COURSE GUIDE

EHS 207
GENERAL BIOCHEMISTRY FOR ENVIRONMENTAL HEALTH

Course Team Dr. O. A. Saliu (Course Developer/Writer) – NOUN
Dr. O. A. Idowu (Co-Writer) – UniIlorin
Prof. A. T. Oladiji (Course Editor) UniIlorin
Prof. G. C. Okoli-Nnabuenyi (Programme Leader) - NOUN

NATIONAL OPEN UNIVERSITY OF NIGERIA

National Open University of Nigeria
Headquarters
University Village
Plot 91, Cadastral Zone
NnamdiAzikiwe Expressway
Jabi, Abuja

Lagos Office
14/16 Ahmadu Bello Way
Victoria Island, Lagos

e-mail: centralinfo@nou.edu.ng
URL: www.nou.edu.ng

Printed 2019, 2024

ISBN: 978-978-786-025-0

CONTENTS **PAGE**

INTRODUCTION

EHS 207 title "General Biochemistry" is a three (3) Unit course with four (4) Modules and fifteen (15) Units. Biochemistry is the study of biomolecules. It can also be defined as the application of chemistry to the study of biological processes in living organisms. Biochemistry is both a life science and a chemistry science; it explores the chemistry of living organisms and the molecular basis for the changes occurring in living cells.

Millions of complex chemical reactions are going on in the human body at any given time, ranging from the balance of the endocrine system to the storage and utilization of fuel molecules such as glucose. By studying and understanding this highly complex reaction, biochemists have found better ways to fight infections and diseases not just at the molecular level but also at the cellular level. Since an Engineer cannot repair a vehicle if he does not understand how it works, so a biochemist must understand how the human body functions and the various mechanisms involved in process.

Much of biochemistry also deals with the structures and functions of cellular components such as proteins, carbohydrates, lipids and nucleic acids collectively known as biomolecules. The main purpose of all the efforts of Biochemistry is to benefit humans in all forms particularly in the diagnosis and treatment of different diseases. For example, investigation of diabetes mellitus is completely based upon the laboratory test in Biochemistry laboratories, where the presence of sugar in urine is tested by Benedict's test. Similarly, investigations of other disorders such as albuminuria, lactosuria, etc are a few of so many ailments that are investigated in Biochemistry laboratories.

WHAT YOU WILL LEARN IN THE COURSE

In this course, you will learn about the branches of biochemistry and its relevance to other life sciences, biochemistry of living cells, biological oxidation and electron transport chain, buffer, acidity, alkalinity, pH, pKa values and their roles in cellular metabolism. You will learn about the metabolism of biomolecules such as carbohydrate, proteins as well as lipids. The structure of the DNA will also be discussed. The knowledge that will be acquired in this course will assist you in understanding the various biochemical reactions that takes place in the living system.

COURSE AIM

The aim of this course is to build your foundation in the knowledge of biochemistry as it relates to the proper physiological functioning of the human system.

COURSE OBJECTIVE

At the completion of this course, you should be able to:

- explain the branches and relevance of biochemistry, biochemistry of living cells, biological oxidation and electron transport chain, buffer, acidity, alkalinity, pH, pKa values and their roles in cellular metabolism.
- understand the metabolism of major biomolecules such as carbohydrate, proteins, lipids as well as nucleic acid.

WORKING THROUGH THE COURSE

As a student of this course you are expected to register for this course online which is available at the NOUN website before you can have access to all the materials. You will be expected to read every module along with all assigned readings to prepare you for assessment.

Reading the reference materials will enhance your understanding of the course.

Note that each unit has self-assessment exercises which you are advised to do and at certain periods during the course, you will be expected to submit your assignment for the purpose of assessment. There will be final examination

THE COURSE MATERIALS

The main components of the course are:
1. The Course Guide
2. Study Unit
3. References/Further Reading
4. Assignments

STUDY UNITS

There are four (4) modules and fourteen (14) study units in this course
They are as follows:

Module 1 Introduction to General Biochemistry

Unit 1 Definition of Biochemistry
Unit 2 Cell Structure, Cell components and their Functions
Unit 3 Biochemistry of the Plasma Membrane

Module 2 Water, Acids, Bases, Buffer and Macromolecules

Unit 1 Water, Acids, Bases and Buffer
Unit 2 Chemistry of Carbohydrates
Unit 3 Chemistry of Amino Acids and Protein
Unit 4 Chemistry of Lipids
Unit 5 Chemistry of Nucleic Acids

Module 3 Metabolism of Biomolecules

Unit 1 Metabolism of Carbohydrates
Unit 2 Krebs cycle and Oxidative Phosphorylation
Unit 3 Metabolism of Proteins
Unit 4 Metabolism of Lipids

Module 4 Micronutrients (Vitamins and Minerals) and Detoxification

Unit 1 Water Soluble Vitamins
Unit 2 Trace Elements
Unit 3 Detoxification

There are activities related to the lecture in each unit which will help your progress and comprehension of the unit. You are required to work on these exercises which together with the TMAs will enable you to achieve the objectives of each unit.

PRESENTATION SCHEDULE

There is a time-table prepared for the early and timely completion and submissions of your TMAs as well as attending the tutorial classes. You are required to submit all your assignments by the stipulated time and date. Avoid falling behind the schedule time.

ASSESSMENT

There are three aspects to the assessment of this course.
The first one is the self-assessment exercises. The second is the tutor marked assignments and the third is the written examination or the

examination to be taken at the end of the course.

Do the exercises or activities in the unit by applying the information and knowledge you acquired during the course. The tutor-marked assignments must be submitted to your facilitator for formal assessment in accordance with the deadlines stated in the presentation schedule and the assignment file.

The work submitted to your tutor for assessment will count for 30% of your total course work.

At the end of this course, you have to sit for a final or end of course examination of about a three-hour duration which will count for 70% of your total course mark.

TUTOR-MARKED ASSIGNMENT

This is the continuous assessment component of this course and it accounts for 30% of the total score. You will be given four (4) TMAs by your facilitator to answer. Three of which must be answered before you are allowed to sit for the end of course examination.

These answered assignments are to be returned to your facilitator.

You're expected to complete the assignments by using the information and material in your readings, references and study units.

Reading and researching into your references will give you a better deeper understanding of the subject.

1. It is important that each assignment reaches your facilitator on or before the deadline given in the presentation schedule and assignment file. If for any reason you are not able to complete your assignment, make sure you contact your facilitator before the assignment is due to discuss the possibility of an extension. Request for extension will not be granted after the due date except for exceptional circumstances.

2. You will need to revise the whole course content before sitting for the examination. The self-assessment activities and TMAs will be useful for this purpose. The examination concludes the assessment for the course and constitutes 70% of the whole course. All areas of the course will be examined and you will be informed the time for the examination.

COURSE MARKING SCHEME

Assignment	Marks
Assignments 1 – 4	Four assignments, best three marks of the four count at 10% each–30% of course marks.
End of course examination	70% of overall course marks
Total	100% of course materials.

FACILITATORS/TUTORS AND TUTORIALS

Sixteen (16) hours are provided for tutorials for this course. You will be notified of the dates, times and location for these tutorial classes.

As soon as you are allocated a tutorial group, the name and phone number of your facilitator will be given to you.

These are the duties of your facilitator: He or she will mark and comment on your assignment. He will monitor your progress and provide any necessary assistance you need. He or she will mark your TMAs and return them to you as soon as possible.

Do not hesitate to contact your facilitator by telephone or email if you need assistance. The following might be circumstances in which you would have to contact your facilitator if you:

- do not understand any part of the study or the assigned readings
- have difficulty with the self-tests
- have a question or problem with an assignment, with your tutor's comments or with the grading of an assignment.

You should endeavor to attend the tutorials. This is the only chance to have face to face with your course facilitator and to ask questions which are answered instantly. You can raise any problem encountered in the course of your study.

SUMMARY

General biochemistry is the branch of life science that introduces you to chemical and physio-chemical processes such as respiration, digestion and metabolism of various biomolecules that occur within living organisms.

On completion of this course you will have an understanding of the components of the living cell, biological oxidation and electron transport chain, metabolism of carbohydrates, proteins and lipids as well as their roles in cellular metabolism and detoxification of harmful substances.

You are expected to apply the knowledge you have acquired during this course to your practical life.

Furthermore, you should be able to answer the following questions:

- define biochemistry
- discuss the metabolism of carbohydrates, proteins and lipids
- give an account of oxidative phosphorylation and electron transport chain
- explain the detoxification processes of harmful substances.

We wish you success in this course.

MAIN COURSE

CONTENTS **PAGE**

MODULE 1 INTRODUCTION TO GENERAL BIOCHEMISTRY

UNIT 1 DEFINITION OF BIOCHEMISTRY

CONTENTS

1.0 INTRODUCTION

The essence of studying biochemistry is for the purpose of understanding the various chemical reactions that occur in living organisms at both the cellular and molecular levels. Biochemistry as a life science is applicable and relevant in different fields of study such as medicine, agriculture, pharmacy, nursing etc.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

- define biochemistry
- understand the relevance of biochemistry to other life sciences (nursing, medicine, pharmacy)
- describe different branches of biochemistry.

3.0 MAIN CONTENT

3.1 Definition of Biochemistry

Biochemistry is the study of biomolecules. It can also be defined as the application of chemistry to the study of biological processes in living

organisms. Biochemistry is both a life science and a chemical science; it explores the chemistry of living organisms and the molecular basis for the changes occurring in living cells.

Millions of complex chemical reactions are going on in the human body at any given time, ranging from the balance of the endocrine system to the storage and utilisation of fuel molecules such as glucose. By studying and understanding these highly complex reactions, biochemists have found better ways to fight infections and diseases at the molecular level. Since an Engineer cannot repair a vehicle if he does not understand how it works, so a biochemist must understand how the living system works in order to proffer solutions in disease states. Thus much of biochemistry deals with the structures and functions of cellular components such as proteins, carbohydrates, lipids and nucleic acids collectively known as biomolecules. The main focus of biochemistry is in understanding how biological molecules give rise to the processes that occur within living cells, which in turn relates greatly to the study and understanding of the whole organism (human being).

3.2 Relevance of Biochemistry to other life Sciences

Biochemistry provides foundation for other life sciences such as medicine, nursing, pharmacy, zoology, microbiology etc. as well as agriculture.

In pharmacy biochemistry provides an

- ✓ understanding of the constitution of drugs, the half-life of drugs and drug metabolism.

In agriculture, the knowledge of biochemistry plays a valuable role in farming, fishery, poultry, sericulture etc as it

- ✓ helps in the prevention and treatment of diseases
- ✓ gives an idea of how the use of fertilizers can increase plants growth, their yield and quality of food
- ✓ can help to evaluate pesticide residues or other toxic waste in plants, food grain and seed through biochemical test
- ✓ help in the monitoring of the quality of milk in animal husbandry which can be checked by biochemical test.

In medicine, biochemistry gives an insight into the changes and physiological alterations that take place in the body. It also assists in clinical diagnosis of diseases.

Biochemists have contributed greatly to the discovery of new drugs to treat chronic diseases such as cancer, viral infections and metabolic disorders. They are able to do this because they have thorough

understanding of what happens at the molecular and cellular levels of living organisms.

3.3 Branches of Biochemistry

i. **Toxicology:** This field studies the adverse effects of toxic or foreign chemical substances on the organisms. Environmental and food toxicology also fall under this branch of biochemistry.
ii. **Enzymology:** This is the study of enzymes, their functions, deficiency and the consequence of such deficiency in diseases.
iii. **Molecular biology and Biotechnology:** This field evolved directly from Nucleic acid biochemistry and it involves manipulation of DNA to improve drug research and solve health problems. It has wide applications in other fields of science which includes cancer research.
iv. **Lipid and Carbohydrate biochemistry:** This field studies the biochemical basis of metabolic disorders such as diabetes, obesity and Cardiovascular diseases.
v. **Natural products biochemistry:** This is a new area of research in biochemistry; it evolved as a result of interest of scientists across the world in searching for new drugs from plants. Quinine and Artesunate (antimalarial drugs) were isolated from plants.

4.0 CONCLUSION

In this introductory unit, biochemistry has been introduced a life science with important contribution to the field of nursing, medicine, agriculture etc. The five main branches of biochemistry discussed above have different dimensions of improving human life.

5.0 SUMMARY

The primary aim of this unit is to enlighten you about biochemistry as a field of science, its branches as well as its relevance in the field of nursing, medicine, pharmacy and agriculture.

6.0 TUTOR-MARKED ASSIGNMENT

1. Define biochemistry.
2. Name and explain three (3) branches of biochemistry.
3. Discuss the relevance of biochemistry to other life sciences.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). *Medical Biochemistry and Biotechnology*. (1st ed.).

Murray, R.K., Bender, D. A., Botham, K., M., Kennelly, P.J., Rodwell V.W. & Well, P.A. (2012). *Harper's Illustrated Biochemistry (29th ed.).* McGraw-Hill Medical.

Nelson, D.L. & Cox M. M. (2009). Lehninger Principles of Biochemistry (4th ed.).

UNIT 2 CELL STRUCTURE, COMPONENTS OF THE CELL AND THEIR FUNCTIONS

1.0 INTRODUCTION

The living cell we are to discuss here is not different from the cell you learnt in Biology when you were in secondary school. Cells are the basic building blocks of all living organism. The human body is composed of trillion of cells. Cells have many parts, each with a different function. Some of these parts called organelles are specialized structures that perform certain tasks within the cell. Biochemical arrangement of cells and how these cells interact to perform various functions in man are not only fascinating but also very interesting. Imagine the sensitivity of cells responsible for taste; different region of your tongue detects different taste.

Some cells are replaced every 72 hours in our body while some spend up to ten years before they die. Also, some cells remain in our body throughout our lifetime. There are two basic types of cells in nature and these are prokaryotic and eukaryotic cells. Prokaryotic cells are the simplest cells and are without a nucleus and cell organelles while eukaryotic cells are sophisticated cells with a well-defined nucleus and cell organelles. A group of cells forms tissue, various tissues forms an organ and different organs make up the body.

It is important to understand compartmentalization and the functions of various organelles present in the cells. Most biochemical reactions take place inside the cell but in different organelles; for example, energy generation takes place inside the mitochondria. Thorough understanding of cell structure will help you to understand the root causes of many diseases and the biochemical mechanisms of their treatment.

2.0 OBJECTIVES

At the end of this unit, you will learn about the cell, structure of the animal cell, cell organelles and their functions.

3.0 MAIN CONTENT

3.1 Structure of Animal Cell

A living cell is defined as the fundamental unit of life and it is the smallest unit capable of exhibiting the characteristics of life. The cell was discovered in 1665 by Robert Hooke while examining a thin slice of cork under his new crude microscope. He observed numerous porous structures and named it the cell. The animal cells have different shapes and sizes; some are circular, spherical, cylindrical, fibrous etc. Red blood cells called erythrocytes are one of the smallest animal cells while ova are among the largest. In terms of length, nerve cells are the longest. For ease of representation, circular structure is commonly used to illustrate the structure of the animal cell Figure 1.1.

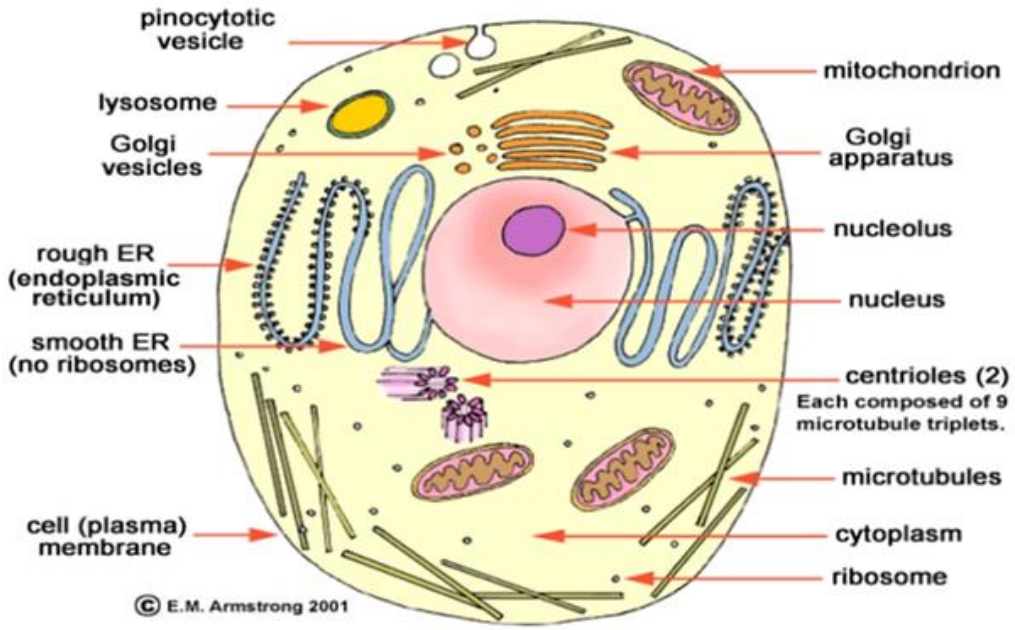


Figure 1.1: Structure of the animal cell

Source: Armstrong (2001).

A cell can be subdivided into 3 parts namely:

i. **The plasma membrane:** This is the thin cover that separates a cell from its environment. It also protects the components of the cell from leakage. It prevents the fluid outside the cell called extracellular fluid (ECF) from mixing with the fluid inside the cell called intracellular fluid (ICF). Plasma membrane regulates the materials that enters or leaves the cell, for this reason, it is said to be semi-permeable. In addition, the plasma membrane has some glycoproteins and glycolipids on its surface; these molecules serve as signal molecule between cells.

ii. **The cytoplasm:** This is the fluid-like space between the plasma and nuclear membrane. Cytoplasm is the cavity where the organelles are found. It provides space for the movement of synthesized products from one compartment to another for further processing. The organelles are suspended in the cytoplasm by cytoskeleton network that resemble nets.

iii. **Nucleus:** This is the most important part of the cell, the nucleus is always centrally located. It has its own membrane called nuclear membrane which protects the content of the nucleus. Nucleus is very important to the cell because it contains the genetic materials (DNA and RNA) that control all the activities of the cell. Nucleus regulates the rate and time of cell division. It also determines the materials that enter or exit the cell.

3.2 Functions of cell organelles

i. Rough Endoplasmic Reticulum: It is a vast system of interconnected, membranous, sacks that are located in the cell's cytoplasm and it is responsible for the synthesis of protein (due to the presence of ribosomes attached to it) and degradation of worn out organelles.

ii. Smooth Endoplasmic Reticulum: It is located in the cell's cytoplasm and transports materials throughout the cell. It contains enzymes which produce and digest lipids (fats) and membrane proteins. The smooth endoplasmic reticulum is therefore responsible for the synthesis of lipids and steroids, storage and metabolism of calcium and detoxification of toxic substances.

iii. Golgi Apparatus: It is a flattened sac-like organelle that looks like a stack of pancakes. It is located near the nucleus. It produces the membranes that surround the lysosomes. The golgi apparatus packages proteins and carbohydrates into membrane-bound vesicles for export from the cell.

iv. Lysosome: These are round organelles surrounded by a membrane where the digestion of cell nutrients takes place due to presence of the digestive enzymes. It contains more than 40 different hydrolytic enzymes and they are collectively known as LYSOZYMES which are actively involved in the degradation of macromolecules, worn out organelles and the removal of excess secretory products. Lysosome has the thickest membrane to prevent the leakage of hydrolytic enzymes.

v. Peroxisomes: These are single membrane spherical organelles,

also called micro-bodies. They contain antioxidant enzymes such as catalase and peroxidases which are involved in the detoxification of hydrogen peroxide and other radicals.

vi. Mitochondria: The mitochondrion is known as the power house of the cell as it generates energy in form of ATP (adenosine triphosphate), the energy currency of all living cells. It is spherical in shape and has double membrane i.e. inner and outer mitochondrion membrane.

vii. Ribosomes: These are small organelles rich in ribonucleic acid (RNA) and are active in the synthesis of proteins.

ix. Vacuole: The vacuole is a fluid-filled, membrane-surrounded cavity inside a cell. The vacuole fills with food being digested and waste material that is on its way out of the cell. There are specialized vacuoles which function to store fat as fat droplets.

