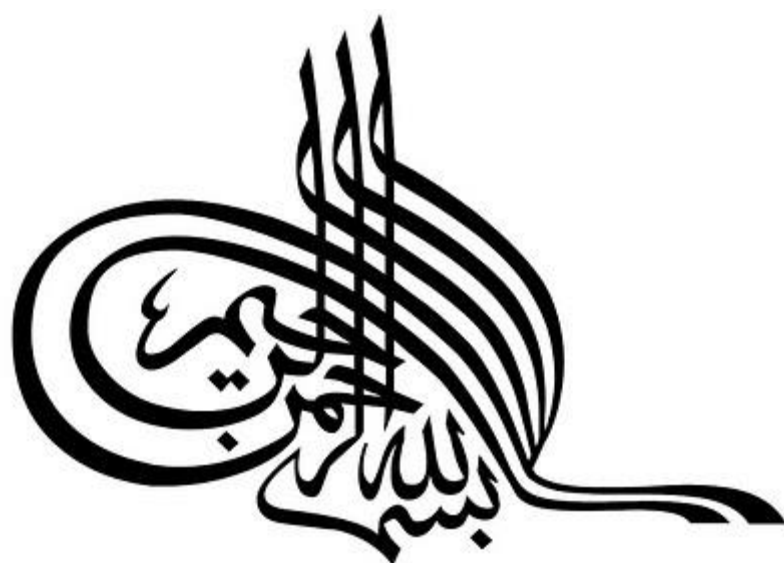


Pharmacy Exam Guide
Step I
PHARMACEUTICAL BIO-CHEMISTRY-I

-1st Edition
(P1C3)



*In the name of Allah,
the Most Beneficent,
the Most Merciful*

**PHARMACY EXAM
GUIDE
STEP I
PHARMACEUTICAL
BIO-CHEMISTRY-I
1ST EDITION
(P1C3)**

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The authors, editors, and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accordance with the current recommendations and practice at the time of publication.

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DEDICATED TO OUR PARENTS
AND TEACHERS

ACKNOWLEDGEMENT

The future belongs to those who believe in the beauty of their dreams.

The preparation of this book "**Pharmacy Exam Guide**" was just a dream of some students of **Doctor of Pharmacy, University of Central Punjab**, which could not be fulfill without the help and support of our teachers and parents.

We appreciate the tireless efforts of ***Our Teachers*** who encouraged us always to achieve our endeavor, no matter, how hard they can be.

We are much indebted to ***Our Parents*** for inspiring and motivating us to achieve the great goals in life.

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Chapter 1 INTRODUCTION TO BIOCHEMISTRY

1.1 BIOCHEMISTRY

- Biochemistry is the application of chemistry to the study of biological processes at the cellular and molecular level.
- It emerged as a distinct discipline around the beginning of the 20th century when scientists combined chemistry, physiology and biology to investigate the chemistry of living systems by:
- Studying the structure and behavior of the complex molecules found in biological material and
- The ways these molecules interact to form cells, tissues and whole organism

1.2 PRINCIPLES OF BIOCHEMISTRY

- Cells (basic structural units of living organisms) are highly organized and constant source of energy is required to maintain the ordered state.
- Living processes contain thousands of chemical pathways. Precise regulation and integration of these pathways are required to maintain life
- Certain important pathways e.g. Glycolysis is found in almost all organisms.
- All organisms use the same type of molecules: carbohydrates, proteins, lipids & nucleic acids.
- Instructions for growth, reproduction and developments for each organism is encoded in their DNA

1.3 PRINCIPLE AREAS OF BIOCHEMISTRY

- Structure and function of biological macromolecules
- Metabolism – anabolic and catabolic processes
- Molecular Genetics – How life is replicated. Regulation of protein synthesis

1.4 HISTORY OF BIOCHEMISTRY

1.4.1 VITALISM

Idea that substances and processes associated with living organisms did not behave according to the known laws of physics and chemistry

1.4.2 EVIDENCE:

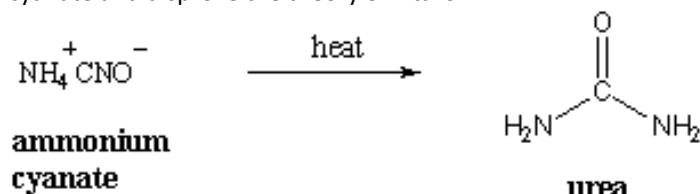
- Only living things have a high degree of complexity

- Only living things extract, transform and utilize energy from their environment
- Only living things are capable of self-assembly and self-replication

1.4.3 FALLACY #1: BIOCHEMICALS CAN ONLY BE PRODUCED BY LIVING ORGANISMS

1.4.3.1 1828 FRIEDRICH WOHLER

Produces ammonia a biochemical from ammonium cyanate and disprove the theory of vitalism.



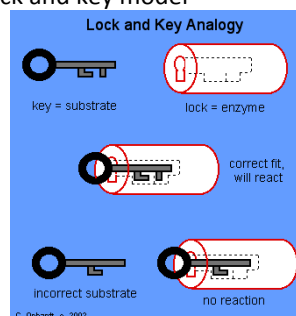
1.4.4 FALLACY #2: COMPLEX BIOCONVERSION OF CHEMICAL SUBSTANCES REQUIRE LIVING MATTER

1.4.4.1 1897 EDUARD BUCHNER

Produces Alcohol from glucose and dead yeast
Glucose + Dead Yeast = Alcohol

1.4.4.2 EMIL FISCHER

Presented lock and key model



1.4.5 1944 AVERY, MACLEOD AND MCCARTY

Identified DNA as information molecules

1.4.6 1953 WATSON AND CRICK

Proposed the structure of DNA

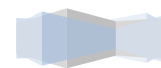
1.4.7 1958 CRICK

Proposed the central dogma of biology

1.5 ORGANIZATION OF LIFE

1.5.1 ELEMENTS

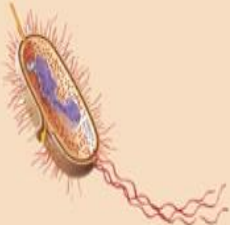
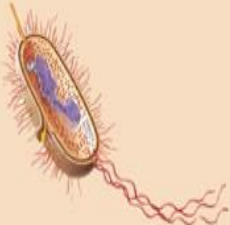
- simple organic compounds (monomers)
- macromolecules (polymers)
- supramolecular structures
- organelles
- cells
- tissues
- organisms
- Range of the sizes of objects studies by Biochemist and Biologist



1.5.2 IMPORTANT ELEMENT

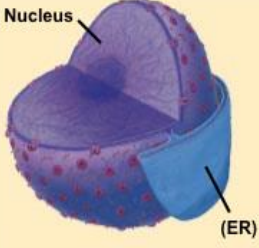
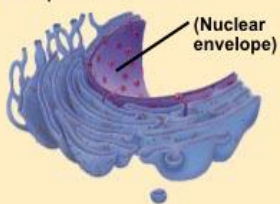
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Table 4.2 Principal Differences between Prokaryotic and Eukaryotic Cells

Characteristic	Prokaryotic	Eukaryotic
		
		
Size of Cell	Typically 0.2–2.0 μm in diameter	Typically 10–100 μm in diameter
Nucleus	No nuclear membrane or nucleoli	True nucleus, consisting of nuclear membrane and nucleoli
Membrane-Enclosed Organelles	Absent	Present; examples include lysosomes, Golgi complex, endoplasmic reticulum, mitochondria, and chloroplasts
Flagella	Consist of two protein building blocks	Complex; consist of multiple microtubules
Glycocalyx	Present as a capsule or slime layer	Present in some cells that lack a cell wall
Cell Wall	Usually present; chemically complex (typical bacterial cell wall includes peptidoglycan)	When present, chemically simple (includes cellulose and chitin)
Plasma Membrane	No carbohydrates and generally lacks sterols	Sterols and carbohydrates that serve as receptors
Cytoplasm	No cytoskeleton or cytoplasmic streaming	Cytoskeleton; cytoplasmic streaming
Ribosomes	Smaller size (70S)	Larger size (80S); smaller size (70S) in organelles
Chromosome (DNA)	Usually single circular chromosome; typically lacks histones	Multiple linear chromosomes with histones
Cell Division	Binary fission	Involves mitosis
Sexual Recombination	None; transfer of DNA only	Involves meiosis

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1.5.8 FUNCTION OF CELL ORGANELLE

	Cell Component	Structure	Function
The eukaryotic cell's genetic instructions are housed in the nucleus and carried out by the ribosomes	Nucleus 	Surrounded by nuclear envelope (double membrane) perforated by nuclear pores. The nuclear envelope is continuous with the endoplasmic reticulum (ER).	Houses chromosomes, made of chromatin (DNA, the genetic material, and proteins); contains nucleoli, where ribosomal subunits are made. Pores regulate entry and exit of materials.
	Ribosome 	Two subunits made of ribosomal RNA and proteins; can be free in cytosol or bound to ER	Protein synthesis
The endomembrane system regulates protein traffic and performs metabolic functions in the cell	Endoplasmic reticulum 	Extensive network of membrane-bound tubules and sacs; membrane separates lumen from cytosol; continuous with the nuclear envelope.	Smooth ER: synthesis of lipids, metabolism of carbohydrates, Ca^{2+} storage, detoxification of drugs and poisons Rough ER: Aids in synthesis of secretory and other proteins from bound ribosomes; adds carbohydrates to glycoproteins; produces new membrane
	Golgi apparatus 	Stacks of flattened membranous sacs; has polarity (<i>cis</i> and <i>trans</i> faces)	Modification of proteins, carbohydrates on proteins, and phospholipids; synthesis of many polysaccharides; sorting of Golgi products, which are then released in vesicles.
	Lysosome 	Membranous sac of hydrolytic enzymes (in animal cells)	Breakdown of ingested substances, cell macromolecules, and damaged organelles for recycling
	Vacuole 	Large membrane-bound vesicle in plants	Digestion, storage, waste disposal, water balance, cell growth, and protection
Mitochondria and chloroplasts change energy from one form to another	Mitochondrion 	Bounded by double membrane; inner membrane has infoldings (cristae)	Cellular respiration
	Chloroplast 	Typically two membranes around fluid stroma, which contains membranous thylakoids stacked into grana (in plants)	Photosynthesis
	Peroxisome 	Specialized compartment bounded by a single membrane	Contains enzymes that transfer hydrogen to water, producing hydrogen peroxide (H_2O_2) as a by-product, which is converted to water by other enzymes in the peroxisome



Chapter 2 CARBOHYDRATES

2.1 CARBOHYDRATES

- Carbohydrates provide fuel, or energy, for the human body. These organic (carbon-containing) compounds are an integral part of both plant and animal life, and, as stated above, life as we know it could not exist without them.
- Carbohydrates are made up of three elements: carbon, hydrogen and oxygen—carbohydrates. As you will learn in a later lesson, fats are also comprised of carbon, hydrogen and oxygen, but they have less oxygen and more carbon and hydrogen than carbohydrates.
- Carbohydrates, along with proteins and fats, comprise the major components of living matter and are used for maintenance of cellular functional activities and as reserve and structural materials for cells
- Carbohydrate simply means hydrates of carbon i.e., (C + H₂O)
- They are also called saccharide, which means “sugars.”
- They are the most abundant organic compound found in nature
- Carbohydrates have the general formula C_x(H₂O)_y

2.2 THE IMPORTANCE OF CARBOHYDRATES

- Even the process of digestion could not occur without the energy provided by carbohydrates.
- Without carbohydrates we would not be able to think or move and our heart couldn't beat.
- Whether it be digestion or circulation, thinking or walking, all life activities are dependent upon carbohydrates.
- When insufficient carbohydrates are available from the diet, the body converts fat reserves to carbohydrates for its use, and amino acids are utilized as carbohydrates instead of being used to make body protein.

Simple carbohydrates

Simple carbohydrates are found in foods such as fruits, milk, and vegetables

Cake, candy, and other refined sugar products are simple sugars which also provide energy but lack vitamins, minerals, and fiber



ADAM.

Complex carbohydrates

Complex carbohydrates provide vitamins, minerals, and fiber

Foods such as breads, legumes, rice, pasta, and starchy vegetables contain complex carbohydrates



ADAM.

2.3 CARBOHYDRATES ORIGIN

- Plants and photosynthesis
- Chlorophyll captures light energy which is transformed into chemical energy - ATP
- Chemical energy is used to combine CO₂ and H₂O to form glucose. The by-product is oxygen
- Extra glucose is stored in plants as starch

2.4 DEFINITION

Carbohydrates are defined as polyhydroxy aldehydes or ketones or substances that hydrolyze to yield polyhydroxy aldehydes and ketones

2.5 TYPE OF CARBOHYDRATES

2.5.1 REDUCING SUGAR



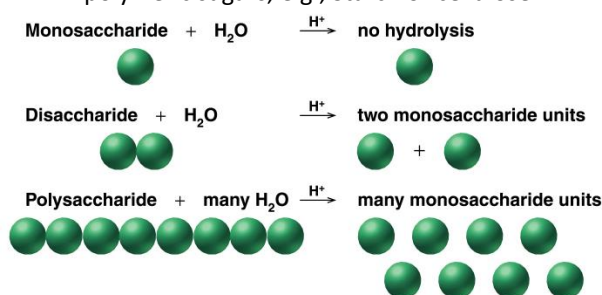
Reducing sugar is that sugar who have a free functional group (free aldehyde or keto group) e.g. sucrose

2.5.2 NON REDUCING SUGAR

Reducing sugar is that sugar who does not possess free functional group (free aldehyde or keto group) e.g. Starch.

2.6 CLASSIFICATION OF CARBOHYDRATES

- Monosaccharides – carbohydrates that cannot be hydrolyzed to simpler carbohydrates; e.g., Glucose or fructose.
- Disaccharides – carbohydrates that can be hydrolyzed into two monosaccharide units; e.g., Sucrose, which is hydrolyzed into glucose and fructose.
- Oligosaccharides – carbohydrates that can be hydrolyzed into a few monosaccharide units. (normally 2 to 10)
- Polysaccharides – carbohydrates that are polymeric sugars; e.g., Starch or cellulose.



2.6.1 MONOSACCHARAIDES

- Consist of 3-6 carbon atoms typically
- A carbonyl group (aldehyde or ketone)
- Several hydroxyl groups
- 2 types of monosaccharide structures: Aldoses and ketoses

2.6.2 ALDOSES

Aldoses are monosaccharides with an aldehyde group with many hydroxyl (-OH) groups.

- *triose* (3C atoms)
- *tetrose* (4C atoms)
- *pentose* (5C atoms)
- *hexose* (6C atoms)

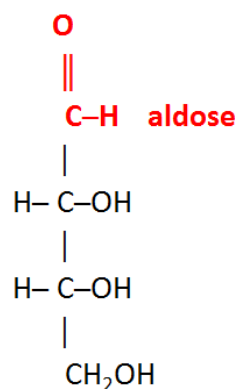
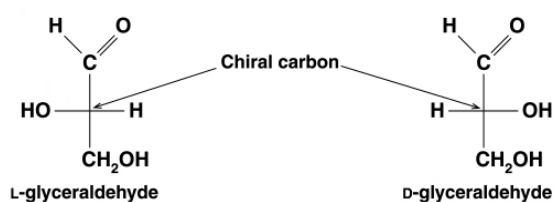


FIGURE 1: ERYTHROSE, AN ALDOTETROSE

2.6.3 KETOSES

Ketoses are monosaccharides with a ketone group with many hydroxyl (-OH) groups.

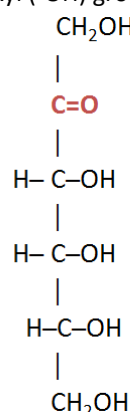


FIGURE 2: FRUCTOSE, A KETOHEXOSE

2.6.4 SOME IMPORTANT MONOSACCHARAIDES

No of Carbons	Category Name	Relevant examples
3	Triose	Glyceraldehyde, Dihydroxyacetone
4	Tetrose	Erythrose
5	Pentose	Ribose, Ribulose, Xylulose
6	Hexose	Glucose, Galactose, Mannose, Fructose
7	Heptose	Sedoheptulose
9	Nonose	Neuraminic acid, also called sialic acid

2.6.5 STRUCTURES OF MONOSACCHARAIDES

2.6.5.1 D AND L NOTATIONS

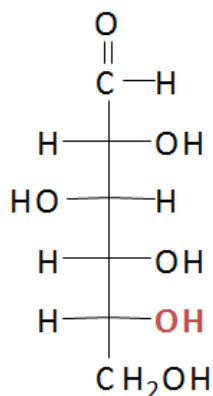
- In a Fischer projection, the -OH group on the chiral carbon *farthest from the carbonyl group* determines an L or D isomer.
- Left is assigned the letter L for the L-form.
- Right is assigned the letter D for the D-form.



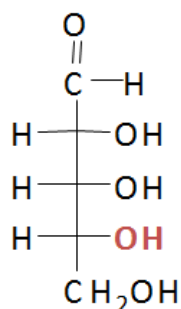
2.6.6 CHIRAL CARBON

An asymmetric **carbon** atom is a **carbon** atom that is attached to four different ... that cannot be superimposed on their own mirror image are said to be **chiral**.

2.6.7 EXAMPLES OF D AND L ISOMERS OF MONOSACCHARAIDES



D-glucose

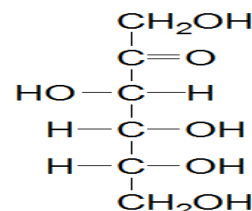


D-ribose

- D-glucose is found in fruits, corn syrup, and honey.
- An aldohexose with the formula $\text{C}_6\text{H}_{12}\text{O}_6$.
- Known as blood sugar in the body.
- The monosaccharide in polymers of starch, cellulose, and glycogen.

2.6.9 D-FRUCTOSE

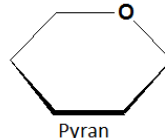
- D-fructose is a ketohexose $\text{C}_6\text{H}_{12}\text{O}_6$
- It is the sweetest carbohydrate
- It is found in fruit juices and honey
- Converts to glucose in the body



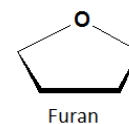
D-Fructose

2.6.10 CYCLIC STRUCTURES

Cyclic structures are the prevalent form of monosaccharaides with 5 or 6 carbon atoms.



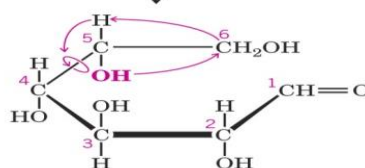
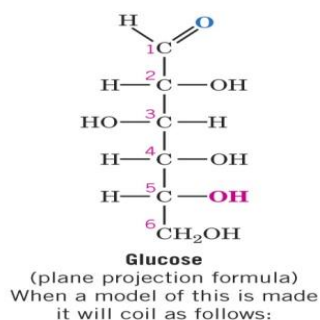
Pyran



Furan

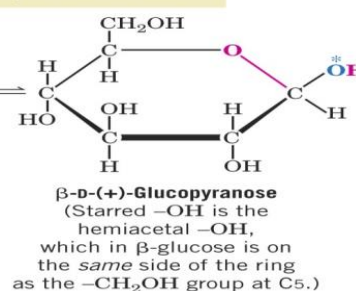
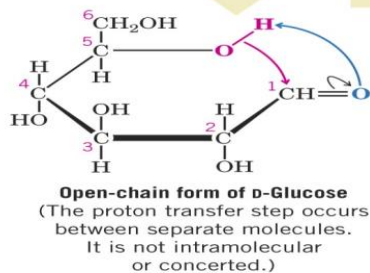
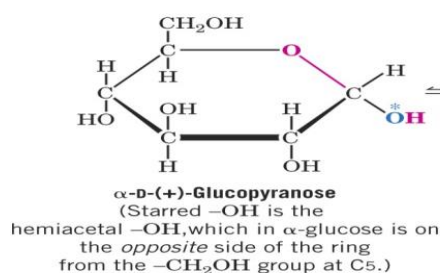
Cyclic structures form when the hydroxyl group on C-5 reacts with the aldehyde group or ketone group.

2.6.8 D-GLUCOSE



If the group attached to C4 is pivoted as the arrows indicate, we have the structure below.

This —OH group adds across the $\text{C}=\text{O}$ to close a ring of six atoms and make a cyclic hemiacetal.

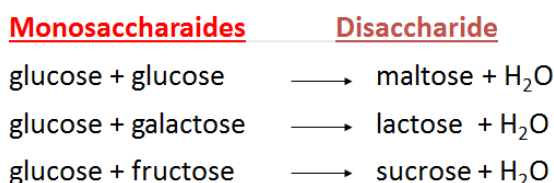


2.7 DISACCHARIDES

Disaccharide	Description	Component monosaccharides
sucrose	common table sugar	glucose 1 α →2fructose
maltose	product of starch hydrolysis	glucose 1 α →4 glucose
trehalose	found in fungi	glucose 1 α →1 glucose
lactose	main sugar in milk	galactose 1 β →4 glucose
melibiose	found in legumes	galactose 1 α →6 glucose

2.7.1 IMPORTANT DISACCHARIDES

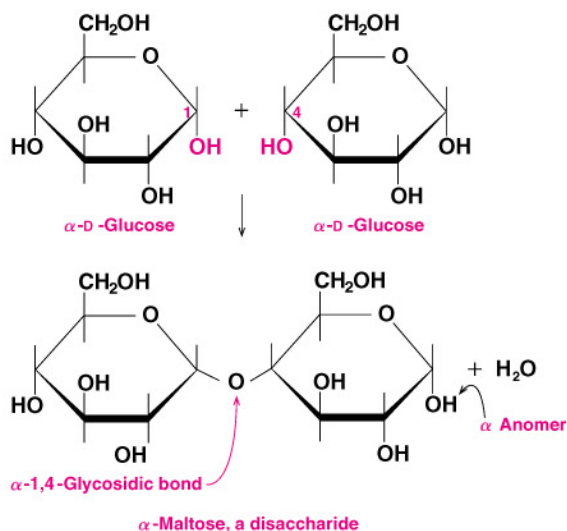
A disaccharide consists of two monosaccharides.



2.7.2 MALTOSE

- Maltose is a disaccharide also known as *malt sugar*.
- Composed of two D-glucose molecules
- Obtained from the hydrolysis of starch
- used in cereals, candies, and brewing
- found in both the α - and β -form

2.7.2.1 FORMATION OF MALTOSE

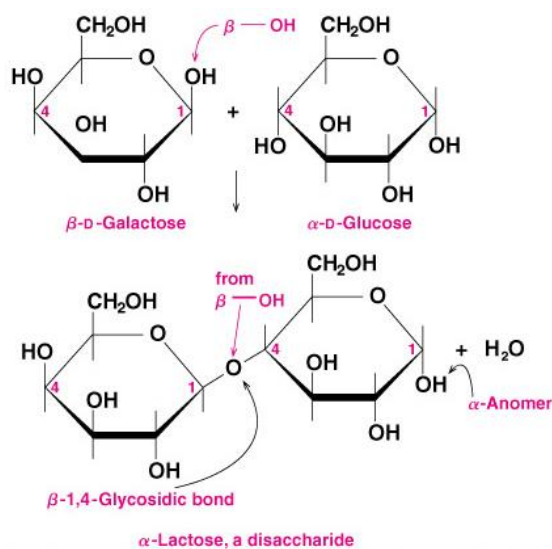


2.7.3 LACTOSE

- It is of interest because it is associated with lactose intolerance which is the intestinal distress caused by a deficiency of lactase, an

intestinal enzyme needed to absorb and digest lactose in milk.

- Undigested lactose ferments in the colon and causes abdominal pain, bloating, gas, and diarrhea.
- Yogurt does not cause these problems because lactose is consumed by the bacteria that transform milk into yogurt,
- It is a disaccharide of β -D-galactose and α - or β -D-glucose.
- Contains a β -1,4-glycosidic bond.
- It is found in milk and milk products.

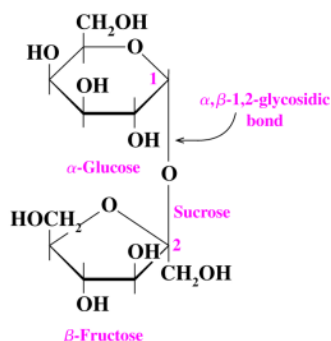


2.7.4 SUCROSE

- Sucrose or *table sugar*
- Sucrose, also called saccharose, is ordinary table sugar refined from sugar cane or sugar beets. It is the main ingredient in turbinado sugar, evaporated or dried cane juice, brown sugar, and confectioner's sugar
- It is obtained from sugar cane and sugar beets.
- Consists of α -D-glucose and β -D-fructose..
- It has an α , β -1,2-glycosidic bond.

2.7.5 TREHALOSE & CELLOBIOSE

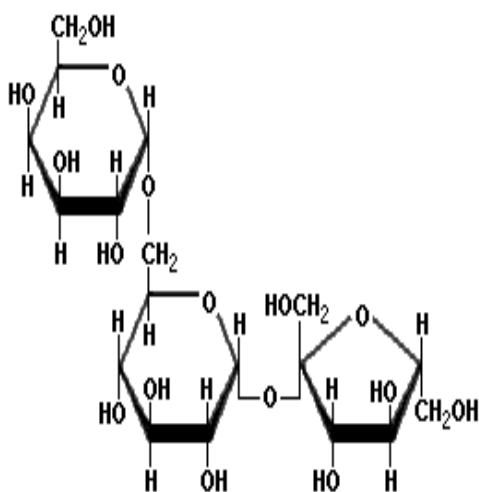
Trehalose has two α -D-glucose molecules connected through carbon number one in a $1\alpha \rightarrow 1$ linkage. Cellobiose is a disaccharide consisting of two β -D-glucose



molecules that have a $1\beta \rightarrow 4$ linkage as in cellulose. Cellobiose has no taste, whereas maltose and trehalose are about one-third as sweet as sucrose.

2.8 TRISACCHARIDES

Raffinose, also called melitose, is a trisaccharide that is widely found in legumes and cruciferous vegetables, including beans, peas, cabbage, brussels sprouts, and broccoli. It consists of galactose connected to sucrose via a $1\alpha \rightarrow 6$ glycosidic linkage.

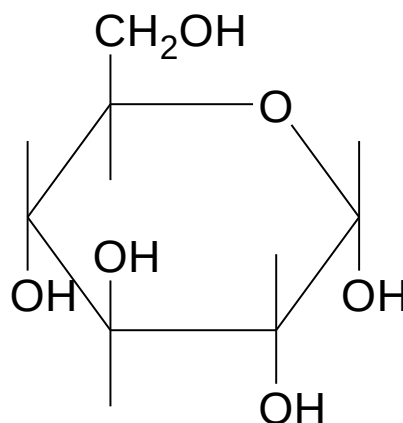


2.8.1 RAFFINOSE

Humans cannot digest saccharides with this linkage and the saccharides are fermented in the large intestine by gas-producing bacteria. Tablets containing the enzyme alpha-galactosidase, such as Beano, are frequently used as digestive aids to prevent gas and bloating. The enzyme is derived from selected strains of the food grade fungus *Aspergillus niger*.

2.9 POLYSACCHARIDES

- Polysaccharides are polymers of D-glucose.
- Include amylose and amylopectin, starches made of α -D-glucose.
- Include glycogen (animal starch in muscle), which is made of α -D-glucose.
- Include cellulose (plants and wood), which is made of β -D-glucose.

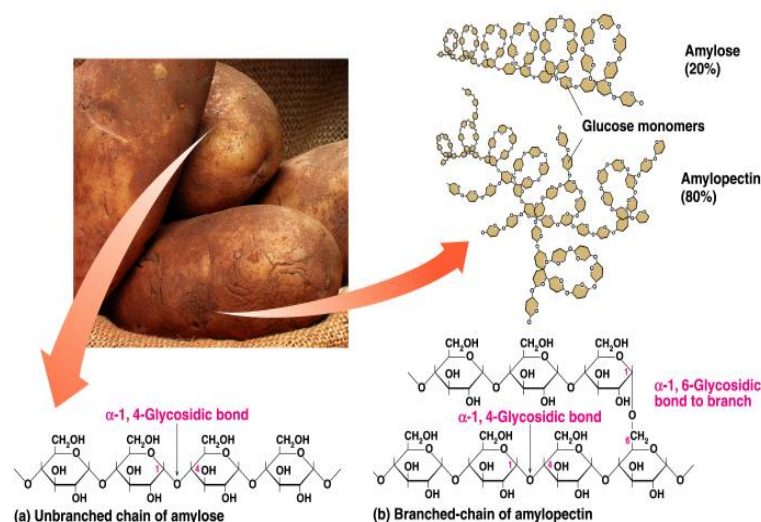


α -D-Glucose

2.9.1 POLYSACCHARIDES ARE POLYMERS OF SIMPLE SUGARS

Many polysaccharides, unlike sugars, are insoluble in water. Dietary fiber includes polysaccharides and oligosaccharides that are resistant to digestion and absorption in the human small intestine but which are completely or partially fermented by microorganisms in the large intestine. The polysaccharides described below play important roles in nutrition, biology, or food preparation.

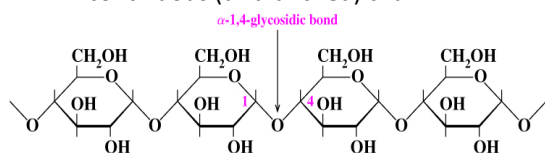
2.10 STRUCTURES OF AMYLOSE AND AMYLOPECTIN



Timberlake, General, Organic, and Biological Chemistry. Copyright © Pearson Education Inc., publishing as Benjamin Cummings

2.10.1.1 AMYLOSE

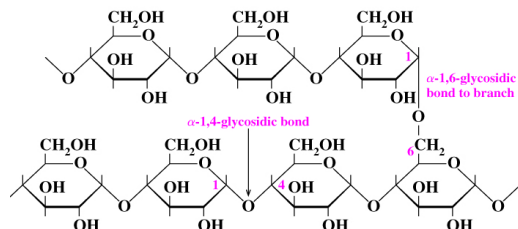
- Amylose molecules consist typically of 200 to 20,000 glucose units which form a helix as a result of the bond angles between the glucose units.
- Amylose is a polymer of α -D-glucose molecules.
- It is linked by α -1,4 glycosidic bonds.
- A continuous (unbranched) chain.



(a) Unbranched chain of amylose

2.10.1.2 AMYLOPECTIN

- Amylopectin differs from amylose in being highly branched. Short side chains of about 30 glucose units are attached with $1\alpha \rightarrow 6$ linkages approximately every twenty to thirty glucose units along the chain. Amylopectin molecules may contain up to two million glucose units.
- Amylopectin is a polymer of α -D-glucose molecules.
- It is a branched-chain polysaccharide.
- Has α -1,4-glycosidic bonds between the glucose units.
- It has α -1,6 bonds to branches.



Branched chain of amylopectin

2.10.2 DEXTRINS

- Starches like amylose and amylopectin hydrolyze to dextrins (smaller polysaccharides)
- Contain 3-8 glucose units
- Dextrins are a group of low-molecular-weight carbohydrates produced by the hydrolysis of starch. Dextrins are mixtures of polymers of D-glucose units linked by $1\alpha \rightarrow 4$ or $1\alpha \rightarrow 6$ glycosidic bonds

2.10.3 MALTODEXTRIN

Maltodextrin is partially hydrolyzed starch that is not sweet and has a DE value less than 20. Syrups, such as corn syrup made from corn starch, have DE values from 20 to 91. Commercial dextrose has DE values from 92 to 99

2.10.4 CORN SYRUP SOLIDS

Corn syrup solids, which may be labeled as soluble corn fiber or resistant maltodextrin, are mildly sweet semi-crystalline or powdery amorphous products with DEs from 20 to 36 made by drying corn syrup in a vacuum or in spray driers. Resistant maltodextrin or soluble corn fiber are not broken down in the digestive system, but they are partially fermented by colonic bacteria thus providing only 2 Calories per gram instead of the 4 Calories per gram in corn syrup

2.10.5 HIGH FRUCTOSE CORN SYRUP (HFCS)

High Fructose Corn Syrup (HFCS), commonly used to sweeten soft drinks, is made by treating corn syrup with enzymes to convert a portion of the glucose into fructose. Commercial HFCS contains from 42% to 55% fructose, with the remaining percentage being mainly glucose. There is an effort underway to rename High Fructose Corn Syrup as Corn Sugar because of the negative public perception that HFCS contributes to obesity.

2.10.6 STARCH

Starch is the major form of stored carbohydrate in plants. Starch is composed of a mixture of two substances: *amylose*, an essentially linear polysaccharide, and *amylopectin*, a highly branched polysaccharide. Both forms of starch are polymers of α -D-Glucose. Natural starches contain 10-20% amylose and 80-90% amylopectin. Amylose forms a colloidal dispersion in hot water (which helps to thicken gravies) whereas amylopectin is completely insoluble.

