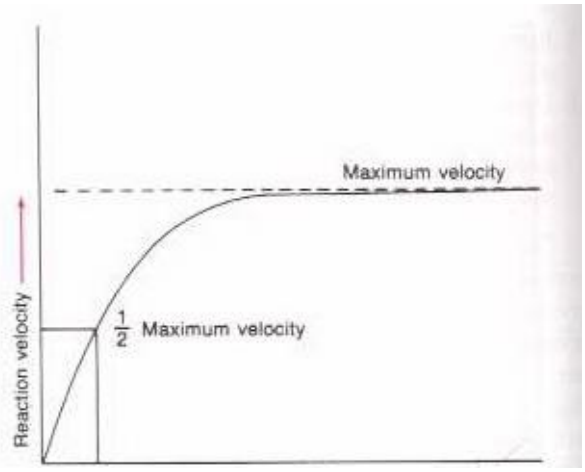


Fig.(5) Substrate Concentration

2-Enzyme concentration :

The velocity of the reaction is proportional to the enzyme concentration . the higher the enzyme level ,the faster the reaction will proceed because more enzyme is present to bind with the substrate . **Fig.(6)**

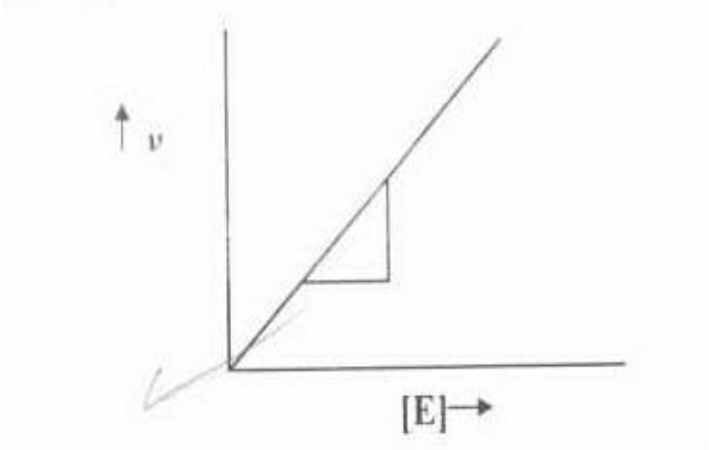


Fig.(6) Enzyme concentration

3-PH :

Changes in PH may denature an enzyme or influence its ionic state ,resulting in structural changes , hence each enzyme operates within a specific PH range and maximally at a specific PH .most enzymatic reactions occur in the PH range of 7.0 to 8.0 but some enzymes are active in wider PH ranges than other ,for example the optimum PH of pepsin is approximately 1.6 and glucose -6-phosphatase is 7.8 . **Fig.(7)**