4.0 CONCLUSION

The cell is the structural and functional basic unit of life. The human body contains several billions of cells that perform various functions. There are specialized structures called cell organelles present within the cell through which the cell performs these various functions.

5.0 SUMMARY

In this unit, you have learnt about the cell, types of cells, structure of the animal cell, cell organelles and their functions.

6.0 TUTOR-MARKED ASSIGNMENT

1. Draw a well labeled structure of the animal cell
2. List four cell organelles and their functions.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology. 1st edition.

Devlin T.M. (2010). Textbook of Biochemistry with Clinical Correlation 7th Edition. John Wiley & Sons Inc.

UNIT 3 BIOCHEMISTRY OF THE PLASMA MEMBRANE

1.0 INTRODUCTION

The cell or plasma membrane can be referred to as 'the wall of a city. It protects the components of the cell and also regulates what enters or leaves the cell. The plasma membrane is very important to all cells since the cell owes its survival to an intact and functional cell membrane. If there is any injury to the cell membrane, the whole cell may be destroyed. Technically, the cell membrane is a liquid. At room temperature, it has about the same consistency as vegetables oil. Lipids, proteins and carbohydrates in the plasma membrane can diffuse freely throughout the cell membrane; they are essentially floating across its surface. This process is known as the fluid mosaic model, which was coined by S. J. Singer and G. L. Nicolson in 1972.

2.0 OBJECTIVES

At the end of this unit, you be able to describe the plasma membrane. You will also get to know the various mechanism of transport of materials across the plasma membrane.

3.0 MAIN CONTENT

3.1 Components of the plasma membrane

Plasma membrane mainly consists of phospholipids, cholesterol and proteins. There is a wide variation in lipid- protein ratio for different cell membranes. The functions performed by the cell and the location determine the quantity of proteins and lipids present in the plasma membrane.

Membrane Lipids
There are several types of membrane lipids. The fundamental building blocks of cell membranes are the **phospholipids**. Membrane lipids are ***amphipathic molecules*** (they have both hydrophilic and hydrophobic

ends, hydrophilic means “water loving”; this part readily associates with water while hydrophobic ends means “water hating”; they tend to move away from water). When cellular membranes form, phospholipids assemble into two layers because of their hydrophilic and hydrophobic properties. The phosphate heads in each layer face the aqueous or watery environment on both side, and the tails hide away from the water between the layers of heads, because they are hydrophobic (Figure 1.2).

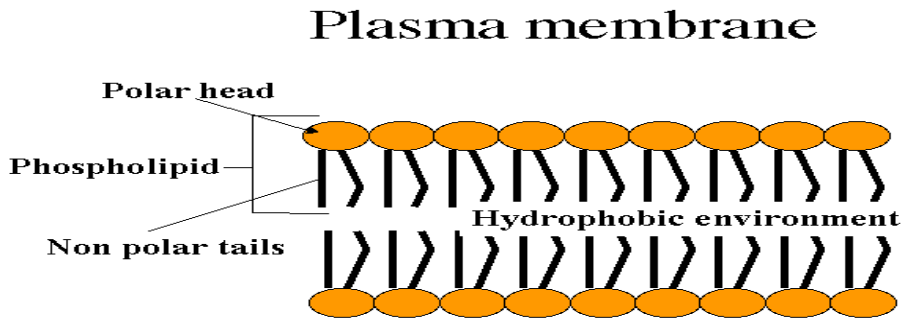


Figure 1.2: Structure of plasma membrane bilayer
Source: Sadler (2004).

Cholesterol

Cholesterol is another important membrane lipid found exclusively in the plasma membrane of mammalian cells. The cholesterol molecules are randomly distributed across the phospholipid bilayer, helping the bilayer stay fluid in different environmental conditions. It holds the phospholipids together so that they don’t separate too far thereby letting unwanted substances in, or compact too tightly, restricting movement across the membrane. Without cholesterol, the phospholipids in the plasma membrane will start to get closer together when exposed to cold, making it more difficult for small molecules, like gases to squeeze in between the phospholipids like they normally do. Also the presence of cholesterol prevents phospholipids from separating from each other which could have resulted in large gaps.

Membrane Proteins

Membrane proteins can be classified as being either peripheral or integral on the basis of their association with the membrane lipids. Integral membrane proteins interact extensively with the hydrocarbon chains of membrane lipids. Most of these integral proteins span the lipid bilayer, protruding at both ends. They have high percentage of non-polar amino acids and represent about 70% of total membrane proteins. Examples are membrane enzymes, hormone receptors, pumps and channels. Integral proteins are helpful for transporting larger molecules like glucose across the cell membrane. In contrast, peripheral proteins are bound to the surface of lipid bilayer primarily by electrostatic and hydrogen bonds. Many peripheral membrane proteins are also bound to the surfaces of integral proteins, on either the cytosolic or extra cellular

side of the membrane. Examples include cytochrome c and acetyl choline esterase.

3.2 Functions of the plasma membrane

i. **Protection:** The primary function of the plasma membrane is to protect the cytoplasm and the organelles present in the cell. It is responsible for the maintenance of shape and size of cells.

ii. **Transportation:** The cell membrane act as semi permeable membrane which allows only some substances to pass through it thereby acting as a barrier for other substances. For example, small hydrophobic molecules such as CO_2, O_2 and small lipids dissolve in the membrane and pass through readily. Ions and most nutrient molecules do not move freely through the membrane, but are often carried by the transport protein channels, either with or without the use of energy.

3.3 Mechanism of transportation of materials across the plasma membrane

Passive Transport: Passive transport in cells involves the process of diffusion; the diffusion can be simple or facilitated.

Simple diffusion – In terms of cellular activity, the rate of simple diffusion can be affected by temperature, molecular size, concentration of the gradient. Materials that are moved through membranes by simple diffusion include: water, carbon dioxide, oxygen, some lipid soluble molecules such as alcohol.

Facilitated diffusion – Most molecules cannot move freely through the membrane, but do cross membranes with the help of membrane transport proteins, which temporarily bind to the substance to be moved through the membrane, a process called facilitated diffusion. No energy is involved in the process since both carrier proteins and channel proteins are involved. Materials that pass through membranes by facilitated diffusion include glucose, amino acids and many small ions. The movement of water through membranes also involves facilitated diffusion. The special protein channel used for this is called *aquaporins*, and it facilitates the movement of water at a rate needed for cell activities. Facilitated diffusion process may be coupled to the movement of other molecules in the same direction or opposite direction. In co-transport, the transport of one molecule depends on sequential transfer of another molecule. Co-transport may be symport or antiport. A symport moves two molecules in the same direction e.g. sodium-glucose

transporter. Antiport system moves two molecules in opposite direction. It is also known as counter transport e.g. sodium-potassium transporter.

Active transport – Energy requiring transport across membranes. Active transport is involved in the movement of molecules across the cell membrane from a region of lower concentration to a region of higher concentration i.e. against the concentration gradient. Generally, most cells need to move substances through the membrane in a direction counter to the gradient or move substances that are too large or bulky with the use of energy. Some transport proteins (carrier proteins) can move substances through the membrane against the concentration gradient. Active transport typically requires two carrier protein active sites. One recognizes the substances to be carried while the other releases ATP to provide energy for the protein carrier. In some cases, concentration gradients of ions typically (H^+) protons or (Na^+) sodium ions can be used to provide the energy needed to move molecules through the membranes.

Active transport is classified into two types according to the source of energy used. Primary active transport derives its energy directly from the hydrolysis of ATP while the secondary active transport uses an indirect energy of an electrochemical gradient or membrane potential produced originally by primary active transport. An example of primary active transport is sodium-potassium pump (Na^+ - K^+ ATPase). It is the protein or enzyme responsible for the transportation of Na^+ and K^+ across the cell membrane. The enzyme is known as sodium-potassium Adenosine triphosphatase.

The energy required for the transportation of sodium and potassium ions are derived from the hydrolysis of ATP. For every three Na+ pumped out of the cell, two K^+ are released into the cytosol.

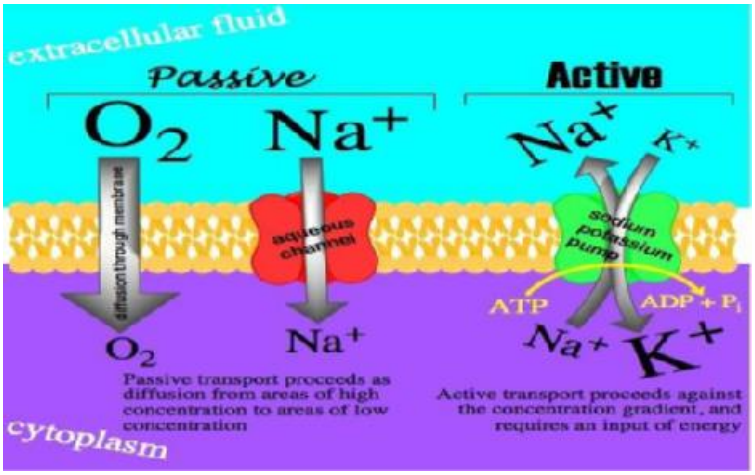


Figure 1.3: Active and passive transport across the plasma membrane

Source: Delvin (2010).

4.0 CONCLUSION

The plasma membrane is a semi-permeable membrane that controls the entry and exit of molecules within the cell. The chemical structure of the plasma membrane explains the process of transportation across different gradients of the cell.

5.0 SUMMARY

In this unit, you have learnt about the lipids and protein components of the cell membrane. We also discussed the different mechanism of transportation of material across the cell membrane with explanation of the factors that drive such exchange.

6.0 TUTOR-MARKED ASSIGNMENT

1. Write short notes on the lipids and protein components of the plasma membrane
2. Explain the passive mechanism of transportation across the cell membrane, draw diagrams to illustrate your answers.
3. Differentiate between the active and passive methods of transportation.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology. 1st edition

Devlin T.M. (2010) Textbook of Biochemistry with Clinical Correlation 7th Edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P.J., Rodwell V. W. and Well, P. A. (2012). Harper's Illustrated Biochemistry (29th Edition) McGraw-Hill Medical.

Nelson, D.L. and Cox M.M., (2009). Lehninger Principles of Biochemistry 4th edition

Sadler, T. W. (2004). Langman's Medical Embryology 9th edition.

MODULE 2 WATER, ACIDS, BASES, BUFFER AND MACROMOLECULES

UNIT 1 WATER, ACIDS, BASES AND BUFFER

1.0 INTRODUCTION

Water is the most abundant matter on earth and also a major component of the body. Typically, organisms are constituted of 70 to 90 % water. It must be present before any metabolic activity can take place in the cell and it is referred to as a weak electrolyte because it can undergo partial dissociation into a proton (H^+) and hydroxyl ion (OH^-).

Water is made up of oxygen and two hydrogen atoms. Oxygen has a tendency to pull the electrons more towards itself, thereby becoming electronegative and leaving the hydrogens electropositive. This results in the creation of a dipole due to the fact that each water molecule is surrounded by four other water molecules. The bond between 'H' of one water molecule and 'O' of the other is known as hydrogen bond. In this unit we shall also be discussing acids and bases which are defined with respect to their ability to gain or lose protons and the importance of buffers in biological system.

2.0 OBJECTIVES

At the end of this unit, you should understand the properties of water, the importance of water as the major component of living organisms and

be able to define acid, base and a buffer. You will also learn how to calculate pH, pOH and pKa of a given solution.

3.0 MAIN CONTENT

3.1 The properties of water

i. Water is the predominant chemical component of all living organisms.
ii. Most chemical reactions in the cell take place in aqueous environment.
iii. It has a high boiling and melting points when compared to other liquids.
iv. It has a specific heat of vaporization
v. Hydrogen bonds hold the oxygen and hydrogen atoms together in a water molecule.
vi. The oxygen of water is very electronegative, while hydrogen is electropositive; as a result water is dipolar and exhibit tendency to dissociate.

3.2 Biological importance of water

i. **Water helps in the digestion of food:** It helps to break down food so that the body can absorb the nutrients.
ii. **It regulates the body temperature:** Water that is stored in the middle layers of the skin comes to the skin's surface as sweat when the body heats up. As it evaporates, it cools the body.
iii. **It cushions the brain, spinal cord and other sensitive tissues:** Dehydration can affect brain structure and function. It is also involved in the production of hormones and neurotransmitters. Prolonged dehydration can lead to problems with thinking and reasoning.
iv. **It boosts skin health and beauty:** With dehydration, the skin can become more vulnerable to skin disorders and premature wrinkling.
v. **It delivers oxygen throughout the body:** Blood is more than 90 percent, and blood carries oxygen to different parts of the body.
vi. **It lubricates the joint:** Cartilage, found in joints and the disks of spine contains around 80 percent water. Long-term dehydration can reduce the joints shock-absorbing ability, leading to joint pain.
vii. The strong dipole and high dielectric constant of water enables it to dissolve large quantities of charged compounds.
viii. The presence of hydrogen bond also enables water to dissolve many organic molecules that contain functional groups.

ix. Water provides environment for macromolecules to achieve stable structure in solution

3.3 Acid, Base and Buffer

An acid is a proton donor. It is also a compound that dissociates in aqueous solution to produce (H^+) proton and a conjugate base (A^-).

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

Acid may dissociate partially (called weak acid e.g. ethanoic acid, water) or completely (called strong acid e.g. hydrochloric acid) in solution. In solution, weak acid establishes equilibrium between the proton and its conjugate base. Weak acids are those which have a slight tendency to give up protons e.g. acetic acid. On the other hand, strong acids give up protons readily e.g. HCl.

$$HCl \longrightarrow H^+ + Cl^-$$

$$CH_3COOH \longrightarrow CH_3COO- + H^+$$

A Base is a compound that accepts proton in aqueous environment. Just like an acid, there are strong bases and weak bases. For example, sodium hydroxide is a strong base which releases hydroxyl ions very easily, and water is a weak base as it is a poor source of hydroxyl ions.

$$NaOH \longrightarrow Na^+ + OH^-$$

$$H_2O \longrightarrow H^+ + OH^-$$

pH of a solution is simply defined as the negative logarithm of the hydrogen ion concentration in a media. In simple terms it is a value that gives the amount of hydrogen ions present in a solution. This value is expressed in a reverse or negative form i.e. higher the pH value lower is the hydrogen ion concentration and lower the pH value higher is the hydrogen ion concentration. The pH of all solutions ranges between 0 and 14 only. pH of value 7.0 is neutral e.g. water and pH ranging from 0 to 0.69 is acidic and 7.1 to 14 is basic or alkaline.

The normal pH of the blood plasma ranges between 7.35 and 7.45, average being 7.4. The intracellular pH of the tissues is 7.25 to 7.35 averaging to 7.30 and pH of extracellular fluid is 7.30 to 7.40 with an average of 7.35. A decrease in the pH of blood is termed as acidosis and an increase in the pH of blood is termed as alkalosis. Alkalosis is more fatal than acidosis.

Mathematically,

$pH = - \log [H^+]$ and

$pOH = - \log [OH^-]$

The equilibrium constant is called the acid dissociation constant and it is represented as:

$$K_a = = \frac{[H+]\,[A-]}{[HA]}$$

Where K is the equilibrium constant and $_a$ is the acid.

Calculation of pH, pOH and pKa

Example 1: If the H^+ concentration of a solution is 4.2×10^{-3} calculate the pH of the solution.

Solution:

$pH = - \log [H^+]$, $\log[4.2 \times 10^{-3}] = \log 4.2 + \log 10^{-3} = 0.62 - 3 = -2.38$. Substitute for $\log [H^+]$ in the equation.
$pH = -(-2.38)$, the two negative values canceled out, $pH = 2.38$

Example 2: Calculate the $[H^+]$, $[OH^-]$ and pH of 0.01M ethanoic acid, given that ($K_a = 1.76 \times 10^{-5}$).

Solution:

Note that ethanoic acid is a weak acid, it dissociates partially in solution, therefore $HA = H^+ + A^-$, if the conjugates are represented by x, then $HA = 0.1 - x \approx 0.1$ (value of x is negligible)

$$Ka = \frac{[H^+]\,[A^-]}{[HA]}$$

$Ka = 1.76 \times 10^{-5} = X2/0.1$
$X2 = 1.76 \times 10^{-6}$, X is equal to the square root of 1.76×10^{-6}

This is equal to 1.33×10^{-3}, therefore,

$$[H^+] = 1.33 \times 10^{-3}$$

$pH = -\log 1.33 \times 10^{-3} = 0.12-3$, if you take away 3 from 0.12, this will give you a negative value (-2.88).

$$pH = 2.88 .$$

To calculate the pOH, the dissociation of pure water will be considered. $H_3O = H^+ + OH^-$,

$[H^+] + [OH^-] = 1.0 \times 10^{-14}$,

$[OH-] = 1.0 \times 10^{-14} / [H^+]$

$= 1.0 \times 10^{-14} / 1.33 \times 10^{-3}$,

[OH-] =7.52 x 10-12.

But pOH = -log 7.52 x 10-12. This is equal to 0.88 – 12,
pOH = 11.12

Buffer

A buffer is a solution that resists changes in pH (hydrogen ion concentration) when an acid or a base is added. A buffer contains a weak acid and its conjugate base. Examples of buffer solutions are Acetate buffer (acetic acid and acetate salt), Bicarbonate buffer (carbonic acid and bicarbonate salt), phosphate buffer (sodium hydrogen phosphate and potassium hydrogen phosphate) etc.

Regulation of pH solution by buffer

If (H^+) hydrogen ions are added to a buffer solution, the conjugate base reacts with the excess hydrogen ions to form the acid. On the other hand, if (OH^-) hydroxyl ions are added, they react with the acid present in the buffer to produce water and conjugate base.

Preparation of buffer

To prepare buffer, Henderson-Hasselbalch equation is usually used to calculate the concentrations of acid and base components of the buffer to be prepared.

The equation is $pH = pKa + \log \frac{[A^-]}{[HA]}$

3.4 Biological importance of buffer

Buffers are chemical substances that help to maintain a relatively constant pH in a solution. Buffering is important in living systems as a means of maintaining a fairly constant internal environment also known as homeostasis. The following are examples of buffers in biological

system and their importance:

i. The maintenance of blood pH is regulated via the bicarbonate buffer. This system consists of carbonic acid and bicarbonate ions. When the blood pH drops into the acidic range, this buffer acts to form carbon dioxide gas. The lungs expel this gas out of the body during the process of respiration. During alkaline conditions, this buffer brings the pH back to neutral by causing excretion of the bicarbonate ions through the urine.

ii. The phosphate buffer system acts in a manner similar to the bicarbonate buffer, but only that it has a much stronger action. The internal environment of all cells contains this buffer comprising hydrogen phosphate ions and dihydrogen phosphate ions. Under conditions when excess hydrogen enters the cell, it reacts with the hydrogen phosphate ions, which accepts them. Under alkaline conditions, the dihydrogen phosphate ions accept the excess hydroxide ions that enter the cell.