Starches are transformed into many commercial products by hydrolysis using acids or enzymes as catalysts.

Hydrolysis is a chemical reaction in which water is used to break long polysaccharide chains into smaller chains or into simple carbohydrates.

The resulting products are assigned a Dextrose Equivalent (DE) value which is related to the degree of hydrolysis. A DE value of 100 corresponds to completely hydrolyzed starch, which is pure glucose (dextrose).

2.10.7 MODIFIED STARCH

Modified starch is starch that has been changed by mechanical processes or chemical treatments to stabilize starch gels made with hot water. Without modification, gelled starch-water mixtures lose viscosity or become rubbery after a few hours

2.10.8 HYDROGENATED GLUCOSE SYRUP (HGS)

Hydrogenated glucose syrup (HGS) is produced by hydrolyzing starch, and then hydrogenating the resulting syrup to produce sugar alcohols like maltitol and sorbitol, along with hydrogenated oligo- and polysaccharides.

2.10.9 POLYDEXTROSE (POLY-D-GLUCOSE)

Polydextrose (poly-D-glucose) is a synthetic, highly-branched polymer with many types of glycosidic linkages created by heating dextrose with an acid catalyst and purifying the resulting water-soluble polymer. Polydextrose is used as a bulking agent because it is tasteless and is similar to fiber in terms of its resistance to digestion

2.10.10 RESISTANT STARCH

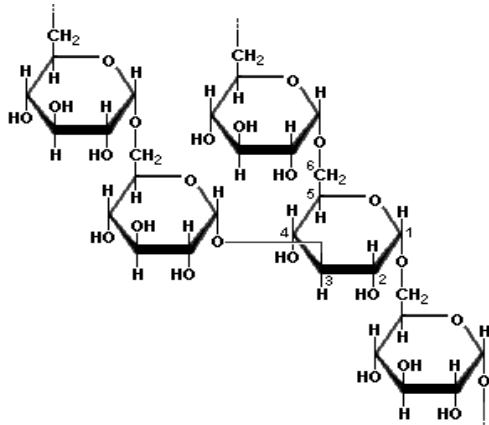
The name resistant starch is applied to dietary starch that is not degraded in the stomach and small intestine, but is fermented by microflora in the large intestine.

2.10.11 INVERT SUGAR

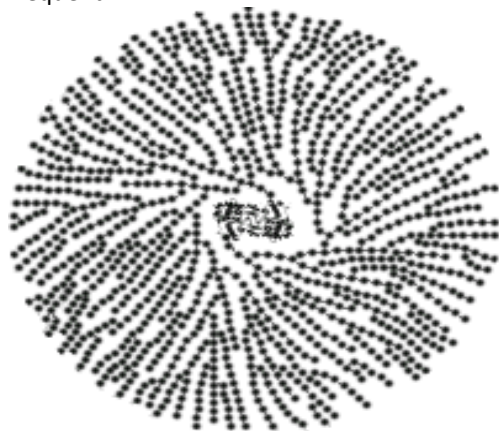
Invert sugar is a mixture of glucose and fructose, it is obtained by splitting sucrose into two components.

2.10.11.1 GLYCOGEN

Glucose is stored as glycogen in animal tissues by the process of glycogenesis. When glucose cannot be stored as glycogen or used immediately for energy, it is converted to fat. Glycogen is a polymer of α -D-Glucose



identical to amylopectin, but the branches in glycogen tend to be shorter (about 13 glucose units) and more frequent.



The glucose chains are organized globularly like branches of a tree originating from a pair of molecules of glycogenin, a protein with a molecular weight of 38,000 that acts as a primer at the core of the

structure. Glycogen is easily converted back to glucose to provide energy.

2.10.12 DEXTRAN

fructose	173
invert sugar*	120
HFCS (42% fructose)	120
sucrose	100
xylitol	100
tagatose	92
glucose	74
high-DE corn syrup	70
sorbitol	55
mannitol	50
trehalose	45
regular corn syrup	40
galactose	32
maltose	32
lactose	15

FIGURE 3: RELATIVE SWEETNESS OF VARIOUS CARBOHYDRATES

Dextran is a polysaccharide similar to amylopectin, but the main chains are formed by $1\alpha \rightarrow 6$ glycosidic linkages and the side branches are attached by $1\alpha \rightarrow 3$ or $1\alpha \rightarrow 4$ linkages. Dextran is an oral bacterial product that adheres to the teeth, creating a film called plaque. It is also used commercially in confections, in lacquers, as food additives, and as plasma volume expanders

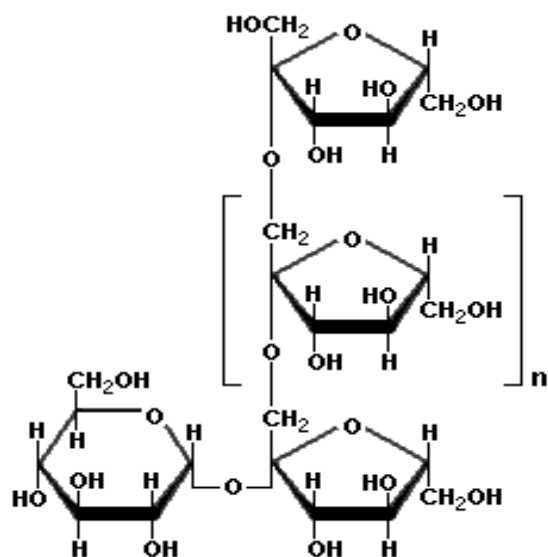
2.10.12.1 INULIN

Some plants store carbohydrates in the form of inulin as an alternative, or in addition, to starch

Inulins are present in many vegetables and fruits, including onions, leeks, garlic, bananas, asparagus, chicory, and Jerusalem artichokes.

Inulins, also called fructans, are polymers consisting of fructose units that typically have a terminal glucose



Inulin $n = \text{approx. } 35$

2.10.13 OLIGOFRUCTOSE & INULIN

Oligofructose has the same structure as inulin, but the chains consist of 10 or fewer fructose units. Oligofructose has approximately 30 to 50 percent of the sweetness of table sugar. Inulin is less soluble than oligofructose and has a smooth creamy texture that provides a fat-like mouthfeel. Inulin and oligofructose are nondigestible by human intestinal enzymes, but they are totally fermented by colonic microflora. The short-chain fatty acids and lactate produced by fermentation contribute 1.5 kcal per gram of inulin or oligofructose. Inulin and oligofructose are used to replace fat or sugar and reduce the calories of foods like ice cream, dairy products, confections and baked goods.

2.10.14 CELLULOSE

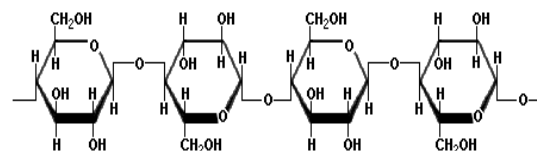
Cellulose is a polymer of β -D-Glucose, which in contrast to starch, is oriented with $-\text{CH}_2\text{OH}$ groups alternating above and below the plane of the cellulose molecule thus producing long, unbranched chains.

The absence of side chains allows cellulose molecules to lie close together and form rigid structures.

Cellulose is the major structural material of plants. Wood is largely cellulose, and cotton is almost pure cellulose.

Cellulose can be hydrolyzed to its constituent glucose units by microorganisms that inhabit the digestive tract of termites and ruminants.

Cellulose may be modified in the laboratory by treating it with nitric acid (HNO_3) to replace all the hydroxyl groups with nitrate groups ($-\text{ONO}_2$) to produce cellulose nitrate (nitrocellulose or guncotton) which is an explosive component of smokeless powder. Partially nitrated cellulose, known as pyroxylin, is used in the manufacture of collodion, plastics, lacquers, and nail polish.



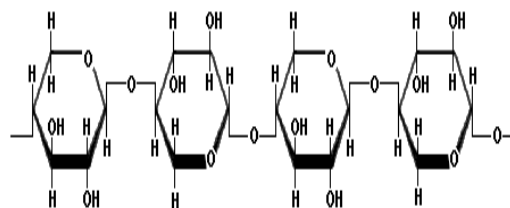
2.10.15 CELLULOSE GUM OR CARBOXYMETHYL CELLULOSE (CMC)

Cellulose Gum or Carboxymethyl Cellulose (CMC) is a chemical derivative of cellulose where some of the hydroxyl groups ($-\text{OH}$) are substituted with carboxymethyl groups ($-\text{CH}_2\text{COOH}$). The properties of cellulose gum depend on the degree of substitution and the length of the cellulose chains. The degree of substitution (DS) is the number of carboxymethyl groups per glucose unit and may vary in commercial products from 0.4 to 1.5. Cellulose gum is non-toxic and becomes very viscous when combined with water. It is used as a thickener for foods and as an emulsion stabilizer in products like ice cream. Cellulose gum is also used in personal lubricants, diet pills, water-based paints, detergents and paper coatings.

2.10.16 HEMICELLULOSE

The term "hemicellulose" is applied to the polysaccharide components of plant cell walls other than cellulose, or to polysaccharides in plant cell walls which are extractable by dilute alkaline solutions. Hemicelluloses comprise almost one-third of the carbohydrates in woody plant tissue. The chemical structure of hemicelluloses consists of long chains of a variety of pentoses, hexoses, and their corresponding uronic acids

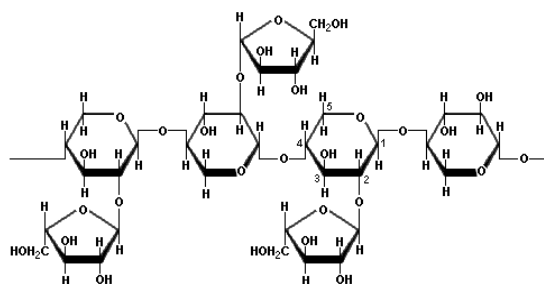
Hemicelluloses may be found in fruit, plant stems, and grain hulls. Although hemicelluloses are not digestible, they can be fermented by yeasts and bacteria. The polysaccharides yielding pentoses on hydrolysis are called pentosans. Xylan is an example of a pentosan consisting of D-xylose units with $1\beta \rightarrow 4$ linkages.



Xylan

2.10.17 ARABINOXYLAN

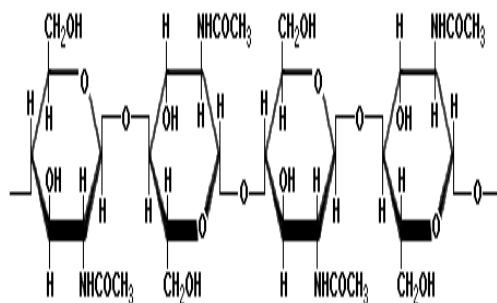
Arabinoxylans are polysaccharides found in the bran of grasses and grains such as wheat, rye, and barley



Arabinoxylans consist of a xylan backbone with L-arabinofuranose (L-arabinose in its 5-atom ring form) attached randomly by $1\alpha\rightarrow2$ and/or $1\alpha\rightarrow3$ linkages to the xylose units throughout the chain. Since xylose and arabinose are both pentoses, arabinoxylans are usually classified as pentosans. Arabinoxylans are important in the baking industry. The arabinose units bind water and produce viscous compounds that affect the consistency of dough, the retention of gas bubbles from fermentation in gluten-starch films, and the final texture of baked products.

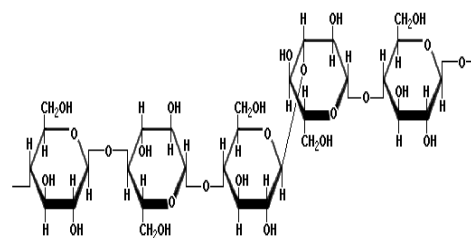
2.10.18 CHITIN

Chitin is an unbranched polymer of N-Acetyl-D-glucosamine. It is found in fungi and is the principal component of arthropod and lower animal exoskeletons, e.g., insect, crab, and shrimp shells. It may be regarded as a derivative of cellulose, in which the hydroxyl groups of the second carbon of each glucose unit have been replaced with acetamido ($-\text{NH}(\text{C}=\text{O})\text{CH}_3$) groups.



2.10.18.1 BETA-GLUCAN

Beta-glucans consist of linear unbranched polysaccharides of β -D-Glucose like cellulose, but with one $1\beta\rightarrow3$ linkage for every three or four $1\beta\rightarrow4$ linkages. Beta-glucans form long cylindrical molecules containing up to about 250,000 glucose units. Beta-glucans occur in the bran of grains such as barley and oats, and they are recognized as being beneficial for reducing heart disease by lowering cholesterol and reducing the glycemic response. They are used commercially to modify food texture and as fat substitutes.



2.10.19 GLYCOSAMINOGLYCANS

Glycosaminoglycans are found in the lubricating fluid of the joints and as components of cartilage, synovial fluid, vitreous humor, bone, and heart valves.

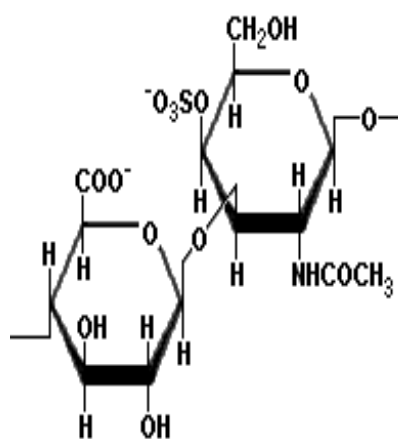
Glycosaminoglycans are long unbranched polysaccharides containing repeating disaccharide units that contain either of two amino sugar compounds -- N-acetylgalactosamine or N-acetylglucosamine, and a uronic acid such as glucuronate (glucose where carbon six forms a carboxyl group).

Glycosaminoglycans are negatively charged, highly viscous molecules sometimes called *mucopolysaccharides*.

The physiologically most important glycosaminoglycans are hyaluronic acid, dermatan sulfate, chondroitin sulfate, heparin, heparan sulfate, and keratan sulfate.

2.10.20 CHONDROITIN SULFATE

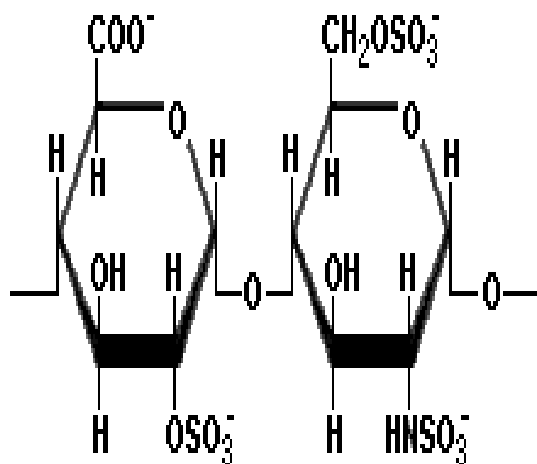
Chondroitin sulfate is composed of β -D-glucuronate linked to the third carbon of N-acetylgalactosamine-4-sulfate as illustrated here. It is used for solving joints problems.



2.10.20.1 HEPARIN

Heparin is a complex mixture of linear polysaccharides that have anticoagulant properties and vary in the degree of sulfation of the saccharide units. Heparin is used as anti-coagulant.

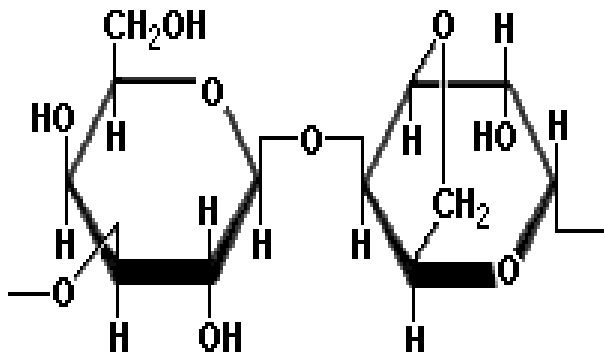




2.10.20.2 AGAR

Agar (agar agar) is extracted from seaweed and is used in many foods as a gelling agent. Agar is a polymer of agarobiose, a disaccharide composed of D-galactose and 3,6-anhydro-L-galactose. Highly refined agar is used as a medium for culturing bacteria, cellular tissues, and for DNA fingerprinting. Agar is used as an ingredient in desserts in Japan and other Asian countries. The gels produced with agar have a crispier texture than the desserts made with animal gelatin.

Agarobiose is the repeating disaccharide unit in agar



2.10.21 CARRAGEENAN

Carrageenan is a generic term for several polysaccharides also extracted from seaweed. Carrageenan compounds differ from agar in that they have sulfate groups ($-\text{OSO}_3^-$) in place of some hydroxyl groups. Carrageenan is also used for thickening, suspending, and gelling food products.

2.10.22 ALGINIC ACID/ ALGINATES

Alginate is extracted from seaweeds, such as giant kelp (*Macrocystis pyrifera*).

The chemical constituents of alginate are random sequences of chains of β -D-mannuronic and α -L-guluronic acids attached with 1 $\rightarrow$ 4 linkages.

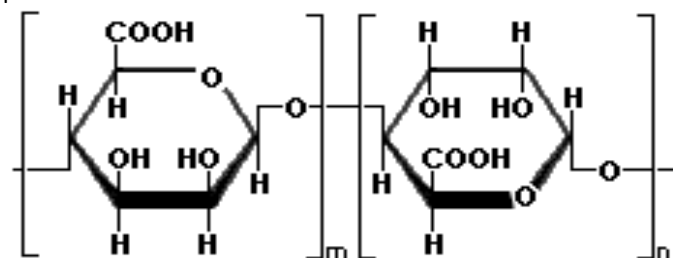
Alginates are insoluble in water, but absorb water readily. They are useful as gelling and thickening agents.

Alginates are used in the manufacture of textiles, paper, and cosmetics.

The sodium salt of alginic acid, sodium alginate, is used in the food industry to increase viscosity and as an emulsifier.

Alginates are found in food products such as ice cream and in slimming aids where they serve as appetite suppressants.

In dentistry, alginates are used to make dental impressions



2.11 PHYSICAL PROPERTIES OF SOME CARBOHYDRATES

2.11.1 GLUCOSE

Formula	$\text{C}_6\text{H}_{12}\text{O}_6$
Formula Mass	180.16 g/mol
Physical Appearance	White crystalline powder
Melting Point	150-152 °C
Density	1.54 g/cm ³ (30 °C)
Solubility in Water	Soluble
Uses	Preparation of products such as High Fructose Syrups, Gibberellic acid D-Ribose, Mannitol, Vitamin C. Use as energy source by body

2.11.2 FRUCTOSE

Formula	$\text{C}_6\text{H}_{12}\text{O}_6$
Formula Mass	180.16 g/mol
Physical Appearance	White Crystalline Solid
Melting Point	119-122 °C
Density	1.59 g/cm ³
Solubility in Water	Soluble
Uses	Preparation of honey, High Fructose Syrups, Aroma, Sucrose etc. Gives fruit a sweet taste To increase Shelf Life as a sweetener

2.11.3 GALACTOSE

Formula	$\text{C}_6\text{H}_{12}\text{O}_6$
Formula Mass	180.16 g/mol
Physical Appearance	White powder
Melting Point	168-170 °C

Density	1.5 g/cm ³		peritoneal dialysis
Solubility in Water	Soluble less than glucose		Grains contain high levels of raffinose
Uses	as a basic food and drink ingredient, energy drinks acceleration of senescence (aging)		
2.11.4 MALTOSE		2.11.8 STARCH	
Formula	C ₁₂ H ₂₄ O ₁₂	Formula	(C ₆ H ₁₀ O ₅) _n
Formula Mass	360.31 g/mol	Physical Appearance	white fine crystalline powder
Physical Appearance	White crystalline powder	Melting Point	256-258°C
Melting Point	119-121 °C	Density	1.5 g/cm ³
Density	1.54 g/cm ³	Solubility in Water	Not soluble
Solubility in Water	Soluble less than glucose	Uses	Preparation of Cationic starch, D-Sorbitol, Glucose syrup, dried Spiramycin, Gibberellic acid & L-Lactic acid etc. Used as thickeners and stabilizers in foods such as puddings Used in Ironing Dress Shirts Store energy in plants
Uses	A disaccharide commonly found in foods and commonly utilized in brewing processes. Preparation of Liquid glucose, IMP.		
2.11.5 LACTOSE		2.11.9 GLYCOGEN	
Formula	C ₁₂ H ₂₂ O ₁₁	Formula	(C ₆ H ₁₀ O ₅) _n
Formula Mass	342.3 g/mol	Physical Appearance	White to off-white powder
Physical Appearance	white crystals or powder	Melting Point	270-280 °C
Melting Point	222.8°C	Density	1.83 g/cm ³
Density	1.52 g/cm ³	Solubility in Water	Soluble but not clear solution
Solubility in Water	Soluble	Uses	Preparation of ribonucleic acid for injection Store energy in animals
Uses	Preparation of Abamectin, Lactulose & Pepsin etc. Present in Milk		
2.11.6 SUCROSE			
Formula	C ₁₂ H ₂₂ O ₁₁		
Formula Mass	342.3 g/mol		
Physical Appearance	White crystalline powder		
Melting Point	185-187 °C		
Density	1.59 g/cm ³		
Solubility in Water	Soluble		
Uses	Yuanzhen sugar is a polysaccharide polymer, containing a certain amount of fructooligosaccharides. Preparation of D-Sorbitol, Invertose & lactic acid etc.		
2.11.7 RAFFINOSE			
Formula	C ₁₈ H ₃₂ O ₁₆		
Formula Mass	504.44 g/mol		
Physical Appearance	white powder or crystals		
Melting Point	81°C		
Density	1.81 g/cm ³		
Solubility in Water	Soluble		
Uses	Preparation of Lactic acid, Sucralose as an osmotic agent for		



Chapter 3 LIPIDS

3.1 LIPID

The lipids are a large and heterogeneous group of substances of biological origin that are easily dissolved in organic solvents such as methanol, acetone, chloroform, and benzene. By contrast, they are either insoluble or only poorly soluble in water. Their low water solubility is due to a lack of polarizing atoms such as O, N, S, and P.

3.2 CLASSIFICATION OF LIPIDS

Lipids can be classified into substances that are either
Hydrolysable - able to undergo hydrolytic cleavage
e.g. ester and phospholipid

Non-hydrolysable - able to undergo hydrolytic cleavage
e.g. alkanes and carotenoids

3.3 IMPORTANCE OF LIPIDS

3.3.1 FUEL

Lipids are an important source of energy in the diet. In quantitative terms, they represent the principal energy reserve in animals. Neutral fats in particular are stored in specialized cells, known as adipocytes. Fatty acids are released from these again as needed, and these are then oxidized in the mitochondria to form water and carbon dioxide, with oxygen being

consumed. This process also gives rise to reduced coenzymes, which are used for ATP production in the respiratory chain.

3.3.2 NUTRIENTS

Amphipathic lipids are used by cells to build membranes. Typical membrane lipids include phospholipids, glycolipids, and cholesterol. Fats are only weakly amphiphilic and are therefore not suitable as membrane components.

3.3.3 INSULATION

Lipids are excellent insulators. In the higher animals, neutral fats are found in the subcutaneous tissue and around various organs, where they serve as mechanical and thermal insulators. As the principal constituent of cell membranes, lipids also insulate cells from their environment mechanically and electrically. The impermeability of lipid membranes to ions allows the formation of the membrane potential

3.3.4 SPECIAL TASKS

Some lipids have adopted special roles in the body. Steroids, eicosanoids, and some metabolites of phospholipids have signaling functions. They serve as hormones, mediators, and second messengers. Other lipids form anchors to attach proteins to membranes. The lipids also produce cofactors for enzymatic reactions—e. g., vitamin K and ubiquinone. The carotenoid retinal, a light-sensitive lipid, is of central importance in the process of vision.



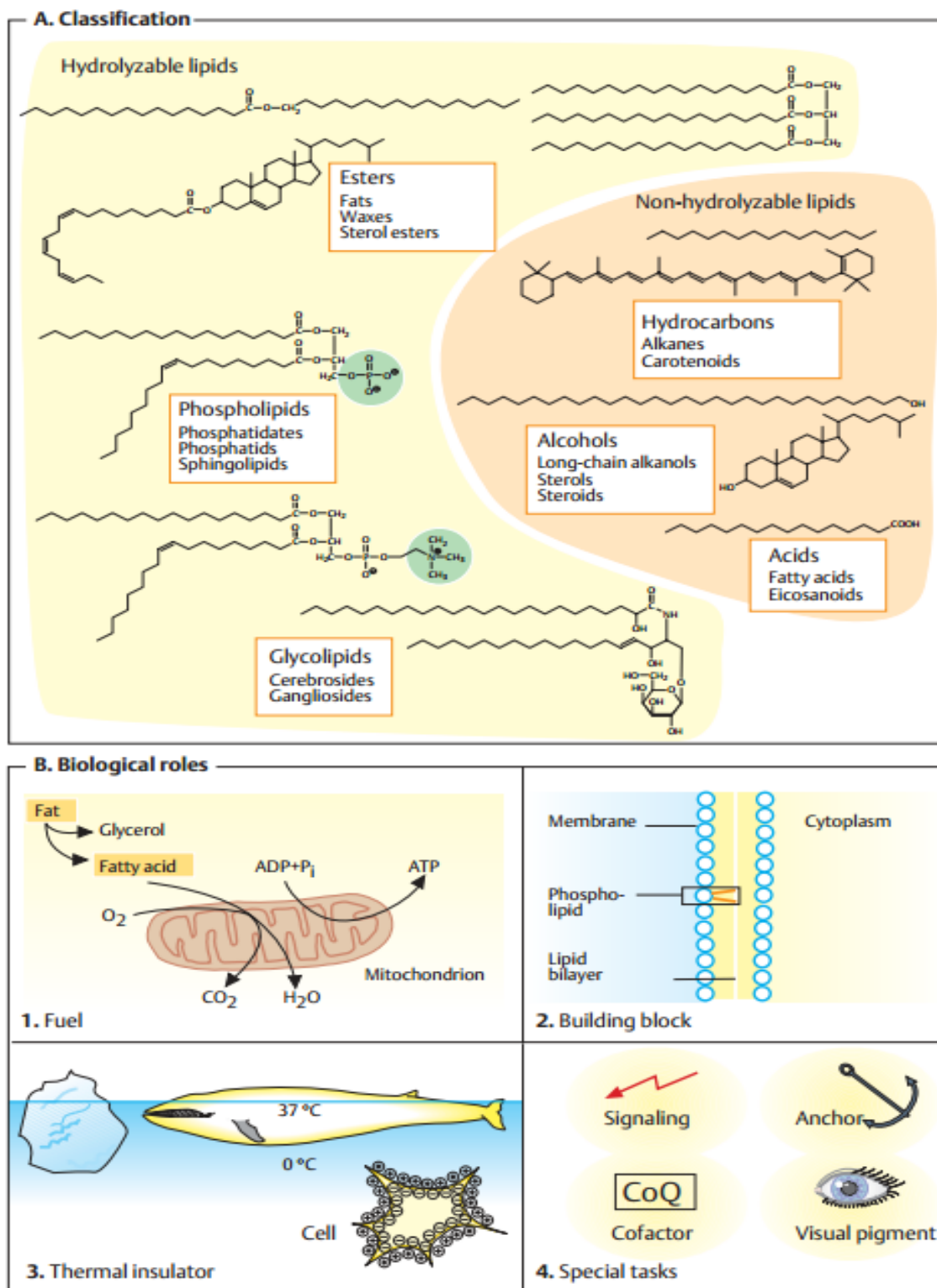


FIGURE 4: CLASSIFICATION AND IMPORTANCE OF LIPIDS

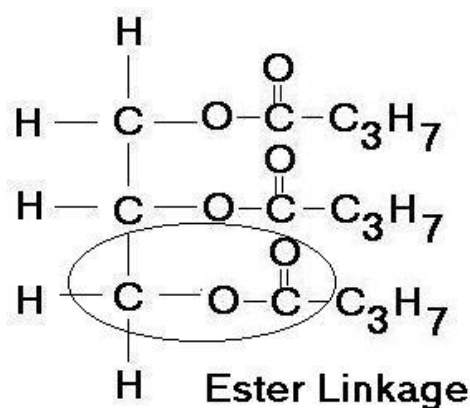
3.4 CARBOXYLIC ACID

Carboxylic is an organic acid characterized by the presence of at least one carboxyl group.

3.5 ESTER BOND

Ester bonds are formed by the reaction of an acid and alcohol. In biological molecules you find ester bonds in lipids where the carboxyl group of a fatty acid reacts with the hydroxyl group of triglycerol.





3.6 PHOSPHOLIPIDS

Phospholipids are a class of lipids that are a major component of all cell membranes as they can form lipid bilayers. Most phospholipids contain a diglyceride, a phosphate group, and a simple organic molecule such as choline; one exception to this rule is sphingomyelin, which is derived from sphingosine instead of glycerol.

3.7 GLYCOLIPIDS

Glycolipids are lipids with a carbohydrate attached. Their role is to provide energy and also serve as markers for cellular recognition.

3.8 FATTY ACIDS

In chemistry, and especially in biochemistry, a **fatty acid** is a carboxylic acid with a long aliphatic tail (chain), which is either saturated or unsaturated.

3.8.1.1 SATURATED FATTY ACIDS

If the carbon atoms in fat molecules have a single bond between them and as many hydrogen atoms as possible are bonded to the carbon atoms, then it is said to be saturated fat. E.g. Palmitic acid and stearic acid.

3.8.1.2 UNSATURATED FATTY ACID

The fat is unsaturated fat if the bond between the carbon atoms is a double bond and the molecule can absorb more hydrogen atoms. Or, in other words, unsaturated fat is a fat or fatty acid in which there are one or more double bonds in the fatty acid chain. E.g. Linoleic acid and Linolenic acid.

3.8.1.3 ESSENTIAL FATTY ACID

Essential fatty acids, or EFAs, are fatty acids that humans and other animals must ingest because the body requires them for good health but cannot synthesize themselves e.g. linoleic acid, linolenic acid and arachidonic acid.

3.8.1.4 NON – ESSENTIAL FATTY ACID

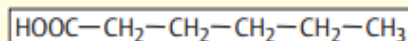
Non – Essential fatty acid include those fatty acid which body can synthesize itself. E.g. Palmitic acid is the first fatty acid synthesized in our body.

3.8.2 IMPORTANT CARBOXYLIC ACID



A. Carboxylic acids

Name	Number of carbons	Number of double bonds	Position of double bonds
Formic acid	1:0	0	
Acetic acid	2:0	0	
Propionic acid	3:0	0	
Butyric acid	4:0	0	
Valerianic acid	5:0	0	
Caproic acid	6:0	0	
Caprylic acid	8:0	0	
Capric acid	10:0	0	
Lauric acid	12:0	0	
Myristic acid	14:0	0	
Palmitic acid	16:0	0	
Stearic acid	18:0	0	
Oleic acid	18:1; 9	1	
Linoleic acid	18:2; 9,12	2	
Linolenic acid	18:3; 9,12,15	3	
Arachidic acid	20:0	0	
Arachidonic acid	20:4; 5,8,11,14	4	
Behenic acid	22:0	0	
Erucic acid	22:1; 13	1	
Lignoceric acid	24:0	0	
Nervonic acid	24:1; 15	1	

Not contained
in lipids

Caproic acid

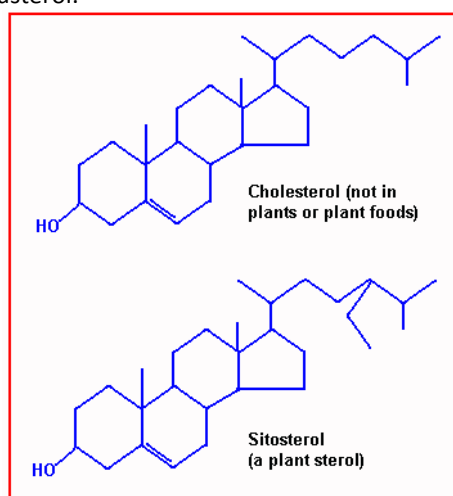
 Essential in human nutrition
3.9 STRUCTURE OF FATS, PHOSPHOLIPIDS
AND GLYCOLIPIDS

3.11 STEROID

A **steroid** is a type of organic compound that contains a characteristic arrangement of four cycloalkane rings that are joined to each other.

3.12 STEROLS

Sterols, also known as steroid alcohols, are a subgroup of the steroids and an important class of organic molecules. They occur naturally in plants, animals, and fungi, with the most familiar type of animal sterol being cholesterol. Cholesterol is vital to animal cell membrane structure and function and a precursor to fat-soluble vitamins and steroid hormones. Other example includes ergosterol, β -sitosterol, and stigmasterol.