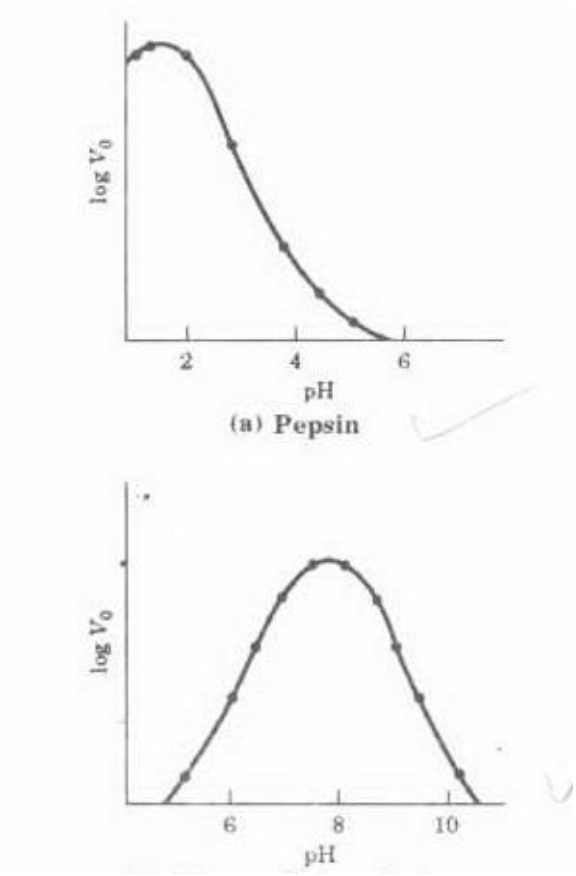


Fig.(7) PH

4- Temperature :

The temperature is high enough to denature the protein composition of the enzyme .for each 10◦ increase in temperature , the rate of reaction approximately double until ,of course the protein is denatured. The rate of denaturation increases as the temperature increases and is significant at 40 ◦ to 50◦c.each enzyme functions at optimum temperature ,which is influenced by other reaction especially the total time for reaction. **Fig.(8)**

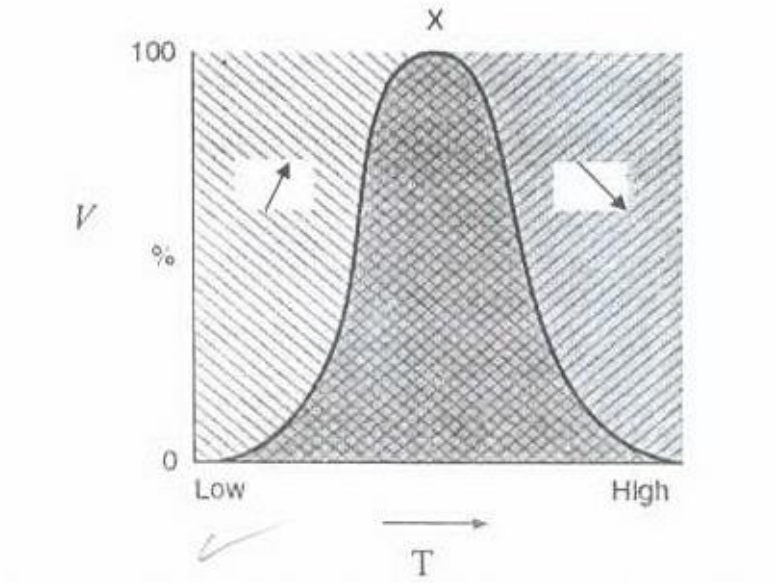
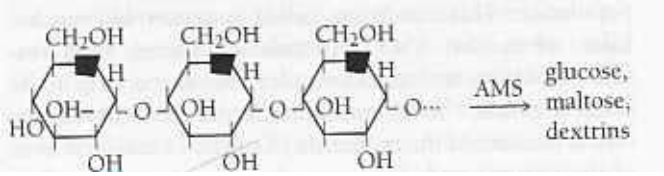


Fig.(8) Temperature

Amylase :

Amylase (AMS) is an enzyme belong to the class of hydrolases that catalyze the breakdown of starch and glycogen . AMS attacks only α-1-4 glycosidic bonds to produce glucose , maltose and intermediate chains ,called dextrins .



Tissue Source :

Pancreas and the salivary glands are the major tissue sources of AMS . Lesser concentration are found in skeletal muscle and the small intestine .AMS is the smallest enzyme with a molecular weight of 50,000 to 55,000 ,because its small size , it is filtered by the renal glomerulus and also appears in the urine .

Diagnostic Significance

1- AMS measurements is in the diagnosis of acute pancreatits .
2- Elevated AMS level in salivary gland lesions such as mumps .
3-Elevation of AMS in renal insufficiency and diabetic ketoacidosis .

Reference Range of AMS 25-130 U/h

Urine

Urine is a complex aqueous solution of inorganic salts and organic waste products of body metabolism .