4.0 CONCLUSION

Water is life and a core component of all other fluids that make chemical reactions possible in the body. Acids, bases and buffers serve different biological purposes in the living system.

5.0 SUMMARY

In this study unit, you have learnt about the properties of water and its biological importance, acid, base and buffers. You are also introduced to the Henderson-Hasselbalch equation

6.0 TUTOR-MARKED ASSIGNMENT

1. What are the properties of water?
2. Define an acid and a base.
3. Give examples of two buffers and explain how they regulate pH in the living system.
4. Calculate the pH of a solution of weak acid whose Molarity is 0.0008.
5. Calculate the $[H^+]$, $[OH^-]$ and pH of 2.5×10^{-3} M ethanoic acid, given that ($Ka = 1.48 \times 10^{-5}$).

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010) Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V.W. and Well, P. A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 2 CHEMISTRY OF CARBOHYDRATES

1.0 INTRODUCTION

Carbohydrates (CHOs) are compounds containing C, H and O (Carbon, Hydrogen and Oxygen) with the general formula $C_nH_{2n}O_n$. They are widely distributed in plants and animals where they play important structural and metabolic roles. Glucose is the most important carbohydrate.

Most dietary CHO is absorbed into the bloodstream as glucose formed by the hydrolysis (breakdown) of dietary starch and disaccharides. Other sugars are also converted to glucose in the liver. Glucose is the major metabolic fuel of mammals and a universal fuel for the fetus. It is the precursor for the synthesis of all other CHOs in the body, including glycogen which is the storage form of carbohydrates in man. Diseases associated with CHO metabolism include Diabetes Mellitus, Galactosemia, Glycogen storage diseases and Lactose intolerance.

2.0 OBJECTIVES

At the end of this unit, you should be able to know the classification of carbohydrates into various sugars, the isomers of glucose and the roles of carbohydrates in biological membrane.

3.0 MAIN CONTENT

3.1 Classification of Carbohydrates (CHO)

Carbohydrates are classified according to the number of sugar units in the molecule as follows:

Monosaccharides: These are sugars that contain one sugar unit and cannot be further hydrolyzed. They represent the end product of CHO digestion in the human body. They are classified as trioses, tetroses,

pentoses, hexoses or heptoses, depending on the number of carbon (C) atoms, and as aldoses and ketoses depending on whether they have an aldehyde or ketone group. Examples of monosaccharaides hexoses are glucose and galactose.

Table 2.1: Classification of Sugars

Classification based on number of Carbon atom	**Aldoses**	**Ketoses**
Trioses ($C_3H_6O_3$)	Glyceraldehyde	Dihydroxyacetone
Tetroses ($C_4H_8O_4$)	Erythrose	Erythrulose
Pentoses ($C_5H_{10}O_5$)	Ribose	Ribulose
Hexoses ($C_6H_{12}O_6$)	Glucose	Fructose
Heptoses ($C_7H_{14}O_7$)	-	Sedoheptulose

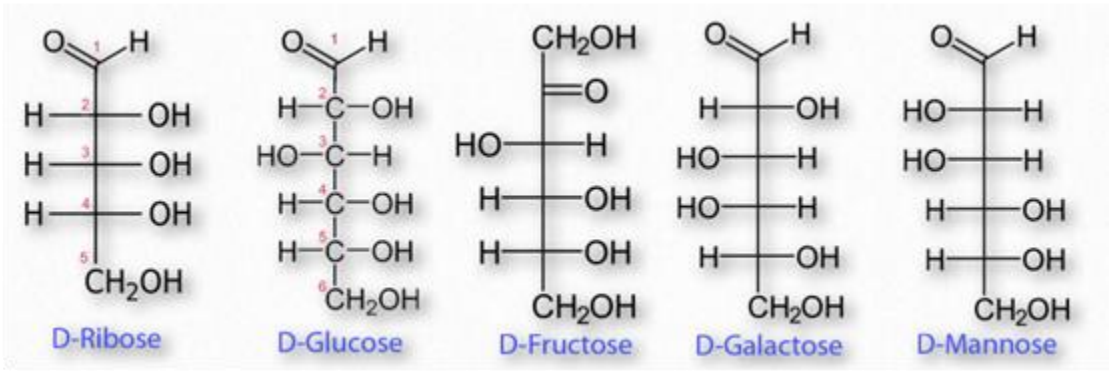


Figure 2.1: Sugars with different no of carbon atoms
Source: Nelson and Cox (2010).

Disaccharides: These are condensation products of 2 monosaccharide units e.g. lactose (galactose + glucose), maltose (2 glucose i.e. glucose + glucose) and sucrose (glucose + fructose).

Oligosaccharides: These are condensation products of 3-10 monosaccharides. Most are not digested by human enzymes rather they play structural roles.

Polysaccharides: These are condensation products of 10 or more monosaccharide units.. Food contains a wide variety of other polysaccharides, collectively known as non-starch polysaccharides which are not digestible by the human enzymes and are the major components of dietary fibre. Examples include cellulose (a glucose

polymer from plant cell walls) and inulin (a fructose polymer which the storage CHO in some plants. Examples of polysaccharides are glycogen, starch and dextrin which may be linear or branched polymers

Glycogen: It is known as animal starch. It is made up of α-1, 4 linkages in the linear and α-1, 6 linkages at the branching points. It is highly branched. Glycogen is the storage form of energy (glucose) in each and every cell of the body. Liver and muscle contains the highest amount of glycogen. At least 5% of glycogen is present in each cell even under severe fasting/starvation condition. It gives a red colour with iodine.

Starch: It is made up of α-D-glucose units, hence known as glucosan. It is composed of amylose and amylopectin.

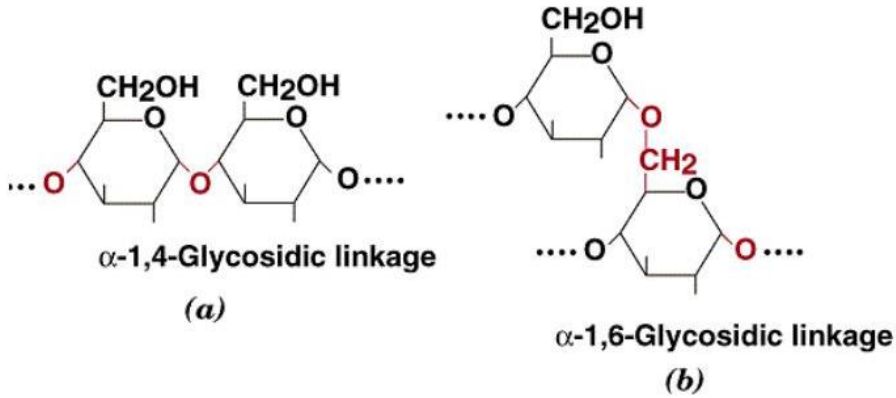


Figure 2.2: Structure of glycogen showing glycosidic linkage
Source: Nelson and Cox (2010).

Structure of Glucose

The straight chain structural formula of glucose can account for some of its properties, but a cyclic structure formed by a reaction between the aldehyde group and an OH group is thermodynamically more favoured and accounts for other properties. The cyclic structure results from the reaction between the aldehyde group in C_1 and the OH group in C_5, which forms a hemiacetal linkage and produce either of 2 stereoisomers. The structure can also be represented in form of a chair, with the 6 membered rings containing one oxygen atom as shown in Figure 2.3.

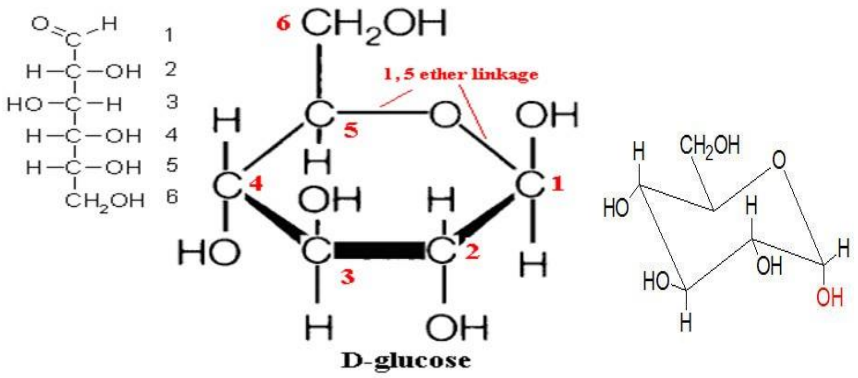


Figure 2.3: Structures of glucose
Source: Nelson and Cox (2010).

3.2 Isomers of Glucose

Isomerism is the occurrence of compounds with the same chemical formula but different structural formula. The important types of isomerism found in glucose are **D and L isomerism.** The designation of a sugar isomer as the D form or of its mirror image as the L form is determined by its spatial relationship to the parent compound of the carbohydrates. The orientation of the –H and –OH groups around the C atom adjacent to the terminal primary alcohol carbon determines whether the sugar belongs to D or L series (when the –OH group on this C is on the right, the sugar is called D isomer and when it is on the left, it is called L-isomer) Most of the naturally occurring monosaccharide are D sugars. The presence of asymmetric C atom also confers optical activity on the compound. When a beam of plane-polarized light is passed through a solution of an optical isomer, it rotates either to the right (known to be + dextrorotatory,) or to the left (known to be - levorotatory).

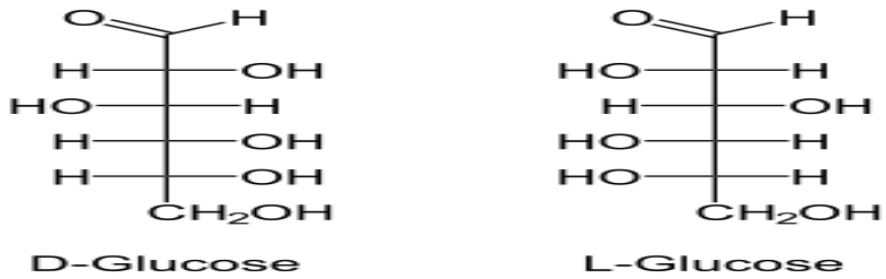


Figure 2.4: D and L isoforms of Glucose
Source: Nelson and Cox (2010).

Epimers: These are isomers differing as a result of variations in

configurations of the –OH and –H on C atoms 2, 3 and 4 of glucose. The most important biological isomers of glucose are mannose (differs in configuration at C2) and galactose (differs in confriguration at C4).

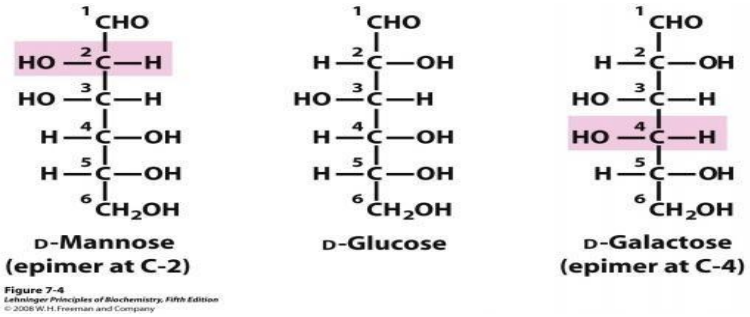


Figure 2.5: Epimers of Glucose
Source: Nelson and Cox (2010).

3.3 Functions of carbohydrates

1. Provide instant energy to the body*:* This is the primary function of carbohydrates in the body. Carbohydrates which we consume as food in the form of starch get digested in the body to release glucose. This glucose after being absorbed into blood reaches all the body tissues and cell. It gets metabolized to release energy in the form of ATP in the presence of oxygen inside the mitochondria.

2. Reserve food: Carbohydrate is also stored as the reserve food in the body. This is a precautionary measure for the body to cope up in times of hunger. The excess glucose which is obtained by food is converted to glycogen in the body. This conversion of glucose to glycogen happens in the presence of the hormone insulin. This glycogen is stored in the liver and to a small extent in the skeletal muscles. In times of starvation, this glycogen converts back to glucose and provides energy.

3. Detoxification of the body by metabolism: Many drugs and toxic wastes in the body are metabolized for easy excretion in the body. Some of these are water-insoluble and hence they are difficult to be expelled in urine. The body converts them into glucuronosyl conjugates using the glucuronosyl moiety derived from carbohydrates. A carbohydrate moiety like glucose combines with uronic acid to form glucuronate. These conjugates of insoluble substances with glucuronosyl are more water-soluble and easily excreted from the body. Thus detoxification of physiological importance is carried out to some extent with carbohydrate derivatives.

4. Constitute genetic material: Carbohydrates form a part of DNA and RNA in the form of deoxyribose and ribose sugars. These are five carbon sugars.

5. They are constituents of all the cellular organelles: Carbohydrates are also components of cell organelles like the cell membrane, mitochondria, nucleus, endoplasmic reticulum, etc. They provide structural integrity, mechanical strength in combination with proteins and lipids. They help make up the body mass by being included in all the parts of the cell and tissues. For example, in cell membranes, there are two constituents, i.e., glycolipid layer and glycoprotein layer. Here the term "glyco" is a carbohydrate.

6. Transport of oxygen: Glucose is taken by red blood cells which lack mitochondria and other cell organelles required for producing energy. The energy in the form of ATP is produced by a non-oxidative pathway (anaerobic glycolysis). This energy thus produced is necessary for hemoglobin to bind to oxygen molecules which are transferred from lungs to the different tissues.

4.0 CONCLUSION

Carbohydrates are one of the important biomolecules that are widely distributed in plants and animals and they play important structural and metabolic roles in the living cell.

5.0 SUMMARY

In this unit, you have learnt the various classifications of carbohydrates with examples, the isomers of glucose and the biological roles of carbohydrate.

6.0 TUTOR-MARKED ASSIGNMENT

1. Explain the classification of carbohydrates and give two examples each
2. What is isomerism and list the isomers of glucose
3. Enumerate the functions of carbohydrates

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology. 1st edition.

Devlin T.M. (2010) Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R.K., Bender, D.A., Botham, K., M., Kennelly, P.J., Rodwell V.W. and Well, P.A., (2012). Harper's Illustrated Biochemistry (29th Edition) McGraw-Hill Medical.

Nelson, D.L. and Cox M.M., (2009). Lehninger Principles of Biochemistry 4th edition.

Sadler, T.W. (2004). Langman's Medical Embryology 9th edition.

UNIT 3 CHEMISTRY OF AMINO ACIDS AND PROTEINS

1.0 INTRODUCTION

Amino acids are the basic structural units of proteins. Proteins in all species from bacteria to humans are made from the same set of twenty amino acids. Amino acids take part in many types of reactions, but the most important of these is the formation of a peptide bond. This involves the joining of the α- carboxyl group of one amino acid to the α-amino group of another amino acid, with the loss of a water molecule. Amino acids are grouped according to the nature of their side chains. Since amino acids are weak acids, their strength is expressed as pKa (negative log of ionization constant). The net charge on an amino acid depends on the pKa of its functional groups and the pH of the surrounding medium.

2.0 OBJECTIVES

At the end of this unit you will have an understanding of the chemical nature of amino acids, different ways of classifying amino acids and proteins, formation of peptide bonds and the role of proteins in biological process.

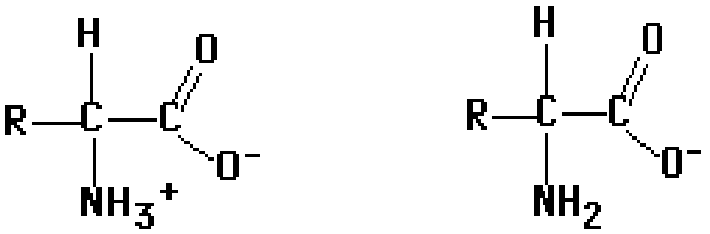
3.0 MAIN CONTENT

3.1 Chemical nature of amino acids

An amino acid consists of amino group, a carboxyl group (-COOH), a hydrogen atom (H) and a distinctive R group bonded to a carbon atom, called the α- carbon. The R group is specific to each amino acid.

Amino acids in solution at neutral pH are predominantly dipolar ions also called a Zwitterions. In the dipolar form, the amino group is

protonated ($-NH_3^+$) while the carboxyl group is dissociated (-COO-). The ionization state of an amino acid varies with pH. At physiological pH, carboxyl groups exist almost entirely as -COO- and amino groups predominantly as $-NH_3^+$.



pH 7 pH 11

Figure 2.6: Structure of amino acid at ionization states as a function of pH
Source: Nelson and Cox (2010).

3.2 The 20 amino acids found in proteins

Proteins found in living organisms contain only twenty (20) different kinds of amino acids. The same 20 standard amino acids make up the proteins in all living cell either in virus, bacteria, yeast, plant or human cell. These 20 amino acids combine in different sequences and numbers to form various kinds of proteins. The table below shows the 20 standard amino acids.

Table 2.2: The twenty (20) amino acids

Amino acid	Three –letter abbreviation	One-letter symbol
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamine	Gln	Q
Glutamic acid	Glu	E
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S

Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

3.3 Classification of amino acids

Amino acids may be classified based on the following:

Classification based on nutritional requirement

1. Essential Amino Acids

These are amino acids which are not synthesized in the body but must be provided in the diet to meet the body's metabolic needs. About ten of the amino acids are grouped under this category indicating that mammals require about half of the amino acids in their diet for growth and maintenance of normal nitrogen balance. Examples are Arginine*, Histidine*, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan, Valine.

Note that *Arginine and *Histidine are also grouped as semi essential amino acids

2. Non- Essential Amino Acids

These amino acids are amino acids that need not be provided through diet, because they can be biosynthesized in adequate amounts within the organism. Examples are Alanine, Asparagine, Aspartic acid (aspartate), Cysteine, Glutamic Acid (glutamate), Glutamine, Glycine, Proline, Serine, and Tyrosine.

3. Semi-essential Amino Acids

These are amino acids that can be synthesized within the organism but their synthesis is not in sufficient amounts, however they should also be provided in the diet. Two amino acids are grouped under semi-essential amino acids and they are Arginine and Histidine.

Classification based on the fate of each amino acid in mammals

Amino acids can be classified here as Glucogenic (i.e. potentially can be converted to glucose), ketogenic (i.e. potentially be converted to ketone bodies).

1. Glucogenic Amino Acids

Glucogenic amino acids are those amino acids in which their carbon skeleton gets degraded to pyruvate, α ketoglutarate, succinyl CoA, fumarate and oxaloacetate and then converted to glucose and glycogen. These include Alanine, Cysteine, Glycine, Arginine, Glutamine, Isoleucine, and Tyrosine.

2. Ketogenic Amino Acids

Those amino acids in which their carbon skeleton is degraded to acetoacetyl CoA, or acetyl CoA and then get converted to acetone and β-hydroxy butyrate which are referred to ketone bodies. These include Phenylalanine, Tyrosine, Tryptophan, Isoleucine, Leucine, and Lysine.

These amino acids have the ability to form ketone bodies which is particularly evident in untreated diabetes mellitus in which large amounts of ketone bodies are produced by the liver. Degradation of Leucine which is an exclusively ketogenic amino acid makes a substantial contribution to the formation of ketone bodies especially during starvation.