3.13 BILE ACIDS

Bile acids are steroid acids found predominantly in the bile of mammals. Bile salts are bile acids compounded with a cation, usually sodium.

Cholic acid and chenodeoxycholic acid are primary bile acids that are formed by the liver. Their dehydroxylation at C-7 by microorganisms from the intestinal flora gives rise to the secondary bile acids lithocholic acid and deoxycholic acid.

3.14 STEROID HORMONES

A **steroid hormone** (abbreviated as sterone) is a steroid that acts as a hormone. Humans have six steroid hormones: progesterone, cortisol, aldosterone, testosterone, estradiol, and calcitriol.



Chapter 4 AMINO ACID

Amino acids are the product form by the carboxylic group and amino group attach to the same carbon.

4.1 FUNCTION OF AMINO ACID

- Components of peptides and proteins - Only the 20 proteinogenic amino acid are included in the genetic code and therefore regularly found in proteins.
- Amino acids or their derivatives are also form components of lipids—e. g., serine in phospholipids and glycine in bile salt
- Amino acids function as neurotransmitters themselves
- Specific amino acids form precursors for other metabolites—e. g., for glucose in gluconeogenesis, for purine and pyrimidine bases, for heme, and for other molecules.

4.2 OPTICAL ACTIVITY

The natural amino acids are mainly α -amino acids, in contrast to β -amino acids such as β -alanine and taurine. Most α -amino acids have four different substituents at C-2 (C_α). The α atom therefore represents a chiral center—i. e., there are two different enantiomers (L- and D-amino acids). Among the proteinogenic amino acids, only glycine is not chiral ($R=H$). In nature, it is almost exclusively L-amino acids that are found. D-Amino acids occur in bacteria—e. g., in murein—and in peptide antibiotics.

4.3 DISSOCIATION CURVE OF HISTIDINE

All amino acids have at least two ionizable groups, and their net charge therefore depends on the pH value. The COOH groups at the α -C atom have pK values of between 1.8 and 2.8 and are therefore more acidic than simple monocarboxylic acids. The basicity of the α -amino function also varies, with pK values of between 8.8 and 10.6, depending on the amino acid. Acidic and basic amino acids have additional ionizable groups in their side chain.

Histidine can be used here as an example of the pH-dependence of the net charge of an amino acid. In addition to the carboxyl group and the amino group at the α -C atom with pK values of 1.8 and 9.2, respectively, histidine also has an imidazole residue in its side chain with a pK value of 6.0. As the pH increases, the net charge (the sum of the positive and negative charges) therefore changes from +2 to -1. At pH 7.6, the net charge is zero, even though the molecule contains two almost completely ionized groups in these conditions. This pH value is called the isoelectric point. At its isoelectric point, histidine is said to be zwitterionic, as it has both anionic and cationic properties. Most other amino acids are also zwitterionic at neutral pH.

4.4 PROTEINOGENIC AMINO ACID

The amino acids that are included in the genetic code are described as proteinogenic. There are 20 proteinogenic amino acids.

4.4.1 CLASSIFICATION OF PROTEINOGENIC AMINO ACID



Aliphatic					Sulfur-containing	
Glycine (Gly, G)	Alanine (Ala, A)	Valine (Val, V) ☆	Leucine (Leu, L) ☆	Isoleucine (Ile, I) ☆	Cysteine (Cys, C)	Methionine (Met, M) ☆
H	CH_3	$\text{H}_3\text{C}-\text{CH}-\text{CH}_3$	$\text{H}_3\text{C}-\text{CH}-\text{CH}_2-\text{CH}_3$	$\text{H}_3\text{C}-\text{CH}-\text{CH}_2-\text{CH}_3$	CH_2-SH pK _a value 8.3	$\text{CH}_2-\text{CH}_2-\text{S}-\text{CH}_3$
-2.4	-1.9	-2.0	-2.3	-2.2	-1.2	-1.5
Aromatic			Cyclic		Neutral	
Phenylalanine (Phe, F) ☆	Tyrosine (Tyr, Y)	Tryptophan (Trp, W) ☆	Proline (Pro, P)	Serine (Ser, S)	Threonine (Thr, T) ☆	
$\text{CH}_2-\text{C}_6\text{H}_5$	$\text{CH}_2-\text{C}_6\text{H}_4-\text{OH}$ 10.1	$\text{CH}_2-\text{Indole ring}$	COO^- Pyrrolidine ring	CH_2-OH	$\text{H}_3\text{C}-\text{CH}-\text{OH}$	
+0.8	+6.1	+5.9	+6.0	+5.1	+4.9	
☆ Essential amino acids						□ Chiral center
Neutral		Acidic		Basic		
Asparagine (Asn, N)	Glutamine (Gln, Q)	Aspartic acid (Asp, D)	Glutamic acid (Glu, E)	Histidine (His, H)	Lysine (Lys, K) ☆	Arginine (Arg, R)
$\text{CH}_2-\text{CONH}_2$	$\text{CH}_2-\text{CH}_2-\text{CONH}_2$	CH_2-COO^- 4.0	$\text{CH}_2-\text{CH}_2-\text{COO}^-$ 4.3	$\text{CH}_2-\text{Imidazole ring}$ 6.0	$\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{NH}_3^+$ 10.8	$\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{NH}-\text{C}(\text{NH}_2)_2$ 12.5
+9.7	+9.4	+11.0	+10.2	+10.3	+15.0	+20.0

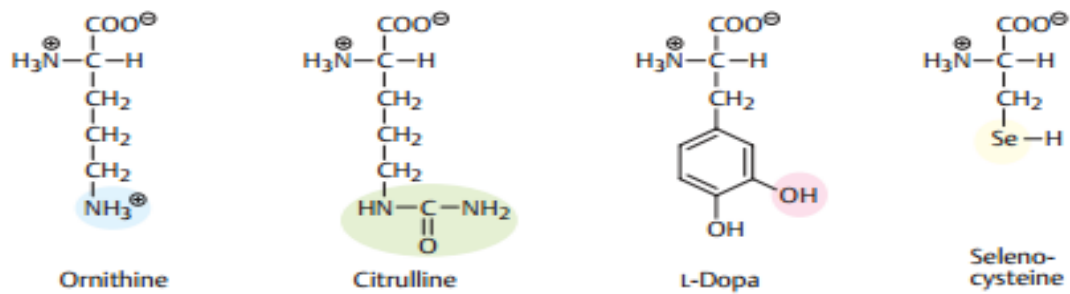
In addition to the 20 proteinogenic amino acids, there are also many more compounds of the same type in nature known as non – proteinogenic amino acid.

4.5 NON – PROTEINOGENIC AMINO ACID

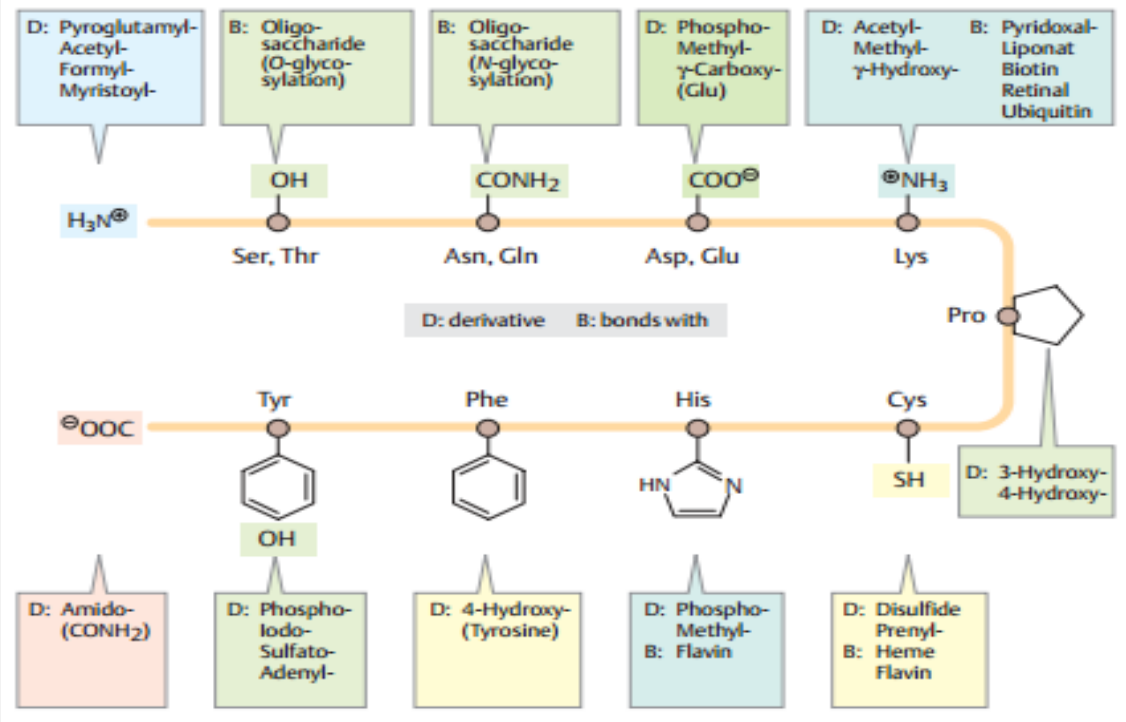
4.5.1 CLASSIFICATION OF NON- PROTEINOGENIC AMINO ACID



A. Rare amino acids



B. Post-translational protein modification



C. Biogenic amines

Amino acid	Amine	Function	Amino acid	Amine	Function
Serine	Ethanol-amine	Glutamate	Glutamate	γ -Amino-butyrate	Neurotransmitter (GABA)
Cysteine	Cysteamine	Component of coenzyme A	Histidine	Histamine	Mediator, neurotransmitter
Threonine	Amino-propanol	Component of vitamin B ₁₂	Dopa	Dopamine	Neurotransmitter
Aspartate	β -Alanine	Component of coenzyme A	5-Hydroxy-tryptophan	Serotonin	Mediator, neurotransmitter



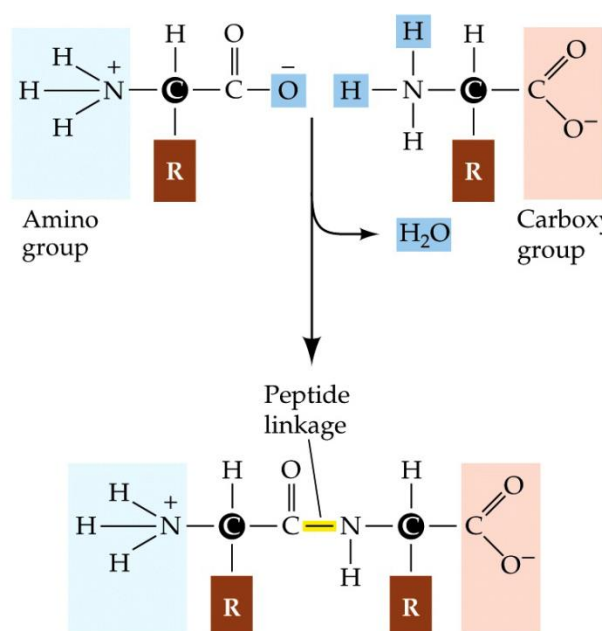
Chapter 5 PROTEINS

5.1 PROTEIN

Proteins are large biological molecules consisting of one or more chains of amino acids.

5.2 PEPTIDE BOND

A peptide bond (amide bond) is a covalent chemical bond formed between two molecules when the carboxyl group of one molecule reacts with the amino group of the other molecule, causing the release of a molecule of water (H_2O), hence the process is a dehydration synthesis reaction (also known as a condensation reaction), and usually occurs between amino acids.



5.3 FUNCTION OF PROTEIN

5.3.1 ESTABLISHMENT AND MAINTENANCE OF STRUCTURE

Structural proteins are responsible for the shape and stability of cells and tissues. Histones are also structural proteins. They organize the arrangement of DNA in chromatin. The basic components of chromatin, the nucleosomes consist of an octameric complex of histones, around which the DNA is coiled.

5.3.2 TRANSPORT

A well-known transport protein is hemoglobin in the erythrocytes. It is responsible for the transport of oxygen and carbon dioxide between the lungs and tissues. The blood plasma also contains many other

proteins with transport functions. Prealbumin, for example, transports the thyroid hormones thyroxine and triiodothyronine. Ion channels and other integral membrane proteins facilitate the transport of ions and metabolites across biological membranes.

5.3.3 PROTECTION AND DEFENSE

The immune system protects the body from pathogens and foreign substances. An important component of this system is immunoglobulin G.

5.3.4 CONTROL AND REGULATION

In biochemical signal chains, proteins function as signaling substances (hormones) and as hormone receptors. The small peptide hormone insulin is an example. DNA-binding proteins are decisively involved in regulating the metabolism and in differentiation processes. The structure and function of the catabolite activator protein and similar bacterial transcription factors have been particularly well investigated.

5.3.5 CATALYSIS

Enzymes, with more than 2000 known representatives, are the largest group of proteins in terms of numbers. The smallest enzymes have molecular masses of 10–15 kDa. Intermediate sized enzymes, such as alcohol dehydrogenase are around 100–200 kDa, and the largest— including glutamine synthetase with its 12 monomers can reach more than 500 kDa

5.3.6 MOVEMENT

The interaction between actin and myosin is responsible for muscle contraction and cell movement. Myosin with a length of over 150 nm, is among the largest proteins. Actin filaments (F-actin) arise due to the polymerization of relatively small protein subunits (G-actin). Along with other proteins, tropomyosin, which is associated with F-actin, controls contraction.

5.3.7 STORAGE

Plants contain special storage proteins, which are also important for human nutrition. In animals, muscle proteins constitute a nutrient reserve that can be mobilized in emergencies.

5.4 STRUCTURE OF PROTEIN

A protein function depends upon on its specific conformation. The primary structure of a protein is determined by the gene corresponding to the protein. In molecular biology protein structure describes the various levels of organization of protein molecules, which includes:-

- Primary structure
- Secondary structure
- Tertiary structure
- Quaternary structure

5.4.1 PRIMARY STRUCTURE



The primary structure of protein is the unique sequence of amino acids.

5.4.2 SECONDARY STRUCTURE

The secondary structure of protein results from hydrogen bond at regular intervals along the polypeptide backbone.

The typical shapes that develop from secondary structure are:-

1. An Alpha Helix (Coil)
2. Beta Pleated Sheet (Fold)

5.4.3 TERTIARY STRUCTURE

Tertiary structure refers to three-dimensional structure of a single protein molecule. The tertiary structure of protein results from varieties of attraction between the R groups or between the R group and the polypeptide backbone. The interactions includes

1. Hydrogen Bonds (among polar areas)
2. Ionic Bonds (among charged R – group)
3. Hydrophobic interactions (among hydrophobic R-group)
4. Van Der Waals Interactions (among hydrophobic R-group)
5. Disulfide bridges (Strong covalent bond that form between sulfhydryl groups (SH) of cysteine monomers, stabilize the structure)

5.4.4 QUATERNARY STRUCTURE

Quaternary structure results from the aggregation of two or more polypeptide subunits. The quaternary structure is stabilized by the same non-covalent interactions and disulfide bonds as the tertiary structure.

5.5 EXAMPLE:-

5.5.1 HEMOGLOBIN

The protein hemoglobin is made up (primarily) of 4 polypeptides. Typically, when a protein is made up of multiple polypeptides, each polypeptide is simply called a protein subunit. However, in the case of hemoglobin, the subunits are each called globin. The 4 globins are of two types. 2 of them with identical amino acid sequences (primary structure) are called alpha-globins (a-globins), while the other 2 also have identical amino acid sequences and are called beta-globins (b-globins). Every hemoglobin molecule contains 2 a-globins and 2 b-globins. Each of the globins is folded into a secondary and tertiary structure. Then, all four are put together into the hemoglobin molecule's quaternary structure.

5.5.2 INSULIN

Insulin is composed of two peptide chains referred to as the A chain and B chain. A and B chains are linked together by two disulfide bonds, and an additional disulfide is formed within the A chain. In most species,

the A chain consists of 21 amino acids and the B chain of 30 amino acids. It is a dimer of an A-chain and a B-chain, which are linked together by disulfide bonds.

5.5.3 ALBUMIN

The general structure of albumin is characterized by several long α (alpha) helices, this allows it to maintain a relatively static shape, something essential for regulating blood pressure.

Serum albumin contains eleven distinct binding domains for hydrophobic compounds. One heme and six long-chain fatty acids can bind to serum albumin at the same time.

5.5.4 MYOGLOBIN (DOES NOT POSSESS QUATERNARY STRUCTURE)

Myoglobin consists of a single protein chain with 153 amino acids and one heme group that stores oxygen in the muscle cells. Myoglobin has a stronger affinity for oxygen than hemoglobin, which enables the oxygen to shift from one to the other.

5.5.5 GLOBULIN

It has helices and strands, 13 and 19 respectively. The major beta-sheets of globulin are named the A-sheet and the B-sheet. The 13 helices are each lettered beginning with letter A. The molecule has five cysteine residues but has no disulfide bonds; so sulfur is not responsible for holding together globulin structure.



Chapter 6 NUCLEIC ACID

6.1 BASICS

6.1.1 IMPORTANCE OF NUCLEIC ACID

Nucleic Acid in form of DNA and RNA helps in following:

- Synthesis of Protein
- As essential component of coenzymes
- Regulation of cell metabolism
- Gene Regulation
- Safeguard against mutation allowing some variations via semi-conservative type of replication.

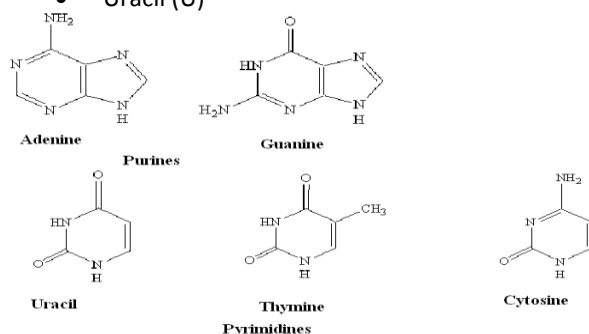
6.1.2 TYPE OF NITROGENOUS BASE

6.1.2.1 1. PURINE

- Adenine (A)
- Guanine (G)

6.1.2.2 2. PYRIMIDINE

- Cytosine (C)
- Thymine (T)
- Uracil (U)



6.1.3 TYPE OF SUGAR

There are two types of Sugar present in nucleoside

- Deoxyribose (present in DNA)
- Ribose (present in RNA)

6.1.4 NUCLEOTIDE

A compound consists of a nitrogenous base linked to a pentose sugar (via glycosidic linkage to anomeric carbon of sugar) which is further attach to phosphate (via ester bond to hydroxyl group of sugar)

6.1.5 NUCLEOSIDE

A compound composes of a nitrogenous base linked to pentose sugar.

6.1.5.1 TYPE OF NUCLEOSIDE

6.1.5.1.1 ADENOSINE

Deoxyribose sugar or Ribose Sugar which is attach to phosphate group by ester bond and Adenine (a nitrogenous base).

6.1.5.1.2 GUANOSINE

Deoxyribose sugar or Ribose Sugar which is attach to phosphate group by ester bond and Guanine (a nitrogenous base).

6.1.5.1.3 CYTIDINE

Deoxyribose sugar or Ribose Sugar which is attach to phosphate group by ester bond and Cytosine (a nitrogenous base).

6.1.5.1.4 THYMIDINE

Deoxyribose sugar which is attach to phosphate group by ester bond and Thymine (a nitrogenous base).

6.1.5.1.5 URIDINE

Ribose Sugar which is attach to phosphate group by ester bond and uracil (a nitrogenous base).

6.1.6 POLYNUCLEOTIDE

Polynucleotide consists of repeating units of nucleotides

6.2 DNA (DEOXYRIBONUCLEIC ACID)

DNA stands for Deoxyribonucleic Acid. DNA is the genetic material present in the cell. In case of Eukaryotes the DNA is present in the nucleus while some amount is present in mitochondria. It is double stand.

6.2.1 CHROMATIN

DNA is bound to a protein forming a complex called Chromatin.

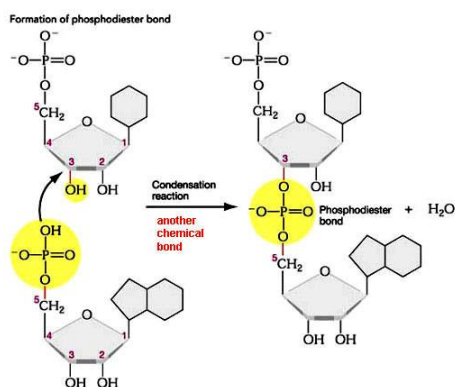
6.2.2 FORMS OF DNA

- B-form (Watson and Crick)
- A-form
- Z-form

6.2.3 PHOSPHODIESTER BOND

A phosphodiester bond is a group of strong covalent bonds between a phosphate group and two carbon ring carbohydrates by two ester bonds. It is chemical bond that holds together the polynucleotide chains of RNA and DNA by joining a specific carbon.





6.2.4 CHARGAFF'S RULE

By studying the hydolysates of DNA, Chargaff established the following facts:

- The sum of purine is equal to the sum of pyrimidine.
- The molar proportion of adenine is equal to that of thymine.
- The molar proportion of guanine equal to that of cytosine.

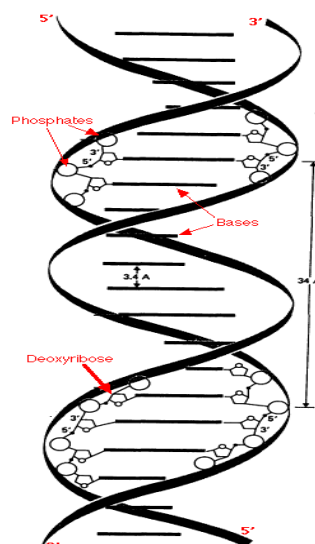
6.2.5 STRUCTURE OF DNA

6.2.5.1 PRIMARY STRUCTURE

- The polynucleotide strand forms the primary structure of DNA

6.2.5.2 SECONDARY STRUCTURE

- Two polynucleotide strands joined by hydrogen bonds between the bases to form the secondary structure.
- Adenine = Thymine (two hydrogen bond)
- Guanine ≡ Cytosine (three hydrogen bond)
- The base pairing of the two strands is complementary.
- The two polynucleotide strands are antiparallel to one another.
- The distance between two nucleotides is 11 Å.
- They are twisted to form double helix.
- The diameter of the helix is 20 Å.
- A single turn of helix is 34 Å.
- The helix has a major groove and minor groove.
- The number of base pair per turn in
 - A-form is 11
 - B-form is 10
 - Z-form is 12



6.2.5.3 TERTIARY STRUCTURE

- Tertiary structure of DNA includes supercoiling of double helix.
- **HISTONES** consisting of basic proteins (like arginine and lysine), which help in stabilization of DNA by forming salt bridges due to its acidic nature.
- **NUCLEOSOME**: The two molecule of each histone (H2A, H2B, H3 and H4) form a core around which 140 base pairs of DNA which is called nucleosome.
- **HISTONE H1**: It joins one nucleosome to the next is complex.

6.2.6 MELTING TEMPERATURE OF DNA

The temperature at which the half of the helical structure of DNA is lost is called melting temperature.

6.2.7 DENATURATION

Denaturation is the loss of helical structure.

6.2.8 RENATURATION

The process of reformation of double helix of DNA strand is called renaturation.

6.2.9 GENETIC CODE

6.2.10 Genetic Code: GENETIC CODE IS A

DICTIONARY OF CODONS THAT SPECIFIES ALL THE AMINO ACIDS FOUND IN PROTEINS.

CODON: A codon is a sequence of three bases in mRNA that codes for a particular amino acid.

ANTI-CODON: the sequence of three bases present on t-RNA that is complementary to codon.

STOP CODON: Out of 64 codons, three are used to termination protein synthesis and is called stop codon i.e. UAA, UAG and UGA.



START CODON: Reading of codon begins from start i.e. AUG (methionine) from 5' to 3' end of mRNA.

	U	C	A	G	
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

GENETIC CODE

6.2.11 CHARACTERISTIC OF GENETIC CODON

6.2.11.1 DEGENERATE

The code is degenerate or redundant which means that many amino acids can be coded by more than one codon e.g. Arginine is specified by six different codons. The codons that code for same amino acid are called **SYNONYMS**.

*Only tryptophan and methionine are coded by one codon.

6.2.11.2 SPECIFIC

The same codon specifies the same amino acid in almost all the species with very few exceptions.

6.2.11.3 COMMA-LESS OR NON-OVERLAPPING

The code is read from a fixed point in continuous manner and don't overlap e.g. abc def ghi jkl represent four codons.

6.3 RNA (RIBONUCLEIC ACID)

6.3.1 DIFFERENCE OF DNA AND RNA

	RNA	DNA
Sugar	Ribose	Deoxyribose
Bases	Adenine Cytosine Guanine Uracil	Adenine Cytosine Guanine Thymine
Structure	Single stranded polynucleotide chain. Folds to form loops (cloverleaf shaped)	Double helix made of 2 anti-parallel polynucleotide chains.

6.3.2 STRUCTURE OF RNA

6.3.2.1 PRIMARY STRUCTURE

The single strand chain of polynucleotide linked by 3'-5' phosphodiester bonds make up the primary structure of protein.

6.3.2.2 SECONDARY STRUCTURE

The single strand structure is capable of coiling at its complementary base sequence which is stabilized by hydrophobic interactions.

6.3.3 TYPES OF RNA

6.3.3.1 mRNA (MESSENGER RNA)

mRNA comprises of 5% of the cellular RNA. It carries genetic information from DNA to the cytosol.

Cap: The eukaryotic mRNA consists of a structure called a cap at the 5' end which is a 7'-methylguanosine triphosphate (mGTP) cap. This Cap promotes translation by increasing the mRNA binding to the 40S ribosomal subunit.

Tail: A poly (A) tail, made up of nearly 200 adenine residues exists at the 3' end. The poly (A) tail may help in transporting the mRNA from the nucleus to the cytoplasm.

6.3.3.2 tRNA (TRANSFER RNA)

tRNA also known as soluble RNA (sRNA) is present in cytosol. It comprises about 10-20% of the cellular RNA. The primary structure is made up of 60-110 nucleotides. tRNA include modified nucleotides that are

- Pseudouridine (ψ)
- Ribothymidine (T)
- Dihydrouridine (DHU)

tRNA consists of an adaptor (that carries specific protein), an anti-codon and four loops that are

- DHU loop
- Variable loop
- T ψ loop
- Anticodon loop

tRNA has -CCA part present at the adaptor at which the amino acid attaches.

The three dimensional structure of tRNA is like a twisted L.

The tRNA containing the amino acids with it is called charged tRNA while tRNA which is not carrying the amino acid with it is called uncharged amino acid.

6.3.3.3 rRNA (RIBOSOMAL RNA)

There are four types of RNA present in Eukaryotes

1. 18 S
2. 28 S
3. 5 S
4. 5.8 S

The 28S, 5S and 5.8S combine to form 60S subunit of ribosome, while the 18S rRNA forms 40S ribosomal subunit.



Both the subunit (60S and 40S) combines to form 80S functional ribosome.

*'S' denotes Svedberg unit which refers to the rate of sedimentation in the centrifuge.

6.3.4 OTHER TYPES OF RNA

OLIGONUCLEOTIDES: serve as primers for DNA replication

HETEROGENEOUS RNAs (HNRNAs): capping, tailing and splicing to generate mature mRNA.

SMALL NUCLEAR RNAs (SNRNAs): associated with proteins in small nuclear ribonucleoprotein (snurps). Also help in capping, tailing and splicing to generate mature mRNA.

6.4 Wobble Hypothesis

According to Wobble hypothesis, the codon of the mRNA pairs with its respective anti-codon on the tRNA. The first two bases of the codon always make strong base pairing while the third (wobble base) forms loose pairing.

6.4.1 BENEFITS OF Wobble Hypothesis

The wobble base contributes to specificity, and also helps in rapid dissociation of tRNA from its codon.

6.5 MUTATION

6.5.1 MUTATION

A mutation is defined as heritable change in DNA due to an alteration in the base sequence.

6.5.2 SUBSTITUTION

6.5.2.1 TRANSITION

Substitution of one purine for another purine OR one pyrimidine for another pyrimidine is called transition.

6.5.2.2 TRANSVERSION

Substitution of a purine to a pyrimidine OR pyrimidine to purine is called transversion.

6.5.3 POINT MUTATION

Alteration in any one single nucleotide base on the mRNA could result in point mutation.

6.5.3.1 EFFECT OF POINT MUTATION

6.5.3.1.1 SILENT MUTATION

In silent mutation, there is no change in result as the change codon codes for the same amino acid. E.g. if CGA is changed to CGG there is no change in result because both codes of arginine.

6.5.3.1.2 MISSENSE MUTATION

In this type of mutation the change in codon results in code of another amino acid. There are three type of missense mutation:

6.5.3.1.2.1 Acceptable: A PARTIAL CHANGE IN CODON THAT CHANGES THE AMINO ACID BUT DOES NO EFFECT THE FUNCTION OF PROTEIN.

PARTIALLY ACCEPTABLE: A change in codon that changes amino acid but does a little effect on the function of protein. E.g. In sickle cell anemia, the mutation involves an A → T transversion.

UNACCEPTABLE: A change in codon that changes amino acid and totally retards the function of protein.

6.5.3.1.3 NONSENSE MUTATION

The codon containing the changed base may become a terminating codon, thus stop the translation process prematurely.

6.5.3.1.4 OTHER MUTATION

INSERTION: Insertion occurs when one or more nucleotides are added to DNA.

DELETION: Deletion occurs when one or more nucleotides are removed which results in the altered mRNA.

FRAME SHIFT MUTATION: Includes the insertion or deletion of nucleotides by numbers of nucleotides in DNA that are not multiple of three. It happens in hemoglobin Wayne, and Cystic fibrosis.

TRIPLET EXPANSION: The mutation in which a triplet of nucleotide is added. It happens in Huntington's disease.

6.6 CENTRAL DOGMA OF PROTEIN SYNTHESIS

6.6.1 GENE

Specific sequence of polynucleotide (DNA) that codes for a particular protein is called gene.

6.6.2 CENTRAL DOGMA OF PROTEIN SYNTHESIS

The flow of information from DNA to RNA is named as the Central Dogma of Protein Synthesis.

6.7 CELL CYCLE

The cell cycle is the series of events that take place in a cell leading to its division and duplication (replication). A continuously dividing human cell takes approximately 22 hours to divide. It consists of two periods:

1. Interphase (the period of non-apparent division)
2. Mitotic Phase (the period of division)

6.7.1 INTERPHASE

The period of life cycle between two consecutive divisions is termed as interphase.

G1 (GAP 1 OR POST MITOTIC PHASE) is the period of extensive metabolic activity in which cell normally



grows in size, specific enzymes are synthesized and DNA base units are accumulated for the DNA synthesis.

S PHASE (SYNTHESIS PHASE) during which the DNA is synthesized and the number of chromosome is double. The S phase almost always lasts for 8 hours.

G2 PHASE (PRE MITOTIC PHASE) is the preparing of the cell for division.

G0 PHASE (RESTING PHASE) is a phase in which the growth and replication ceases and cell goes in non-dividing state for some time or in some case for life time.

MITOSIS is a type of division which insures same number of chromosomes in the daughter cells as that in the parent cell.

MEIOSIS is the type of division which reduces the diploid number of chromosomes to the haploid number of gametes.

6.8 REPLICATION

6.8.1 SUPPOSE MODEL OF REPLICATION

Three model of replication was proposed

6.8.1.1 CONSERVATIVE

According to this model full DNA model is converse and a new double stranded DNA is formed which is exact copy of it with all new nucleotides

6.8.1.2 SEMI-CONSERVATIVE

According to this model, the double helix DNA split into two different strands and a new strand is form by the attachment of complementary nucleotides to the existing strand, which conserves half of the DNA.

6.8.1.3 DISPERSIVE MODEL

According to this model all the DNA molecule is broken down into its basic nucleotides and two new DNA strands are prepared from mixing of old and new nucleotide together.

Meselson and Stahl proved the semi-conservative model of replication.