The term nonprotein nitrogen (NPN)compounds arise from the catabolism of proteins and nucleic acids . the biochemistry , and analytical methods for measurement of the (NPN)compounds (urea , uric acid , creatinine , creatine and ammonia) table (1).

Urea

The NPN compound present in highest concentration in the blood is urea . urea is the major product of protein metabolism . it is formed in the liver from amino groups (-NH2) and free ammonia during protein catabolism ,urea nitrogen (urea N)is a more appropriate term .

Physiology :

Protein metabolism produces amino acids that can be oxidized to produce energy or stored as fat and glycogen . these processes release nitrogen , which is converted to urea and excreted as a waste product .following synthesis in the liver , urea is carried in the blood to the kidney , where it is readily filtered from the plasma by the glomerulus.

Most of the urea in the glomerular filtrate is excreted in the urine , some urea is reabsorbed by the renal tubules . the amount reabsorbed depends on urine flow rate and extent of hydration . small quantities of urea (10% of the total) are excreted through the gastrointestinal tract and skin .

The concentration of urea in the plasma is determined by renal function and perfusion , the protein content of the diet , and the rate of protein catabolism.

Pathophysiology:

An elevated concentration of urea in the blood is called **azotemia** .very high plasma urea concentration accompanied by renal failure is called **uremia** , or the **uremic syndrome .**

Condition causing increased plasma urea are classified according to cause into three main categories : **prerenal , renal , and postrenal .**

-**Perrenal azotemia** is caused by reduced renal blood flow, consequently , less urea is filtered .causative factors include : congestive heart failure , shock , hemorrhage , dehydration , high protein diet or increased protein catabolism such as stress , fever and gastrointestinal hemorrhage may increase urea concentration.

-Renal causes of elevated urea include: acute and chronic renal failure , glomerular nephritis , tubular necrosis , and other intrinsic renal disease .

-Postrenal azotemia can be due to obstruction of urine flow in the urinary tract by renal calculi , tumors of the bladder or prostate , or sever infection .

The major causes of decreased plasma urea concentration include: low protein intake and sever liver disease , plasma urea concentration is decreased during late pregnancy and infancy as a result of increased protein synthesis .

Normal value of urea in plasma or serum adult : **6-20 mg / dl**
Normal value of urea in urine adult: **12 – 20 g / day**

Uric acid

Uric acid is the product of catabolism of the purine nucleic acids . although it is filtered by the glomerulus and into the urine, most uric acid is reabsorbed in the proximal tubules and reused . uric acid is relatively insoluble in plasma and , at high concentration ,can be deposited in the joints and tissue , causing painful inflammation .

-Physiology :

Purines , such as adenine and guanine from the break down of ingested nucleic acids , are converted into uric acid , primarily in the liver .uric acid is transported in the plasma from the liver to the kidney , where it is filtered by the glomerulus . reabsorption of 98% to 100% of the uric acid from the glomerular filtrate occurs in the proximal tubules . small amounts of uric acid are secreted by the distal tubules into the urine .

Renal excretion accounts for about 70% of uric acid elimination , the remainder passes into the gastrointestinal tract and is degraded by bacterial enzymes .

Nearly all of the uric acid in plasma is present as **monosodium urate** .at the PH of plasma PH 7 , urate is relatively insoluble , at concentrations greater than 6.8mg /dl , the plasma is saturated .as a result, urate crystals may form and precipitate in the tissues .

Normal value of uric acid in plasma or serum: **3.5- 7.2 mg / dl** in adult male
Normal value of uric acid in plasma or serum: **2.6 – 6.0 mg / dl** in adult female
Normal value of uric acid in urine adult: **250 – 750 mg / day**

Pathophysiology:

Elevated plasma uric acid concentration **hyperuricemia** is found in: gout , increased catabolism of nucleic acids , renal disease ,hemolytic or anemia .