Classification depending on the charge

1. Neutral amino acids: These are amino acids that do not contain any charge on the 'R' group. They are further classified into

- Aliphatic amino acids which contains a chain of carbon atoms e.g. Glycine, Alanine, Seine, Threonine, Valine, Leucine, Isoleucine, Asparagine, Glutamine
- Aromatic amino acid which have an aromatic shape or contains benzene ring e.g. Phenylalanine, Tyrosine, Tryptophan.
- Heterocyclic amino acids which have heterocyclic ring i.e. any of the ring structures which contain different atoms.
- Sulphur containing which are amino acids which contain Sulphur atom e.g. Cysteine and Methionine.

2. Acidic amino acids: These are amino acids that contain a negative charge or an acidic group e.g. Aspartate, Glutamate

3. Basic amino acids: These contain a positive charge or a basic group e.g. Arginine, Lysine and Histidine.

Formation of peptide bonds

The most important reaction of amino acids is the formation of a peptide bond. This involves the joining of the α- carboxyl group of one amino acid to the α- amino group of another amino acid, with resultant loss of a water molecule. The biosynthesis of peptide bonds requires an input of free energy, whereas their hydrolysis is thermodynamically favorable. Many amino acids (usually > 100) are joined by peptide bonds to form a polypeptide chain.

3.4 Classification of proteins

Proteins are macromolecules with a backbone formed by polymerization of amino acids. They are nitrogenous compounds of high molecular weight which play a vital or prime role in living organisms.

Proteins may be classified on the basis of their composition, solubility, shape and their biological functions.

Classification based on composition

A. Simple protein: These proteins yield only amino acids during hydrolysis with no other major organic or inorganic hydrolysis products.

B. Conjugated Proteins

These yields amino acids and other organic and inorganic components e.g. Nucleoprotein (a protein containing Nucleic acids), Lipoprotein (a protein containing lipids), Phosphoprotein (a protein containing phosphorous), Metalloprotein (a protein containing metal ions of Fe^{2+}), Glycoprotein (a protein containing carbohydrates)

Classification based on Solubility

a) **Albumins:** These proteins such as egg albumin and serum albumin are readily soluble in water and coagulated by heat.
b) **Globulins:** These proteins are present in serum, muscle and other tissues and are soluble in dilute salt solution but sparingly in water.
c) **Histones:** Histones are present in glandular tissues (thymus, pancreas etc.) and are soluble in water. They combine with nucleic acids in cells and on hydrolysis to yield basic amino acids.

Classification based on Shape

A. Fibrous proteins

These proteins are made up of several coiled cross-linked polypeptide chains. They are insoluble in water and highly resistant to enzyme digestion. A few sub groups are listed below:

1. Collagens: These are major proteins of the connective tissue. They are insoluble in water, acids or alkalis but are convertible to water-soluble gelatin and are easily digestible by enzymes.
2. Elastins: present in tendons, arteries and other elastic tissues, not convertible to gelatin.
3. Keratins: these are proteins found in the hair and nails etc.

B. Globular proteins: These are globular or ovoid in shape, soluble in water and constitute the enzymes, oxygen carrying proteins, hormones etc.

Classification based on biological functions

Proteins are sometimes described as the "workhorses" of the cell because they do so many things like:

- act as enzymes e.g. kinases, transaminases etc.
- act as storage proteins e.g. myoglobin, ferritin
- act as regulatory proteins e.g. peptide hormones, DNA binding proteins
- act as structural protein e.g. collagen, proteoglycan
- act as protective proteins e.g. blood clotting factors, Immunoglobins,
- act as transport protein e.g. hemoglobin, plasma lipoproteins
- act as contractile or motile proteins e.g. actin, tubulin

3.5 Roles of proteins in biological processes

Proteins play crucial roles in virtually all biological processes. Some of these roles include:

Enzymatic catalysis: Nearly all chemical reactions in biological systems are catalyzed by enzymes. Chemical transformations rarely occur at perceptible rates *in vivo* in the absence of enzymes. Most enzymes are proteins. Thus, proteins play the unique role of determining the pattern of chemical transformations in biological systems.

Transport and storage: Many small molecules and ions are transported by specific proteins e.g. Hb (hemoglobin) transports oxygen in erythrocytes while myoglobin transports oxygen in muscle. Transferrin carries iron in the plasma of blood to the liver where it is stored as a complex with ferritin, another protein.

Co-ordinated motion: Proteins are the major components of muscle. Muscle contraction is accomplished by the sliding motion of two kinds of protein filaments. On the microscopic scale, coordinated motion such as the movement of chromosomes in mitosis and the propulsion of sperm by their flagella are also produced by contractile assemblies consisting of proteins.

Mechanical support: The high tensile strength of skin and bone is due to the presence of collage, a fibrous protein.

Immune protection: Antibodies are highly specific proteins that recognize and combine with foreign substances such as viruses, bacteria and cells from other organisms.

Generation and transmission of nerve impulses: The response of nerve cells to specific stimuli is mediated by receptor proteins e.g. rhodopsin is the photoreceptor protein in retinal rod cells.

Control of Growth and Differentiation: Controlled sequential expression of genetic information is essential for the orderly growth and differentiation of cells. Repressor proteins are important control elements that silence specific segments of the DNA of a cell. Nerve growth factor, a protein complex serves to guide the formation of neutral networks in higher organisms.

4.0 CONCLUSION

Proteins are nitrogenous organic compounds of high molecular weight which play a primary role in living organisms. They are polymers of amino acids and are essential nutrients for tissue growth, repairs and replacement.

5.0 SUMMARY

In this unit you have learnt about the chemical nature of amino acids, different classification of amino acids and proteins, formation of peptide bonds and the role of proteins in biological system.

6.0 TUTOR-MARKED ASSIGNMENT

1. Describe the chemical nature of amino acids.
2. Identify the 20 amino acids which make up proteins.
3. Explain the formation of peptide bond.
4. State the biological role of protein in the living system.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th Edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V.W. and Well, P. A. (2012). Harper's Illustrated Biochemistry (29th Edition) McGraw-Hill Medical.

Nelson, D.L. and Cox M.M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 4 CHEMISTRY OF LIPIDS

1.0 INTRODUCTION

The word lipid was derived from the Greek word *lipos* meaning fats. Lipids are heterogeneous group of compounds related either directly or indirectly to fatty acids. They are insoluble in water but soluble in non-polar organic solvents such us benzene, chloroform, and ether. They are present in all living organisms.

2.0 OBJECTIVES

At the end of this unit, you will learn about fatty acids, classification of lipids and the biological functions of lipids.

3.0 MAIN CONTENT

3.1 Fatty Acids

Fatty acids (FA) are the monocarboxylic acids with a long hydrocarbon chain. The minimum number of carbon atoms required to be called as fatty acid is 4. They are two types of fatty acids namely saturated and fatty unsaturated.

1. Saturated fatty acids are the fatty acids without double bonds i.e. they contain only single bonds along the length of the carbon chain.

Name of fatty acids	**Number of carbon atoms**
Butyric acid	4
Lauric acid	12
Myristic acid	14
Palmitic acid	16
Stearic acid	18
Arachidic acid	20

All these fatty acids are solids at room temperature.

2. Unsaturated fatty acids are the FA that contains one or more double bonds along the length of the hydrocarbon chain. Most naturally occurring unsaturated FAs have a cis-configuration i.e. the hydrogen atoms are on the same side of the chain. To represent the position of the double bond in a fatty acid, it is represented as Delta n (Δ), where n shows the position of double bond between the nth carbon atom and the carbon atom next to it towards the omega (last) carbon atom. Unsaturated fatty acids are all liquids at room temperature. They can be further classified depending on the number of double bonds present per fatty acid into:

(a). **Monounsaturated Fatty Acids (MUFA):** They contain only one double bond per fatty acid. Oleic acid is the most abundant monounsaturated FA in nature with C18 atoms and cis Δ^9 (cis Δ^9 means position of the double bond). Palmitoleic acid is another example of MUFA, and it is present nearly in all fats. Palmitoleic has C16 atoms and cis Δ^9 (cis Δ^9 means position of the double bond)

Name of fatty acid	**Number of carbon atoms**	**Position of the double bond**
Palmitoleic acid	16	cis Δ^9
Oleic acid	18	cis Δ^9

(b). **Polyunsaturated fatty acids (PUFA) –** These are the FAs obtained from plant seeds. They usually contain 2 or more double bonds. In PUFA, double bonds are usually separated by a methylene (CH_2) group. PUFA are present in oils such as soya bean oil, groundnut oil, sunflower, benne-seed oil etc. Examples of PUFA are *linoleic, linolenic and arachidonic* acids; they are also called omega 6 and omega 3 fatty acid respectively. These two PUFA are also referred to as essential PUFA because animals cannot synthesize them, therefore they must be supplied to the body in the diet.

Name of fatty acid	**Number of carbon atoms**	**Number of double bonds**	**Position of the double bond**
Linoleic acid	18	2	cis $\Delta^{9,12}$
Linolenic acid	18	3	cis $\Delta^{9,12,15}$
Arachidonic acid	20	4	cis $\Delta^{5,8,11,14}$

3.2 Classification of Lipids

Lipids can be classified into the following:

1. **Simple lipids**: - These are esters of fatty acids with different alcohols. They are further classified as:

Neutral Fats: - These are esters of fatty acids with glycerol. They are known as triacylglycerols (TAG) or triglycerides.

Waxes: - Esters of fatty acids with high molecular weight monohydric alcohols

Triacylglycerols

These are esters of fatty acids with a glycerol and are storage forms of lipids in mammals. Triacylglycerols also called triacylglycerides exist as simple or mixed types depending on the type of fatty acids that form esters with the glycerol.

Triacylglycerols are mainly found in special cells called adipocytes (fat cells), of the mammary gland, abdomen and under skin of animals.

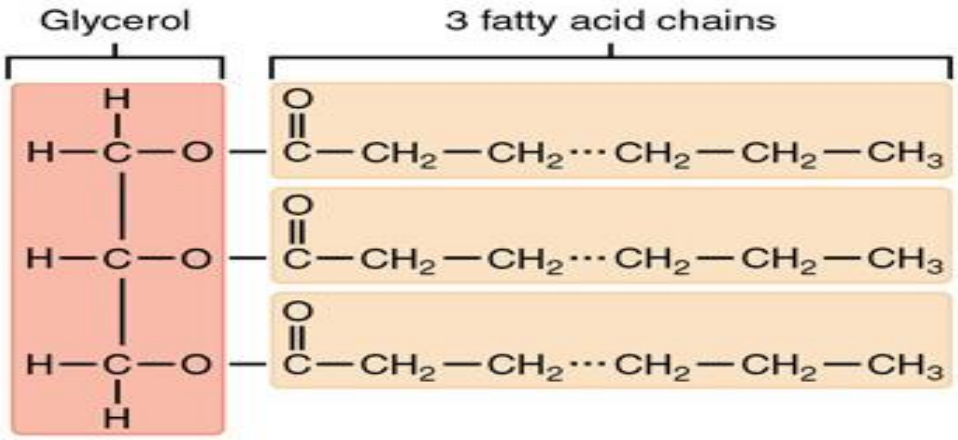


Figure 2.7: Structure of Triacylglycerides

2. **Compound lipids**: - Simple lipids in combination with some other groups are called compound lipids. Depending upon the group (prosthetic group) attached the compound lipids are further classified as:

(a). Phospholipids: - They contain a phosphoric acid as the prosthetic group. Depending upon the alcohol present they are grouped into Glycerophospholipids (the alcohol is glycerol) e.g. phosphatidyl choline, phosphatidyl ethanolamine, phosphatidyl serine, phosphatidyl inositol etc and Sphingophospholipids (the alcohol is sphingosine) e.g. sphingomyelin which contains a fatty acid at the amino group.

(b). Glycolipids: - These lipids contain a fatty acid, sphingosine and carbohydrate residues. They are also known as cerebroside.

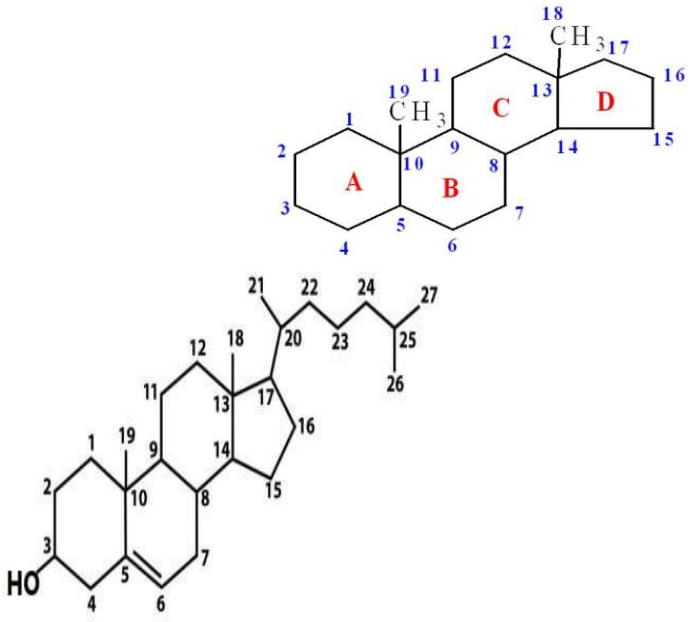
3. **Derived lipids:** Derived lipids are the hydrolytic products of the simple and compound lipids. They include fatty acids and steroids.

Steroids

All compounds containing the cyclo-pentano-perhydro-phenanthrene ring are called steroids. Example of steroids is cholesterol. Cholesterol is the major sterol in the body. It is a constituent of cell membrane and provides rigidity to it. It acts as the precursor for all the other steroids in the body.

Biological importance of cholesterol

- For the synthesis of bile salts that are important in lipid digestion and absorption.
- For the synthesis of steroid hormones that are biologically important like the sex hormones estrogen and progesterone.
- For the synthesis of vitamin D3
- As a structural material in biological membranes.
- As a component of lipoproteins which is a transport form of lipid based energy.



Cylo-pentano-perhydro-phenanthrene
Cholesterol

Symptoms of essential fatty acids deficiency

When essential fatty acids (omega-3 and omega-6 fatty acids) are not present in our diets, our body will not be able to produce prostaglandins and sterols (this is just one of many functions of these FA). We know that hormones are very important for reproduction in man and woman, deficiency of material required to synthesize them will result in inadequate or complete absence of the hormones. The result is infertility. So, foods that are rich in essential fatty acids are good for our health, examples of such foods are fish, poultry products, fruits, vegetables, nuts (especially walnuts), legumes (especially soya beans), beef etc. The symptoms of essential fatty acids deficiency are:

i. Growth retardation
ii. Poor wound healing
iii. Dermatitis and hair loss
iv. Kidney and liver diseases
v. Infertility
vi. Depression

The most noticeable symptoms of essential fatty acids deficiency are skin disorders such as scaly dermatitis. It usually occur on the hands, shoulders, forearms and face however it can show up on other parts of the body. When essential fatty acids are included in the diets, these symptoms disappear within 7 days.

3.3 General functions of lipids

i. They serve as efficient energy sources: Lipids provide energy higher amount of energy for the body than carbohydrates and protein.
ii. They are structural components of the cell membrane: Cell membranes are made up of lipids such as phospholipids and cholesterol that gives cell stability.
iii. They assist in digestion: Lipids dissolve fat soluble vitamins (Vit. A, D, E, K) and therefore help in their digestion.
iv. They occur as free fatty acids in the plasma where they act as transporter of various biological molecules, especially plasma albumin.
iv. They serve as thermal insulators.
v. Lipids serve as precursors for hormones especially steroid hormones.

4.0 CONCLUSION

Lipids are efficient energy sources for the body and also one of the structural components of the plasma membrane. Deficiency of essential

fatty acids which are a class of lipid in our body give rise to symptoms like growth retardation, poor wound healing, dermatitis and hair loss etc.

5.0 SUMMARY

In this unit, you have learnt about fatty acids, classification of lipids and the symptoms of fatty acid deficiency.

6.0 TUTOR-MARKED ASSIGNMENT

1. List the classes of lipids and give 2 examples in each
2. Enumerate the biological functions of lipids
3. Differentiate between saturated and unsaturated fatty acids, give two examples of each
4. Enumerate the symptoms of fatty acids deficiency

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th Edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V.W. and Well, P. A. (2012). Harper's Illustrated Biochemistry (29th Edition) McGraw-Hill Medical.

Nelson, D.L. and Cox M.M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 5 CHEMISTRY OF NUCLEIC ACID

1.0 INTRODUCTION

Nucleic acids are acidic compounds first discovered in the cell nucleus. Later they were found in the cytoplasm. They are high molecular weight nitrogenous organic compounds which play an important role in storage, transmission and control of all the cellular activities. They are defined as polynucleotides i.e. chain-like polymers of up to thousands of nucleotide units. Each nucleotide is a molecular complex of nucleoside and phosphoric acid.

2.0 OBJECTIVES

On the completion of this unit you will get to understand the chemical components of nucleic acids, the structure of the DNA and RNA.

3.0 MAIN CONTENT

3.1 Nucleic acids

The term nucleic acid is the overall name for DNA i.e. deoxyribonucleic acid and RNA i.e. ribonucleic acid. They are composed of nucleotides, which are the monomers made of three components: a 5-carbon sugar, a phosphate group and a nitrogenous base.

Nucleic acids are the most important macromolecules in all living things because it is the genetic material responsible for the transfer of genetic information from one generation of organisms to another. The traits we share with our parents are due to the genes inherited from them. This is not limited to physical appearance, colour of skin, size of eye balls, intelligence etc.

Nucleic acids are present in nucleus, mitochondria and chloroplast in plant. They are found in two basic structural forms, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

The structure of DNA

Deoxyribonucleic acid (DNA) is the principal informational macromolecule of the cell which stores, translates and transfers the genetic information. In prokaryotes, the DNA is found mostly in the nuclear zone. In eukaryotes it is found in the nucleus, mitochondria and chloroplast. The structure of the DNA is based on the discovery of Watson and Creek in 1953.

Double helical structure of DNA as proposed by Watson and Crick Model

The three dimensional structure of DNA as proposed by Watson and Crick and the recent advances in it are summarized below:

1. DNA is made of two helical chains coiled around the same axis, to form a right-handed double helix.
2. The two chains in the helix are anti-parallel to each other i.e. the 5'-end of the polynucleotide chain and the 3'-end of the other polynucleotide chain is on the same side and close together.
3. The distance between each turn is 3.6 nm
4. There are 10 nucleotides per turn
5. The spatial relationship between the two strands creates major and minor grooves between the two strands. In these grooves some protein interact.
6. The hydrophilic backbones of alternating deoxyribose and negatively charged phosphate groups are on the outside of the double bond helix.
7. The hydrophobic pyrimidine and purine bases are inside the double helix, which stabilizes the double helix of the DNA.
8. The double helix is also stabilized by inter-chain hydrogen bond formed between a purine and pyrimidine base.
9. A particular purine base, pairs by hydrogen bonds, only with a particular pyrimidine base i.e. Adenine (A) pairs with Thymine (T) and Guanine (G) pairs with Cytosine only.
10. Two hydrogen bonds pairs Adenine and Thymine (A = T) whereas three hydrogen bonds pairs Guanine and Cytosine (G = C).
11. The base pairs A = T and (G = C) are known as complementary base pairs.
12. Due to the presence of complementary base pairing, the two chains of the DNA double helix are complementary to each other. Hence the number of 'A' bases are equal to the number of 'T' bases (or 'G' is equal to 'C') in a given double stranded DNA.
13. One of the strands in the double helix is known as sense strand i.e. which codes for

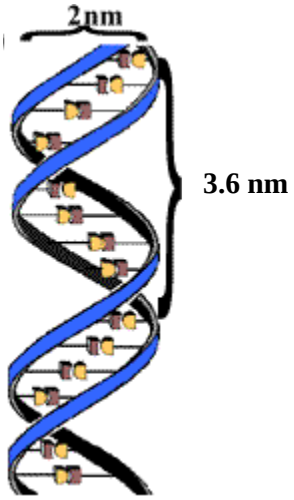


Figure 2.8: Double helical structure of the DNA
Source: Amanullah (2011).