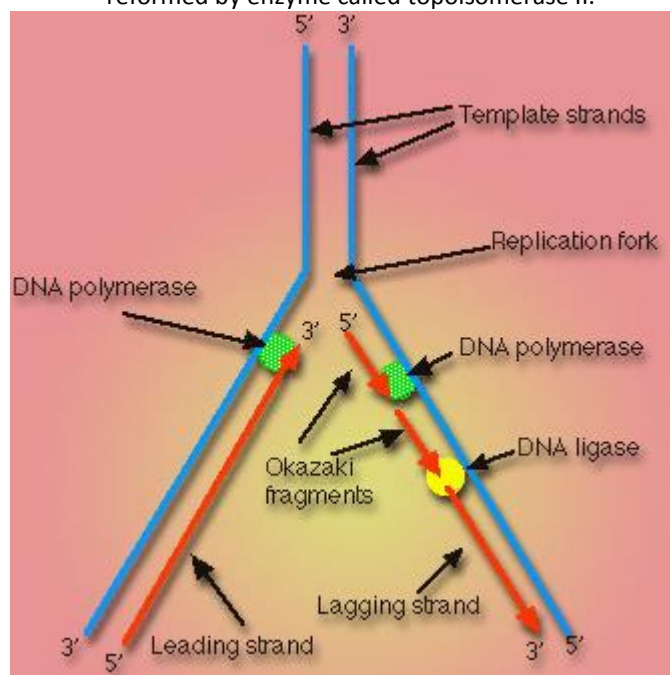
6.8.2 REPLICATION:

The process of copying of existing DNA is called as replication.

6.8.2.1 STEP OF REPLICATION:

- The DNA strands are unzipped by an enzyme Helicase, which break the hydrogen bond between the opposite strands.
- A DNA polymerase enzyme is used for the formation of new DNA strand. DNA polymerase works under two conditions:
 - It needs RNA primer.
 - It moves in 5' to 3' direction

- The replication fork is a structure that forms within the nucleus during DNA replication. It is created by helicases, which break the hydrogen bonds holding the two DNA strands together. The resulting structure has two branching "prongs", each one made up of a single strand of DNA. It gives rise to two strands
- The leading strand is the template strand of the DNA double helix so that the replication fork moves along it in the 3' to 5' direction.
- The lagging strand is the strand of the template DNA double helix that is oriented so that the replication fork moves along it in a 5' to 3' manner.
- On the lagging strand, primase "reads" the DNA and adds RNA to it in short, separated segments, forming Okazaki fragments.
- The enzyme ligase joins the Okazaki fragment.
- RNA primers are removed and the gaps formed due to it are filled by repaired DNA polymerase.
- The DNA configuration is again maintain or reformed by enzyme called topoisomerase II.

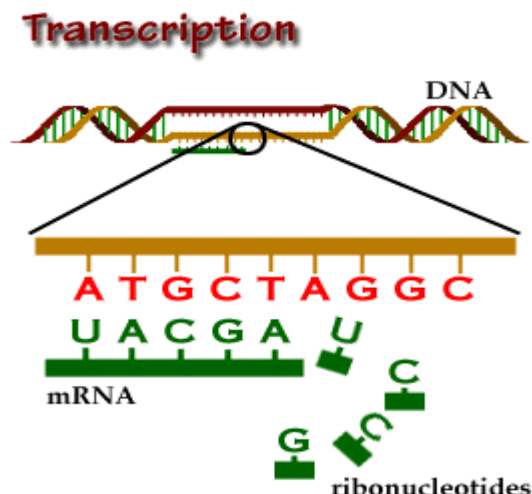


List of major DNA replication enzymes in the replication

Enzyme	Function
DNA Helicase	Unwinds the DNA double helix at the Replication Fork.
DNA Polymerase	Builds a new duplex DNA strand by adding nucleotides in the 5' to 3' direction. Also performs proof-



	reading and error correction.
DNA clamp	A protein which prevents DNA polymerase III from dissociating from the DNA parent strand.
Topoisomerase	Relaxes the DNA from its super-coiled nature.
DNA Gyrase	Relieves strain of unwinding by DNA helicase.
DNA Ligase	Re-anneals the semi-conservative strands and joins Okazaki Fragments of the lagging strand.
Primase	Provides a starting point of RNA (or DNA) for DNA polymerase to begin synthesis of the new DNA strand.
Telomerase	Lengthens telomeric DNA by adding repetitive nucleotide sequences to the ends of eukaryotic chromosomes



6.9 TRANSCRIPTION

Transcription is a process by which the genetic information present in DNA is used to specify a complementary sequence of bases in an mRNA chain by the help of enzyme.

6.9.1 STEPS IN TRANSCRIPTION

Three Steps are involved in RNA synthesis

6.9.1.1 INITIATION

In this step the RNA polymerase bind to the region of DNA having the promoter site (a region made up of different number of nucleotide called Hogness or TATA box and CAAT box).

6.9.1.2 ELONGATION

Once the promoter is recognized by the holoenzyme, the RNA polymerase begins to synthesis the transcript.

6.9.1.3 TERMINATION

The elongation continues until a termination signal is encountered.

6.9.2 POST- TRANSCRIPTION MODIFICATIONS

A poly (A) tail, made up of nearly 200 adenine residues exists at the 3' end. The poly (A) tail may help in transporting the mRNA from the nucleus to the cytoplasm.

6.10 TRANSLATION

The process in which the genetic information presents in mRNA specifies the sequence of amino acids during protein synthesis. It occurs in endoplasmic reticulum with the help of tRNA and rRNA.

6.10.1 Requirement for Translation

- Amino Acids
- tRNA
- Amino-acyl-tRNA synthetases
- mRNA
- Functional ribosomes (rRNA)
- Protein factors
- ATP and GTP (for energy)

6.10.2 STEPS IN TRANSLATION

6.10.2.1 ACTIVATION

- Amino acids are activated and attached to the corresponding tRNA with the help of aminoacyl-tRNA.

6.10.2.2 INITIATION

- The initiation codon is AUG (methionine).
- Methionyl tRNA binds to small ribosomal subunit to make a complex by the help of GTP and on hydrolysis a larger subunit bind with it which completes the ribosome.
- The ribosome contains two binding sites for tRNA. 'P' site or peptidyl site and 'A' site r aminoacyl site. And an 'E' site which is actually occupied by Empty tRNA as it exits the ribosome.
- During initiation the met tRNA binds to P site.



6.10.2.3 ELONGATION

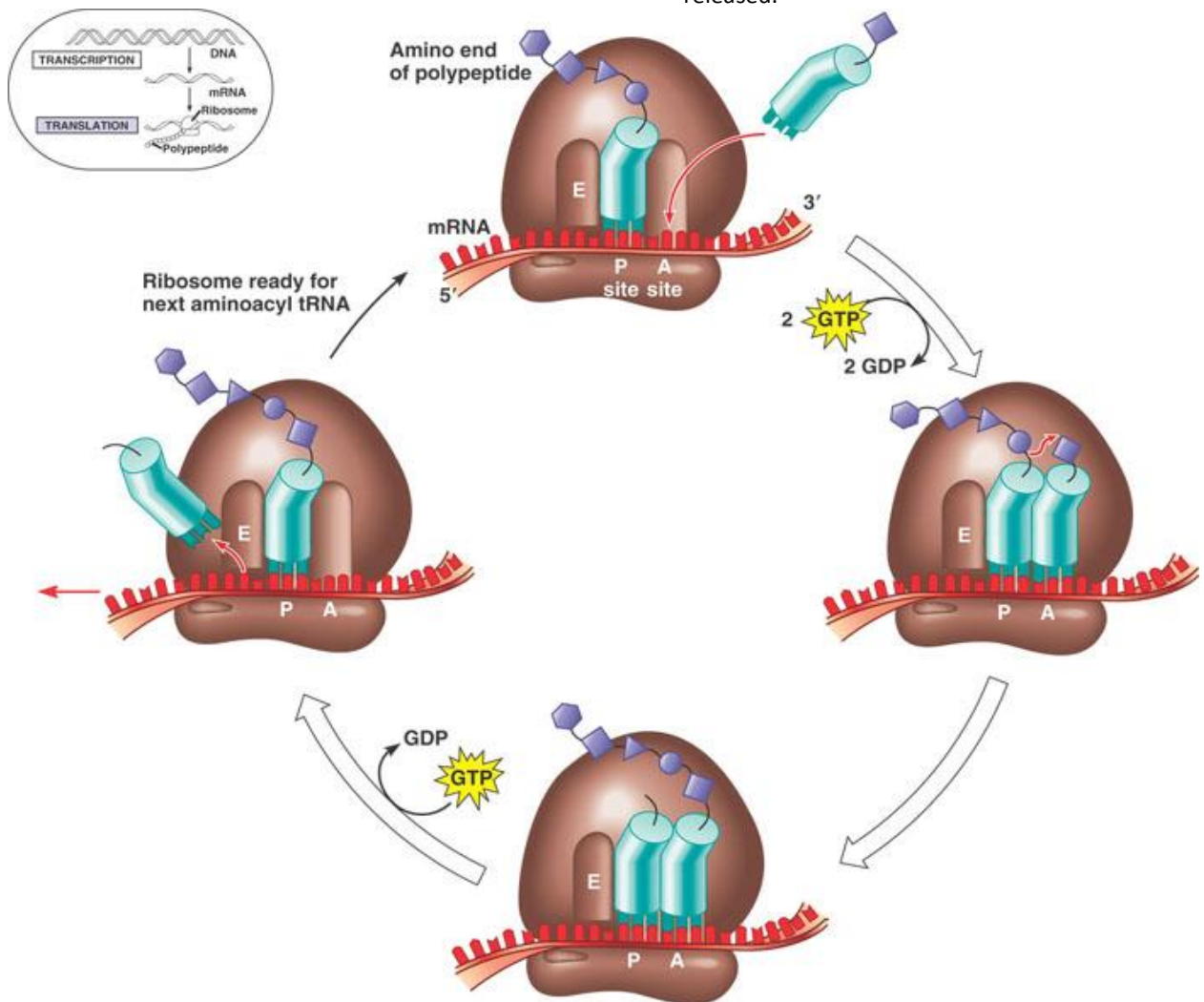
- The next aminoacyl tRNA now makes its way toward the ribosome containing complementary bases to the next codon.
- Before binding of the aminoacyl tRNA, it first combines with GTP and elongation factor.
- The next aminoacyl tRNA goes and occupies the 'A' site on the ribosome.
- Peptidyl transferase catalyzes the formation of a peptide bond.
- The methionine now moves from the 'P' site to a site leaving the tRNA specific for methionine with no amino acid.
- Removal of this tRNA occurs with the help of another elongation

factor which also requires GTP. The 'P' site is now empty.

- Translocation of tRNA with the peptide to 'P' site occurs which requires elongation factor and GTP is utilized again.
- The unloaded tRNA in the 'P' site is moved to 'E' site. Now the 'A' site is empty to receive the next aminoacyl-tRNA.
- This process repeats till one of the three nonsense codons is encountered in the 'A' site of the ribosome.

6.10.2.4 TERMINATION

- The nonsense codons are recognized by a single releasing factor. The newly synthesized peptide is released.



6.11 SIGNAL HYPOTHESIS

The major mechanism whereby proteins that insert into or cross a membrane are synthesized by a



membrane-bound ribosome. The first thirteen to thirty-six amino acids synthesized, termed a signal peptide, are recognized by a signal recognition particle that draws the ribosome to the membrane surface by interaction with a docking protein. The signal peptide may later be removed from the protein.

6.12 CANCER

6.12.1 TUMOR

A tumor is an abnormal growth of body tissue. Tumors can be cancerous (malignant) or noncancerous (benign).

BENIGN TUMOR is not transferred to other part of the body they are small in size and localized.

MALIGNANT TUMOR may transfer to other part of the body i.e. they are not localized.

CANCER is the uncontrolled growth of abnormal cells in the body.

6.12.2 DIFFERENCE OF CANCEROUS CELL TO

NORMAL CELL

- Cancer cells are less differentiated than normal cells
- Grows Rapidly
- Have high nucleus to cytoplasmic ratio
- Prominent nucleoli

6.13 NECROSIS AND APOPTOSIS

APOPTOSIS: internal program of events and sequence of morphological changes by which cell commits suicide is collectively called apoptosis.

NECROSIS: in contrast to suicide, the cell damage due to tissue damage is called necrosis, during which the cell swells and burst, releasing intercellular contents, which can damage neighbor cells and cause inflammation.

6.14 OTHER DEFINITION

BACTERIOPHAGE: A virus capable of replicating within a bacterial cell.

CLONE: The descendants of single cell is called clone.

CLONING: The production of large number of identical DNA molecules or cells from a single, ancestral DNA molecule or cell is called cloning.

GENE SPLICING: The enzymatic attachment of one gene or part of a gene to another

PLASMID: an extra-chromosomal independently replicating small circular DNA molecule commonly employed in genetic engineering

POLYMERASE CHAIN REACTION (PCR): a repetitive procedure that results in geometric amplification of a specific DNA sequence.

PROBE: A labeled fragment of a nucleic acid containing a nucleotide sequence complementary to a gene or genomic sequence that one wishes to detect in a hybridization experiment.

RECOMBINANT DNA: DNA formed by the joining of genes into new combinations.

RESTRICTING FRAGMENTS: segments of double stranded DNA produced by action of restriction endonucleases on larger DNA.



Chapter 7 ENZYMES

7.1 ENZYMES

Any protein which originates from living cells and is capable of producing certain chemical changes in organic substances by catalytic action. For example, pepsin which helps in digestion. Without enzymes the reaction would proceed at very slow speed making life impossible.

7.1.1 ACTIVE SITE

The catalytic activity of enzyme is restricted to small portion of the globular protein which is called active site. It consists of few amino acids only. The rest of bulk of amino acids maintains the globular structure of protein. It is further divided into

- Binding site (that help in the recognition and binding of proper substrate)
- Catalytic site (transforms the substrate into product(s))

7.1.2 SUBSTRATE

The reactant that attaches to the active site of protein is called substrate.

7.1.3 CO-FACTOR

The non-protein part attach to the enzyme which is important for proper function of enzyme is called co-factor. The co-factor acts as a bridge between substrate and enzyme. Co-factor sometimes acts as source of chemical energy for the catalytic reaction.

7.1.3.1 PROSTHETIC GROUP

If the non-protein part (co-factor) is covalently bonded to the protein part, it is known as prosthetic group.

7.1.3.2 CO-ENZYMES

If the non-protein (co-factor) is loosely attached to protein part, it is known as co-enzyme. E.g. NAD, FAD

7.1.4 ACTIVATOR

The detachable co-factor is known as activator, if it is an inorganic ion, e.g. Mg^{2+} and Fe^{2+} .

7.1.5 APO-ENZYME

An enzyme with its coenzyme, or prosthetic group removed is designated as apoenzyme.

7.1.6 HOLO-ENZYME

An activated enzyme consisting of a polypeptide chain and a cofactor is known as holoenzyme.

7.2 CHARACTERISTIC OF ENZYMES

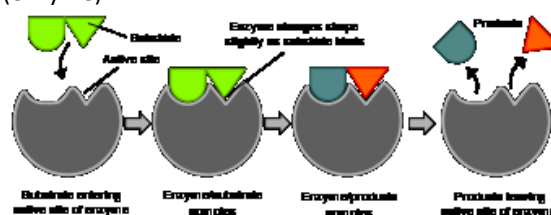
1. All enzymes are globular proteins.
2. They increase the rate of reaction without themselves being used.
3. Their presence does not affect the nature or properties of end products.

4. Small amounts of an enzyme can accelerate chemical reaction.
5. They are very specific in nature.
6. They are sensitive to even a minor change in pH, temperature, substrate concentration.
7. Some enzymes require a co-factor for their proper functioning.
8. They lower the activation energy of the reactions.
9. They are produced by living cells for use in or near the site of production.
10. Many enzymes are simply dissolved in cytoplasm, while other are tightly bounded to certain subcellular organelles.

7.3 MECHANISM OF ENZYME ACTION (CATALYSIS)

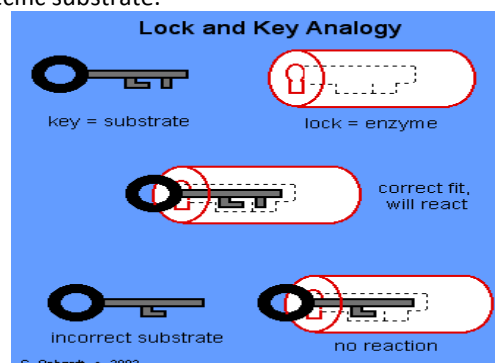
Every enzyme is specific in its action which reacts with a specific substrate to form an intermediate which is enzyme substrate complex. This complex is then converted into product. For example:

Maltose (substrate) + Maltase (enzyme) $\rightleftharpoons$ maltase maltose complex $\rightleftharpoons$ 2 Glucose (product) + Maltase (enzyme)



7.3.1 LOCK AND KEY MODEL

The specific action of an enzyme with a single substrate can be explained using a Lock and Key analogy first postulated in 1894 by Emil Fischer. In this analogy, the lock is the enzyme and the key is the substrate. Only the correctly sized key (substrate) fits into the key hole (active site) of the lock (enzyme). Smaller keys, larger keys, or incorrectly positioned teeth on keys (incorrectly shaped or sized substrate molecules) do not fit into the lock (enzyme). Only the correctly shaped key opens a particular lock. Which means only the specific enzyme reacts with the specific substrate.



According to Lock and Key Model the active site is rigid and there is no flexibility in the active site before, during or after the enzyme action and it is used as template. Later studies did not support this model in all reaction.

7.3.2 INDUCED-FIT THEORY

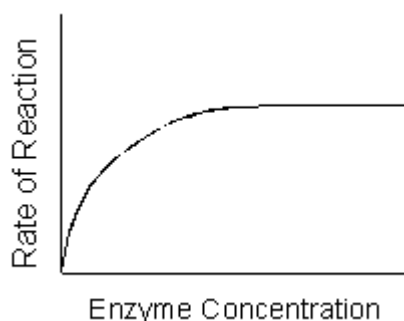
The induced-fit theory assumes that the substrate plays a role in determining the final shape of the enzyme and that the enzyme is partially flexible. This explains why certain compounds can bind to the enzyme but do not react because the enzyme has been distorted too much. Other molecules may be too small to induce the proper alignment and therefore cannot react. Only the proper substrate is capable of inducing the proper alignment of the active site.

7.4 FACTORS AFFECTING THE RATE OF ENZYME ACTION

7.4.1 ENZYME CONCENTRATION

The rate of reaction depends directly on the amount of enzyme present at a specific time at unlimited substrate concentration. If the amount of enzyme is double the reaction rate is double.

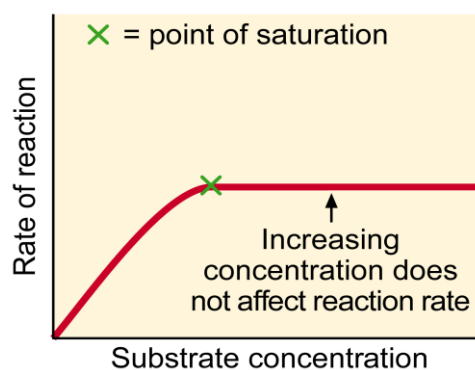
By increasing the enzyme molecules there is increase in the number of active site which will convert the substrate molecules into product in the given period of time. After a certain limiting concentration the rate of reaction no longer depend upon this increase.



7.4.2 SUBSTRATE CONCENTRATION

At low concentration of substrate the reaction rate is directly proportional to the substrate available.

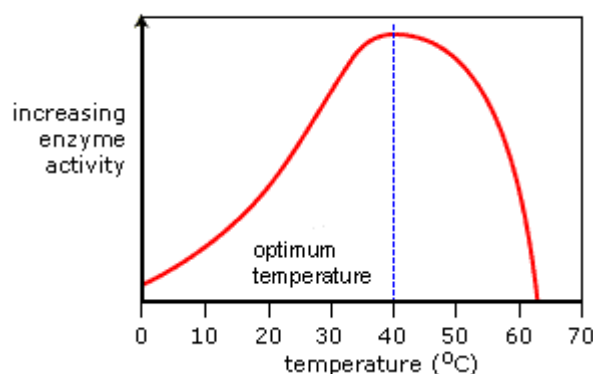
If the enzyme concentration is kept constant and the amount of substrate is increased, a point is reached when a further increase in the substrate does not increase the rate of reaction any more. This is because at high substrate level all the active sites of the enzyme are occupied and further increase in the substrate does not increase the reaction rate.



7.4.3 TEMPERATURE

The rate of enzyme action may increase with increase in temperature but up to a certain limit. All enzymes can work at their maximum rate at specific temperature called the **optimum temperature**. For enzymes of human body 37 °C is the optimum temperature.

Heat provides activation energy and therefore, chemical reactions are accelerated at high temperature. Heat also supplies kinetic energy to reacting molecules, causing them to move rapidly. Thus the reactant move more quickly and chances of their collision with each other are increase. However, further increase in heat energy also increases the vibrations of atoms which make up the enzyme molecule. If the vibrations become too violent, globular structure essential for enzyme activity is lost and the enzyme is said to be denatured.



7.4.4 pH VALUE

Every enzyme functions most effectively over a narrow range of pH known as **optimum pH**.

A slight change in pH can change the ionization of the amino acids at the active site. Moreover, it may affect the ionization of the substrates. Under these changed conditions enzyme activity is either retarded or blocked completely.

Extreme changes in pH cause the bonds in the enzyme to break, resulting in the enzyme denaturation.

Enzyme	Optimum pH
Pepsin	2.00
Sucrase	4.50

Enterokinase	5.50		
Salivary amylase	6.80		
Catalase	7.60	4	Lyases (synthases)
Chymotrypsin	7.00-8.00		
Pancreatic lipase	9.00		
Arginase	9.70		

7.4.5 INHIBITORS

An inhibitor is a chemical substance which can react in place of substrate with the enzyme but is not transformed into product and this blocks the active site temporarily or permanently. This process is called **enzyme inhibition**.

7.4.5.1.1 EXAMPLE

Poisons like cyanide, antibiotics, anti-metabolites and some drugs are example of inhibitors.

7.4.5.2 IRREVERSIBLE INHIBITORS

They check the reaction rate by occupying the active sites or destroying the globular structure. They occupy the active sites by forming covalent bonds or they may physically block the active sites.

7.4.5.3 REVERSIBLE INHIBITORS

They form weak linkages with the enzyme. Their effect can be neutralized completely or partially by an increase in the concentration of the substrate. They are further divided into

7.4.5.3.1 COMPETITIVE INHIBITORS

Because of the structure similarity with the substrate they may be selected by the binding site, but are not able to activate the catalytic site, thus there is no production of any product.

7.4.5.3.2 NON-COMPETITIVE INHIBITORS

They form enzyme inhibitor complex at a point other than active site. They alter the structure of the enzyme in such a way that even if genuine substrate binds the active site, catalysis fails to take place.

7.5 ENZYME CLASSES

1	Oxidoreductases	Catalyze the transfer of reducing equivalents from one redox system to another (require co-enzyme)
2	Transferases	Catalyze the transfer of other groups from one molecule to another (require co-enzyme)
3	Hydrolases	Catalyze the transfer of groups from one molecule to another

but the acceptor is always water molecule

Catalyze reactions involving either the cleavage formation of chemical bonds with double bonds either arising or disappearing

5 Isomerase

Move groups within a molecule, without changing the gross composition of the substrate

6 Ligases (synthetases)

Are energy dependent and are therefore always coupled to the hydrolysis of nucleoside triphosphate



Chapter 8 VITAMINS

1. Lipid soluble vitamins
2. Water soluble vitamins

8.1 VITAMINS

Vitamins are vital amines

There are classified into two group

8.2 SOME IMPORTANT VITAMINS

8.2.1 LIPID SOLUBLE VITAMINS

Vitamin	Important Functions
D (cholecalciferol)	In response to hypocalcemia, helps normalize serum calcium levels
A (carotene)	Retinoic acid and retinol act as growth regulators, especially in epithelium Retinal is important in rod and cone cells for vision
K	Carboxylation of glutamic acid residues in many Ca^{2+} -binding proteins, importantly coagulation factors II, VII, IX, and X, as well as protein C and protein S
E (α -tocopherol)	Antioxidant in the lipid phase. Protects membrane lipids from peroxidation and helps prevent oxidation of LDL particles thought to be involved in atherosclerotic plaque formation

8.2.2 WATER SOLUBLE VITAMINS



Vitamin or Coenzyme	Enzyme	Pathway	Deficiency
Biotin	Pyruvate carboxylase Acetyl CoA carboxylase Propionyl CoA carboxylase	Gluconeogenesis Fatty acid synthesis Odd-carbon fatty acids, Val, Met, Ile, Thr	MCC* (rare): excessive consumption of raw eggs (contain avidin, a biotin-binding protein) Alopecia (hair loss), bowel inflammation, muscle pain
Thiamine (B ₁)	Pyruvate dehydrogenase α -Ketoglutarate dehydrogenase Transketolase	PDH TCA cycle HMP shunt	MCC: alcoholism (alcohol interferes with absorption) Wernicke (ataxia, nystagmus, ophthalmoplegia) Korsakoff (confabulation, psychosis) High-output cardiac failure (wet beri-beri)
Niacin (B ₃) NAD(H) NADP(H)	Dehydrogenases	Many	Pellagra: diarrhea, dementia, dermatitis, and, if not treated, death Pellagra may also be related to deficiency of tryptophan (corn major dietary staple), which supplies a portion of the niacin requirement.
Folic acid THF	Thymidylate synthase Enzymes in purine synthesis need not be memorized	Thymidine (pyrimidine) synthesis Purine synthesis	MCC: alcoholics and pregnancy (body stores depleted in 3 months) Homocystinemia with risk of deep vein thrombosis and atherosclerosis Megaloblastic (macrocytic) anemia Deficiency in early pregnancy causes neural tube defects in fetus
Cyanocobalamin (B ₁₂)	Homocysteine methyltransferase Methylmalonyl CoA mutase	Methionine, SAM Odd-carbon fatty acids, Val, Met, Ile, Thr	MCC: pernicious anemia. Also in aging, especially with poor nutrition, bacterial overgrowth of terminal ileum, resection of the terminal ileum secondary to Crohn disease, chronic pancreatitis, and, rarely, vegans, or infection with <i>D. latum</i> Megaloblastic (macrocytic) anemia Progressive peripheral neuropathy
Pyridoxine (B ₆) Pyridoxal-P (PLP)	Aminotransferases (transaminase): AST (GOT), ALT (GPT) δ -Aminolevulinate synthase	Protein catabolism Heme synthesis	MCC: isoniazid therapy Sideroblastic anemia Cheilosis or stomatitis (cracking or scaling of lip borders and corners of the mouth) Convulsions
Riboflavin (B ₂) FAD(H ₂)	Dehydrogenases	Many	Corneal neovascularization Cheilosis or stomatitis (cracking or scaling of lip borders and corners of the mouth) Magenta-colored tongue
Ascorbate (C)	Prolyl and lysyl hydroxylases Dopamine hydroxylase	Collagen synthesis Catecholamine synthesis Absorption of iron in GI tract	MCC: diet deficient in citrus fruits and green vegetables Scurvy: poor wound healing, easy bruising (perifollicular hemorrhage), bleeding gums, increased bleeding time, painful glossitis, anemia
Pantothenic acid CoA	Fatty acid synthase Fatty acyl CoA synthetase Pyruvate dehydrogenase α -Ketoglutarate dehydrogenase	Fatty acid metabolism PDH TCA cycle	Rare



Chapter 9 HORMONES

9.1 HORMONE

Hormones may be defined as the chemical substances that are secreted by the endocrine cells into the extracellular fluids and regulate the metabolic activity of other cells in the body.

9.2 MEDIATOR

Mediators is the term used for signaling sub-stances that do not derive from special hormone-forming cells, but are form by many cell types. They have hormone-like effects in their immediate surroundings. Histamine and prostaglandins.

9.3 NEUROTRANSMITTERS

Neurohormones and neurotransmitters are signaling substances that are produced and released by nerve cells. Growth factors and cytokines mainly promote cell proliferation and cell differentiation.

9.4 OVERVIEW OF FUNCTION OF HORMONES

- Growth and differentiation of cells, tissues, and organs
- Metabolic pathways
- Digestive processes
- Maintenance of ion concentrations (homeostasis)

9.5 HORMONE HIERARCHY

The hierarchical nature of hormone action can be summarized as follows:

1. Hormonal action is controlled ultimately by the central nervous system, which transmits signals to the hypothalamus. It responds by producing factors that either stimulate (called releasing factors) or inhibit the release of hormones from the pituitary.
2. Pituitary hormones do one of the following:

- a. They stimulate other endocrine glands, each of which releases a hormone that acts on a target tissue and elicits a specific metabolic response.

- b. Alternatively, they act directly on a target tissue. The action of a hormone sets in motion events that ultimately limit that action.

- Some pituitary hormones stimulate target tissue directly. For example, prolactin stimulates mammary glands to produce milk.
- Most pituitary hormones act on endocrine glands that occupy an intermediate, or secondary, position in the hierarchy, stimulating them to produce hormones that exert the ultimate actions on target tissues. Pituitary hormones that act on other endocrine glands are called tropic hormones or tropins. An example is adrenal corticotrophic hormone (ACTH), also called β -corticotropin. This peptide is secreted from the anterior pituitary, and it stimulates the adrenal cortex to produce glucocorticoids and mineralocorticoids, which in turn act on a number of tissues.

9.6 TYPES OF HORMONES ON THE BASIS OF ITS EFFECT

9.6.1 ENDOCRINE EFFECT

Hormones transfer signals by migrating from their site of synthesis to their site of action. They are usually transported in the blood. In this case, they are said to have an endocrine effect example: insulin.

9.6.2 AUTOCRINE EFFECT

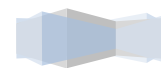
When signal substances also pass effects back to the cells that synthesize them, they are said to have an autocrine effect, example: prostaglandins.

9.6.3 PARACRINE EFFECT

Tissue hormones, the target cells for which are in the immediate vicinity of the glandular cells that produce them, are said to have a paracrine effect, example: gastrointestinal tract hormones.

9.7 MECHANISM OF HORMONE ACTION

- The endocrine system acts by releasing hormones that in turn trigger actions in specific target cells.
- Receptors on target cell membranes bind only to one type of hormone. More than fifty human hormones have been identified; all act by binding to receptor molecules.



- The binding hormone changes the shape of the receptor causing the response to the hormone. There are two mechanisms of hormone action on all target cells.

9.8 LIPOPHILIC HORMONES

9.9 SOME IMPORTANT LIPOPHILIC HORMONE

Lipophilic hormones, which include steroid hormones, iodothyronines, and retinoic acid, are relatively small molecules.

1. STEROID HORMONES

9.9.1.1 PROGESTERONE

Progesterone is a female sexual steroid belonging to the progestin (gestagen) family. It is synthesized in the corpus luteum of the ovaries. The blood level of progesterone varies with the menstrual cycle. The hormone prepares the uterus for a possible pregnancy. Following fertilization, the placenta also starts to synthesize progesterone in order to maintain the pregnant state. The development of the mammary glands is also stimulated by progesterone.

9.9.1.2 ESTRADIOL

Estradiol is the most important of the estrogens. Like progesterone, it is synthesized by the ovaries and, during pregnancy, by the placenta as well. Estradiol controls the menstrual cycle. It promotes proliferation of the uterine mucosa, and is also responsible for the development of the female secondary sexual characteristics (breast, fat distribution, etc.).

9.9.1.3 TESTOSTERONE

Testosterone is the most important of the male sexual steroids (androgens). It is synthesized in the Leydig interstitial cells of the testes, and controls the development and functioning of the male gonads. It also determines secondary sexual characteristics in men (muscles, hair, etc.).

9.9.1.4 CORTISOL

Cortisol, the most important glucocorticoid, is synthesized by the adrenal cortex. It is involved in regulating protein and carbohydrate metabolism by promoting protein degradation and the conversion of amino acids into glucose. As a result, the blood glucose level rises. Synthetic glucocorticoids (e. g.,

dexamethasone) are used in drugs due to their anti-inflammatory and immunosuppressant effects.

9.9.1.5 ALDOSTERONE

Aldosterone, a mineralocorticoid, is also synthesized in the adrenal gland. In the kidneys, it promotes Na^+ resorption by inducing Na^+/K^+ ATPase and Na^+ channels. At the same time, it leads to increased K^+ excretion. In this way, aldosterone indirectly increases blood pressure.

9.9.1.6 CALCITRIOL

Calcitriol is a derivative of vitamin D. On exposure to ultraviolet light, a precursor of the hormone can also arise in the skin. Calcitriol itself is synthesized in the kidneys. Calcitriol promotes the resorption of calcium in the intestine and increases the Ca^{2+} level in the blood.

2. IODOTHYRONINES

The thyroid hormone thyroxine (tetraiodothyronine, T_4) and its active form triiodothyronine (T_3) are derived from the amino acid tyrosine. The iodine atoms at positions 3 and 5 of the two phenol rings are characteristic of them. Post-translational synthesis of thyroxine takes place in the thyroid gland from tyrosine residues of the protein thyroglobulin, from which it is proteolytically cleaved before being released. Iodothyronines are the only organic molecules in the animal organism that contain iodine. They increase the basal metabolic rate, partly by regulating mitochondrial ATP synthesis. In addition, they promote embryonic development.