-Gout is a disease found primarily in men and usually is first diagnosed between 30 and 50 years of age . affected individuals have pain and inflammation of the joints caused by precipitation of sodium urates .in 25% to 30% of these patients , hyperuricemia is a result of overproduction of uric acid .

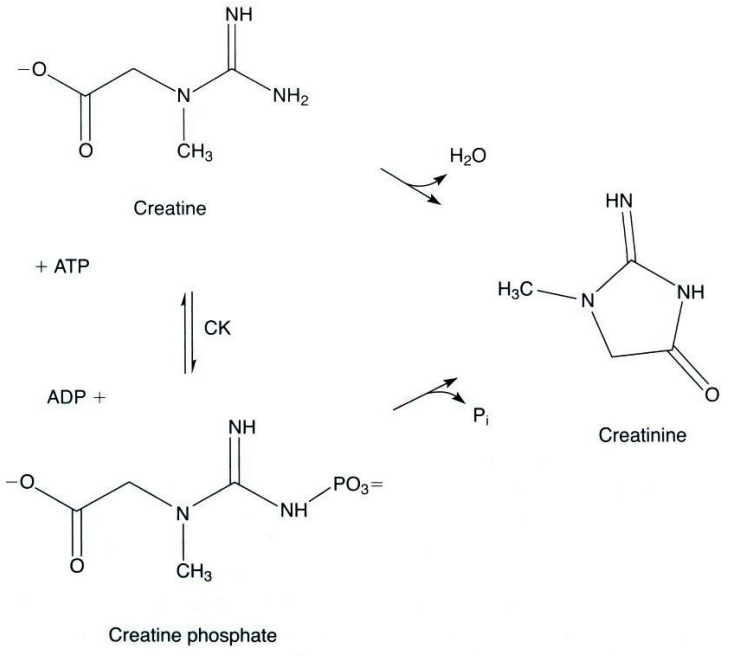
Hypouricemia is less common than hyperuricemia and is usually to sever liver disease or defective tubular re absorption as in Fanconi syndrome .

Creatinine and Creatine:

Creatinine is formed from creatine and creatine phosphate in muscle and is excreted into the plasma at a constant related to muscle mass. Plasma creatinine is inversely related to glomerular filtration rate (GFR) and ,it is commonly used to assess renal filtration function .

Physiology :

Creatine is synthesized primarily in the liver from arginine , glycine , and methionine . it is then transported to other tissues , such as muscle , where it is converted to creatine phosphate ,which serves as a high – energy source . creatine phosphate loses phosphoric acid and creatine loses water to form the cyclic compound , creatinine, which diffuses into the plasma and is excreted in the urine .Fig .(1)



CK = creatine kinase (EC 2.7.3.2)

FIGURE 1 . Interconversion of creatine, creatine phosphate, and creatinine.

Creatinine is released into the circulation and it is filtration by glomerular ,then excreted in the urine . small amounts of creatinine are secreted by the proximal tubule and reabsorbed by the renal tubules .

Normal value of creatinine in plasma or serum: **0.9 – 1.3 mg /dl** in adult male
Normal value of creatinine in plasma or serum : **0.6 – 1.1 mg / dl** in adult female

Pathophysiology :

Elevated creatinine concentration is associated with abnormal renal function . plasma concentration of creatinine is inversely proportional to clearance of creatinine. When plasma creatinine concentration is elevated ,GFR is decreased , indicating renal damage .

Bilirubin

Bilirubin is the end product of haem metabolism:

Red cells are broken down at the end of their life in the reticule - endothelial system , mainly in the spleen . the released Hb is split into globin , which enters the general protein pool , and haem , which is converted to bilirubin after removal of iron
The iron is reutilized , 80% of bilirubin is metabolized daily by this process

Other sources of bilirubin are from the breakdown of red cells in the bone marrow and of Hb – related compounds such as myoglobin and cytochromes .