Ribonucleic acid (RNA)

Ribonucleic acid is a polymeric essential in various biological roles in coding, decoding, regulation and expression of genes.The building unit of RNA is ribonucleotide. A ribonucleotide is made up of (1) ribose sugar, (2) nitrogenous bases namely Adenine, Uracil, Guanine and Cytosine (Note that uracil is present instead of thymine), (3) phosphoric acid. Ribonucleotide contains "O" (i.e. oxygen) in the carbon 2' of the ribose sugar. RNA is the primary structure unlike the DNA that is a secondary structure.

There are three types of RNA functioning to express the genetic information contained in the DNA. Thus these RNAs play important role in protein synthesis. They are:

1. Messenger RNA (mRNA)
2. Transfer RNA (tRNA)
3. Ribosomal RNA (rRNA

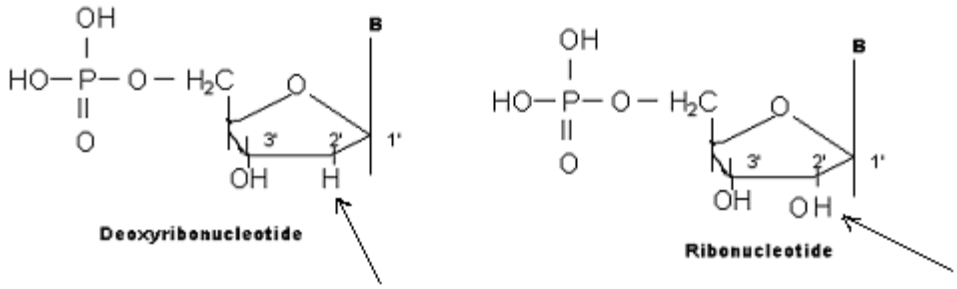


Figure 2.9: Structure of ribose and deoxy-ribose in RNA
Source: Amanullah (2011).

Differences between RNA and DNA

The differences between them are highlighted below:

		DNA	**RNA**
1.	Uracil	Absent	Present
2.	Sugar	Deoxyribose	Ribose
3.	Site	Nucleus, mitochondria but never in cytosol	Nucleus, ribosome, cytosol, Nucleolus, mitochondria
4.	Strands	Two helical strands	Single strand
5.	---------	Carries genetic information	Only m-RNA carries genetic information
6.	Number of Bases	Equal	Not equal
7.	Thymine	Present	Absent

4.0 CONCLUSION

The genetic information is stored in DNA or RNA (RNA viruses). The message contained in the DNA, in the form of nucleotide bases encodes the instructions or traits are transferred from parents to their offspring when cell divides and also provide a template for the production of identical DNA molecules when a cell divides.

5.0 SUMMARY

In this unit, you have learnt about the chemical components of nucleic acid, structure of the DNA and RNA and the differences between them.

6.0 TUTOR-MARKED ASSIGNMENT

1. Describe the chemical components of nucleic acids.
2. Give an account of Watson and Crick description of the DNA.
3. Enumerate the differences between DNA and RNA

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

MODULE 3 METABOLISM OF BIOMOLECULES

UNIT 1 METABOLISM OF CARBOHYDRATES

1.0 INTRODUCTION

Carbohydrates comprises of the polysaccharides such as starch and glycogen, the disaccharides (lactose, maltose, sucrose) and monosaccharaides (like glucose, fructose etc). The complex polysaccharides and disaccharides are converted into simple monosaccharaides which are absorbed by the body. This unit gives the details of the metabolism of carbohydrates.

2.0 OBJECTIVES

No objectives

3.0 MAIN CONTENT

3.1 Digestion of Carbohydrates

Liquid food materials like milk, soup, fruit juice escape digestion in mouth as they are swallowed, but solid foods are masticated thoroughly before they are swallowed to undergo digestion.

1. Digestion in Mouth

Digestion of carbohydrates begins in the mouth, where they come in contact with saliva during mastication. Saliva contains a carbohydrate splitting enzyme called salivary amylase (ptyalin).

Action of ptyalin (salivary amylase)

It is α – amylase that requires chloride (Cl^-) ion for activation and optimum pH 6-7. The enzyme hydrolyzes α- (1, 4) glycosidic linkage from molecules like starch, glycogen and dextrin, producing smaller molecules such as maltose and glucose. Ptyalin action stops in stomach when pH falls to 3.0. There is no digestion of carbohydrates in the stomach as the enzymes for carbohydrate digestion are absent in the gastric secretions.

2. Digestion in Intestine

Food from the stomach reaches the duodenum where it meets the pancreatic juice. The pancreatic juice contains a carbohydrate-splitting enzyme called pancreatic amylase.

a. Pancreatic amylase

It is also an α – amylase with an optimum pH 7.1. Like salivary ptyalin pancreatic amylase also requires Cl^- for its activity. The enzyme hydrolyzes α-(1, 4) glycosidic linkage situated in the polysaccharide molecules thereby liberating free glucose molecules. The pancreatic amylase acts only on α –1, 4 glycosidic linkages, it cannot act on the α – 1,6 glycosidic linkages which are present at the branching points of starch and glycogen. These undigested branching points are known as isomaltose which are digested by an enzyme called isomaltase or α– dextrinase.

The disaccharides are hydrolyzed by respective disaccharides which are secreted by the intestinal mucosa. The disaccharide maltose is digested by the enzyme maltase to yield two glucose units. Lactase splits the disaccharide lactose into glucose and galactose. Sucrose is hydrolyzed by sucrase or invertase into glucose and fructose.

Cellulase cannot be digested by human beings as the enzyme is absent, yet cellulose is specifically included in the diet so as to increase the bulk (fiber) of the food and thus help in the mobility of the food through the gastrointestinal tract. The end products of carbohydrate digestion are glucose, fructose, mannose, ribose etc. some of the sugars are converted into glucose before absorption.

3.2 Absorption of carbohydrates

The monosaccharides are absorbed in the small intestine by three mechanisms- (1) Simple diffusion (2) Active transport and (3) Facilitated transport.

1. **Simple diffusion:** As the digestion proceeds, the concentration of glucose in the intestinal lumen increases more than the blood glucose level. This results in an osmotic difference between the two, due to which glucose simply diffuses downhill from a region of higher concentration of glucose (lumen) to the region of lower concentration of glucose (blood).
2. **Active transport:** Simple diffusion continues till the concentration of glucose in the lumen equals to that of the blood, then glucose is transported by active transport. Here glucose binds to a carrier protein situated in the outer membrane of the intestinal wall. This carrier protein also binds two sodium (Na^+) ions. When both glucose and Na+ are bound to the carrier protein it moves into the cell and releases glucose and Na+ into the cytoplasm of the cell, from where glucose simply diffuses into the blood. To continue the active process Na^+ must be expelled out of the cell, so as to maintain a low concentration of Na^+ inside the cell, when compared to the lumen. Hence Na+ is expelled out of the cell into the blood plasma, in exchange of K^+ through a $Na^{+,}$ K^+ ATPase pump, which hydrolyses ATP for exchanging Na^+ with $K^{+.}$ As this overall process requires energy it is known as active transport. So, during active transport, glucose moves against concentration gradient. Galactose is also absorbed from the intestine in a similar manner as that of glucose active transport.
3. **Facilitated transport:** Fructose is transported by a carrier protein which does not require energy (ATP). Hence it is known as facilitated transport.

3.3 Glycolysis

Glycolysis is the breakdown of glucose or glycogen to pyruvate or lactate. The glycolytic pathway is also called Embden Meyerhoff pathway. It occurs virtually in all tissues. Erythrocytes and nervous tissues derive their energy mainly form glycolysis. This pathway is unique in the sense that it can utilize O_2 if available (‘aerobic’) and it can function in absence of O_2 also (‘anaerobic’). Enzymes involved in glycolysis are present in cytoplasm.

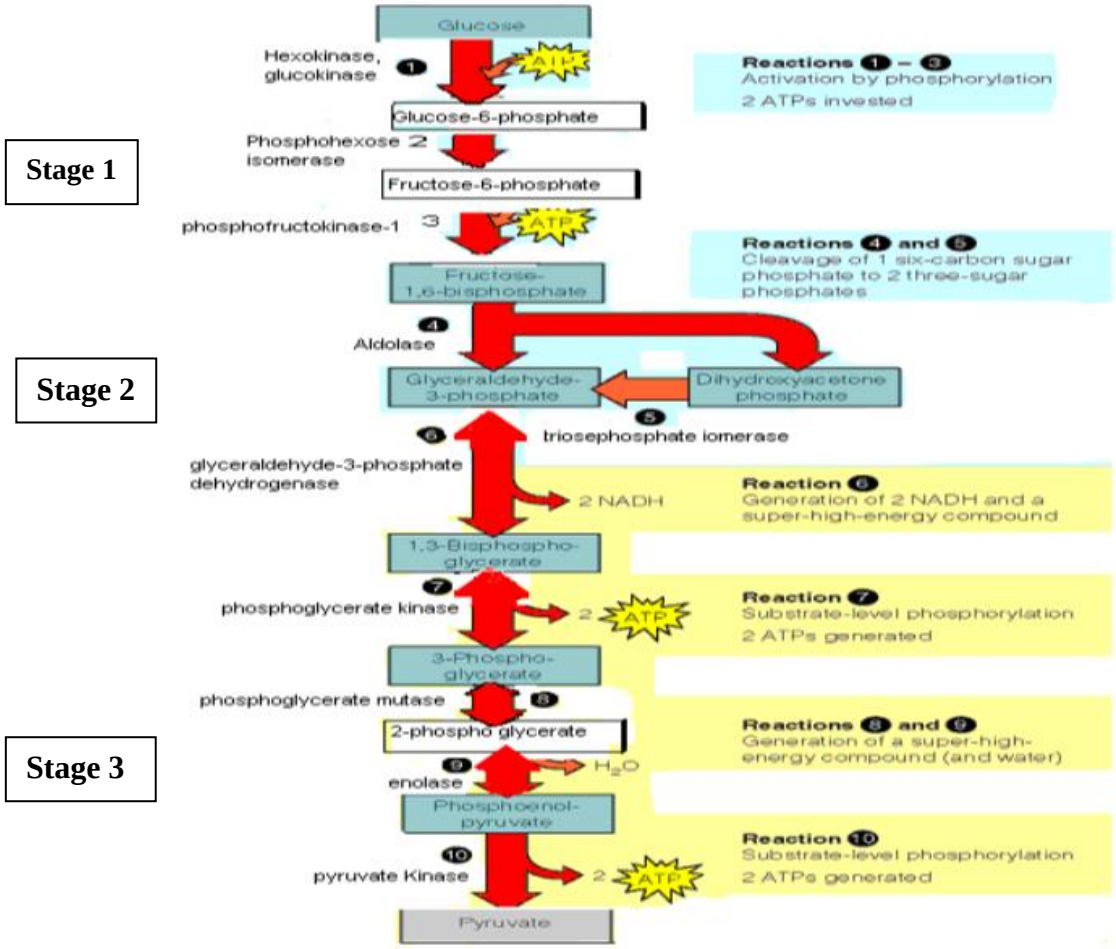


Figure 3.1: Glycolytic pathway
Source: Nelson and Cox (2009).

Aerobic phase of glycolysis
Aerobic phase of glycolysis involves the conversion of glucose to pyruvate.

Anaerobic phase of glycolysis
This is the phase where glucose is converted to lactate.

Reactions of glycolytic pathway
The various reactions are described divided in three stages as shown in Figure 3.1.

Stage 1
1. Phosphorylation of glucose
Glucose is phosphorylated to form glucose – 6- Phosphate. The reaction is catalyzed by the specific enzyme glucokinase in liver cells and by nonspecific hexokinase in the other cells.

ATP acts as the phosphate (PO_4) donor in the presence of Mg. One high energy PO_4 bond is utilized and ADP is produced. The reaction is accompanied by considerable loss of free energy as heat.

2. Conversion of G-6-phosphate to Fructose-6-phosphate

Glucose-6-phosphate after formation is converted to fructose-6-P by phospho-hexose isomerase.

3. Conversion of Fructose-6-phosphate to Fructose 1, 6-disphosphate

Fructose-6-P is phosphorylated with ATP to form fructose 1, 6-disphosphate catalyzed by the enzyme phosphofructokinase.

Note:

Reaction one is irreversible.

One ATP is utilized for phosphorylation of glucose at position 6.

Phosphofructokinase is the key enzyme in glycolysis that regulates the pathway.

Stage 2

This stage involves the cleavage of fructose 1,6-diphosphate into two three-carbon fragments which are glyceraldehyde-3-phosphate and a dihydroxyacetone phosphate catalyzed by aldolase. These resulting three carbon units are readily interconvertible and are catalyzed by phosphotriose isomerase.

Note

The reaction is reversible.

There is neither expenditure of energy nor formation ATP.

Stage 3

In this stage, ATP is harvested when the three carbon-fragments are oxidized to pyruvate. This is an energy-yielding reaction. It consists of the following reactions:

(1). Oxidation of Glyceraldehyde-3-phosphate to 1,3-disphosphoglycerate catalyzed by Glyceraldehyde-3-phosphate dehydrogenase.

(2). 1,3- diphosphoglycerate which is the end- product of the previous stage, still retains the PO_4 group originally derived from ATP in stage 1 and is converted to 3-phosphoglycerate by the enzyme phosphoglycerate kinase which is activated by magnesium ion (Mg^{2+}).

(3). 3-Phosphoglycerate formed in the above reaction is converted to 2-phosphoglycerate, catalyzed by the enzyme phosphoglycerate mutase.

(4). 2-phosphoglycerate is converted to phospoenol pyruvate in a reaction catalyzed by the enzyme enolase which requires the presence of either Mg^{2+} or Mn^{2+}.

(5). Phosphoenol pyruvate is converted to 'Enol' pyruvate. The reaction is catalyzed by the enzyme pyruvate kinase. The high energy phosphate (PO_4) of phosphoenol pyruvate is directly transferred to ADP producing ATP.

In the absence of oxygen (anaerobic condition), pyruvate is converted to lactic acid by the enzyme lactate dehydrogenase.

Significance of glycolysis

1. It is the main route of glucose metabolism.
2. It occurs in all cells of the body.
3. The glycolytic pathway is meant for provision of energy
4. Brain and red blood cells (RBCs) depends only on glucose for oxidation and production of oxygen
5. In the brain aerobic glycolysis occurs whereas in the RBC, there is always anaerobic glycolysis due to the absence of the mitochondria.
6. The initiation of glycolysis is regulated by the ATP concentration in the cytoplasm.
7. In skeletal muscle, aerobic glycolysis occurs in normal conditions but during vigorous muscular contraction, anaerobic glycolysis is the major pathway for energy production as glycolysis provides ATP. In absence of oxygen, muscles can survive under anaerobic condition.

3.4 Clinical conditions associated with impaired glycolysis

Lactic acidosis

It occurs as a result of overproduction of lactate, underutilization of lactate or inhibition of pyruvate dehydrogenase. It may also be as a result of rare congenital disorders where the mitochondria do not function at full capacity or diabetic ketoacidosis as well as liver/kidney disease. It is characterized by Lactate levels > 5 mm/L and serum pH < 7.35.

Symptoms: Nausea, Vomiting, Hyperventilation, Irregular heart rate.

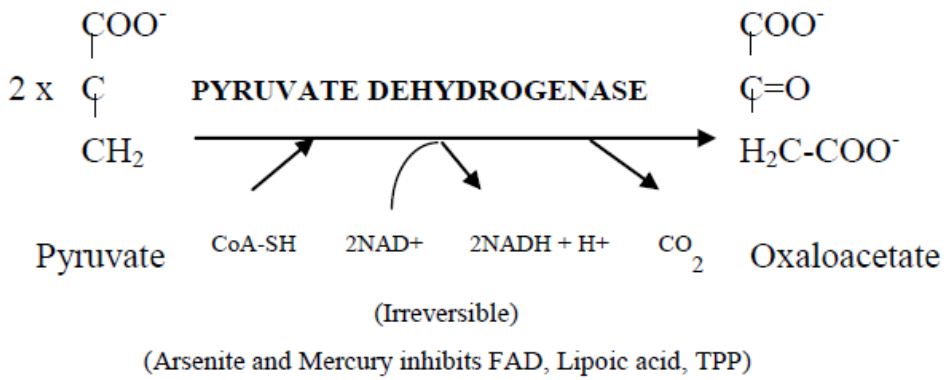
Pyruvate kinase deficiency

The deficiency of pyruvate kinase causes a rare genetic defect of glycolysis which results in hemolytic anemia. In this condition glycolytic intermediates accumulate, whereas pyruvate and lactate concentrations decrease.

3.5 Fate of pyruvate

Pyruvate is an important regulatory point for energy production. The ultimate fate of pyruvate depends on the energy state of the cell and the degree of oxidative phosphorylation taking place. When the energy state of the cell is low (low ADP, low ATP), pyruvate enters the TCA Cycle (Tricarboxylic cycle) as acetyl CoA via the pyruvate dehydrogenase complex and oxidized completely to carbon dioxide and water to yield energy. The pyruvate dehydrogenase complex is one of the most complex proteins in the body and consists of more than 60 subunits.

Pyruvate dehydrogenase complex is a multi-enzyme complex made up of three enzymes which are (1). Pyruvate dehydrogenase (2). Dihydrolipoyl transacetylase and (3) Dihydrolipoyl dehydrogenase. This reaction requires five coenzymes which are (i) Thiamine pyrophosphate (ii) Lipoic acid (iii) Coenzyme A (iv) Flavin adenine dinucleotide (FAD) and (v) Nicotinamide adenine dinucleotide (NAD^+)



4.0 CONCLUSION

Complex carbohydrates (starch) are broken down during digestion into monosaccharaides unit such as glucose and fructose. Glucose is finally oxidized into pyruvate in an aerobic condition or lactate in anaerobic condition both producing different amount of energy in the form of ATP.

5.0 SUMMARY

In this unit you have learnt about the digestion and absorption of carbohydrates, reactions of glycolytic pathway and the significance of the pathway.