9.10 MECHANISM OF ACTION OF LIPOPHILIC HORMONES

1. The second mechanism involves steroid hormones, which pass through the plasma membrane because they are lipid soluble) and act in a two single step process.
2. Steroid hormones bind, once inside the cell, to the nuclear membrane receptors, producing an activated hormone-receptor complex.
3. The activated hormone-receptor complex binds to DNA and activates specific genes, increasing production of proteins.
(activating genes to transcribe messenger RNA, the mRNA is then translated into cytoplasm, resulting in synthesis of new protein)



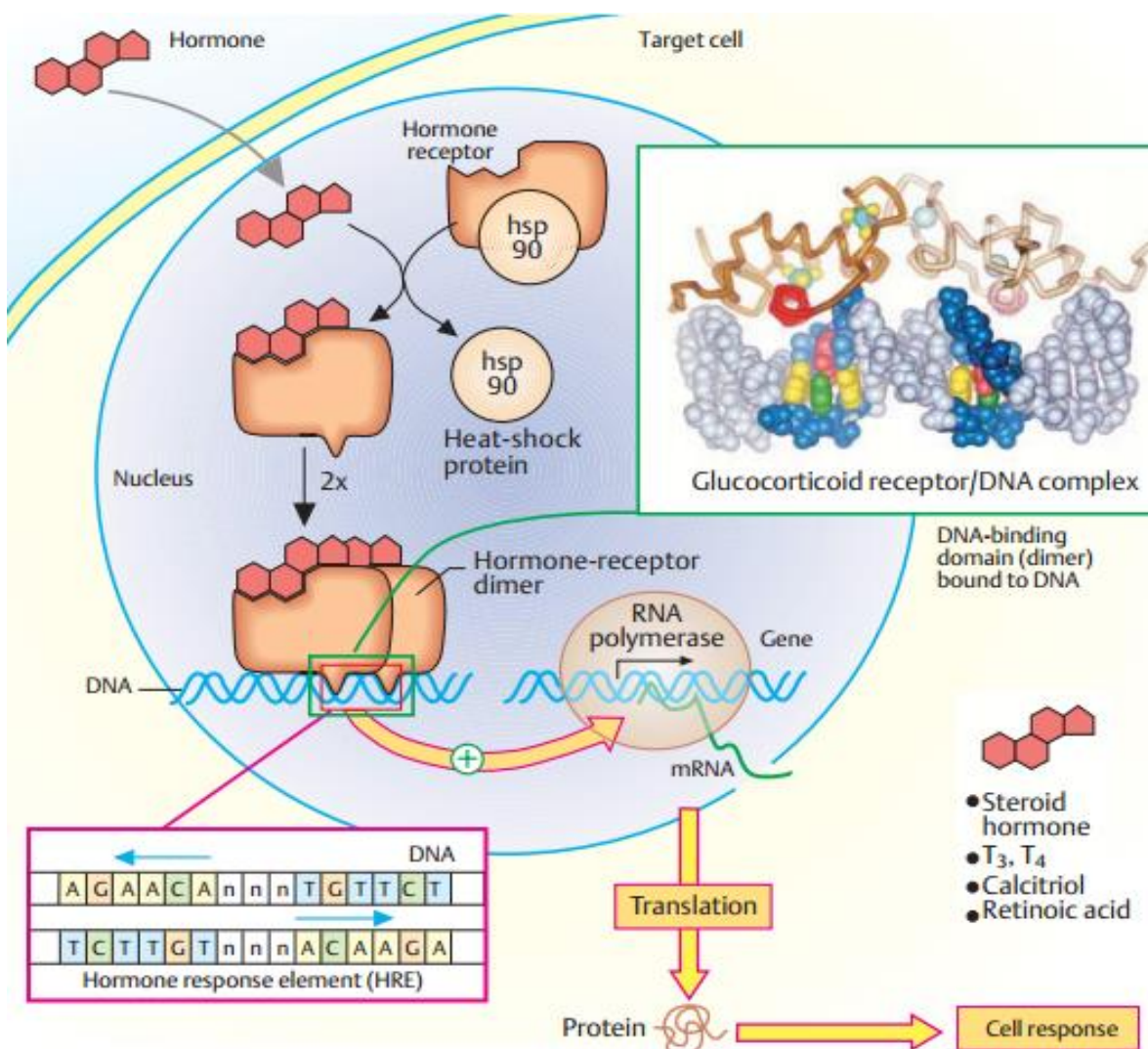


FIGURE 5: MECHANISM OF ACTION OF LIPOPHILIC HORMONES

produced from amino acids by decarboxylation and usually act not only as hormones, but also as neurotransmitters.

9.11 HYDROPHILIC HORMONES

The hydrophilic hormones are derived from amino acids, or are peptides and proteins composed of amino acids. Hormones with endocrine effects are synthesized in glandular cells and stored there in vesicles until they are released. As they are easily soluble, they do not need carrier proteins for transport in the blood. They bind on the plasma membrane of the target cells to receptors that pass the hormonal signal on. Several hormones in this group have paracrine effects.

9.12 SOME IMPORTANT HYDROPHILIC HORMONES

9.12.1 SIGNALING SUBSTANCES DERIVED FROM AMINO ACIDS

Histamine, serotonin, melatonin, and the catecholamines dopa, dopamine, norepinephrine, and epinephrine are known as “biogenic amines.” They are

9.12.1.1 HISTAMINE

Histamine, an important mediator (local signaling substance) and neurotransmitter, is mainly stored in tissue mast cells and basophilic granulocytes in the blood. It is involved in inflammatory and allergic reactions. “Histamine liberators” such as tissue hormones, type E immunoglobulin, and drugs can release it. Histamine acts via various types of receptor. Binding to H₁ receptors promotes contraction of smooth muscle in the Bronchia, and dilates the capillary vessels and increases their permeability. Via H₂ receptors, histamine slows down the heart rate and promotes the formation of HCl in the gastric mucosa. In the brain, histamine acts as a neurotransmitter.

9.12.1.2 EPINEPHRINE

Epinephrine is a hormone synthesized in the adrenal glands from tyrosine. Its release is subject to neuronal

control. This “emergency hormone” mainly acts on the blood vessels, heart, and metabolism. It constricts the blood vessels and thereby increases blood pressure (via α_1 and α_2 receptors); it increases cardiac function (via β_2 receptors); it promotes the degradation of glycogen into glucose in the liver and muscles (via β_2 receptors); and it dilates the bronchia (also via β_2 receptors).

9.12.2 EXAMPLES OF PEPTIDE HORMONES AND PROTEOHORMONES

Numerically the largest group of signaling substances, these arise by protein biosynthesis.

9.12.2.1 THYROLIBERIN

Thyroliberin (thyrotropin releasing hormone, TRH) is one of the neuro-hormones of the hypothalamus. It stimulates pituitary gland cells to secrete thyrotropin (TSH). TRH consists of three amino acids, which are modified in characteristic ways.

9.12.2.2 THYROTROPIN

Thyrotropin (thyroid-stimulating hormone, TSH) and the related hormones lutropin (luteinizing hormone, LH) and follitropin (follicle-stimulating hormone, FSH) originate in the adenohypophysis. They are all dimeric glycoproteins with masses of around 28 kDa. Thyrotropin stimulates the synthesis and secretion of thyroxin by the thyroid gland.

9.12.2.3 INSULIN

Insulin is produced and released by the B cells of the pancreas and is released when the glucose level rises. Insulin reduces the blood sugar level by promoting processes that consume glucose—e. g., glycolysis, glycogen synthesis, and conversion of glucose into fatty acids. By contrast, it inhibits gluconeogenesis and glycogen degradation.

9.12.2.4 GLUCAGON

Glucagon, a peptide of 29 amino acids, is a product of the A cells of the pancreas. It is the antagonist of insulin and, like insulin, mainly influences carbohydrate and lipid metabolism. Its effects are each opposite to those of insulin. Glucagon mainly acts via the second messenger cAMP.

9.13 MECHANISM OF ACTION OF HYDROPHILIC HORMONES

1. Nonsteroid hormones (water soluble) do not enter the cell but bind to plasma membrane receptors, generating a chemical signal (second messenger) inside the target cell.
2. Five different second messenger chemicals, including cyclic AMP have been identified.
3. Second messengers activate other intracellular chemicals to produce the target cell response.

9.13.1 SECONDARY MESSENGER

Second messenger, molecule inside cells that acts to transmit signals from a receptor to a target. The term **second messenger** was coined upon the discovery of these substances in order to distinguish them from hormones and other molecules that function outside the cell as “first messengers” in the transmission of biological information. Many second messenger molecules are small and therefore diffuse rapidly through the cytoplasm, enabling information to move quickly throughout the cell.

9.13.1.1 EXAMPLE:

- Cyclic adenosine monophosphate (cAMP)
- Cyclic guanosine monophosphate (cGMP)



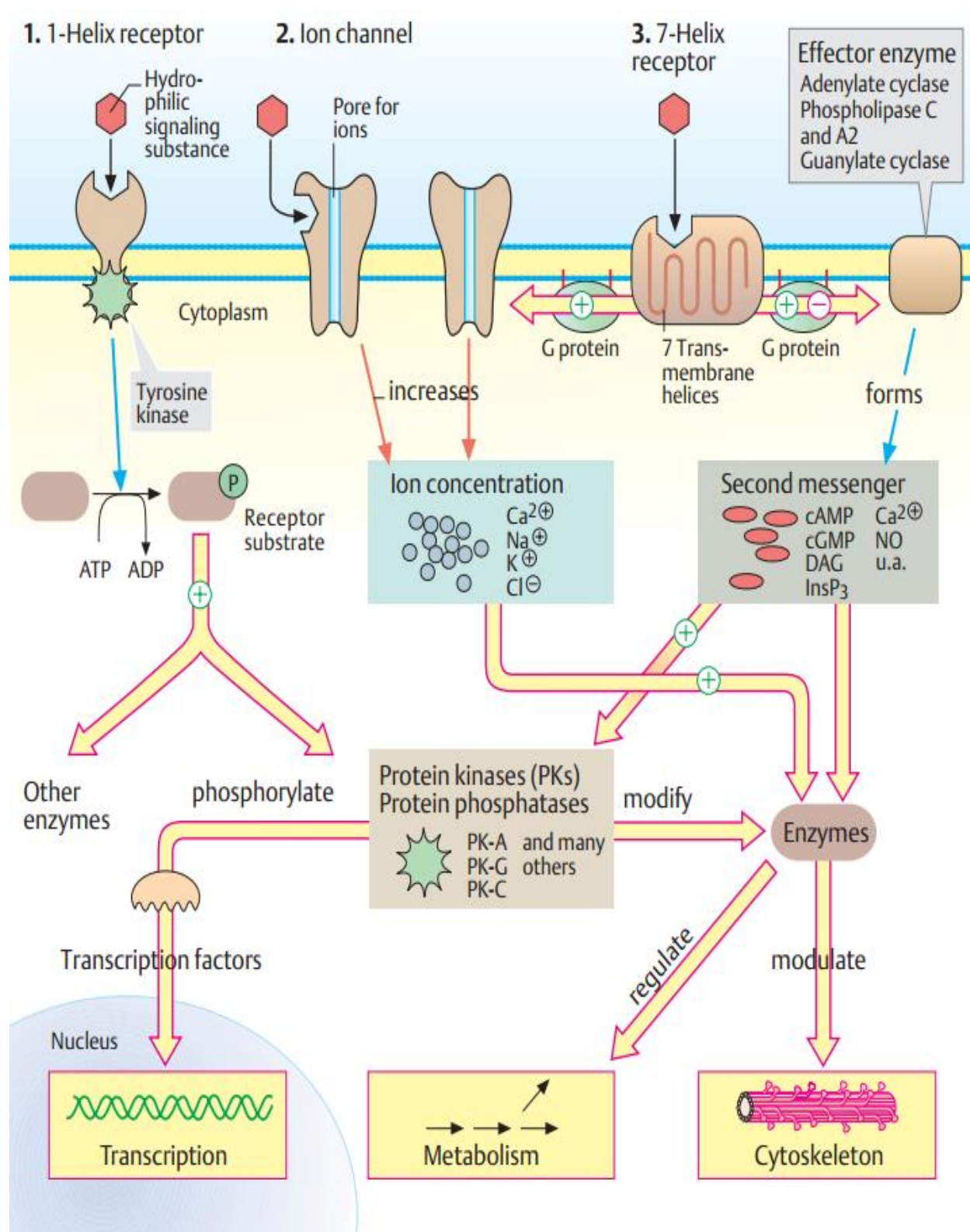


FIGURE 6: MECHANISM OF ACTION OF HYDROPHILIC HORMONE

Chapter 10 OVERVIEW OF ENERGY METABOLISM

10.1 STEPS OF METABOLIZING FOOD

There are four steps of metabolizing food which are as follows:

1. Metabolic fuels are hydrolyzed in the GIT tract to a set of monomeric building blocks.
2. The building blocks are degraded by various pathways to a common intermediate i-e Acetyl CoA.
3. The citric acid cycle (or TCA cycle) oxidizes it to carbon dioxide.
4. The extraction of energy from food by oxidative phosphorylation, in which the energy is released by electron transport chain from NADPH or FADH_2 .

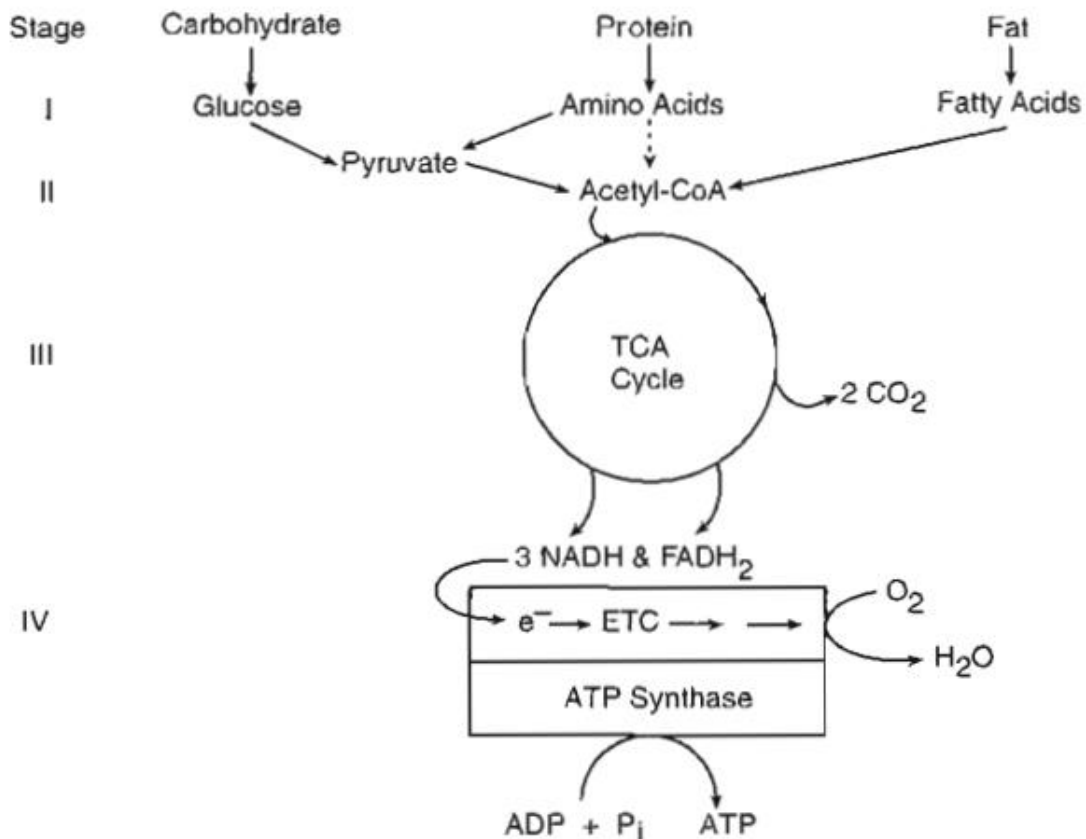


FIGURE 7: OVERVIEW OF ENERGY METABOLISM

10.2 REGULATION OF FUEL METABOLISM

10.2.1 WELL-FED (ADSORPTIVE) STATE

- After the meal, the blood glucose level increases and stimulates the release of insulin.
- Major target for insulin is liver, muscle, adipose tissue.
- Insulin promotes glycogen synthesis.
- After glycogen stores are filled, the insulin converts glucose to fatty acid and triglycerides in liver.
- Two tissues i-e brain and red blood cell are insensitive to insulin. They acquire energy from glucose in both fasting and well-fed state.



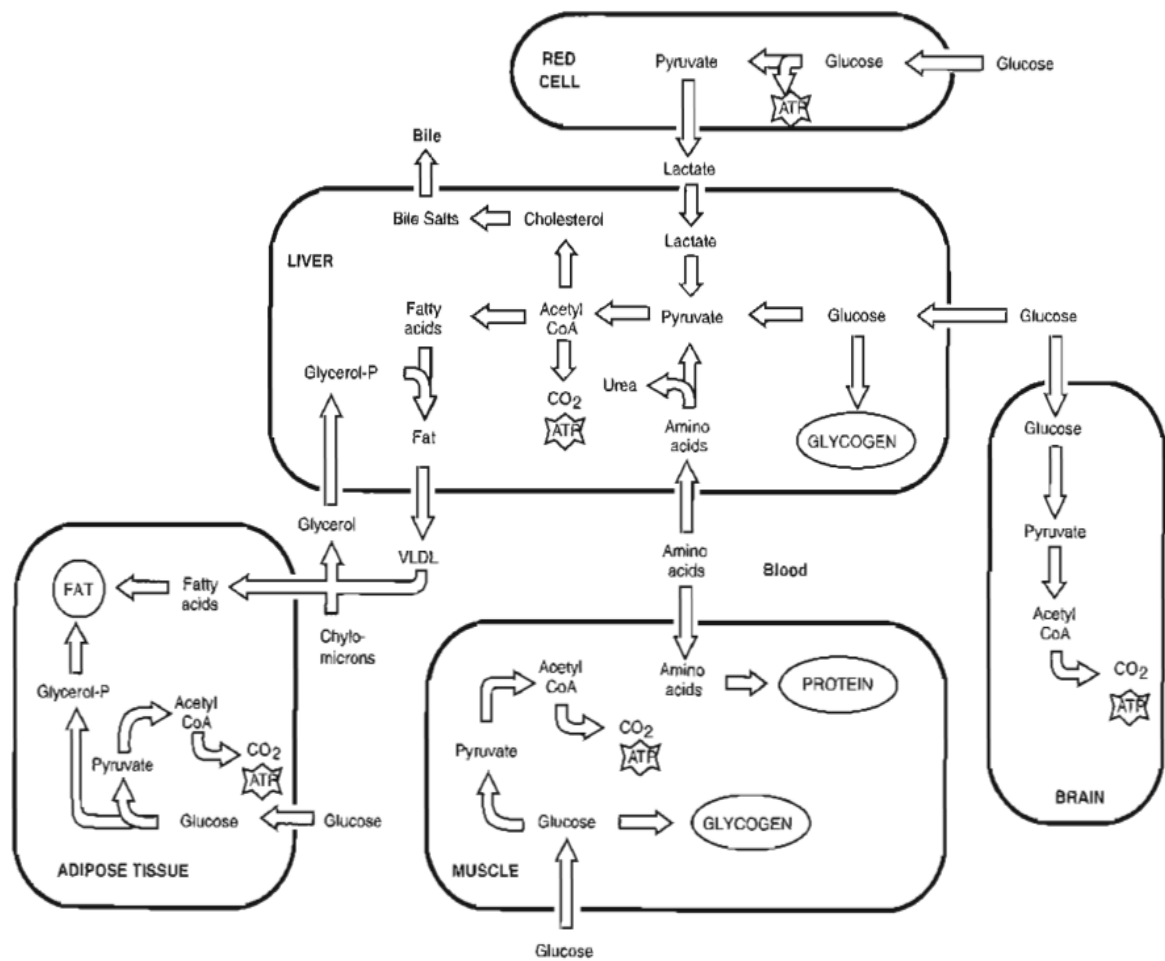


FIGURE 8: WELL-FED (ADSORPTIVE) STATE

10.2.2

10.2.3 POST-ABSORPTIVE STATE

- Glucagon and epinephrine levels rise during overnight fast.

- These hormones exert their effects on skeletal muscle, adipose tissue and liver.
- In liver, glycogen degradation and the release of glucose into the blood are stimulated.
- Hepatic gluconeogenesis is also stimulated by glucagon.



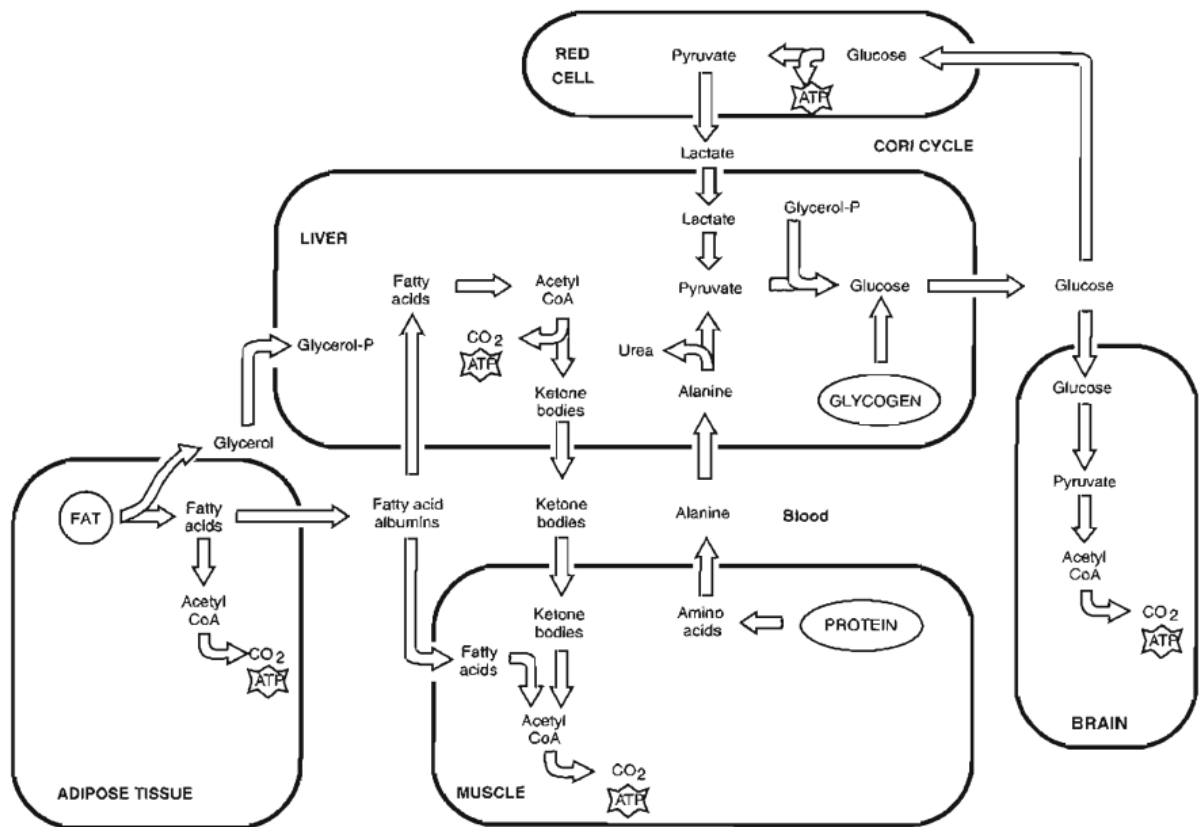


FIGURE 9: POST-ABSORPTIVE STATE

10.2.4 PATTERNS OF FUEL METABOLISM IN TISSUES

Organ	Well-Fed	Fasting
Liver	Glucose and amino acids	Fatty acids
Resting skeletal muscle	Glucose	Fatty acids, ketones
Cardiac muscle	Fatty acids	Fatty acids, ketones
Adipose tissue	Glucose	Fatty acids
Brain	Glucose	Glucose (ketones in prolonged fast)
Red blood cells	Glucose	Glucose



Chapter 11 GLYCOLYSIS AND PYRUVATE DEHYDROGENASE

11.1 OVERVIEW

- All cells can carry out glycolysis.
- In red blood cells, glycolysis represents the only energy yielding pathway.
- The first step in glucose metabolism is its entry inside the cell and phosphorylation by kinase enzyme to prevent glucose from leaving.

11.2 CARBOHYDRATE DIGESTION

- Only small amount of carbohydrate ingested is monosaccharides.
- Most of them are in complex form like starch (amylase and amylopectin) and others are disaccharide (sucrose and lactose) .
- In mouth, salivary amylase is secreted which hydrolyze them to dextrin (<8-10 glucose units).
- Upon entry in stomach, the acid Ph destroys the salivary amylase.
- In intestine, dextrin is hydrolyzed to maltose and isomaltose.
- The digestion process is completed in the brush borders of intestine:
 - I. Maltase cleavage maltose to 2 glucose.
 - II. Isomaltase cleavage isomaltose into 2 glucose.
 - III. Lactase cleavage lactose into glucose and galactose.

- IV. Sucrase cleavage sucrose into glucose and fructose.

11.3 GLUCOSE TRANSPORT

Glucose entry into most of the cell is concentration driven and is independent of concentration of sodium. The normal range of glucose in blood is 4-6Mm (70-110mg/dL).there are four types of glucose transporters.

- GLUT 1 and GLUT 3 mediate basal uptake in most tissues, including brain, nerves, and red blood cells. They have high affinity for glucose.
- GLUT 2 has low affinity for glucose.it mostly captures glucose for storage.GLUT 2 along with insulin is glucose sensor.
- GLUT 4nis in adipose tissue and muscle. It response to glucose level in peripheral blood.

TABLE 1: TYPES OF GLUT

Name	Tissues	K_m , glucose	Functions
GLUT 1	Most tissues (brain, red cells)	~1 mM	Basal uptake of glucose
GLUT 2	Liver Pancreatic β -cells	~15 mM	Uptake and release of glucose by the liver β -cell glucose sensor
GLUT 3	Most tissues	~1 mM	Basal uptake
GLUT 4	Skeletal muscle Adipose tissue	~5 mM	Insulin-stimulated glucose uptake

Normal blood glucose concentration is 4–8 mM.

11.4 GLYCOLYSIS

Glycolysis is a cytoplasmic pathway that converts glucose into two pyruvates, releasing moderate amount of energy captured in two phosphate level phosphorylation and one oxidation reaction.



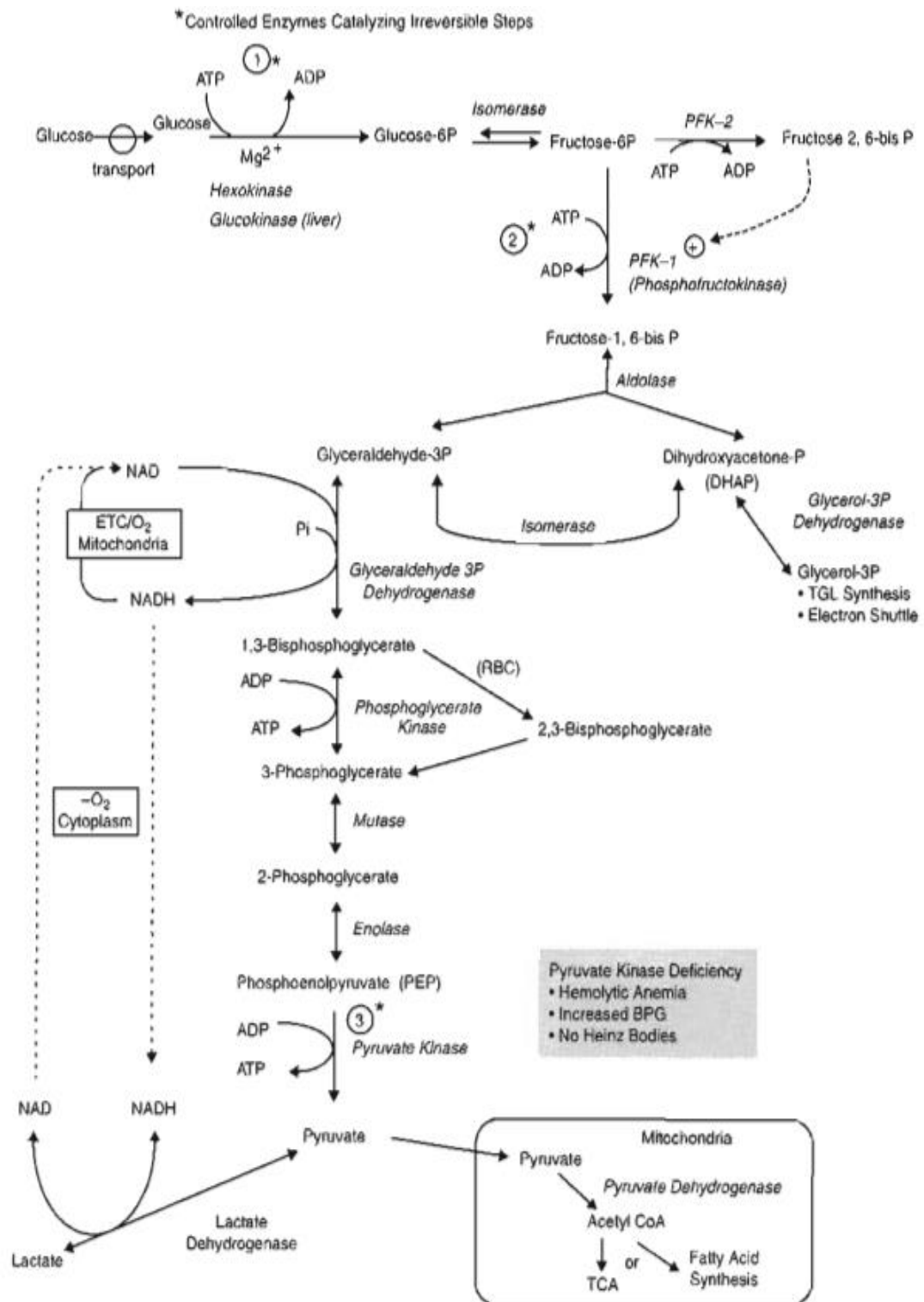


FIGURE 10: GLYCOLYSIS

- If glycolysis is in absence of oxygen it is anaerobic glycolysis.

11.4.1 TYPES OF GLYCOLYSIS

- If glycolysis is in presence of oxygen it is aerobic glycolysis.

11.4.2 COMPARISON OF HEXOKINASE AND GLUCOKINASE

Hexokinase	Glucokinase
Most tissues	Hepatocytes and pancreatic β -islet cells
Low K_m (0.05 mM in erythrocytes)	High K_m (10 mM)
Inhibited by glucose 6-phosphate	Induced by insulin in hepatocytes

PFK-2 is controlled by insulin and glucagon while PFK-1 is controlled by PFK-2

11.4.3 IMPORTANT INTERMEDIATES OF GLYCOLYSIS

- Dihydroxyacetone phosphate (DHAP) is used in liver and adipose tissue for triglyceride synthesis.
- 1,3-Bisphosphoglycerate and phosphoenolpyruvate are high energy intermediates are used to generate ATP.

11.4.4 IMPORTANCE OF LACTATE DEHYDROGENASE

Due to lack of mitochondria in red blood cells cannot utilize the NADH, so in order to regain the NAD required for the glycolysis process, pyruvate is converted to lactate in the presence of lactate dehydrogenase enzyme and it converts NADH back into NAD.

11.4.5 EFFECT OF 2-3 BISPHOSPHOGLYCERATE

Erythrocytes have bisphosphoglycerate mutase, which produces 2,3-bisphosphoglycerate (BPG) from 1,3-BPG in glycolysis. 2, 3- BPG binds to the beta-chains of hemoglobin A (HbA) and decreases its affinity for

oxygen. It occurs mostly due to deficiency of pyruvate kinase.

11.4.6 GLYCOLYSIS IS IRREVERSIBLE

Glycolysis is irreversible at three places which are as follows:

- Glucokinase/hexokinase
- PFK-1
- Pyruvate kinase

11.5 ATP PRODUCTION AND ELECTRON SHUTTLES

- In anaerobic glycolysis 2 ATP yields.
- In aerobic glycolysis 2 ATP plus 2 NADPH yields which can produce ATP further on.

11.5.1 SHUTTLES USED

- Malate shuttle produces 3 ATP by oxidative phosphorylation from cytoplasmic NADPH.
- Glycerol phosphate shuttle yield 2 ATP by oxidative phosphorylation from cytoplasmic NADPH.