Unconjugated bilirubin or indirect bilirubin , that is insoluble in water is carried to the liver bound to plasma albumin. At the hepatic cell membrane , bilirubin is removed from the albumin , then conjugated with glucoronic acid forming bilirubin oneglucoronide or diglucoronide . the reaction is catalyised by the enzyme Uridyl diphosphate glucuronyl transferase (UDP) .The conjugated or direct bilirubin is water soluble . Normally , about 300 mg of bilirubin reaches the liver and is conjugated daily .

Conjugated bilirubin is secreted into bile canaliculus and further to gall bladder for storage , and excretion into small intestine , in the intestine , bacteria deconjugate the bilirubin glucuronate and reduce bilirubin to Urobilinogen . most of this urobilinogen is excreted in the faces as such as Urobilin after oxidation in air .

A small portion is areabsorbed through the enterohepatic circulation to be excreted in the urine . therefore , normal urine contain Urobilinogen but not bilirubin . however , the disappearance of Urobilinogen and appearance of bilirubin (direct) in the urine is an abnormal condition that indicate the presence of obstructive jaundice .

Jaundice is due to an increase in the concentration of bilirubin in blood and is , acommon sign in hepatic or biliary tract disorders .jaundice can be classified into :

1- Prehepatic jaundice (hemolytic) (increase nuconjugated)
Due in acute hemolytic anemia , and in neonatal physiological jaundice .

2- Hepatic jaundice (mainly unconjugated)
Due in conjugation failure , toxic hepatitis and cirrhosis , intrahepatic obstruction (increase conjugated and unconjugated).

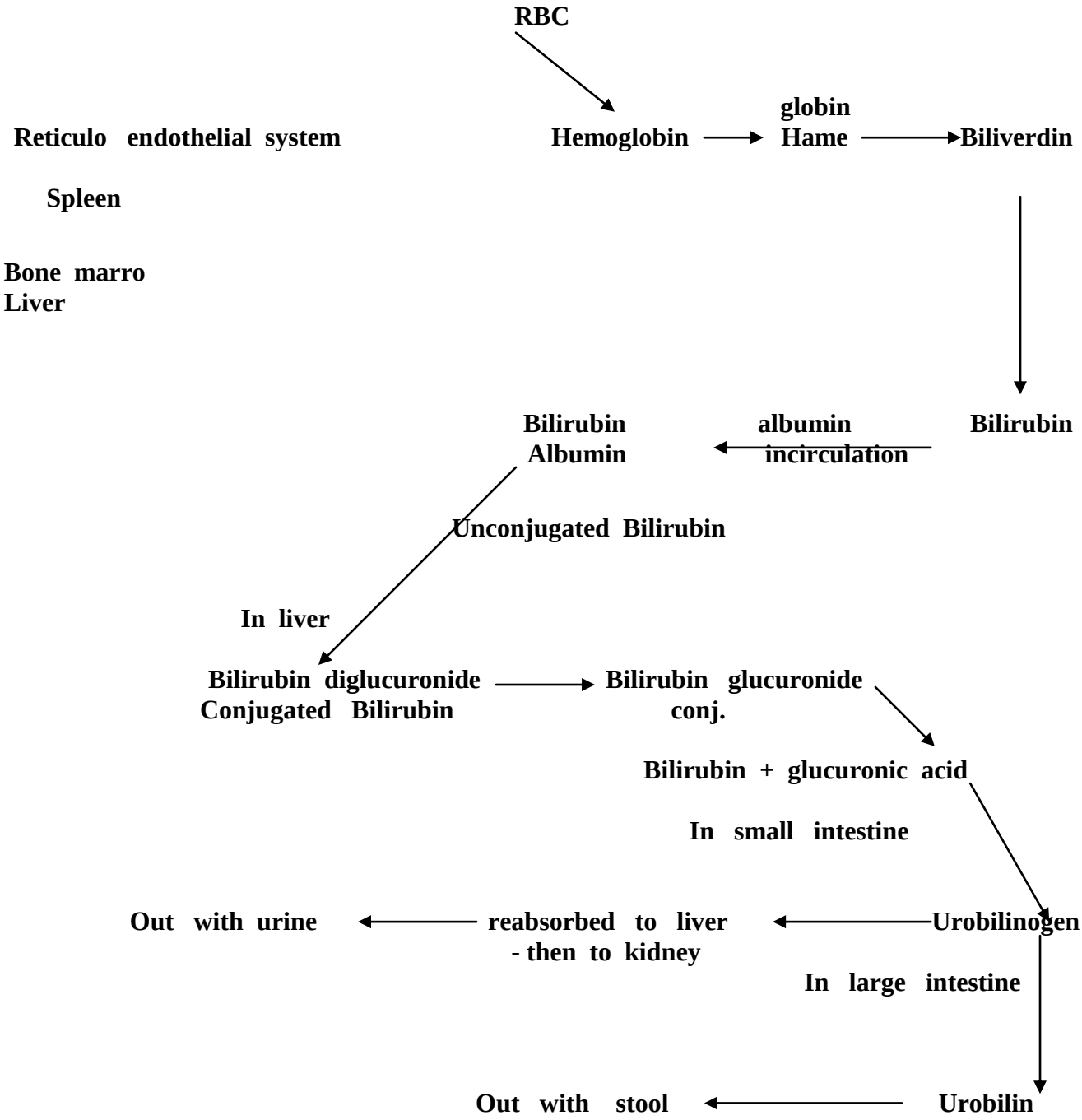
3-Post hepatic jauncice (obstruction of common bile duct due to stones , neoplasms or spasm and stricture (mainly increase conjugated) .