6.0 TUTOR-MARKED ASSIGNMENT

1. Explain the process of carbohydrate digestion
2. Explain the concept of aerobic and anaerobic glycolysis
3. Enumerate the different reactions which make up the pathway and the enzymes which catalyze these reactions
4. Enumerate the significance of the glycolytic pathway
5. State the clinical conditions associated with impaired glycolysis

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 2 KREBS CYCLE AND OXIDATIVE PHOSPHORYLATION

1.0 INTRODUCTION

The Krebs cycle also known as tricarboxylic cycle or the critic acid cycle is named after the scientist Sir Hans Krebs (1900-1981) who discovered it. He proposed the key elements of this pathway in 1937 and was awarded the Nobel Prize in medicine for the discovery in 1953. Krebs cycle is a set of continuous reactions (8 steps) occurring in a cyclic manner in the mitochondrial matrix in eukaryotes and within the cytoplasm in prokaryotes. Acetyl CoA, the fuel of TCA cycle, enters the cycle inside the mitochondrial matrix, and gets oxidized to carbon (IV) oxide (CO_2) and H_2O while at the same time reducing NAD to NADH and FAD to $FADH_2$. The NADH and $FADH_2$ can be used by the electron transport chain to create ATP.

2.0 OBJECTIVES

At the end of this unit, you should understand the TCA cycle, amphibolic and anaplerotic nature of TCA cycle, oxidative phosphorylation and inhibitors of the electron transport chain.

3.0 MAIN CONTENT

3.1 Description of Krebs cycle

In eukaryotes, Krebs cycle takes place in the mitochondria because all the enzymes of the cycle are located inside the mitochondria matrix. The TCA cycle is an important source of precursors or building blocks for the synthesis of molecules such as amino acids, purine bases, cholesterol and porphyrins. The following describes the various steps in TCA cycle.

Step 1

Condensation: In step 1, the two-carbon compound, **acetyl CoA** participates in a condensation reaction with the four-carbon compound, **oxaloacetate** to produce **citrate,** a six-carbon compound catalyzed by the enzyme **citrate synthase.** This is the first stable TCA in the cycle and hence the name TCA cycle.

Step 2

Isomerization of citrate: Step 2 involves moving the hydroxyl group in the citrate molecule so that it can later form α-keto acid. This process involves a sequential dehydration and hydration reaction, to form the **D-isocitrate** isomer (with the hydroxyl group now in the desired α-location), with **cis-aconitase** as the intermediate. A single enzyme, **aconitase** performs this two-step process.

Step 3

Generation of CO_2 and NAD+ linked enzyme: Oxidative decarboxylation takes place in the next reaction. The reaction is catalyzed by the enzyme **isocitrate dehydrogenase.** The reaction involves dehydrogenation to **oxalosuccinate,** an unstable intermediate which spontaneously decarboxylates to give **α-ketoglutarate.** In addition to decarboxylation, this step produces a reduced nicotinamide adenine dinucleotide phosphate (NADH) cofactor.

Step 4

A second oxidative decarboxylation step: This step is performed by a multi-enzyme complex, the **α-ketoglutarate dehydrogenation complex.** The multi-step reaction performed by the α-ketoglutarate dehydrogenation complex is analogous to the **pyruvate dehydrogenase complex,** i.e. an α-keto acid undergoes oxidative decarboxylation with formation of an acetyl CoA i.e. succinyl CoA.

Step 5

Substrate level phosphorylation: Succinyl CoA is a high potential energy molecule. The energy stored in this molecule is used to form a high energy phosphate bond in a guanine nucleotide diphosphate (GDP) molecule. Most of the GTP (Guanine triphosphate) formed is used in the formation of ATP, by the action of nucleoside diphosphate.

Step 6

Flavin dependent dehydrogenation: The succinate produced by **succinyl CoA-synthetase** in the prior reaction needs to be converted to oxaloacetate to complete the Krebs cycle. The first step in the conversion is the dehydrogenation of succinate to yield fumarate facilitated by the enzyme **succinate dehydrogenase.** FAD is covalently

bound to the enzyme (via a histidine residue) which is converted to $FADH_2$ that is oxidized through the ETC producing 2 ATPs.

Step 7

Hydration of a carbon-carbon double bond: Fumarate undergoes a stereo-specific hydration of the C=C double bond, catalyzed by **fumarate hydratase** also known as (**fumarase)** to produce L-malate.

Step 8

Dehydrogenation reaction that will generate oxaloacetate: L-malate (malate) is dehydrogenated to produce oxaloacetate by the enzyme **malate dehydrogenase** during which one molecule of NAD^+ is converted to NADH + H^+. The formation of oxaloacetate completes the Krebs cycle.

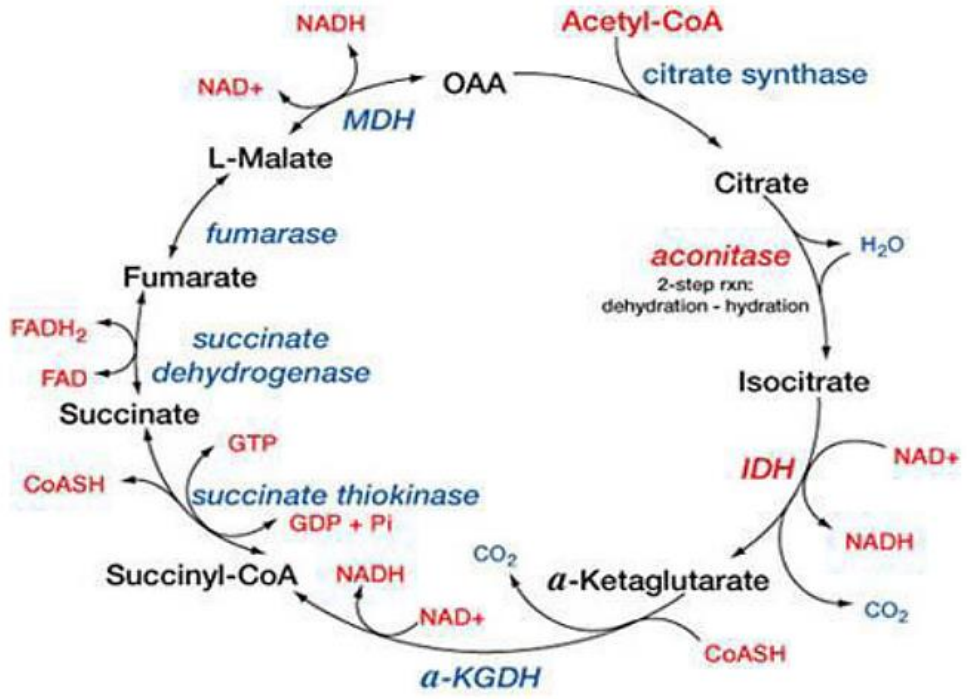


Figure 3.2: The TCA cycle showing the enzymes and the intermediates

Source: Murray *et al.* (2012).

Number of ATP's produced in one Krebs cycle

The TCA cycle produces 3 NADH + H^+ and one $FADH_2$, known as the reducing equivalents. These reducing equivalents are oxidized through the electron transport chain (ETC). When NADH is oxidized through ETC it produces 3 ATPs while oxidation of FADH2 produces 2 ATPs.

Calculation of ATPs produced in each round of citric acid cycle

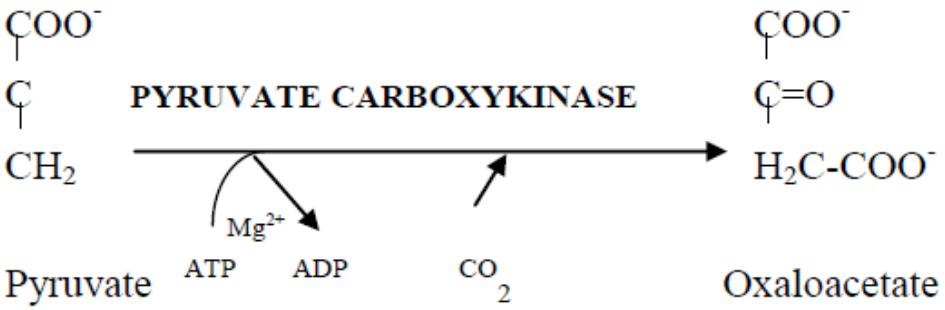
Enzyme involved	Equivalent produced	No. of ATPs produced	The step in TCA
Isocitrate dehydrogenase	NADH	3	Step 3
α-ketogluterate dehydrogenase	NADH	3	Step 4
Succinate thiokinase	GTP	1	Step 5
Succinate dehydrogenase	$FADH_2$	2	Step 6
Malate dehydrogenase	NADH	3	Step 8
		Total ATP produced	**12 ATPs**

3.2 Amphibolic role of TCA cycle

TCA cycle is the common pathway for the oxidation of carbohydrates, fats and proteins (catabolic role). The anabolic role is synthesis of various carbohydrates, amino acids and fats. As its takes part both in anabolism (synthesis of large organic molecules from smaller organic molecules which involves the utilization of energy) and catabolism (breakdown of larger organic molecules to smaller organic molecules accompanied with the release of energy), it is said to be amphibolic pathway of metabolism.

3.3 The Anaplerotic nature of the TCA Cycle

Anaplerosis is the replacement of the depleted intermediates of TCA cycle. As the TCA cycle takes part in the anabolic reactions, the intermediates of TCA cycle are utilized for the synthesis of various compounds. This results in the deficiency of one or more of the TCA cycle intermediates. In order to continue the TCA cycle, those intermediates which are deficient must be filled up by some other process and this process is known as anaplerosis. For example oxaloacetate is utilized for the synthesis of the amino acid aspartic acid and oxaloacetate is replaced via anaplerosis by carboxylation of pyruvate to oxaloacetate by the enzyme pyruvate carboxykinase as shown below.



3.4 Summary of oxidative phosphorylation

The reduced coenzymes (NADH) and $FADH_2$ from the TCA cycle are themselves oxidized when they released their protons and electrons. The electrons are transferred to oxygen, which is the final electron acceptor through a complex chain of electron-carrying molecules known as the electron transport chain. During the electron transferring process, large amount of energy is released and it is conserved in the form of ATP. This process is called oxidative phosphorylation as shown below.

ADP + Pi ⟶ ATP

Inhibitors of electron transport chain
Compounds capable of inhibiting the electron transport chain include Amytal (a barbiturate drug), rotenone (a plant product commonly used as an insecticide), piericidin A, oligomycin etc.

Piericidin A and oligomycin (antibiotics) block the electron flow through the respiratory chain and thereby shut down energy production in their respective targets.

4.0 CONCLUSION

The Krebs cycle is the cycle that takes place in the mitochondrial matrix of cells and it is responsible for the complete oxidation of acetyl CoA to carbon (iv) oxide and water.

5.0 SUMMARY

In this unit, you have learnt about the TCA cycle reactions, amphibolic nature of the TCA cycle, anaplerotic nature of the TCA cycle, oxidative phosphorylation and inhibitors of the electron transport chain.

6.0 TUTOR-MARKED ASSIGNMENT

1. Describe the reactions of TCA cycle in detail
2. Explain the amphibolic nature of the TCA cycle
3. Explain the anaplerotic nature of the TCA cycle
4. Give a summary account of oxidative phosphorylation
5. List two examples of inhibitors of electron transport chain.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 3 AMINO ACIDS METABOLISM

1.0 INTRODUCTION

Amino acids are produced from the breakdown of proteins catalyzed by enzymes called proteolytic enzymes. Unlike the digestion of carbohydrates which begins in the month, the digestion of protein starts in the stomach this is because proteolytic enzymes that degrade proteins are absent in the salivary secretions.

2.0 OBJECTIVES

On completion of this unit, you should have an understanding of the digestion and absorption of proteins, catabolism of amino acids and the reactions of urea cycle.

3. 0 MAIN CONTENT

3.1 Digestion and absorption of protein

The entry of proteins into the stomach stimulates the gastric mucosa to secrete a hormone gastrin which in turn stimulates the secretion of HCl by the parietal cells of the gastric glands and pepsinogen by the chief cells.

The HCl thus produced lower the pH of stomach to (pH 1.5 – 2.5) and acts as an antiseptic killing most of the bacteria and other foreign cells ingested along with food. The acid also denatures the protein by making them susceptible to hydrolysis by the action other proteolytic enzymes called proteases.

Proteases are endopeptidases (a group of enzymes) that attack the internal bonds of proteins and liberate large fragments of peptides. Then pepsinogen, a zymogen (inactive form of an enzyme) is converted into active pepsin which cleaves the ingested protein at their amino terminus

of aromatic amino acids (Phe, Tyr, and Trp.) to produce large peptide fragments and some free amino acids.

Pancreatic Digestion
As the food passes from the stomach to small intestine the low pH of the food triggers the secretion of the hormone 'secretin' into the blood. It stimulates the pancreas to secrets bicarbonate HCO_3 into the small intestine in order to neutralize HCl. The secretion of HCO_3 into the intestine abruptly raises the pH from 2.5 to 7.0 the entry of amino acids into the duodenum releases the hormone 'cholecystokinin' which triggers the release of pancreatic juice (that contains many pancreatic enzymes like trypsinogen, chymotrypsinogen, procarboxypeptidases) by the exocrine cells of the pancreas. Most of these enzymes are produced as zymogens (inactive enzymes) by the pancreas in order to protect the exocrine cells from being digested.

Subsequent to the entry of trypsinogen into the small intestine it is activated to trypsin by enterokinase secreted in the intestinal cells. Chymotrypsin is secreted in an inactive form called chemotrypsinogen which is activated by trypsin. Carboxypeptidase secreted as procarboxypeptidase is activated again by trypsin. Also aminopeptidase secreted as inactive proaminopeptidase is once again activated by trypsin. It is an exopeptidase that cleaves the amino acids from the free amino terminal end.
Dipeptidase acts only on dipeptides and hydrolyzes it into 2 amino acids.

3.2 Catabolism of amino acids

Amino acids are degradation in two steps: Removal of the α-amino group and conversion of the carbon chain to an intermediate of lipid and carbohydrate metabolism.

Removal of the α-amino group (Nitrogen)
Removal of the amino group from amino acids is accomplished by variety of processes such as transamination, oxidative and non-oxidative deamination.

Transamination
Transamination is the transfer of amino group from an amino acid to an α-keto acid or other amino acids.

Alanine + **α-Ketoglutarate** ⟷ **Pyruvate** + **Glutamate**

Oxaloacetate + **Glutamate** ⟷ **Aspartate** + **α-ketoglutarate** (**Urea cycle**)

This reaction is catalyzed by aminotransferases that are dependent on the cofactor pyridoxal phosphate, a derivative of vitamin B_6. The importance of transamination reaction is to collect the amino groups from different amino acid in the form of L-glutamate. The glutamate molecules channel amino groups either into biosynthetic pathway or into sequence of reactions to form nitrogenous compounds. Therefore, transamination reactions are particularly important in the eventual removal of the amino group from amino acids.

The oxidative deamination reaction is catalyzed by glutamate dehydrogenase. This is the major reaction in mammal cells through which ammonia is synthesized. α-ketoglutarate acts as a sink for amino groups by accepting amino groups from various amino acids, with the resultant formation of glutamate. In mammals, all α- amino acids can undergo transamination, except lysine and threonine. The glutamate dehydrogenase (GDH) in animal tissues occurs in the inner matrix of mitochondria and will utilize NAD^+ or $NADP^+$. GDH system use NAD or NADP but not both. The coupling of transamination and deamination reactions, catalyzed by glutamic acid dehydrogenase account for most of the ammonia production in animals. The combined action of amino transferase and glutamate dehydrogenase is referred to as trans deamination and provide a common route for removing and producing nitrogen.

Nitrogen excretion and the Urea cycle:

Excess amino Nitrogen from amino acids is removed as ammonia, which is toxic to the human body. Some ammonia is excreted in urine, but nearly 90% of it is utilized by the liver to form urea, which is highly soluble and is passed in to circulation for being excreted by the kidneys. Daily excretion of urea amounts to about 30 g with a protein intake of nearly 100 g in the food. It is less with lower protein intake. The urea-cycle starts in the mitochondrial matrix of hepatocytes and few of the steps occur in the cytosol: the cycle spans two cellular compartments. The first amino group to enter the cycle is derived from ammonia inside the mitochondria. Some ammonia also arrives at the liver via the portal vein from the intestine, when it is produced by bacterial oxidation of amino acids.

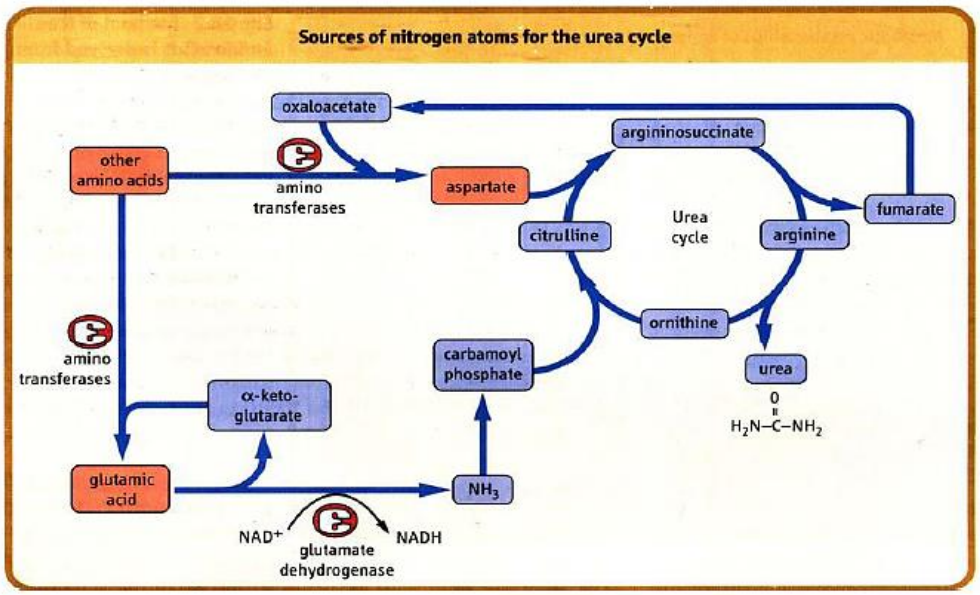


Figure 3.3: Urea cycle
Source: Nelson and Cox (2009).

The reactions of urea cycle are described below:
Step 1 CO_2 from bicarbonate and NH_4 combine together in the liver mitochondria to form carbamoyl phosphate in presence of ATP and Mg^{2}+ by the enzyme Carbamoyl phosphate synthetase I (CPSI).

Step 2 Carbamoyl phosphate reacts with ornithine transferring the carbamoyl moiety to produce citrulline catalyzed by the enzyme ornithine transcarbomylase

Step 3 Argininosuccinic acid is formed by the reaction of Aspartic acid and citrulline: the NH_2 group of the argininosuccinic acid is linked to –CO group of the aspartic acid. The enzyme that catalyzed the reaction is argininosuccinic acid synthase.

Step 4 Argininosuccinic acid is cleaved to form Arginine and fumarate by the enzyme arginiosuccinate lyase. Fumarate goes to the pool of TCA-cycle.

Step 5. Arginine gets cleared off to urea and ornithine by the cytosolic enzyme arginase. Ornithine is thus re-generated and can be transported in to the mitochondrion to initiate another round of the urea - cycle.

Energetics of the urea cycle
The synthesis of one molecule of urea require four high energy phosphate groups
1. 2 ATPs used up to make up carbamoyl Phosphate
2. 1 ATP and two High- energy bonds to make up Arginosuccinate.

4.0 CONCLUSION

Amino acids are degraded by transamination and deamination processes. Transamination of amino acid is catalyzed by transaminases while oxidative deamination is catalyzed by glutamate dehydrogenase and produces ammonia which is toxic to the human body. The toxic ammonia are eliminated from the body as urea via the urea cycle which occurs in the liver and for each molecule of urea produced in the urea cycle, four ATP is required.