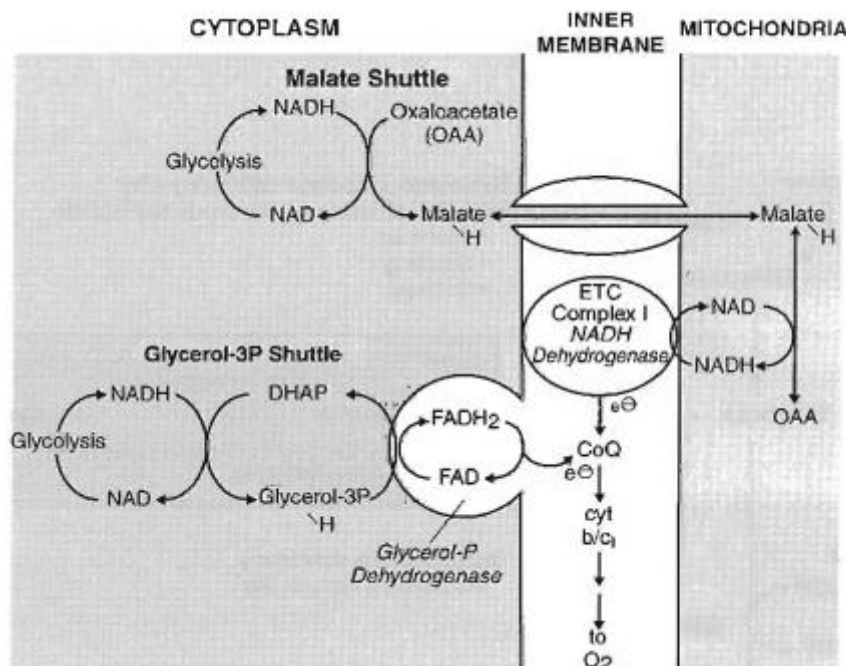


FIGURE 11: MALATE & GLYCEROL-3P SHUTTLE

11.6 GALACTOSE METABOLISM:



Important source of galactose is lactose which is hydrolyzed to glucose and galactose. Galactose reaches the liver with the help of portal blood. The important enzymes are:

- Galactokinase
- Galactose 1-phosphate uridylyltransferase.

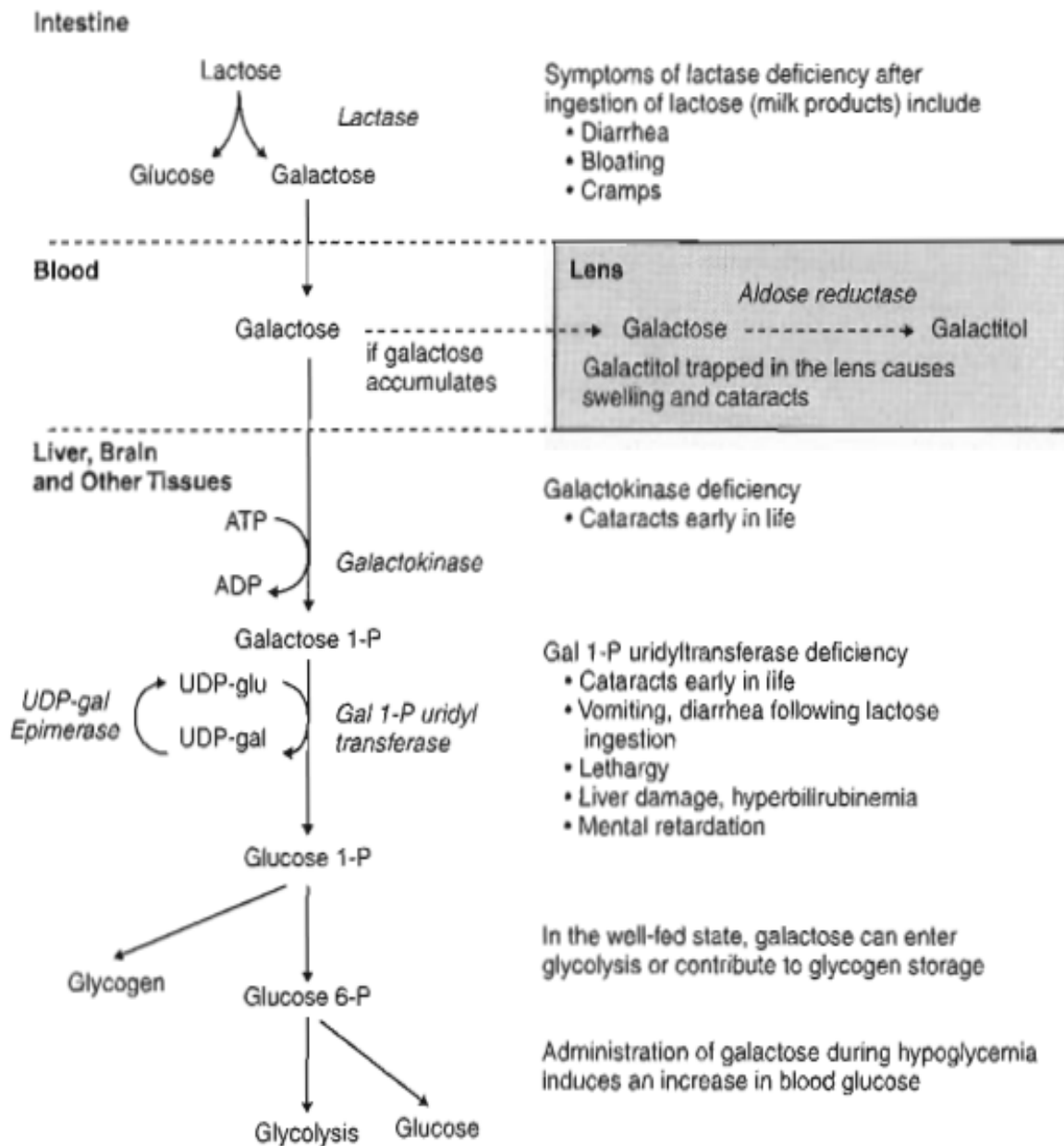


FIGURE 12: GALACTOSE METABOLISM

11.7 FRUCTOSE METABOLISM

Fructose is found in honey and fruit and as part of sucrose. Sucrose is hydrolyzed by intestinal brush

border sucrose and the resulting monosaccharide is fructose and glucose. The important enzymes to remember are:

- Fructokinase
- Fructose 1-P aldolase (aldolase B)



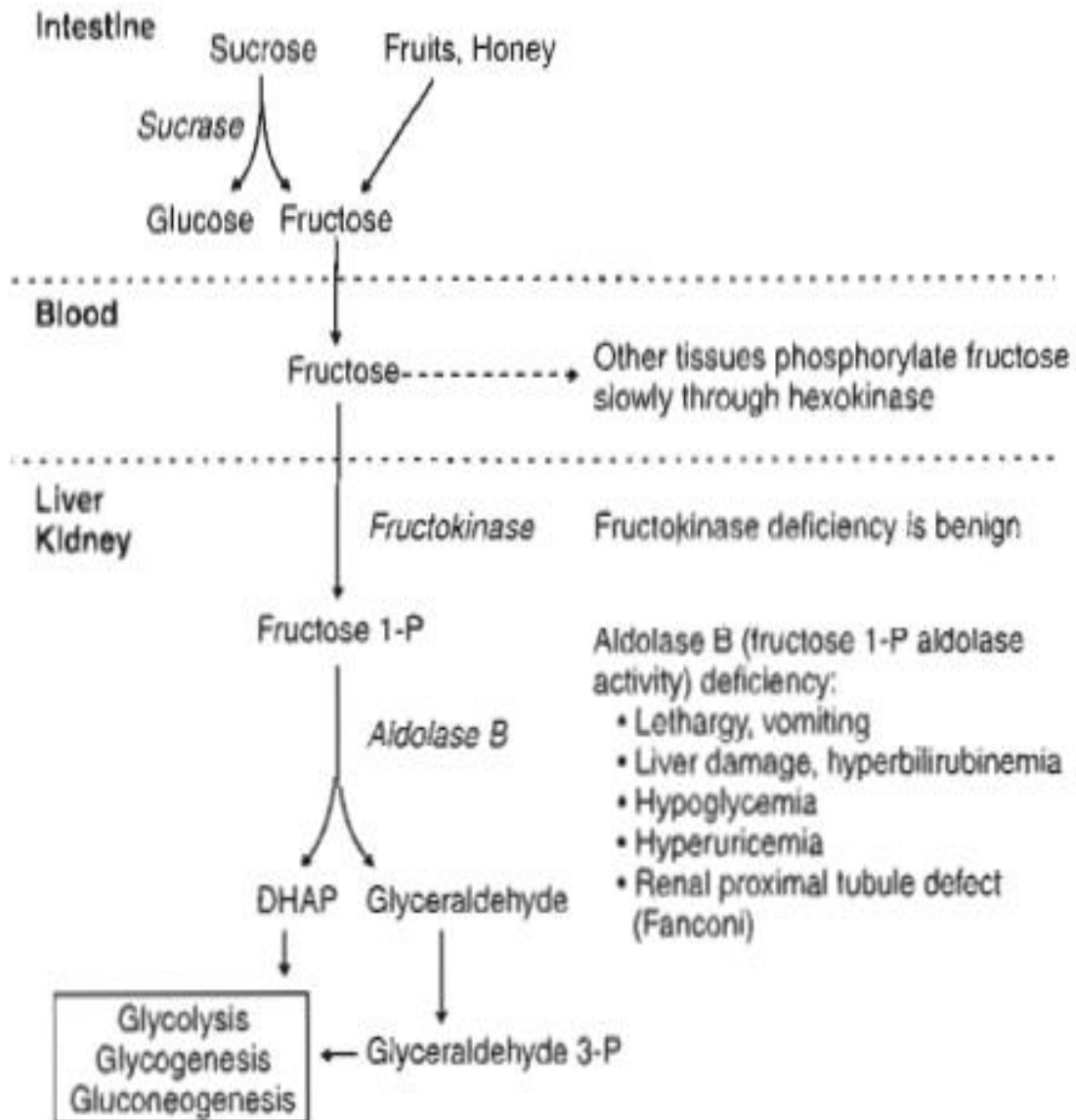


FIGURE 13: FRUCTOSE METABOLISM

11.8 PYRUVATE DEHYDROGENASE

Pyruvate from aerobic glycolysis enters mitochondria where it can be converted to acetyl CoA from which ATP can be extracted. This process is irreversible. Pyruvate dehydrogenase is activated by insulin in

liver, whereas in brain and nerve it is insensitive to hormones. It is inhibited by its product acetyl CoA. Important cofactors and co-enzymes used by pyruvate dehydrogenase include:

- Thiamine phosphate
- Lipoic acid
- Coenzyme A
- FADH_2
- NADPH



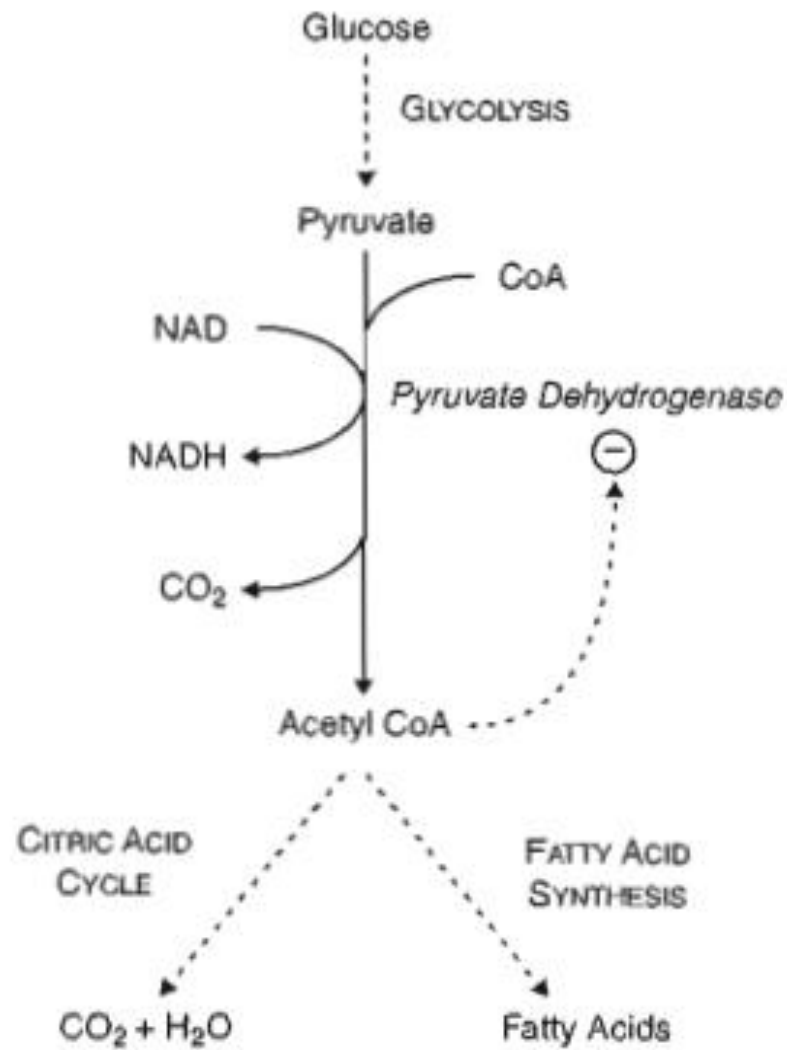


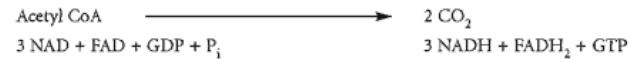
FIGURE 14: PYRUVATE DEHYDROGENASE



Chapter 12 CITRIC ACID CYCLE AND OXIDATIVE PHOSPHORYLATION

12.1 CITRIC ACID CYCLE

- The citric acid cycle is also called Krebs's cycle or tricarboxylic acid cycle.
- It occurs in mitochondria.
- This cycle requires oxygen.
- The primary function of this cycle is the oxidation of acetyl CoA to CO_2 .
- The energy released from this cycle is saved as NADH, FADH_2 And GTP.
- All the enzymes are in mitochondrial matrix except succinate dehydrogenase which is in the inner membrane.



12.2 KEY POINTS

- Isocitrate dehydrogenase, the major control enzyme is inhibited by NADH and ATP .and is activated by ATP.
- Alpha-ketoglutarate is similar to pyruvate dehydrogenase complex.
- Succinyl-CoA synthetase catalyzes substrate level phosphorylation.
- Succinate dehydrogenase present in inner membrane of mitochondria.
- Citrate synthetase condenses the incoming acetyl group with oxaloacetate to form malate.

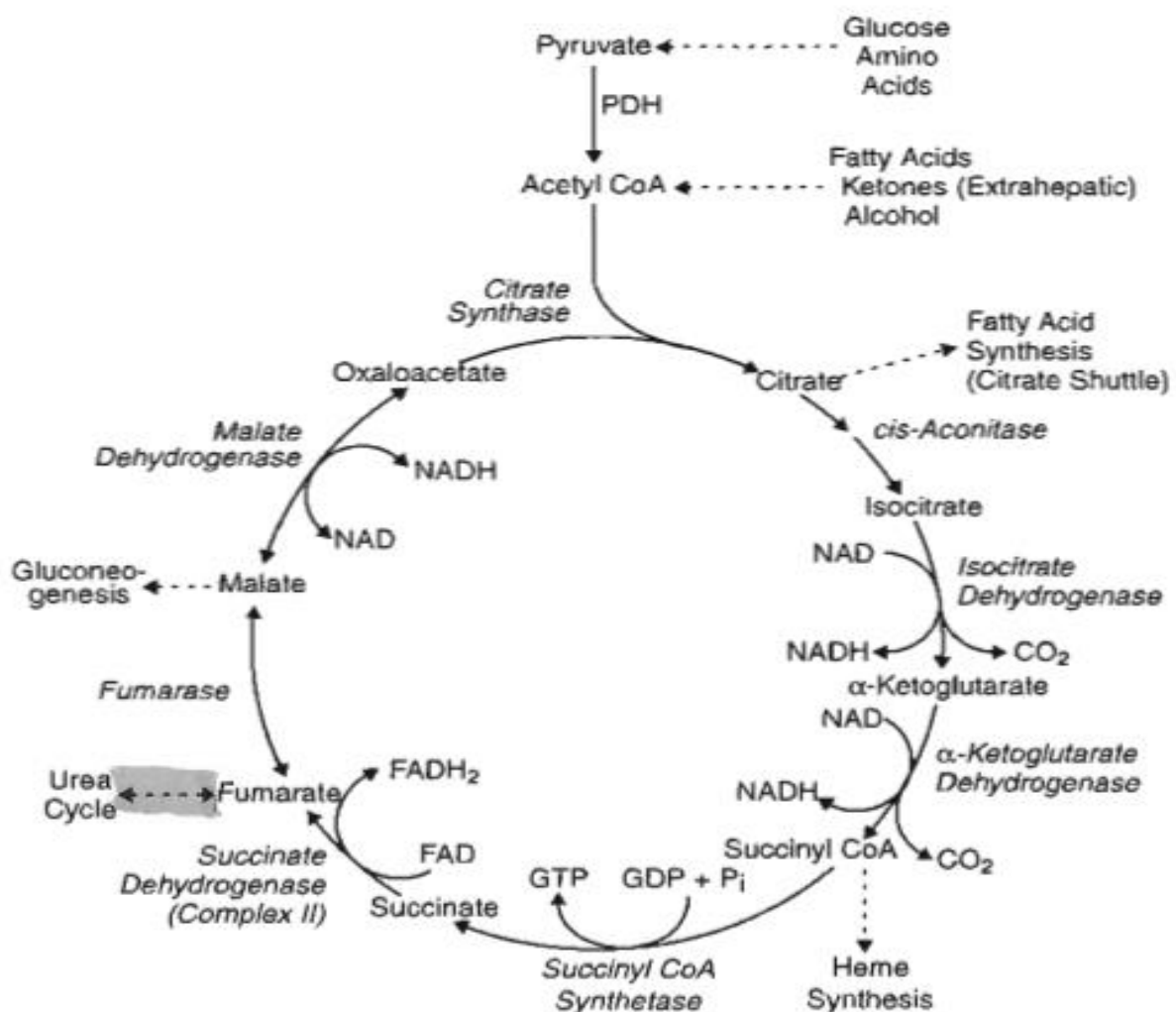
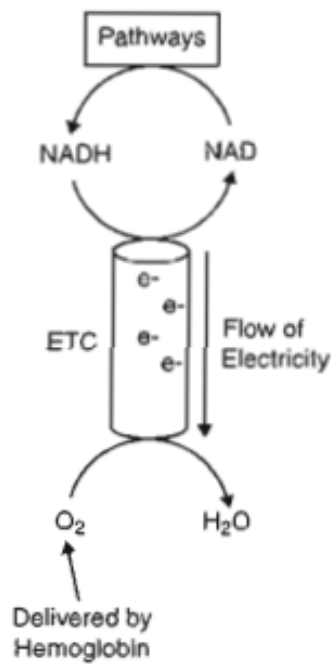


FIGURE 15: KREB'S CYCLE

12.3 IMPORTANT INTERMEDIATE

- Citrate may leave the mitochondria to deliver acetyl CoA to cytoplasm for fatty acid synthesis.
- Succinyl CoA is a high energy intermediate used for heme synthesis.
- Malate can take part in gluconeogenesis.

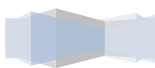
12.4 OVERVIEW OF ELECTRON TRANSPORT CHAIN

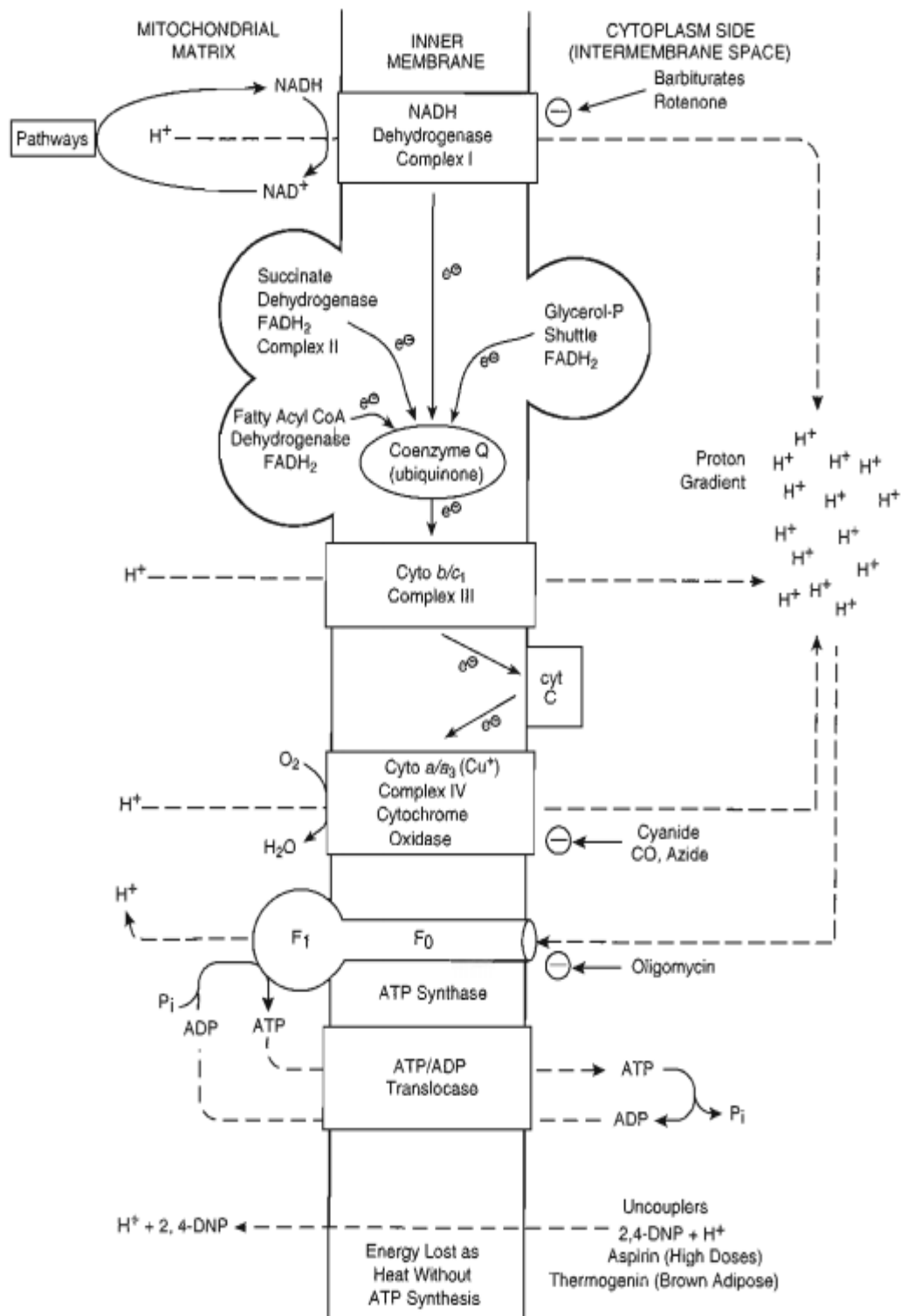


12.5 SOURCES OF NADH, FADH₂ AND O₂:

- Citric acid cycle and pyruvate dehydrogenase produces NADH.
- Succinate dehydrogenase in the TCA cycle and by the alpha-glycerol shuttle produces FADH₂.
- O₂ is delivered to tissues by hemoglobin.

12.6 ELECTRON TRANSPORT CHAIN

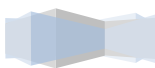




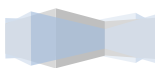
12.7 REACTIVE OXYGEN SPECIES

- When molecular oxygen is partially reduced it produces reactive oxygen species.
- They rapidly react with lipids and causes peroxidation.

- Reactive oxygen species include:
 - Superoxide (O_2^-)
 - Hydrogen peroxide (H_2O_2)
 - Hydroxyl radical (OH)
- Production of these species will be low if oxygen is in high concentration.
- Small quantities of ROS are by-product of ETC.



- These small quantities are destroyed by enzymes catalase.
- The rate of ROS production will increase under certain conditions like reperfusion injury in a tissue that has been deprived of oxygen.
- When oxygen level is suddenly increased which increase the rate of ETC and hence increase in ROS production.



Chapter 13 GLYCOGEN, GLUCONEOGENESIS, AND THE HEXOSE MONPHOSPHATE SHUNT

13.1 GLYCOGEN SYNTHESIS

- From glucose using enzyme glycogen synthetase and branching enzyme in liver and muscle and to some extent in kidney.
- Insulin is the hormone that activates glycogen synthetase and branching enzyme.
- High level of glucose in liver also promotes glycogenesis.

- Synthesis of glycogen granules begins with a core protein glycogenin.

13.2 GLYCOGENOLYSIS

The breakdown of glycogen is called glycogenolysis.

- The rate limiting enzyme of glycogenolysis is glycogen phosphorylase.
- High level of AMP increases glycogenolysis.
- Glucagon and epinephrine promotes glycogenolysis.
- Glycogen phosphorylase and debranching enzyme promotes glycogen breakdown.

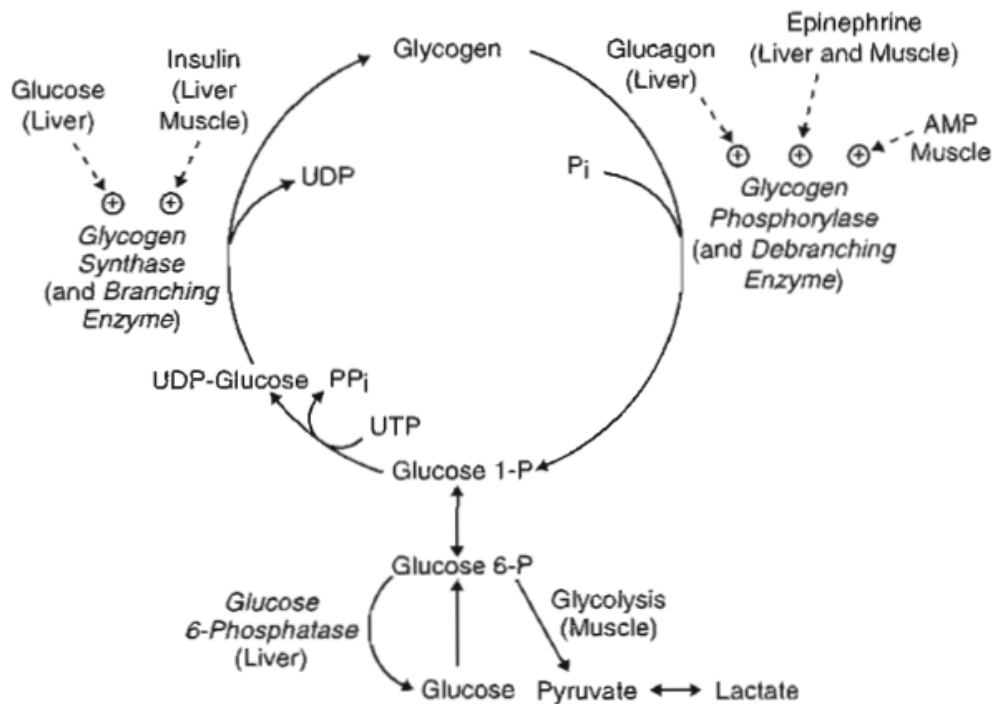


FIGURE 16: GLYCOGEN SYNTHESIS & GLYCOGENOLYSIS

13.3 COMPARISON OF GLYCOGEN SYNTHETASE IN LIVER AND MUSCLE

Glycogen Synthase	Liver	Skeletal Muscle
Activated by	Insulin Glucose	Insulin
Inhibited by	Glucagon Epinephrine	Epinephrine

13.4 GENETIC DEFICIENCIES OF ENZYMES IN GLYCOGEN METABOLISM

The glycogen storage diseases are as follows:

1. Von Gierke

2. Pompe
3. Cori
4. Anderson
5. McArdle
6. Hers



13.7 CORI CYCLE AND ALANINE CYCLE

During fasting, lactate from red blood cells is converted in liver to glucose that can be returned to the red blood cell or muscle. This is called Cori cycle.

The alanine cycle is slightly different version of Cori cycle, in which muscle released alanine, delivering both gluconeogenic substrate and an amino group for urea synthesis.

13.8 HEXOSE MONOPHOSPHATE SHUNT

The hexose monophosphate shunt (HMP) occurs in CYTOPLASM, where it serves two major functions:

- i- NADPH production
- ii- Sources of ribose 5-phosphate for nucleotidesynthesis

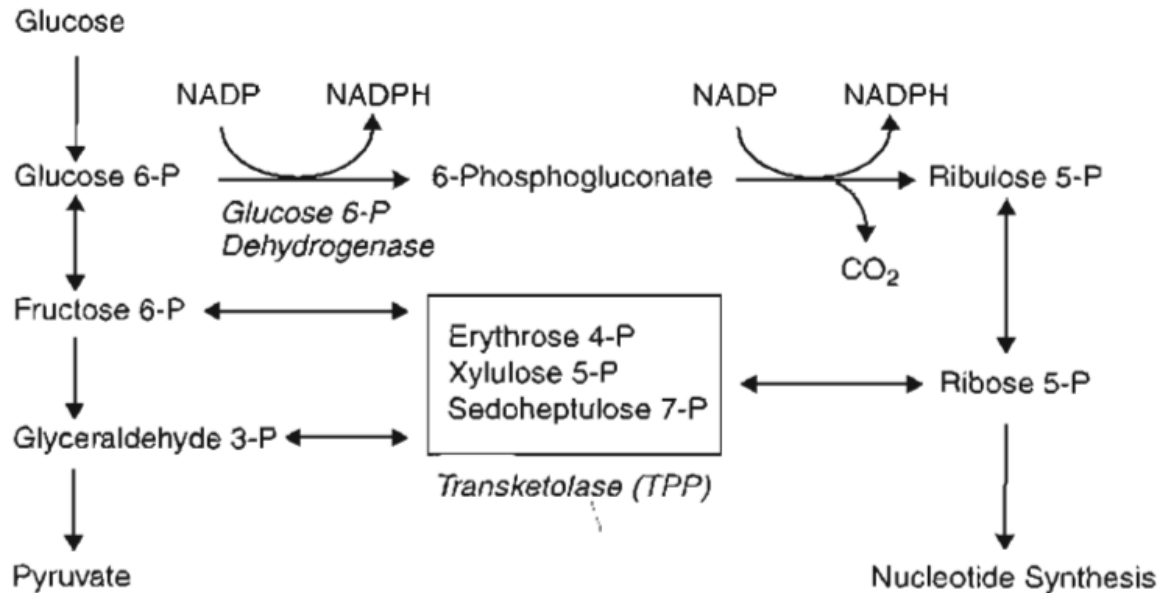


FIGURE 18: HMP SHUNT

13.8.1 FUNCTIONS OF NADPH

- Biosynthesis

- To protect against reactive oxygen species
- Bactericidal activity in polymorphonuclear leukocytes.