Test of Urobilinogen:

Urobilinogen react with Ehrlichs reagent (p-dimethylamino-benzaaldehyde) to give a red - colored product . sodium acetate is add to buffer hydrochloric acid and to enhance the color of the product .

In the test of Urobilinogen in urine should be fresh and not be exposed to light for long periods of time , since the colorless Urobilinogen is easily oxidized to the pigment Urobilin which does not react with Ehrlichs reagent .

Formation and Metabolism of Bilirubin



Diabetes Mellites

Diabetes Mellites

Diabetes mellitus :is actually a group of metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion , insulin action ,or both.

World health organization (WHO) divided diabetes mellitus into the following types:

1- Insulin dependent diabetes mellitus (IDDM) or type 1 diabetes .

2-Non – insulin dependent diabetes mellitus (NIDDM) or type 2 diabetes .

3- Other specific types of diabetes .

4- Gestational diabetes mellitus (GDM).

- 1- Type 1 diabetes mellitus: is a result of autoimmune destruction of the ß-cells of the pancreas , causing deficiency of insulin secretion . type 1 constitutes only 10% to 20% of all cases of diabetes and commonly occurs in childhood and adolescence . this disease usually initiated by an environmental factor or infection (usually a virus) in individuals ,with a genetic predisposition and causes the immune destruction of the ß cells of the pancreas and therefore ,a decreased production of insulin
- 2-Type 2 diabetes mellitus : is a result of an individuals resistance to insulin with an insulin secretory defect , most patients in this type are obese or have an increased percentage of body fat distribution in the abdominal region ,with an increase in age , and with lack of physical exercise .
- 3- Other specific types of diabetes mellitus: are associated with certain condition (secondary) , including genetic defects of ß- cell function or insulin action , pancreatic disease , diseases of endocrine origin , and drug – or chemical- induced insulin receptor abnormalities.

4- Glucocorticoids hormones : primarily cortisol , are released from the adrenal cortex and it increases plasma glucose by decreasing intestinal entry into the cell and increasing gluconeogenesis , liver glycogen , and lipolysis .

5- Growth hormone : is increases plasma glucose by decreasing the entry of glucose into the cells and decrease glycolysis .