5.0 SUMMARY

In this unit you have learnt about the digestion and absorption of proteins and the catabolism of amino acids and the urea cycle.

6.0 TUTOR-MARKED ASSIGNMENT

Discuss:
1. Digestion and absorption of proteins
2. Catabolism of amino acids
3. Reactions of the urea cycle

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 4 LIPID METABOLISM

1.0 INTRODUCTION

Salivary juice produces a lipid hydrolyzing enzyme, especially in infants and children, known as lingual lipase. Lipids are not digested in the mouth, though lingual lipase is present because the high pH of the mouth does not favour the action of lingual lipase and also because the food remains here for a short period of time.

2.0 OBJECTIVES

In this unit you will learn about digestion and absorption of lipids and β-oxidation of fatty acids.

3.0 MAIN CONTENT

3.1 Digestion and Absorption of Lipids

Digestion of lipids in the stomach
As soon as the lipids enter the stomach, they get liquefied due to heat of the stomach. The lipids get emulsified due to the peristaltic movements of the stomach. The gastric juice contains gastric lipase, which is inactive at low pH of the stomach, whereas lingual lipase is active at his pH and it hydrolysis triacylglycerols of short chain fatty acids (which are generally found in milk, so digestion in the stomach is seen only in children). The released fatty acids are absorbed via the stomach wall and enter the portal vein. The TAG with longer chain fatty acids dissolve and form fat droplets and finally enter the intestine.

Digestion of lipids in the intestine
In the intestine, the bile salts (sodium glycocholate and sodium taurocholate) and bile acids (cholic acid, chenodeoxycholic acid and cholesterol) help in emulsifying fats thereby making them susceptible to the digestive enzymes. The presence secretions in the intestine contain

pancreatic lipase which along with the help of a protein called co-lipase and lecithin acts on TAG at the water-oil interface.

Phospholipids are hydrolyzed by phospholipase A, B, C and cholesterol is hydrolyzed by cholesterol esterase. The end products of fat digestion are (1) monoacylglycerols (2) diacylglycerols (3) triacylglycerols (4) free fatty acids (5) glycerol.

Digestion of lipids takes place for a longer duration of time. Until and unless digestion of fats has not taken place, other food materials (carbohydrates and proteins) cannot be digested because of fats will cover the food and prevent enzymes reaching the food (hence take a fatty meal while going on a long journey). The digested lipids enter the intestinal epithelium by diffusion or by a process called pinocytosis. In the intestinal wall the free fatty acids and glycerol re-aggregate to form TAG i.e. here re-synthesis of lipids). These lipids surround a little amount of protein around them to form chylomicrons which enters into systemic circulation. The chylomicrons of the circulation move, towards the adipose tissue, heart, kidney, liver and skeletal muscle. The capillary walls of these tissues contain an enzyme called lipoprotein lipase which hydrolyzes the lipids of the chylomicrons and help in their entry into respective tissue. The lipids are stored as triacylglycerols mainly in the adipose tissue.

3.2 Beta oxidation (β-oxidation) of Fatty Acids

Oxidation of the fatty acids at the β-carbon atom to a carboxylic group is known as β-oxidation. It takes place in the matrix of mitochondria.
The steps involved in the β-oxidation of fatty acids as presented in Figure 3.4 are summarized below:

1. Activation of fatty acids: The fatty acids are activated in the cytosol of the cell wherein the enzyme fatty acyl CoA synthase condenses the fatty acids with coenzyme. A esterification which frequires two high energy bonds.

2. Formation of α-β unsaturated acyl-CoA (Enoyl-CoA): The fatty acyl-CoA undergoes dehydrogenation at the α and β-carbon atoms forming trans α-β unsaturated acyl-CoA.

3. Formation of β-hydroxy acyl-CoA: Enoyl-CoA is then hydrated by the enzyme crotonase (Enoyl-CoA hydratase) which adds water across the double bond. The product formed is β-hydroxy acyl-CoA.

4. Formation of β-keto acyl-CoA: β-hydroxy acyl-CoA undergoes another dehydrogenation to form β-keto acyl-CoA catalyzed by the enzyme β-hydroxy acyl-CoA.

5. Thiolytic cleavage of keto acyl-CoA: β-keto acyl-CoA is then cleaved between the α and β-carbon atom releasing an acetyl CoA and a fatty acyl-CoA catalyzed by the enzyme β-keto thiolase.

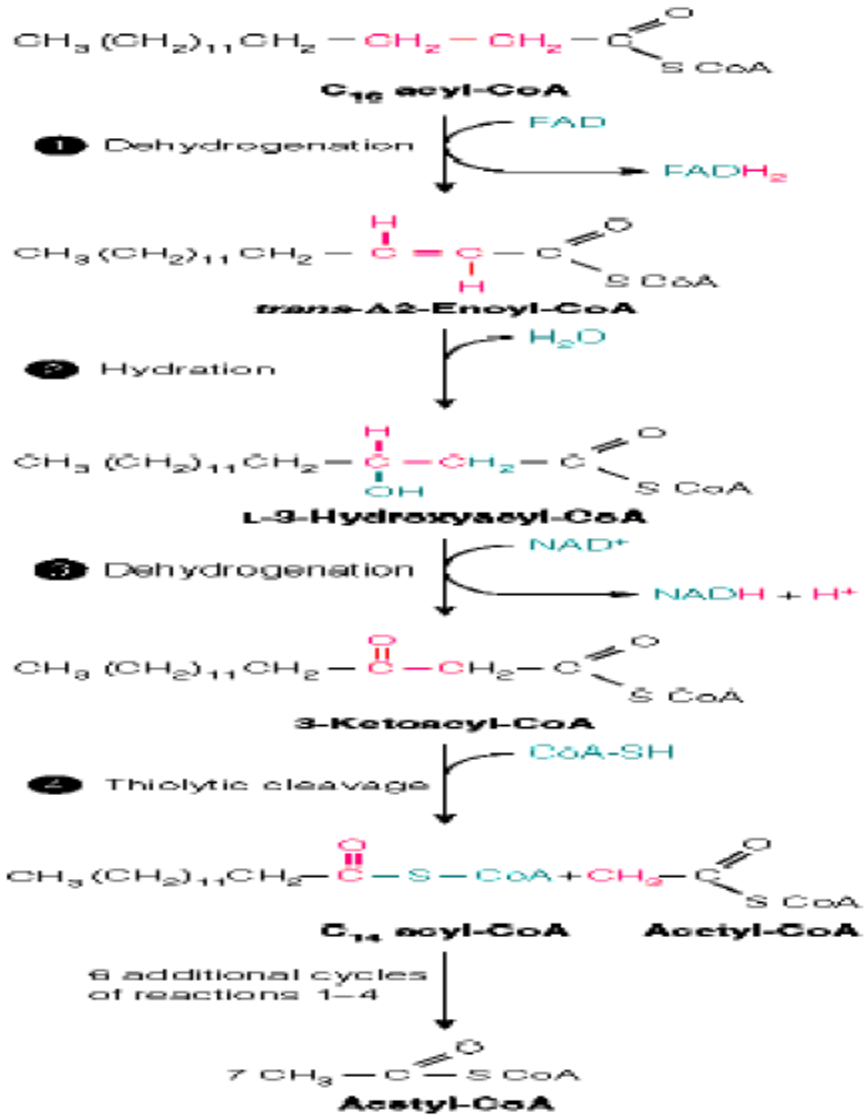


Figure 3.4: β-oxidation of fatty acids
Source: Nelson and Cox (2009)

4.0 CONCLUSION

Digestion of lipids begins in the stomach and is acted upon by group of enzymes called lipase which hydrolyze the lipids into triacylglycerol, free fatty acids and glycerol.

5.0 SUMMARY

In this unit, you have learnt about been the digestion and absorption of lipids, metabolism of fatty acids and triacylglycerol and β-oxidation of fatty acids.

6.0 TUTOR-MARKED ASSIGNMENT

1. Discuss the digestion and absorption of lipids
2. Discuss β-oxidation of fatty acids

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

MODULE 4 MICRONUTRIENTS (VITAMINS AND MINERALS) AND DETOXIFICATION

UNIT 1 WATER SOLUBLE VITAMINS

CONTENTS

1.0 INTRODUCTION

Vitamins organic compounds which cannot be synthesized in the human body and so must be provided in the diet. They are essential for the normal processes of metabolism, including growth and maintenance of health. It is known that the body is able to produce part or even all of its requirements for some of the vitamins. Examples of vitamins such are Vitamin D from cholesterol and Niacin (Vit. B_3) from tryptophan.

2.0 OBJECTIVES

On completion of this unit you should have an understanding of what vitamins are as micronutrients, classes of vitamins and their functions, symptoms associated with deficiency of vitamins.

3.0 MAIN CONTENT

3.1 Water Soluble Vitamins

The water soluble vitamins are the Vitamin B complex and Vitamin C. Vitamin B and C share few common properties besides their solubility characteristics. Since they are water soluble excess can be excreted through urine. Most of the water soluble vitamins act as coenzymes.

The B- Vitamins are essential and must be provided through diet and they include Thiamine (Vit B_1), Riboflavin (Vit B_2), Vit B_3 Niacin (Nicotinic acid (or Nicotinamide), Pantothenic acid (Vit B_5), Vit B_6 (Pyridoxine, pyridoxal, and Pyridoxamine), Vit B_9 (Folic Acid), Vit B_{12} (Cobalamine).

Thiamine (vitamin B_1)
Thiamine is Vitamin B_1. Addition of a pyrophosphate to **thiamine** (from ATP) converts it to thiamine pyrophosphate, a molecule that is the coenzyme for all decarboxylation of keto acids.

Sources: The good sources of thamine are seeds, nuts, wheat, leguminous plants (rich source) and lean meat.

Required daily allowance (RDA): Minimum requirement is 1.0 mg for adults, 0.4-1.3 mg for infants and children. Requirement increases in conditions of anoxia-shock, hemorrhage, injury, illness, fever and hyperthyroidism.

Deficiency causes Beriberi and related deficiency syndromes. It is mainly caused by carbohydrate rich diets. In such individuals TPP dependent reactions are prevented, leading to accumulation of substrates like pyruvate, pentose sugars etc.

Wernicke Korsakoff syndrome which is frequently found in Alcoholics is associated with thiamin deficiency.

Symptoms
Symptoms include Peripheral neuropathy, exhaustion and anorexia. The signs may progress to edema and cardiovascular disorders, neurological and muscular degeneration.

Riboflavin (Vitamin B_2)
Riboflavin, also known as **vitamin B_2**, is a component of the flavin coenzymes, FAD (Flavin adenine dinucleotide and FMN (Flavin monophosphate nucleotide) thereby acting as a co-factor.

Source: meats, nuts, legumes, milk, fish, egg etc.

Required daily allowance (RDA): 1.5-2.5 mg for adults, infants 0.6 mg, children 1.0-1.8 mg

Deficiency: Lack of riboflavin in the diet causes non-fatal syndrome of inflammation of the corner of mouth (angular stomatitis), painful glossitis of tongue (Purple) and scaly dermatitis.

Niacin (Vitamin B_3)
Niacin can be synthesized from tryptophan. However, conversion of tryptophan to niacin is relatively inefficient (60 mg of tryptophan is required to produce 1 mg of Niacin) and occurs only after all the body requirements for tryptophan is met. Thus most people require dietary sources of both tryptophan and niacin.

Source: Milk, lean meat, unrefined grains, cereals and from metabolism of tryptophan.

Required daily allowance (RDA): Adults 17-21 mg, infants 6 mg. The requirement increases with increased intake of calories, illness, severe injury, infection, burns, high corn (maize) diet, pregnancy and lactation.

Deficiency
Deficiency leads to failure of growth, loss of weight and anemia. Pellagra, a disease involving gastrointestinal tract (GIT) and CNS (central nervous system) also develops.

Symptoms
The disease is characterized by intense irritation and inflammation of the mucous membranes of the mouth and other parts of the GIT, leading to gastro- intestinal hemorrhage, dermatitis, dementia and diarrhea. Skin lesion develops when exposed to sunlight, becomes red, thickened and scaly. The patient develops gingivitis and stomatitis (tongue gets swollen)

Vit B_6 (Pyridoxine)
This vitamin exists in three forms: Pyridoxine, Pyridoxal and pyridoxamine and their corresponding phosphates.

Sources: Wheat, corn, egg yolk, liver and muscle meat

RDA: 1.4-2.2 mg for adults, children 0.3-0.4 mg. Patients with anti-tubercular treatment needs more Vitamin B_6.

Deficiency
The deficiency is usually not common, but may result due to intake of drugs like contraceptives. Alcoholics also suffer from such deficiency. Oral contraceptives stimulate the synthesis of the enzyme which requires this vitamin, thus causing deficiency.

Biotin
Biotin is a vitamin and a coenzyme commonly associated with enzymes performing carboxylation reactions. Biotin is typically linked covalently to carboxylase enzymes through the α-amino nitrogen of lysine.

Source: Intestinal bacteria, liver, egg, peanuts and milk.

RDA: 100-200 μg/day. Requirement increase in pregnancy and lactation. Patients on oral antibiotics for a long period of time require more of this vitamin.

Deficiency
The deficiency is rare since it is found in almost all food stuffs. But large consumption of raw egg white may lead to deficiency of Biotin. Avidin, a glycoprotein in egg white binds tightly to biotin and makes it unavailable for the necessary carboxylation reactions.

Symptoms
Dermatitis, glossitis, Muscle pain, depression, alopecia (loss of hair), loss of appetite and nausea.

Vit B_{12} (Cobalamin)
The metal cobalt in **vitamin B_{12}** is coordinated with a tetrapyrrole ring system, called a corrin ring similar to the porphyrin ring of **heme** compounds. The cyanide attached to the cobalt in the structure is an artifact of the isolation and is replaced by water or a hyrdoxyl group in cells. The presence of cobalt and amide nitrogens gives **B_{12}** compounds the name cobamides or cobalamins.

Source: Synthesized by microorganisms

RDA: 3 mg/day.

Deficiency
Deficiency of vitamin B_{12} causes Anemia (a condition where there is low level of red blood cells in the body).

Folic Acid (Vitamin B_9)
The active form of folic acid is Tetra hydro folate (THF). Chemically, **folic acid** is formed from three distinct moieties: (1) a bicyclic, heterocyclic pteridine ring, (2) **6-methylpterin** (**p-aminobenzoic acid, PABA)** (3) **glutamic acid**.

Source: The vitamin is abundant in leafy green vegetables such as spinach, so is named folic acid, from the same root as foliage, whole grain cereals and Liver.

RDA: 100 μg/day. (The RDA during lactation and pregnancy is 500 – 800 μg/day)

Deficiency
The causes of folate deficiency are inadequate intake, impaired absorption, increased demand during pregnancy, lactation and impaired metabolism that leads to megaloblastic anemia. In this condition production of erythrocytes slows down, macrocytic erythrocytes with fragile membrane are formed. Inadequate folate levels during the early stages of pregnancy increases the risk of neural tube defects (a type of birth defect) and spontaneous abortions.

Folate deficiency is common in alcoholics and in people who are on drugs like anti convulsions and oral contraceptives.

Pantothenic Acid (Vitamin B_5) Coenzyme A
Pantothenic acid is a vitamin that forms an essential part of the acyl-carrier moiety known as coenzyme A. **Coenzyme A** (A for acyl) participates in the activation of all acyl groups in including the acetyl group derived from **pyruvate**. The coenzyme is derived metabolically from **ATP**, the vitamin **pantothenic acid**, and **mercaptoethylamine**.

Sources: Eggs, liver, animal tissue, whole grain cereals, yeast and legumes

RDA: 4-7 mg/day

Deficiency
The deficiency is rare due to its wide distribution however the burning foot syndrome in prisoners which is associated with reduced capacity for acetylation is ascribed to pantothenic acid deficiency.

Vitamin C (Ascorbic Acid)
Vitamin C is a water-soluble vitamin and can act as an antioxidant (i.e. fight/prevent against the oxidation of free radicals that causes cell. Tissue and DNA damage in the body).
In general hydroxylation reactions require Vit C. Example: Hydroxylation of cholesterol.

Functions
Vitamin C plays a major role in collagen biosynthesis, degradation of tyrosine, absorption of iron, formation of steroids (Steroidogenesis), adrenaline synthesis, bile acid formation, bone mineral metabolism and acts as potent antioxidant.

White blood cells (WBC) are rich in vit C and play an important role in immunity.

Source: Citrus fruits, potato, tomato and green vegetables

RDA: 60 mg/day

Deficiency
Deficiency of vitamin C causes scurvy.

Symptoms
A symptom of extreme vitamin C deficiency called scurvy is the weakening of collagen fibers caused by the failure to hydroxylate proline and lysine.

Fat soluble Vitamins
Fat soluble vitamins are vitamins that are not readily absorbed into the body from diet. The fats soluble vitamins are vitamins A, D, E and K. Ample reserves of fat soluble vitamins are stored in the tissues as they are not readily absorbed from the food with the exception of Vit. K. Fat soluble vitamins do not serve as coenzymes.

Vitamin A
The vitamin is present in the diet as retinol or as β-carotene some of which is hydrolyzed in the intestine to form retinol. It is a generic term for a collection of three forms of Vitamins, retinol, retinal and retinoic acid (Retinoids) all of which are derived from animal and plant sources. The vitamin is stored mainly in the liver.

Source: A rich source is liver, egg yolk, butter and milk but leafy vegetables and some fruits provide the largest amount of β-carotene,

Functions
β-carotene plays as an antioxidant role and prevents the development of diseases like cancer and cardiovascular disease.

Deficiency

Effects on eye
Vitamin A affects growth and differentiation of epithelial cells of the leading to defective epitheliazation, (a condition affecting the cornea of the eye). It causes formation of abnormal keratin (keratinization) in the mucosal cells or cornea of the eye.

Effect on skin
The deficiency causes dryness and roughness of skin developing keratosis of hair follicles with concomitant deficiency of Vit-B complex.

Effect on bone and teeth
Bone growth is markedly impaired. Osteoclastic activity is also hampered, causing defective bone formation.

Vitamin D
Vitamin D is the only vitamin that is usually not required in the diet, for this reason it is rather assumed to function as a hormone.

Sources
Sunlight, Fish oils, egg yolk are naturally rich sources of Vit D.

Functions
i. It promotes bone mineralization.
ii. It promotes absorption of calcium, phosphates.
iii. It enhances the reabsorption of calcium and phosphate by the kidney.

Deficiency
Deficiency of vitamin D causes rickets (deformation of lower limbs). Rickets is characterized by the production of soft pliable bones due to defective mineralization which is secondary to calcium deficiency.

Usually deficiency of Vitamin D is due to insufficient exposure to sunlight, inadequate dietary intake, GIT disorder, obstructive jaundice and Partial gastrectomy.

Vit D deficiency is also characterized by low concentration of calcium in blood in association with increased serum alkaline phosphatase.

Vitamin E
Vitamin E is required in the human diet but deficiency is rare, except in pregnancy and the new born, where it is associated with hemolytic anemia. It exists in the diet as a mixture of eight closely related compounds called Tocopherols.

Source: The richest source is vegetable oils and nuts

Functions
The main function of Vitamin E is that it acts as an antioxidant.