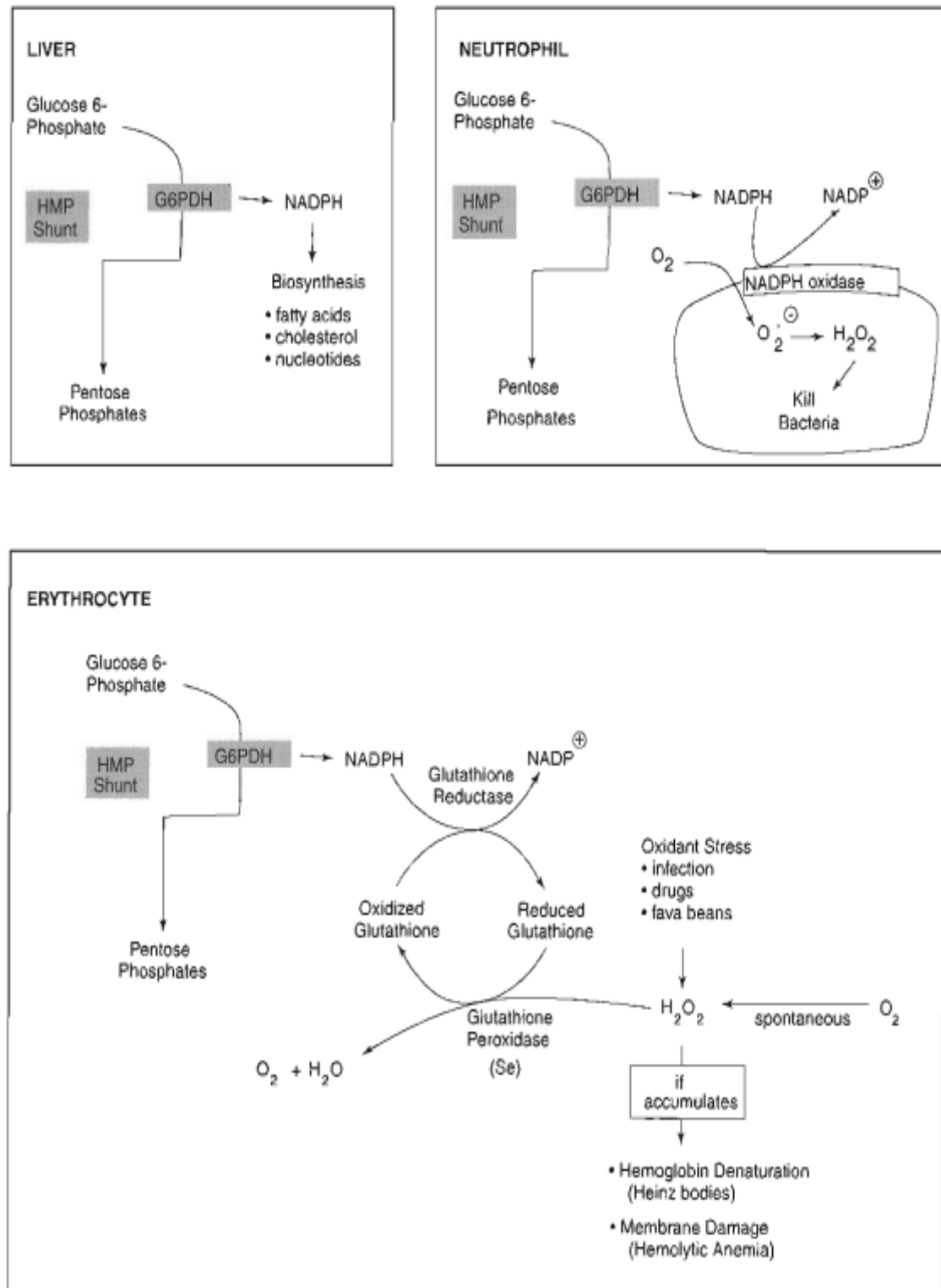


FIGURE 19: FUNCTION OF NADPH



Chapter 14 LIPID SYNTHESIS AND STORAGE

14.1 NOMENCLATURE OF FATTY ACID

- Fatty acid is a long chain carboxylic acid.
- While naming fatty acid, the carbonyl carbon is referred to as carbon 1.
- The carbon contains double bond is considered as carbon 2.
- So the name is given in this fashion (carbon: double bond).

Example: Linoleic C18:2

14.2 UNSATURATED FATTY ACID

Those fatty acid which poses double bond is called unsaturated fatty acid.

14.2.1.1 EXAMPLE:

1. Linolenic C18:3
2. Archidonic C20:4

14.3 SATURATED FATTY ACID

Those fatty acids which do not have double bond in them is called saturated fatty acid.

14.3.1.1 EXAMPLE:

1. Palmitic acid C16:0

14.4 ESSENTIAL FATTY ACID

Those fatty acid which body cannot synthesis is called essential fatty acid.

14.4.1.1 EXAMPLE:

1. Linolenic acid.

14.5 NON-ESSENTIAL FATTY ACID

Those fatty acid which body can synthesis is called non-essential fatty acid.

14.5.1.1 EXAMPLE:

1. Palmitic acid

14.6 NAMING OF UNSATURATED FATTY ACID

- The omega numbering system is used for naming unsaturated fatty acid.
- It describes the position of the last double bond relative to the length of the chain.

14.6.1.1 EXAMPLE:

1. Linolenic C18:3
2. Archidonic C20:4

14.7 ACTIVATION OF FATTY ACID

- When fatty acids are used in metabolism, they are first activated by attaching coenzyme.
- This step is catalyzed by enzyme fatty acyl CoA synthetase.
- This product is generally referred to as fatty acyl CoA.

14.7.1.1 EXAMPLE

Fatty acid + CoA + ATP gives fatty acyl CoA + AMP

14.8 LIPID DIGESTION

- Typical high fatty meals contains gram level of triglyceride and milligram level of cholesterol and cholesterol esters.
- In the intestine, bile is secreted by liver to emulsify fats.
- The pancreas secretes pancreatic lipase, colipase and cholesterol esterase that degrade the fats into fatty acid, 2 monoglyceride and cholesterol.
- These lipids are absorbed and are re-esterified into triglyceride and cholesterol esters and then packed.
- Normally, there is very little fat loss in stools.
- Defects in lipid digestion is called steatorrhea, in which there is excessive loss of lipids in stool.

14.9 FATTY ACID BIOSYNTHESIS

- Excess dietary glucose can be converted to fatty acid and sent to adipose tissue for storage.
- Adipose tissue synthesis smaller quantity of fats.
- Insulin promotes many steps in the conversion of glucose to acetyl CoA in liver:
 1. Glucokinase
 2. PFK-1/PFK-2
 3. Pyruvate dehydrogenase



- Both of the major enzymes for the fatty acid synthesis are also affected by insulin:
 - Acetyl CoA carboxylase
 - Fatty acid synthase.

14.10 CITRATE SHUTTLE AND MALIC ENZYME

- The citrate shuttle transports acetyl CoA groups from the mitochondria to the cytoplasm for fatty acid synthesis.
- Acetyl CoA combines with oxaloacetate in the mitochondria to form citrate.

- But rather than continuing in the citric acid cycle, citrate is transported back to cytoplasm.
- Factors include are insulin and high-energy status.
- In the cytoplasm, citrate lyase splits citrate back into acetyl CoA and oxaloacetate.
- The oxaloacetate returns to the mitochondria to transport additional acetyl CoA.
- This reaction needs NADPH in liver and adipose tissue.

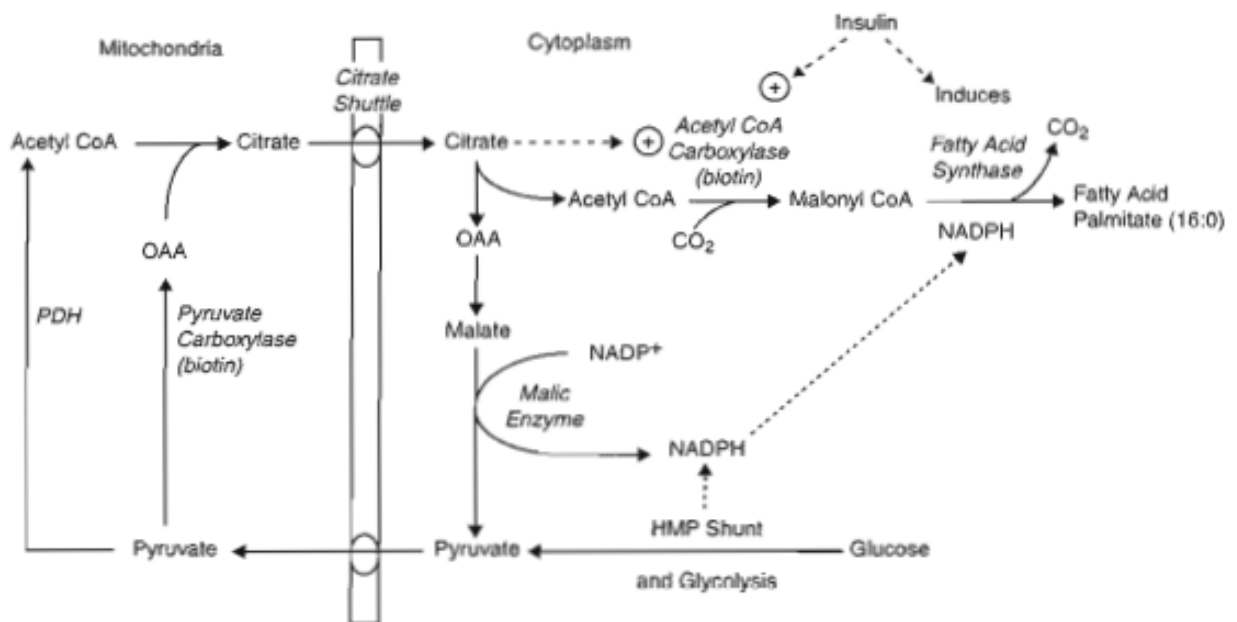


FIGURE 20: SYNTHESIS OF PALMITATE FROM GLUCOSE

14.11 ACETYL CoA CARBOXYLASE

- It is the rate limiting enzyme for fatty acid biosynthesis.
- It is activated by insulin.
- Also by citrate.
- It requires biotin, ATP, CO₂.

14.12 FATTY ACID SYNTHASE

- It may be appropriately called palmitate synthase because palmitate the only fatty acid that can be synthesis in body.

14.13 TRIGLYCERIDE SYNTHESIS AND STORAGE

14.13.1 TRIGLYCERIDE

- Triglyceride, the storage form of fatty acid.
- Triglyceride formation from fatty acid and glycerol 3-P occurs primarily in liver and adipose tissue.
- Liver sends triglycerides to adipose tissue and are packed as very low density lipoproteins (VLDL).

14.13.2 SOURCES OF GLYCEROL 3-P

- Reduction of dihydroxyacetone phosphate (DHAP) in glycolysis by enzyme glycerol 3-P dehydrogenase.
- Phosphorylation of free glycerol by enzyme glycerol kinase.



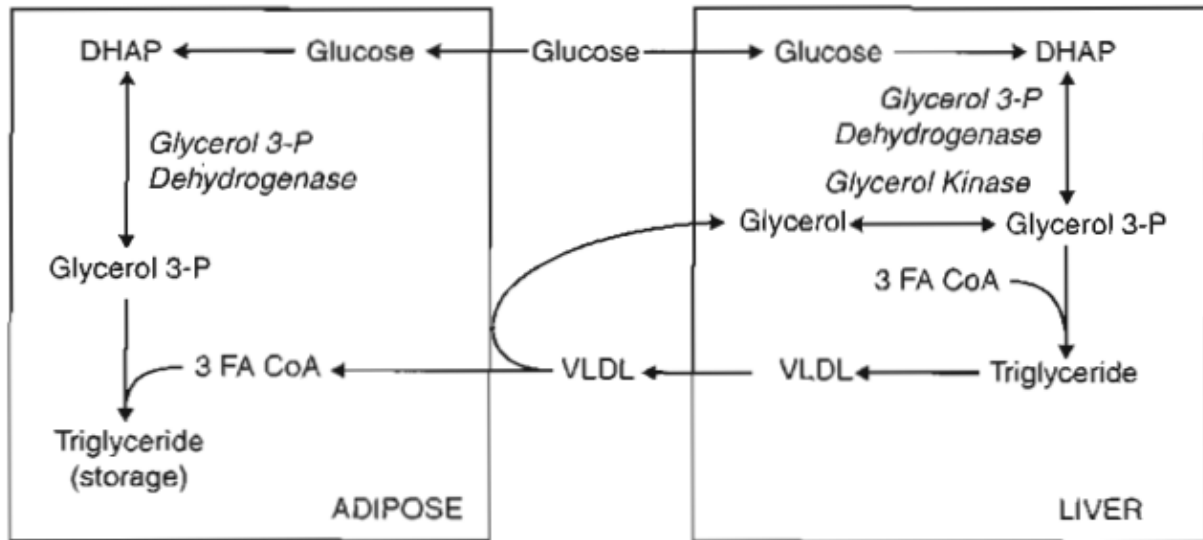


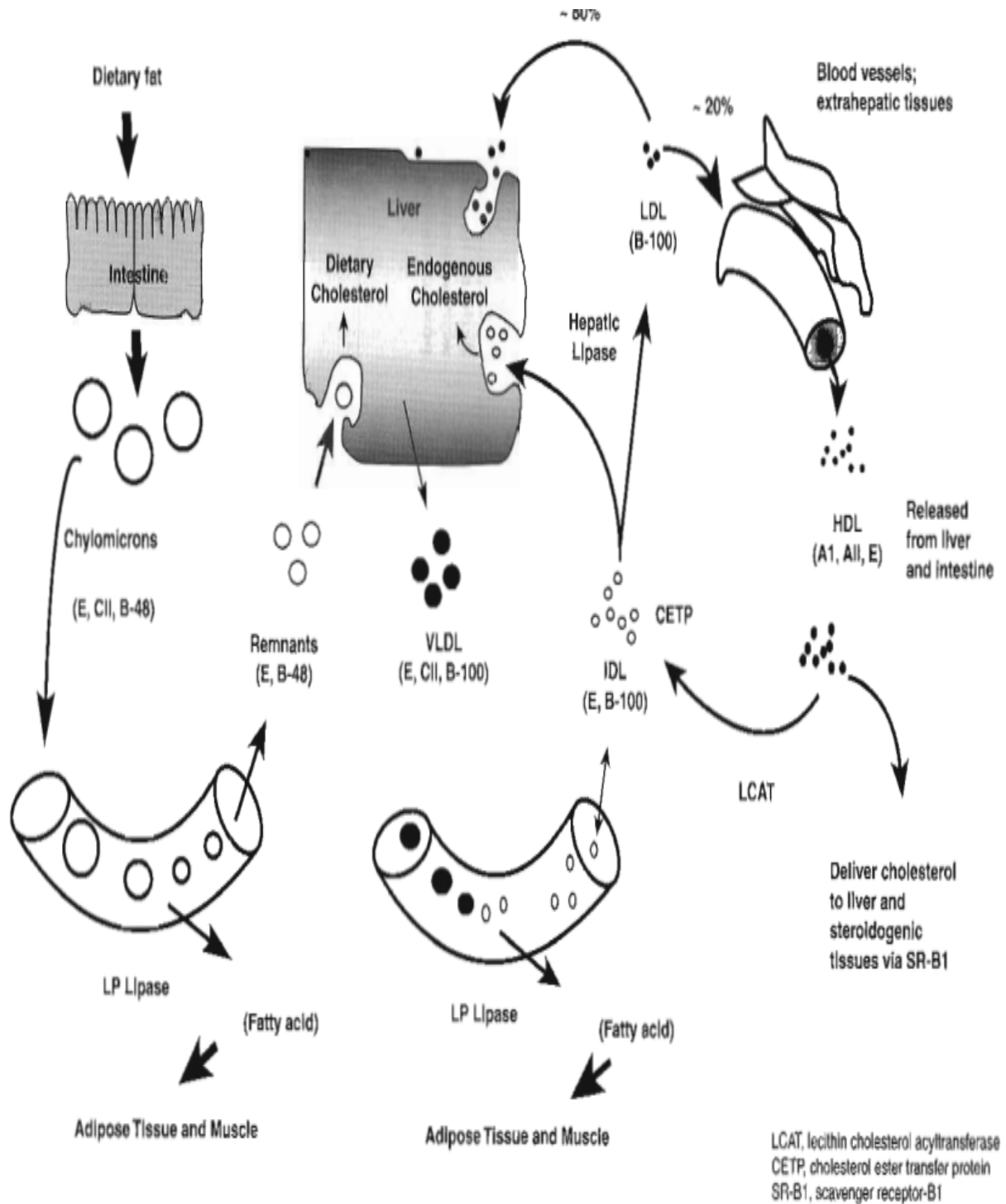
FIGURE 21: TRIGLYCERIDE SYNTHESIS AND STORAGE

14.14 CLASSES OF LIPOPROTEINS

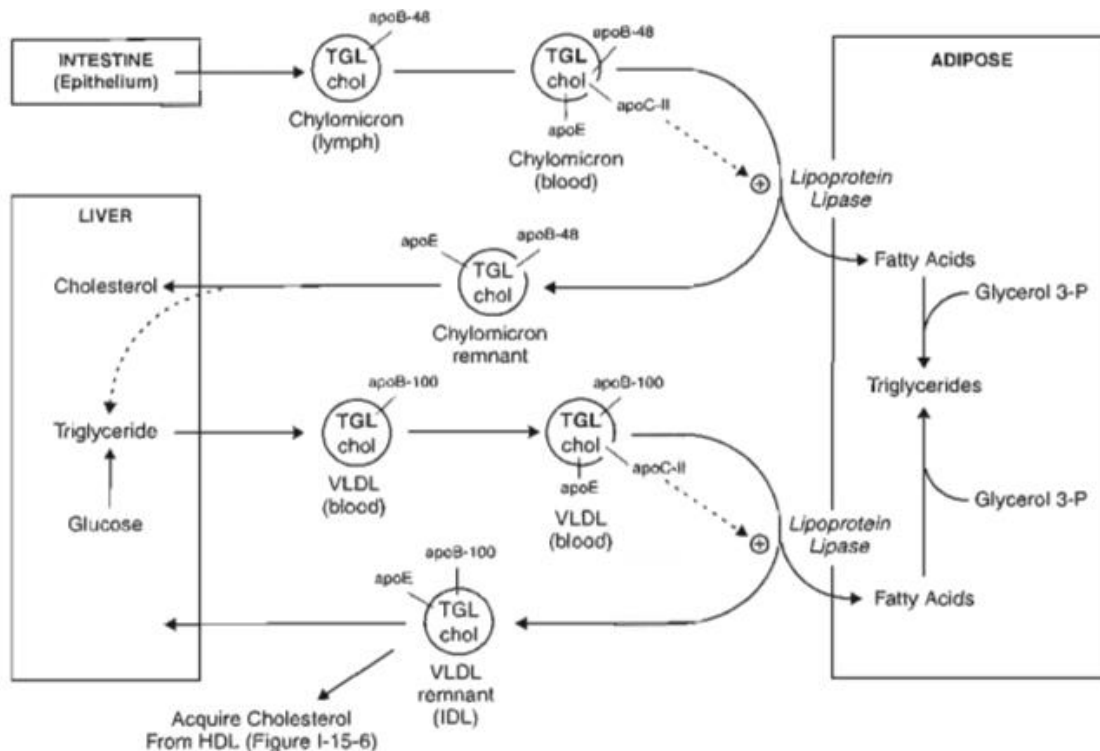
Lipoprotein	Functions	Apoproteins	Functions
Chylomicrons	Transport dietary triglyceride and cholesterol from intestine to tissues	apoB-48 apoC-II apoE	Secreted by epithelial cells Activates lipoprotein lipase Uptake by liver
VLDL	Transports triglyceride from liver to tissues	apoB-100 apoC-II apoE	Secreted by liver Activates lipoprotein lipase Uptake of remnants by liver
LDL	Delivers cholesterol into cells	apoB-100	Uptake by liver and other tissues via LDL receptor (apoB-100 receptor)
IDL (VLDL remnants)	Picks up cholesterol from HDL to become LDL Picked up by liver	apoE	Uptake by liver
HDL	Picks up cholesterol accumulating in blood vessels Delivers cholesterol to liver and steroidogenic tissues via scavenger receptor (SR-B1) Shuttles apoC-II and apoE in blood	apoA-1	Activates lecithin cholesterol acyltransferase (LCAT) to produce cholesterol esters

14.15 OVERVIEW OF LIPOPROTEIN METABOLISM





14.15.1 CHYLOMICRON AND VLDL METABOLISM



14.16 ATHEROSCLEROSIS

- Atherosclerosis (or arteriosclerotic vascular disease) is a condition where the arteries become narrowed and hardened due to an excessive buildup of plaque around the artery wall. The disease disrupts the flow of blood around the body, posing serious cardiovascular complications.
- Arteries contain what is called an *endothelium*, a thin layer of cells that keeps the artery smooth and allows blood to flow easily. Atherosclerosis starts when the endothelium becomes damaged, allowing LDL cholesterol to accumulate in the artery wall. The body sends macrophage white blood cells to clean up the cholesterol, but sometimes the cells get stuck there at the affected site. Over time this results in plaque being built up, consisting of bad cholesterol

(LDL cholesterol) and macrophage white blood cells.

- The plaque clogs up the artery, disrupting the flow of blood around the body. This potentially causes blood clots that can result in life-threatening conditions such as heart attack, stroke and other cardiovascular diseases.
- The condition can affect the entire artery tree, but mainly affects the larger high-pressure arteries.

14.17 CHOLESTEROL METABOLISM

- HMG-CoA is the rate limiting enzyme of this reaction.
- Cholesterol is required for:
 1. Steroids
 2. Bile acids
 3. Vitamin D
 4. Cell membrane.



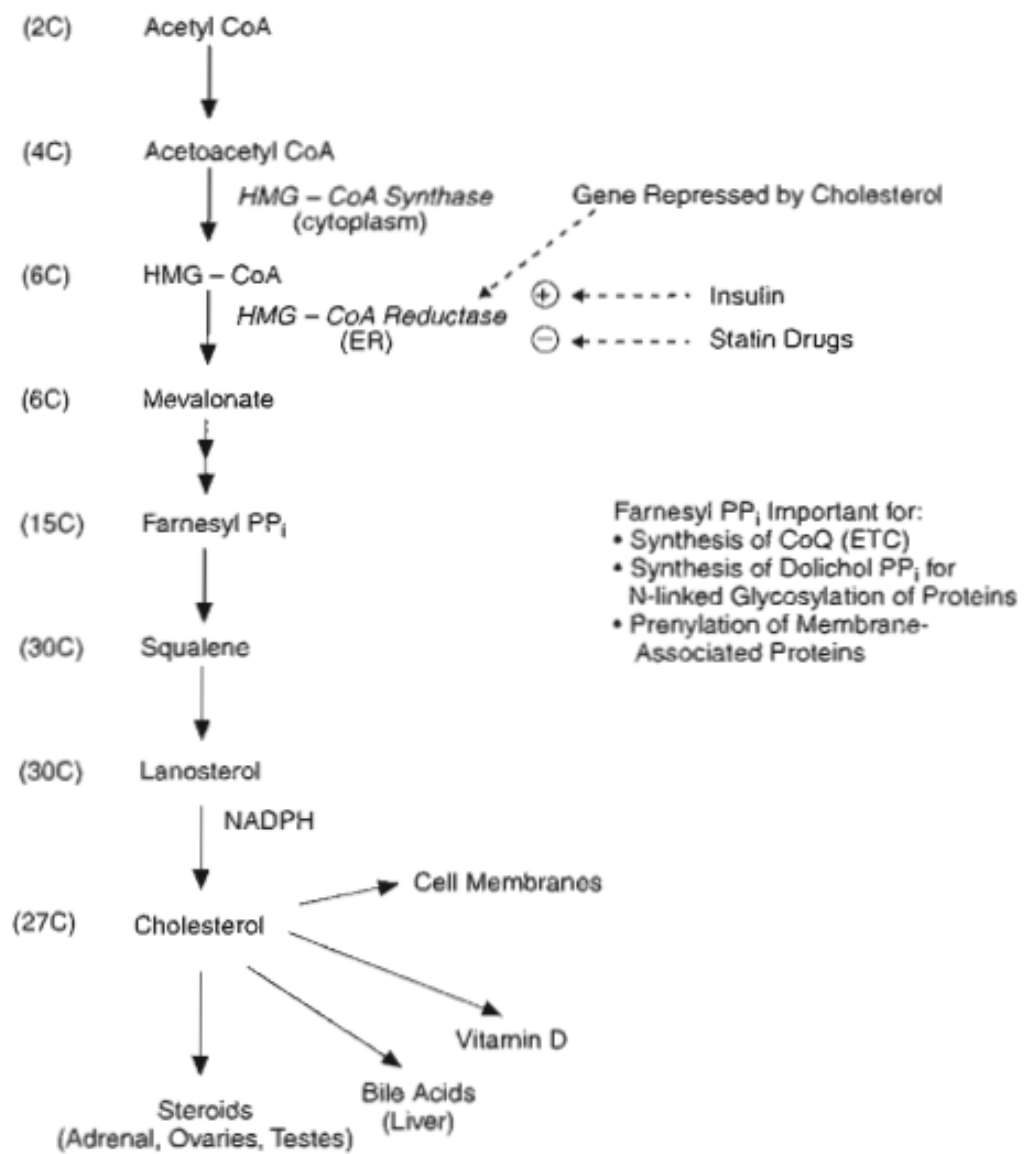


FIGURE 22: CHOLESTEROL METABOLISM



Chapter 15 LIPID MOBILIZATION AND CATABOLISM

15.1 LIPID MOBILIZATION/ LIPOLYSIS OF TGL

- In post absorptive stage, the TGL present in adipose tissue is released and transferred to liver to be used as energy.

- With the fall of level of insulin, the level of cortisol, epinephrine, growth hormone and glucagon increases.
- The increase level of these hormones stimulates the release of hormone sensitive lipase.
- This hormone breaks the TGL into glycerol and fatty acid.
- They go to liver and form energy related products.

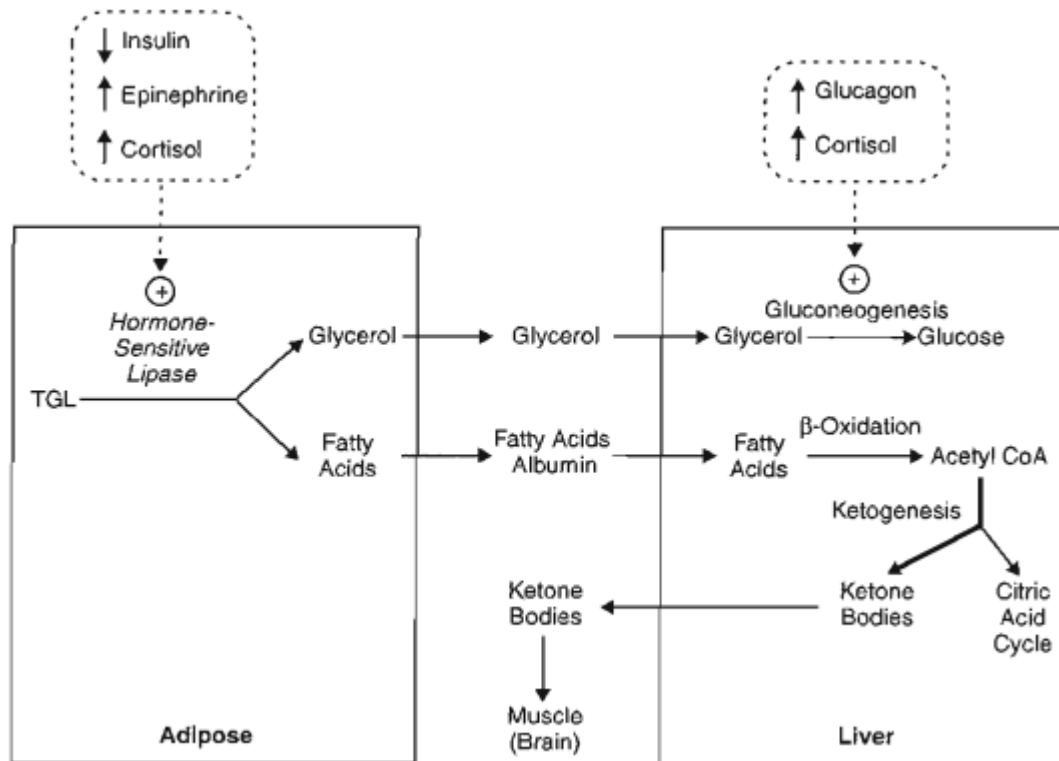


FIGURE 23: LIPOLYSIS OF TGL

Beta oxidation is the reverse the process of the fatty acid synthesis.

15.2 BETA- OXIDATION IN MITOCHONDRIA



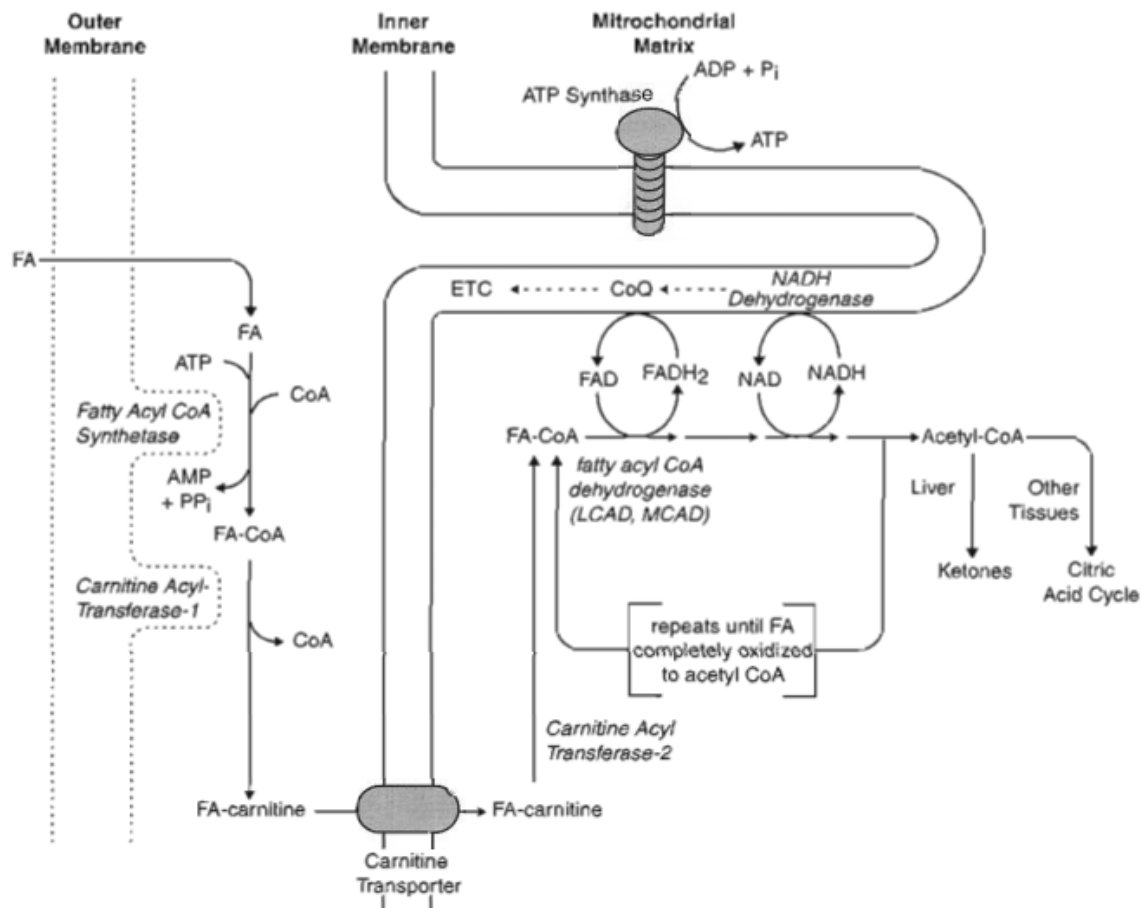


FIGURE 24: BETA OXIDATION OF FATTY ACIDS

15.3 KETONE BODY METABOLISM

- In the fasting state, the liver converts excess acetyl CoA from beta oxidation of fatty acids into ketone bodies which are acetoacetate, 3- hydroxybutyrate and acetate.

15.3.1 KETOGENESIS

The formation of ketone in the liver is called ketogenesis.

15.3.2 KETOGENOLYSIS

The breakdown of ketone is called ketogenolysis which takes place in extrahepatic tissues.