6-Thyroxine hormone : the thyroid gland is stimulated by the production of thyroid –stimulating hormone (TSH)to release thyroxine that increases plasma glucose levels by increasing glycogenolysis , gluconeogenesis , and intestinal absorption of glucose .

Requlation of carbohydrate metabolism by hormones

Control of blood glucose by the following hormones :

1- Insulin hormone : is the hormone responsible for the entry of glucose into the cell . it is synthesized by the cells of islets of Langerhans in the pancreas .it regulates glucose by increasing glycogenesis , lipogenesis , and glycolysis and inhibiting glycogenolysis. Insulin is the only hormone that decreases glucose levels and can be referred to as a hypoglycemic agent .

2-Glucagon hormone : is the hormone responsible for increasing glucose levels . it is synthesized by the ß cells of islets of Langerhans in the pancreas and released during stress and fasting states . glucagon acts by increasing plasma glucose levels by glycogenolysis in the liver and an increase in gluconeogenesis , it can referred to as a hyperglycemic agent .

3- Epinephrine hormone : is produced by the adrenal gland , increases plasma glucose by inhibiting insulin secretion , increasing glycogenolysis and lipolysis, epinephrine is released during times of stress .

- 4- Gestational diabetes mellitus (GDM):causes of(GDM) include metabolic and hormonal changes , this disease is associated with increased perinatal complications and increased risk of diabetes in later years ,infants born to mothers with diabetes are at increased risk for respiratory distress syndrome , hypogalcemia , and hyperbilirubinemia.

Action of Insulin :

- Insulin secretion from pancreatic –ß cells is requlated by glucose levels , in addition to its role in requlation glucose metabolism.
- Insulin is formed from two chain , (A) chain is contain on the 21 amino acid and its contain on the disulfide bond ,(B) chain is contain on the 30 amino acid and two chain are connected with 2 disulfide bond .

- The molecular weight of insulin (5700) daltone , insulin hormone is connected to the insulin receptors (glucoprotein) activation on the cell surface and then its inter glucose from the blood to the cells .

Therapeutic for hyperglycemia

The important of pharmacologic to therapeutic in type 2 diabetes are :

1-The sulfonyl urea (Tolbutamide):

The sulfonyl urea is classes of oral hyperglycemia drugs are referred to as endogenous insulin secretagogues because it is inducse induce the pancreatic release of endogenous insulin .

2-The alpha-Glucosidase inhibitors:

Alpha-glucosidase inhibitors function by interfering with the action of the alpha-glucosidases present in the small intestine,then a reduction in digestion and absorption of glucose into the systemic circulation .

3-Metformin (Biguanides):

Metformin is lower serum glucose levels by suppression of hepatic glucose production and enhancing insulin – stimulated glucose uptake by skeletal muscle.

2-Fructose intolerance:

Fructose intolerance is due from a deficiency of fructose -1-phosphate aldolase that is converted fructose 1,6 di phosphate to di hydroxyl acetone phosphate .

Fructose accumulation leads to symptoms are:

1- Hypoglycemia after fructose ingestion .

2- Nausea and cirrhosis .

3- Vomiting and abdominal pain .

4- Liver damage with hepatomegaly .

5-Jaundice .

3-Glycogen storage disease :

Glycogen storage disease are result of the deficiency of a specific enzyme that an alternation of glycogen metabolism such as :

a- Von Gierke disease :

Von Gierke disease is due from deficiency of glucose -6- phosphatase that is converted glucose -6-phosphate to glucose .

This disease is characterized by:

1-Sever hypoglycemia with acidosis , ketonemia.

2- Glycogen building in the liver causing hepatomegaly .

3-Hyperlipidemia .

4- Uricemia .

5-Growth retardation .

b- Muscular disease :

Muscular disease is due from of deficiency of phosphorylase enzyme in the muscular .and accumulation of glycogen in the muscular .