Deficiency
Vitamin E deficiency is a rare but found in complication of prolonged and severe steatorrhoea, and of prolonged parenteral nutrition. Deficiency of Vitamin E causes anemia. Generally deficiency is investigated by measuring plasma (Vitamin E).

Vitamin K
It refers to a group of related compounds, varying the number of isoprenoid units in its side chain. There are three types, Menaquinone (K2) present in animals, Phylloquinone (K1) present in plants. Like vit

E, the absorption of Vitamin k is dependent on appropriate fat absorption.

Functions
It is the only one acting as co-enzyme from the group of Fat soluble vitamins. This vitamin is also synthesized by intestinal bacteria. It is required for post translational modifications of several proteins required in the coagulation cascade

Deficiency
It is widely distributed in nature and produced by the intestinal micro flora. Virtually ensures that dietary deficiency does not occur in man. However, it is found in patients suffering from liver diseases (obstructive jaundice), in new born infants and in patients with malabsorption. It is associated with bleeding disorders. The placenta is inefficient at passing maternal Vit K to the fetus and immediately after birth the circulation concentration drops, but recovers on absorption of foods. In addition the gut of the new born is sterile, so that the intestinal micro flora does not provide a source of vit K for several days after birth. This is the reason why adults who are on prolonged antibiotic treatment require supplementation of Vit.E.

Specific inhibitors of vitamin D dependent Carboxylation reactions are used in the treatment of thrombosis related diseases. These drugs of the dicoumarin groups e.g. Warfarin, which inhibit the action of Vit K - probably via the mechanisms involved in the regeneration of the active hydroquinone.

Tests to asses Vitamin K status include the prothrombin time-an important test in the investigation and management of jaundiced patients and of those on anticoagulant treatment.

4.0 CONCLUSION

Vitamins are one of the organic molecules required in the body from diet for the proper functioning of the body. Some of them act as co-enzymes that enhances biochemical reactions in the living system while some act as antioxidants that help prevent the development of diseases.

5.0 SUMMARY

In this unit, you have learnt about the water and fats soluble vitamins and symptoms of their deficiencies

6.0 TUTOR-MARKED ASSIGNMENT

1. Define water soluble vitamin and list all.
2. Enumerate the sources and deficiency of all vitamin B complex.
3. State the functions of vitamin A, D and K.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 2 TRACE MINERALS

1.0 INTRODUCTION

Dietary minerals are the chemical elements required by living organisms, other than the four elements carbon, hydrogen, nitrogen, and oxygen present in common organic molecules.

For any nutrient, there is a range of intake between that which is clearly inadequate, leading to clinical deficiency disease, and that which is so much in excess of the body's metabolic capacity that there may be signs of toxicity. Between the 2 extremes, there is a level of intake that is adequate for normal health and the maintenance of metabolic integrity. Individuals do not have the same requirement for nutrients, even when calculated on the basis of body size or energy expenditure. Therefore, in order to assess the adequacy of diets, it is necessary to set a reference level of intake high enough to ensure that no one either suffers from deficiency or is at risk of toxicity. Many of the essential minerals are widely distributed in foods, and most people eating a mixed diet are likely to receive adequate intakes, although supplements can be used when some requirements are not adequately met by the diet, or when chronic or acute deficiencies arise from pathology or injury, etc.

2.0 OBJECTIVES

At the end of this unit, you should have an understanding of macro and micro minerals, functions, food sources, required daily allowance, deficiency and toxicity symptoms of each trace mineral studied.

3.0 MAIN CONTENT

3.1 Macro and Micro minerals

Dietary Minerals include the macro and micro minerals. Macro minerals are required in the diet in large amounts (>100 mg/day). They represent

about 80% of body organic matter and include calcium, phosphorus, potassium, sulfur, sodium, chlorine, and magnesium.

Micro minerals or Trace elements are needed in doses < 100 mg per day. Important "trace" or minor minerals include iron, cobalt, copper, zinc, molybdenum, iodine, selenium and cobalt.

Some minerals are necessary for the body, but their exact functions are unknown. Such include Chromium, Nickel, Bromine, Lithium and Barium. Non-essential minerals found as contaminants in foodstuffs include rubidium, silver, gold and bismuth. Toxic minerals include Al, Pb, Cd and Hg.

3.2 Trace Elements

Zinc

Total zinc content of the body is about 2g, out of which 60% is in skeletal muscles and 30% in bones. The highest concentration of Zinc is seen in Hippocampus area of brain and prostate fluid. More than 300 enzymes are zinc-dependent, including RNA and DNA polymerases, alkaline phosphatase and carbonic anhydrase. It also forms what is known as zinc fingers (Zn^{2+}) co-ordinated to four amino acid side chains), which provide structural stability to many proteins and are important for protein-protein interactions. These are found in many signal transduction proteins. Zn is also involved in DNA and protein synthesis as well as transport of vitamin A, taste perception, wound healing, Zinc plays a vital role in fertility. In males, it protects the prostate gland from infection (prostates) and ultimately from enlargement (prostatic hypertrophy). It also helps maintain sperm count and mobility and normal levels of serum testosterone. Zinc is important during pregnancy, for the growing foetus whose cells are rapidly dividing. Zinc also helps to avoid congenital abnormalities and pre-term delivery. Zinc is vital in ensuring proper growth and development in infants, children and teenagers.

Sources: Meat, shellfish, poultry, whole grains, vegetable, cheese

Required Daily Allowance (RDA): 11 mg for men, 8 mg for women

Deficiency: Zn deficiency in children is marked by poor growth and impairment of sexual development. In both children and adults, it results in poor wound healing and dermatitis as well as impaired immune function. Toxicity effects include loss of appetite, impaired immunity, decreased HDL, iron and copper deficiencies. Toxicity is common in welders due to inhalation of zinc oxide fumes.

Iron

Total body content is 3-5 g, 75% of this is found in blood and the rest in liver, bone marrow and muscles. Iron is present in almost all cells. Blood contains 14.5g of Hb per 100 ml. About 75% of total iron is in hemoglobin, 5% is in myoglobin and 15% in ferritin. Iron carries oxygen as part of haemoglobin in blood or myoglobin in muscles. It is required for cellular energy metabolism. Transferrin is the transport form while Ferritin is the storage form of iron. Transferrin is a glycoprotein, with a mol wt of 76,500 Daltons. Total iron binding capacity (TIBC) is a measure of the blood's capacity to bind iron with transferring. The ref range is about 400mg/100ml. One third of this capacity is saturated with iron. Transferrin has a half-life of 7-19 days, and is a useful index of nutritional status. One molecule of transferrin can bind two ferric ions. In blood, ceruloplasmin is the ferroxidase, which oxidizes ferrous to ferric state. Transferrin receptors are present on most of the body cells, especially on cells which synthesize heme. The iron-transferrin complex is taken up by the body cells by the receptor mechanism.

RDA: for men 8 mg, women (19-50 yrs) 18 mg, women > 50 yrs 8 mg.

Sources: Red meat, fish, poultry, eggs, dried fruits, leafy vegetables, pulses.

Deficiency: Includes anemia characterized by weakness, fatigue, headache and impaired mental and physical performance. It also impaired immunity and pale skin.

Toxicity leads to GIT distress, infections, fatigue, joint pain, skin pigmentation and organ damage.

Copper

Total body copper is about 100 mg. It is found in muscles, liver, bone marrow, brain, kidney, heart and hair. It is a required component of many redox enzymes. Copper containing enzymes are ceruloplasmin, cytochrome oxidase, tyrosinase, superoxide dismutase and others. Required for iron absorption and incorporation of iron into hemoglobin. Only about 10% dietary copper is absorbed. Excretion is mainly through bile.

Sources: Legumes, nuts and seeds, whole grains, organ meats, drinking water.

RDA: 900 μg

Deficiency: Results in microcytic normochromic anemia, cardiovascular diseases, defective cross-linking of connective tissue and hypo pigmentation of hair. Toxicity is manifested as diarrohea and blue-green discoloration of saliva. Copper poisoning may result in hemolysis, hemoglobinuria, proteinuria and renal failure. Toxicity could occur from eating acid foods cooked in uncoated copper cookware or exposure to excess copper in drinking water or other environmental sources. Could result from Copper poisoning, or Wilson's disease Results in vomiting, hematemesis, hypotension, coma, GIT distress, jaundice.

Fluoride

Fluoride is known to prevent caries. In the pits and fissures of premolar and molar teeth, bacterial fermentation of residual food leads to acid production. The acid removes enamel and dentine to expose the pulp, leading to inflammation and toothache. Presence of fluoride will result in a fluoroapatite layer on the enamel, which protects it from decay. The safe limit of F is about 1ppm in water (= 1 mg in 1000 ml of water)

RDA: 4 mg for men, 3 mg for women.

Toxicity leads to fluorosis (pitting and discoloration of teeth with alternate areas of osteoporosis, osteosclerosis and brittle bones), intestinal upset, loss of appetite and loss of weight.

Selenium

Selenium (Se) intake depends on the nature of soil in which food crops are grown. In mammals, glutathione peroxidase is the most important se containing enzyme. 5"-de-iodinase, which converts thyroxin to T3 also contains Se. Selenium concentration in testis is the highest in adult tissue. It is necessary for normal development of spermatozoa. Selenium also acts as a non specific intracellular anti oxidant, its action being complementary to that of Vitamin E.

RDA: 50-100 μg/ day.

Deficiency: Causes Liver necrosis, cirrhosis, cardio myopathy and muscular dystrophy.

Se Toxicity is called selenosis. Symptoms include hair loss, falling of nails, diarrhea, weight loss and garlicky odour in breath.

Iodine

Dietary iodine is efficiently absorbed and transported to the thyroid gland, where it is stored and used for the synthesis of triiodothyronine and thyroxine. These hormones function in regulating the basal metabolic rate of adults and the growth and development of children.

Also functions as antioxidant for extrathyroidal organs such as mammary and salivary glands and for gastric juice production.

Sources: seafood, dairy products, iodized salt **RDA:** 150 μg

Deficiency: Very common results in an enlargement of the thyroid gland (Goitre)

4.0 CONCLUSION

Minerals are organic molecules which are required in the body for bone mineralization and for proper functioning of the body tissues.

5.0 SUMMARY

In this unit, you have been exposed to Macro and Micro minerals.

6.0 TUTOR-MARKED ASSIGNMENT

1. Distinguish between Macro and Micro minerals (Trace elements)
2. List important microminerals (Trace Elements) and enumerate the functions, food sources, required daily allowance, deficiency and toxicity symptoms of each trace mineral studied.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.

UNIT 3 DETOXIFICATION

1.0 INTRODUCTION

Humans are exposed to various foreign chemicals (called xenobiotic) from air, nutrition (food additives, preservatives), therapy for disease (drugs) etc. Hence an understanding of the ability of the body to cope with the chemical onslaught at the cellular level is an important aspect of metabolism. Detoxification is a series of biochemical reactions that convert converts toxic substances into less harmful products and then into more easily excretable forms. Detoxification is often referred to as drug metabolism. All the detoxification reactions majorly occur in the liver, however, the kidney and intestines are also involved to a lesser extent. Several unwanted and harmful substances e.g. drugs get entry into the body by absorption from the gastrointestinal tract and so need to be eliminated regularly to prevent accumulation and prolonged cumulative action.

Compounds that are detoxified are foreign compounds or xenobiotic such as drugs, food additives, insecticides, pollutants etc, compounds produced in the body which are to be eliminated e.g. bilirubin, steroids ammonia etc and compounds produced in the intestine by bacterial putrefaction and fermentation e.g. indole and skatole (from tryptophan), histamine (from histidine), tyramine (from tyrosine) etc.

2.0 OBJECTIVES

On the completion of this unit you will get to know the definition of detoxification, mechanism and reactions of detoxification, and the excretion of xenobiotic.

3.0 MAIN CONTENT

3.1 Mechanism of Detoxification

The overall mechanism of detoxification is to increase the water solubility (polarity) of toxic products and thus facilitate their excretion from the body mostly in urine and also through bile and faeces. Toxic products are rendered water-soluble by adding polar functional groups/conjugates.

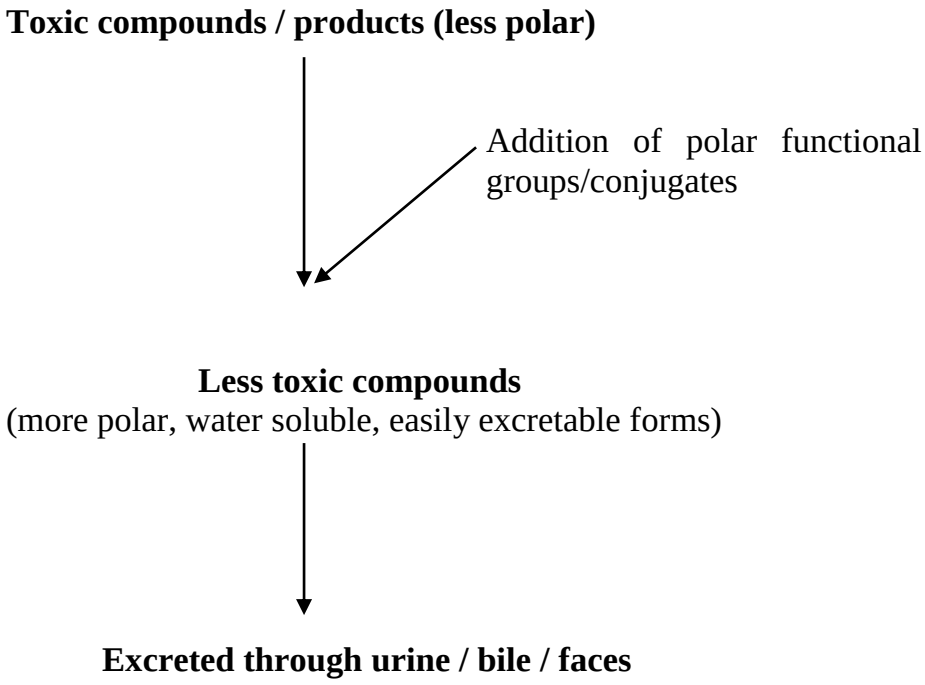


Figure 4.1: Mechanism of detoxification

3.2 Reactions of Detoxification

Foreign substances undergo some preliminary changes which are not different from the metabolic changes occurring to physiological substances. Detoxification reactions are grouped into two phases namely Phase-I and Phase-II detoxification reactions.

Phase I
Phase I detoxification reaction involves oxidation (also known as hydroxylation), reduction or hydrolysis. Minor reactions like deamination, desulfuration, dealkylation etc. are also induced under Phase I

a. **Detoxification by oxidation:** In this reaction hydrocarbons are oxidized to their corresponding alcohols; alcohols to aldehydes

and aldehydes to acids. Also aromatic hydrocarbons are reduced to phenols.
Example is the oxidation of methanol to formic acid, oxidation of benzene to benzoic acid.
Cytochrome P450 (hemeproteins) are enzymes involved in oxidation reaction and are located in the liver microsomes (endoplasmic reticulum). Fifty percent (50%) of drugs are detoxified through this system.

Methanol (**CH_3-OH**) ⟶ Formic acid (**H-COOH**)

Benzoyl ⟶ Benzoic acid

b. **Detoxification by reduction:** This reaction involves the addition of hydrogen atom to hydrocarbons. Examples are given below:

Nitrobenzene ⟶ Amino benzene (Aniline)

Chloral ⟶ Trichloroethanol
(Chloral is a sedative)

c. **Detoxification by hydrolysis:** This reaction involves the hydrolysis of ester, amide, glycosidic bond, ether bond etc by the addition of water. Also Drugs like procaine and acetyl salicylic (aspirin) acid and cardiac glycosides e.g. digitalin, atropine undergo hydrolysis.

H_2O
Aspirin ⟶ salicylic acid + acetic acid

H_2O
Atropine ⟶ tropic acid + tropine

Phase-II
Phase-II detoxification process consists of conjugation reaction. This reaction involves the coupling of the foreign substances after the processes of oxidation, reduction and hydrolysis with some polar substances in the body making the toxic compounds more water soluble and hence easily excretable. The following are some examples:

a. **Glucuronic acids:** Conjugation with glucuronic acid is the most common conjugation reaction. UDP (uridine diphosphate)-glucuronic acid is the glucuronyl donor, UDP-glucuronyl

transferases are the enzymes. Aromatic acids (e.g. benzoic acid) and phenols are conjugated with glucuronic acid. The glucuronic acid is derived from uridine diphosphate glucuronic acid. The drug chloramphenicol and the bile pigments are among the important substances conjugated with glucuronic acid. Derivatives of steroid hormones also are conjugated with glucuronic acid before excretion.

b. **Active sulfate:** It is used to conjugate phenolic compounds. The derivatives are called ethereal sulfates. An increase in their amount in urine excessive intestinal putrefaction or stasis. Adrenal cortical hormones are also excreted after conjugation with sulfuric acid. Yeast and mammalian liver contain enzymes that can activate inorganic sulfate by adding it to 3-phosphoadenosine-5-phosphate. Active sulfate is adenine-3-phosphoribose-5-phosphosulfate. Incorporation of sulfate into sulfated mucopolysaccharaides and conjugation of steroid hormones and others with sulfate are brought about after preliminary activation of sulfate.

c. **Glycine:** This is used to conjugate aromatic acids, cholic acid and also nicotinic acid. The formation of bile acid (glycocholic acid) from cholic acid is also brought about by conjugation with glycine.

d. **Cysteine:** This is used in the conjugation of aromatic compounds like benzene and halogenated ring compounds like bromobenzene.

e. **Acetic acid:** Acetic acid is used to conjugate with aromatic amino compounds like sulfanilamide.

f. **Glutamine:** This is conjugated with phenylacetic acid to form phenylacetylglutamine.

g. **Methyl groups:** Active methionine (s-adenosyl methionine) is used for the conjugation of certain pyridine and other heterocyclic nitrogen containing compounds like nicotinamide.

h. **Interaction of highly toxic cyanides:** There may also be conjugation with thiosulfate to form relatively nontoxic thiocyanates. The enzyme rhodanase converts cyanide to thiocyanate.

3.3 Excretion of detoxified xenobiotic

i. The products of phase-I reactions are either excreted directly or undergo further metabolism by phase-II reactions and then excreted.

ii. In some cases, a xenobiotic may undergo only phase-II reaction without undergoing phase-I reaction.

iii. Occasionally, a xenobiotic may be excreted unchanged.

4.0 CONCLUSION

Detoxification is the breakdown of toxic substances to less harmful substances. Xenobiotic are detoxified by the process of oxidation, reduction and conjugation.

5.0 SUMMARY

In this unit you have learnt about detoxification, mechanism of detoxification and reactions of detoxification.

6.0 TUTOR-MARKED ASSIGNMENT

1. Define detoxification.
2. Explain the mechanism of detoxification.
3. Write in details with examples reactions involved in oxidation, reduction, hydrolysis and conjugation.

7.0 REFERENCES/FURTHER READING

Amanullah, M. (2011). Medical Biochemistry and Biotechnology 1st edition.

Devlin T. M. (2010). Textbook of Biochemistry with Clinical Correlation 7th edition. John Wiley & Sons Inc.

Murray, R. K., Bender, D. A., Botham, K., M., Kennelly, P. J., Rodwell V. W. and Well, P.A. (2012). Harper's Illustrated Biochemistry (29th edition) McGraw-Hill Medical.

Nelson, D. L. and Cox M. M., (2009). Lehninger Principles of Biochemistry 4th edition.