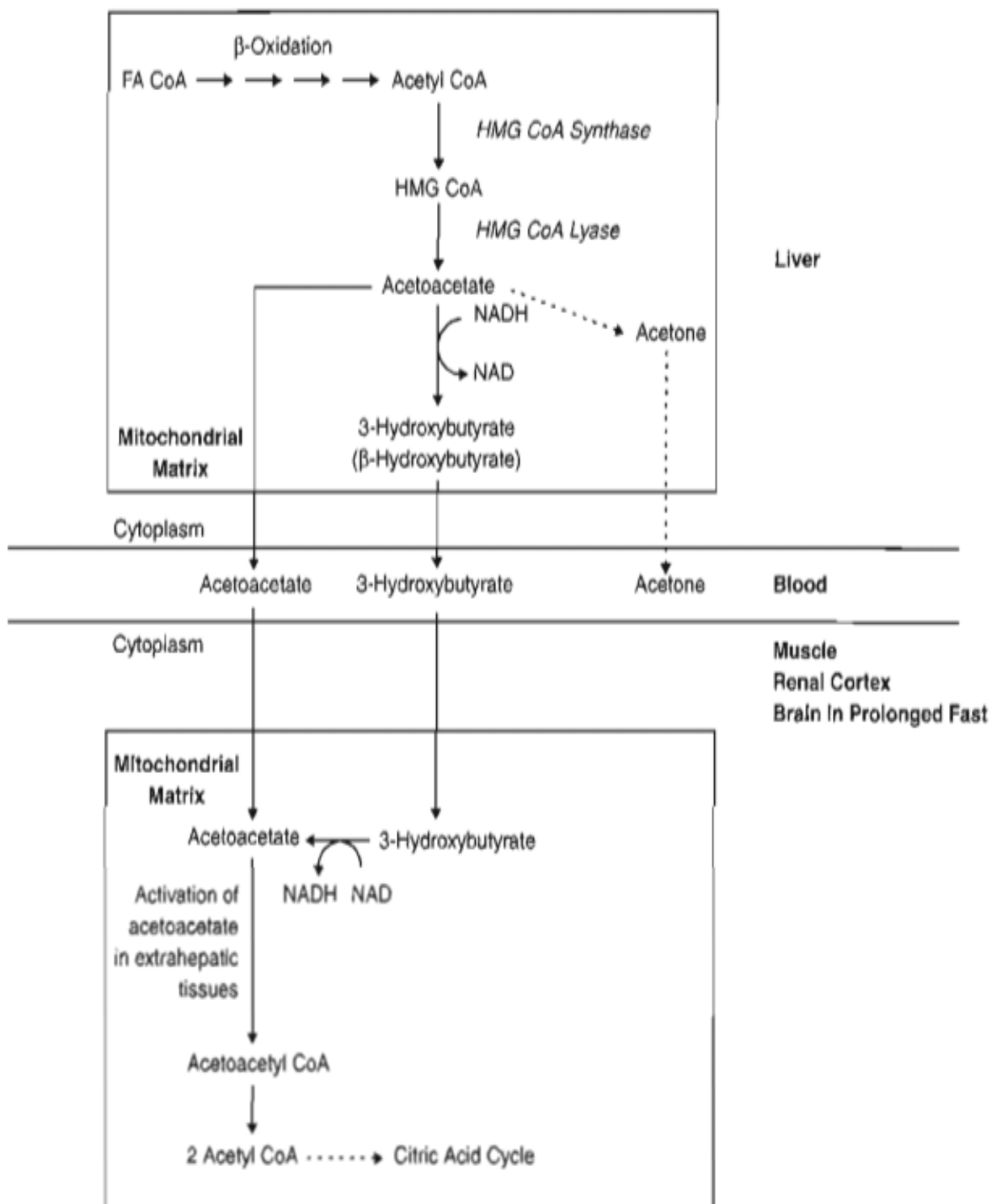


FIGURE 25: KETOGENESIS



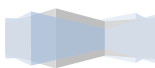
Chapter 16 AMINO ACID METABOLISM

16.1 OVERVIEW

- Proteins obtained from diet or from body can be used as energy source.
- Body protein is catabolized primarily in liver and muscle.
- Amino acid released from proteins usually lose their amino group through deamination or transamination.

16.2 REMOVAL AND EXCRETION OF AMINO GROUPS

- Excess nitrogen is eliminated from the body in the urine.
- Amino group released from deamination forms ammonia.
- Excess nitrogen in the peripheral blood called hyperammonia.



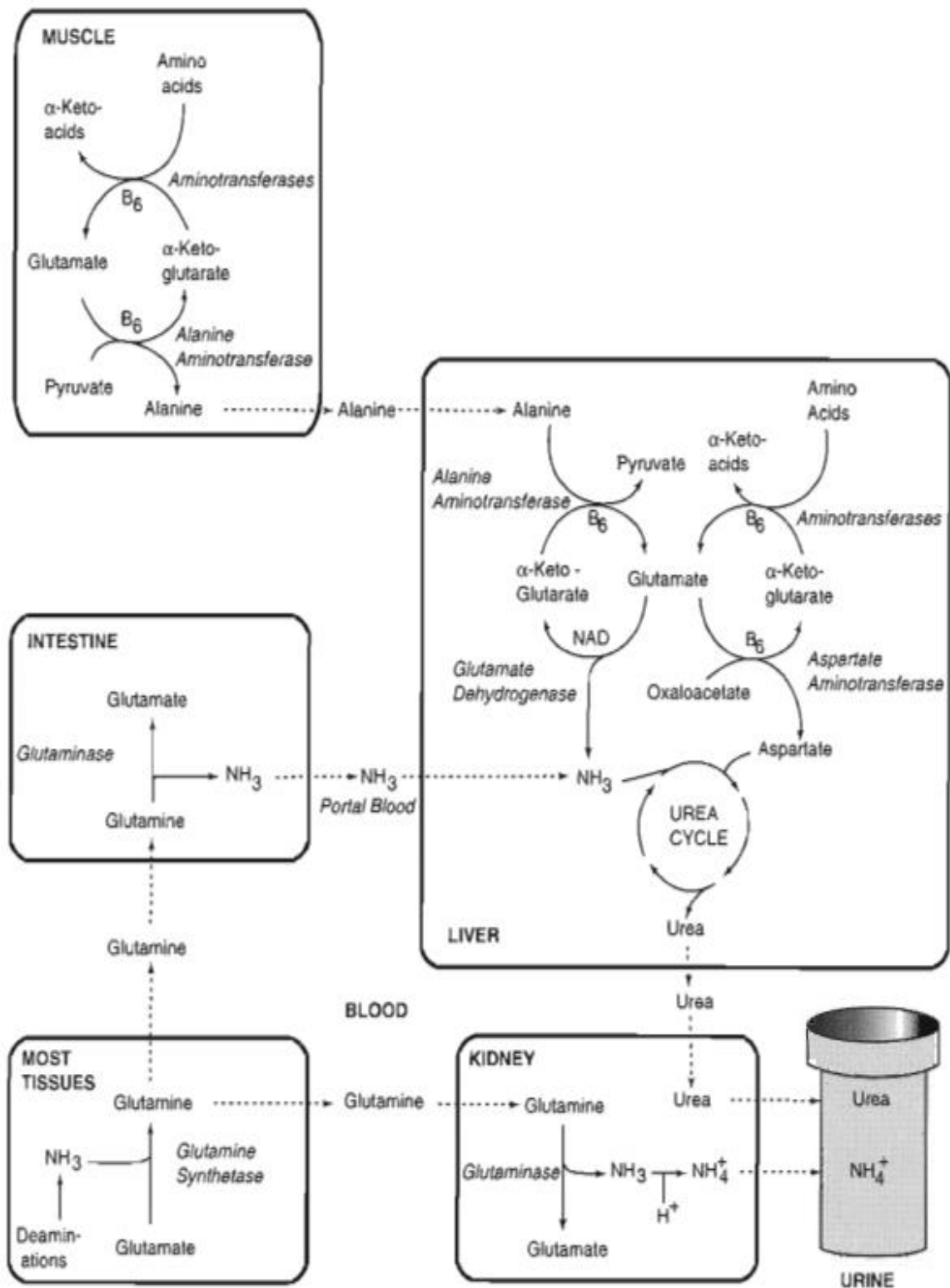


FIGURE 26: REMOVAL AND EXCRETION OF AMINO GROUPS

16.3 UREA CYCLE

- Urea, which contains two nitrogen atoms, is synthesized in the liver from aspartate and

Carbamoyl phosphate, which in turn is produced from ammonium ion and carbon dioxide.

- The urea cycle, like citric acid cycle, acts catalytically.
- The cycle partially in mitochondria and partially in cytoplasm.



- Citrulline enters the cytoplasm and ornithine returns to the mitochondria.
- Carbamoyl phosphate synthetase and ornithine transcarbamoylase are mitochondrial enzyme.
- Aspartate enters the cycle.
- The product urea is formed in cytoplasm and enters the blood for delivery to kidney.

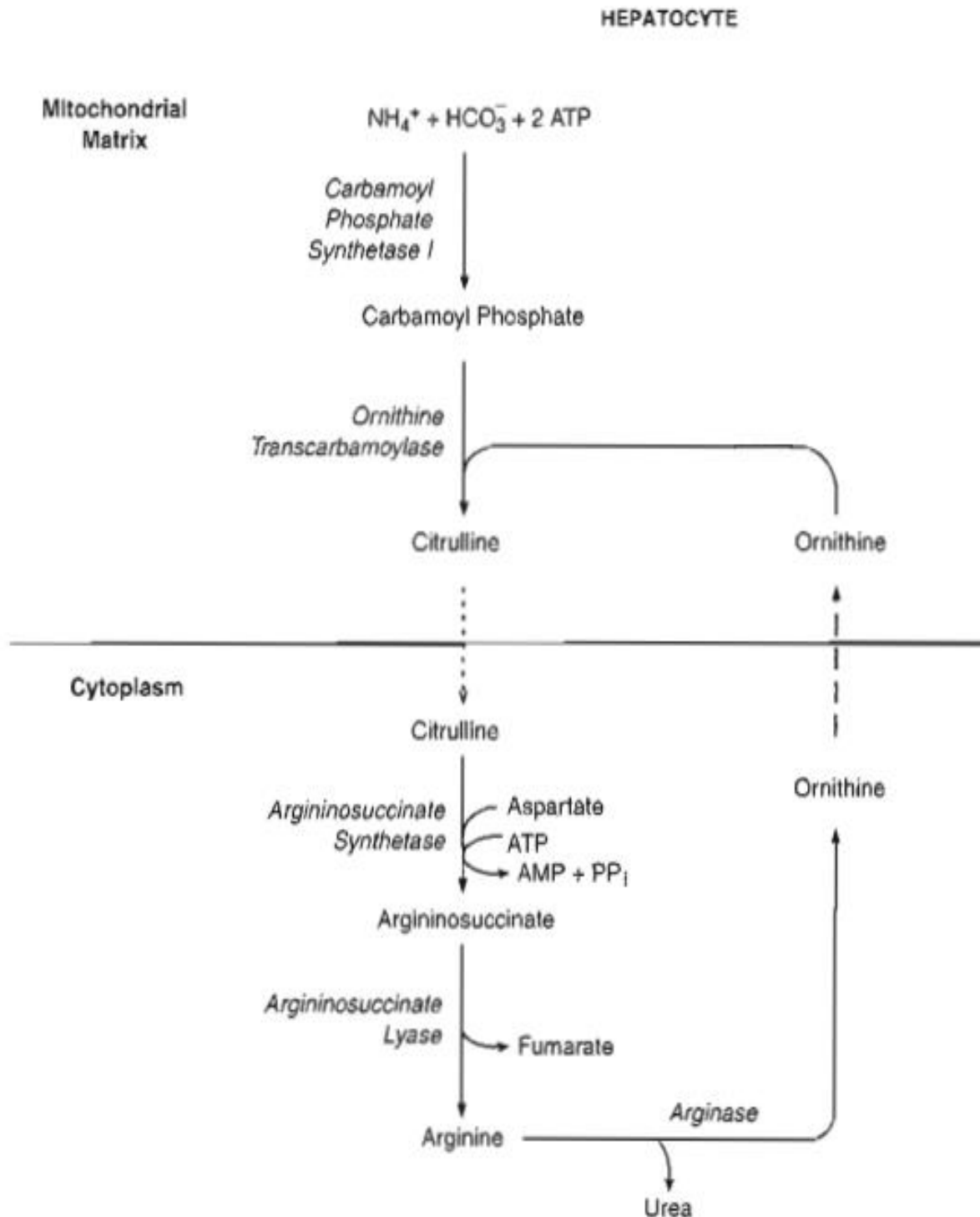
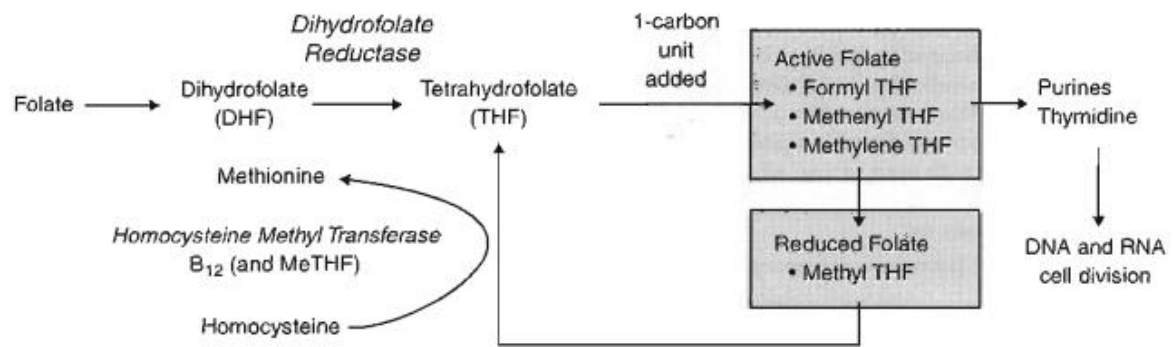


FIGURE 27: UREA CYCLE

16.4 FOLATE METABOLISM





- The enzymes include are catalase, peroxidase.
- In liver, the rate limiting enzyme is alpha-aminolevulinic acid.

16.5 HEME SYNTHESIS

- Heme synthesis occurs in all tissues because heme protein includes not only hemoglobin and myoglobin but all cytochromes.



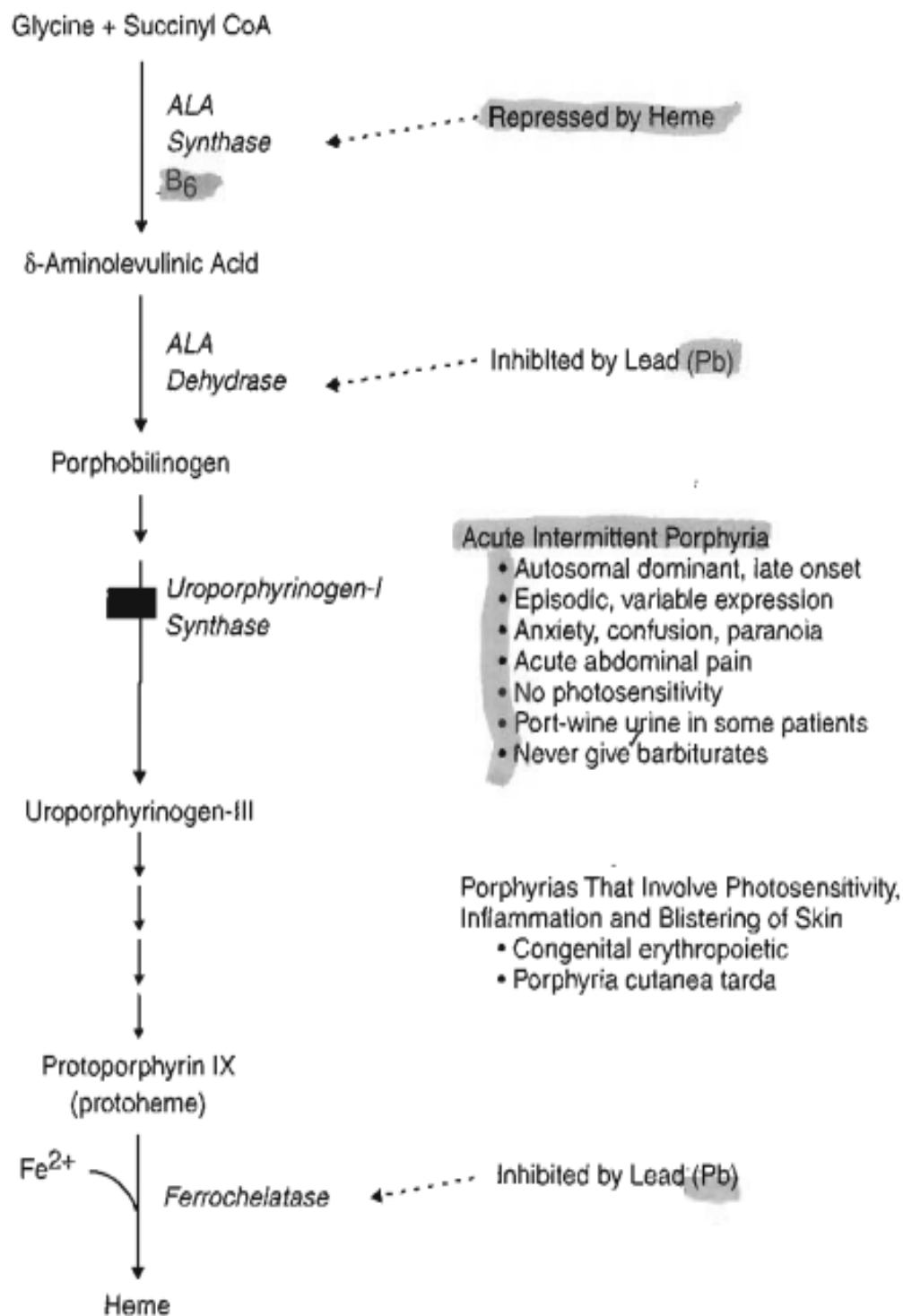


FIGURE 28: HEME SYNTHESIS

16.6 BILIRUBIN METABOLISM

- It is the breakdown product of hemoglobin.
- It is water insoluble that is why they are transported in blood with serum albumin.



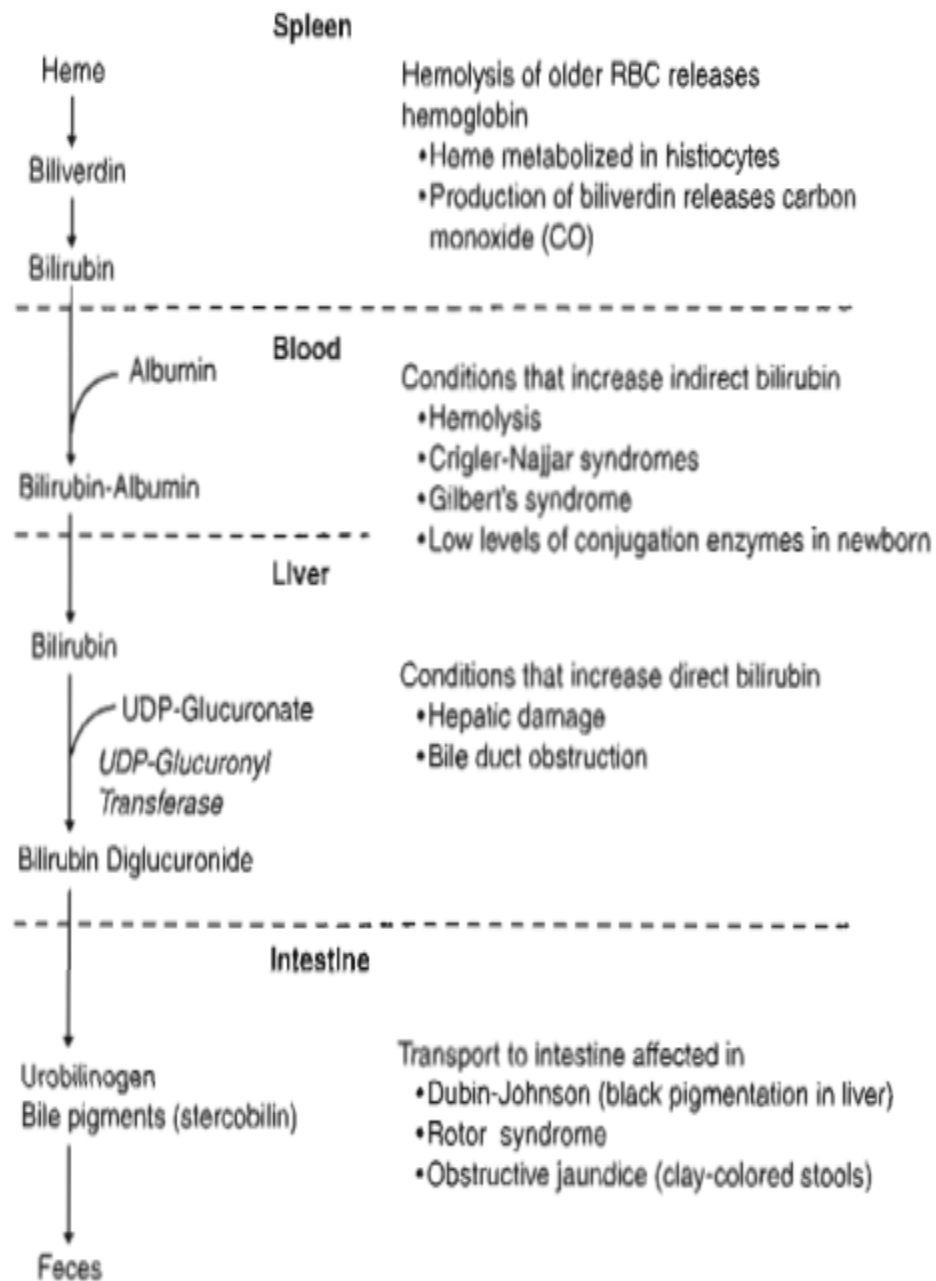


FIGURE 29: BILIRUBIN METABOLISM



Chapter 17 PURINE AND PYRIMIDINE SYNTHESIS

17.1 OVERVIEW

- Nucleotides are needed for DNA and RNA synthesis and for energy transfer.
- Ribose 5-P for nucleotide synthesis comes from hexose monophosphate shunt.
- Cell synthesize nucleotide by two ways:
 - I. De novo
 - II. Salvage pathways.

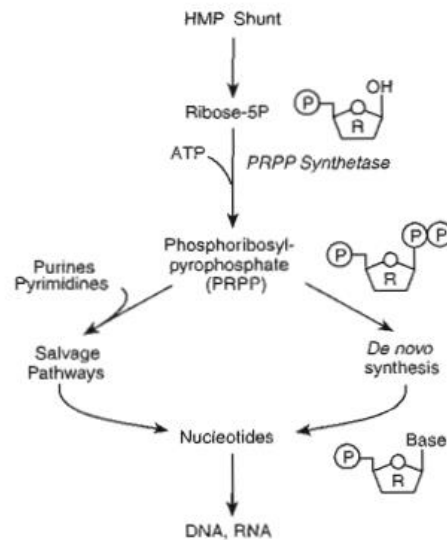
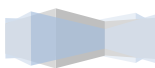


FIGURE 30: NUCLEOTIDES SYNTHESIS

17.2 PYRIMIDINE SYNTHESIS

- Pyrimidine in the cytoplasm is synthesized from aspartate, CO_2 , AND glutamine.
- Synthesis involves cytoplasmic carbamoyl phosphate synthetase.



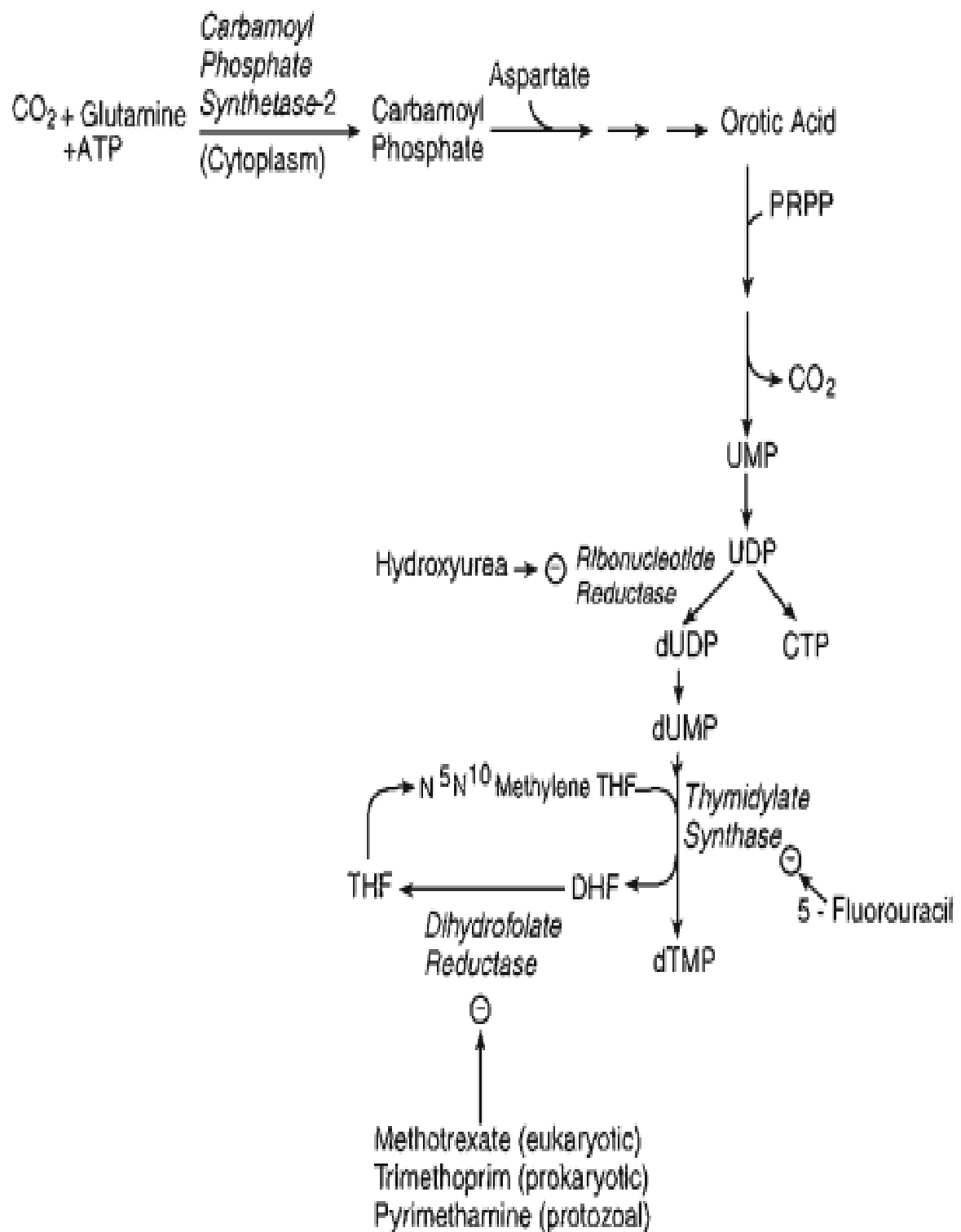


FIGURE 31: DE NOVO PYRIMIDINE SYNTHESIS

17.3 PURINE SYNTHESIS

- PRPP aminotransferase is the rate limiting enzyme for this reaction.

- It is inhibited by three purine nucleotides and end product MP, GMP and TMP.
- The amino acid glycine, aspartate and glutamine are used in purine synthesis.
- Tetrahydrofolate is required for purine synthesis.



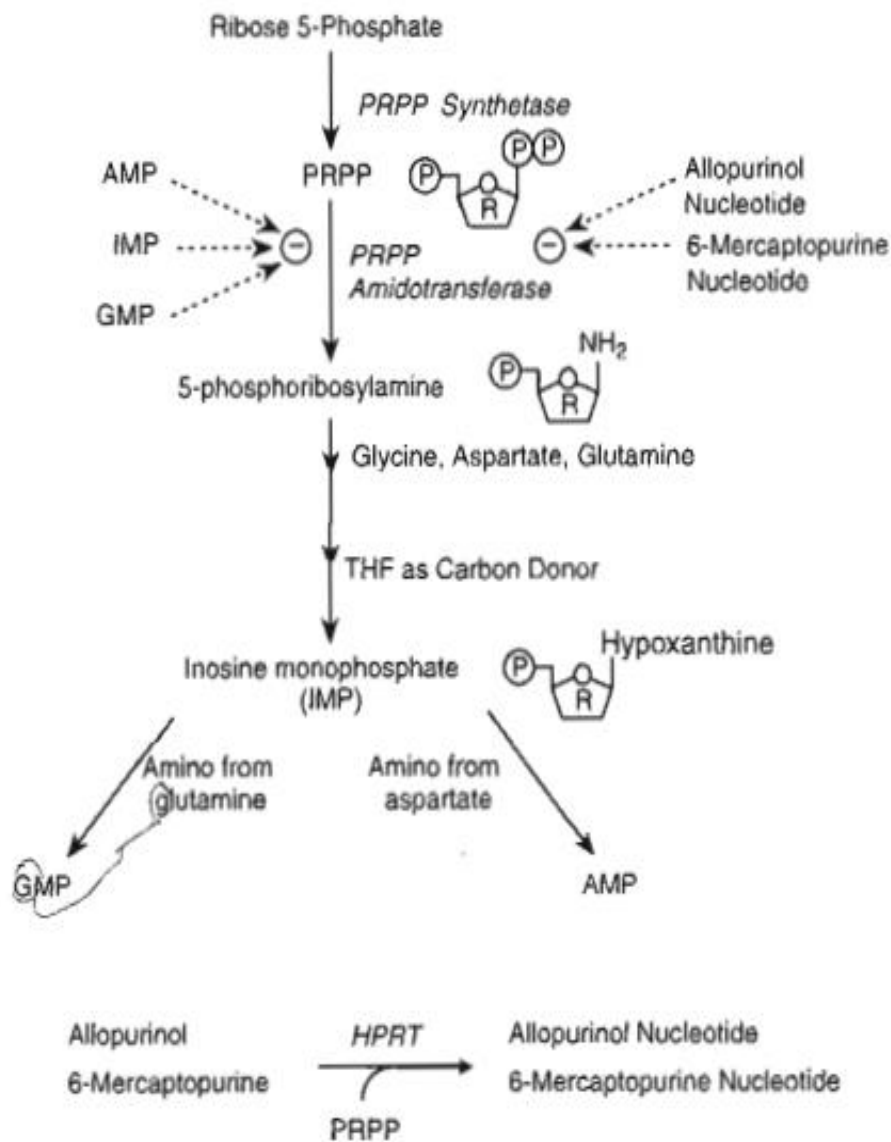


FIGURE 32: DE NOVO PURINE SYNTHESIS

17.4 PURINE EXCRETION AND SALVAGE PATHWAY



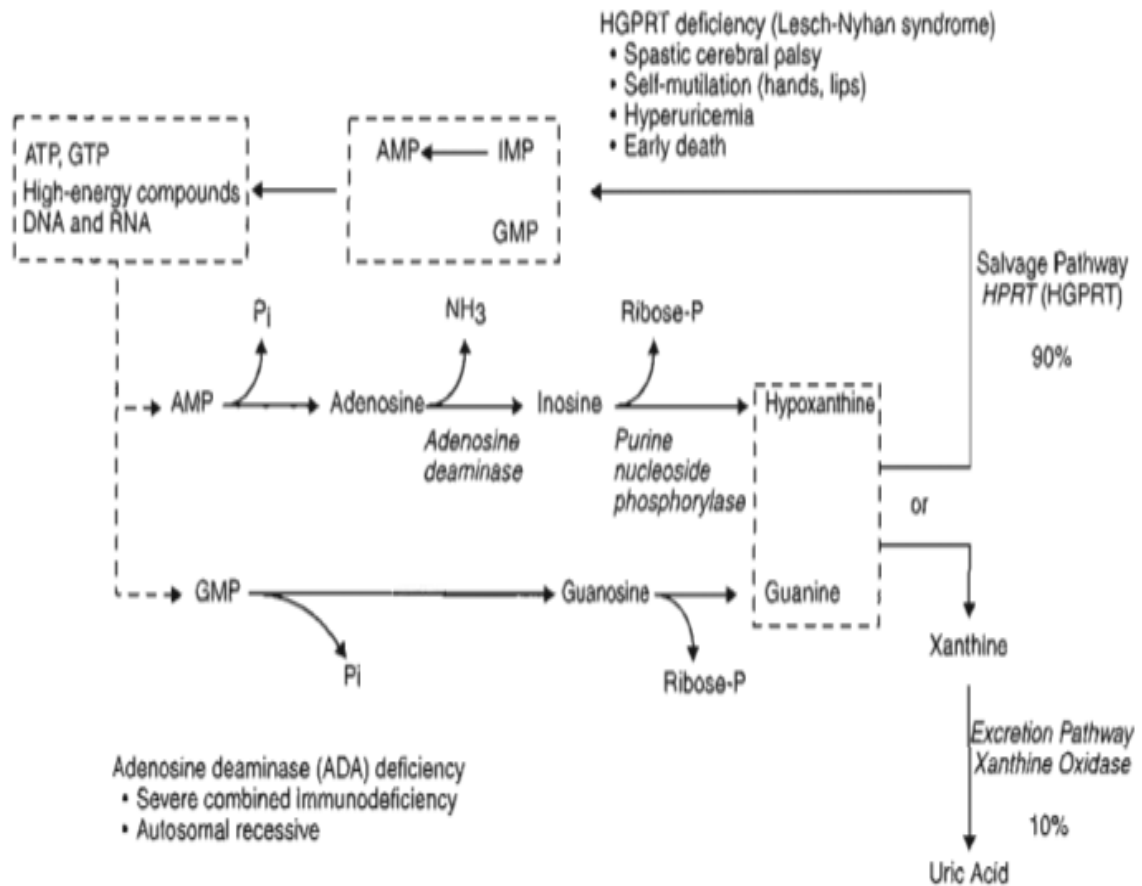


FIGURE 33: PURINE EXCRETION AND SALVAGE PATHWAY



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