# **BIOLOGICAL CHEMISTRY (E- Content)**

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#### **BIOLOGICAL CHEMISTRY**

#### <u>UNIT I</u>

#### ATOMIC THEORY

# What is Atomic Theory?

Dalton's atomic theory was a scientific theory on the nature of matter put forward by the English physicist and chemist John Dalton in the year 1808. It stated that all matter was made up of small, indivisible particles known as 'atoms.

All substances, according to Dalton's atomic theory, are made up of atoms, which are indivisible and indestructible building units. While an element's atoms were all the same size and mass, various elements possessed atoms of varying sizes and masses.

# **Postulates of Dalton's Atomic Theory**

- All matter is made up of tiny, indivisible particles called atoms.
- All atoms of a specific <u>element</u> are identical in mass, size, and other properties. However, atoms of different element exhibit different properties and vary in mass and size.
- Atoms can neither be created nor destroyed. Furthermore, atoms cannot be divided into smaller particles.
- Atoms of different elements can combine with each other in fixed whole-number ratios in order to form compounds.
- Atoms can be rearranged, combined, or separated in chemical reactions.

# Limitations of Dalton's Atomic Theory

- It does not account for subatomic particles: Dalton's atomic theory stated that atoms were indivisible. However, the discovery of <u>subatomic particles</u> (such as protons, electrons, and neutrons) disproved this postulate.
- It does not account for isotopes: As per Dalton's atomic theory, all atoms of an element have identical masses and densities. However, different isotopes of elements have different atomic masses (Example: hydrogen, deuterium, and tritium).
- It does not account for isobars: This theory states that the masses of the atoms of two different elements must differ. However, it is possible for two different elements to share the same mass number. Such atoms are called isobars (Example: <sup>40</sup>Ar and <sup>40</sup>Ca).
- Elements need not combine in simple, whole-number ratios to form compounds: Certain complex organic compounds do not feature simple ratios of constituent atoms. Example: sugar/sucrose (C<sub>11</sub>H<sub>22</sub>O<sub>11</sub>).
- The theory does not account for allotropes: The differences in the properties of diamond and graphite, both of which contain only carbon, cannot be explained by Dalton's atomic theory.



Dalton's Atomic Theory - The Indestructible Atoms

# What are the Merits of Dalton's Atomic Theory?

- 1. The law of multiple proportions, the law of conservation of mass, and the <u>law of constant</u> <u>proportions</u> are not violated by Dalton's atomic theory.
- 2. The theory provides a basis to differentiate between elements and compounds.

#### What Is Atomic Structure?

The atomic structure of an element refers to the constitution of its nucleus and the arrangement of the electrons around it. Primarily, the atomic structure of matter is made up of <u>protons</u>, electrons and neutrons.

The **protons and neutrons** make up the nucleus of the atom, which is surrounded by the electrons belonging to the atom. The **atomic number** of an element describes the total number of protons in its nucleus.



Neutral atoms have equal numbers of protons and electrons. However, atoms may gain or lose electrons in order to increase their stability, and the resulting charged entity is called an ion.

Atoms of different elements have different atomic structures because they contain different numbers of <u>protons and electrons</u>. This is the reason for the unique characteristics of different elements.



#### Formation of a molecule:

- 1. A molecule is formed when two or more atoms join together i.e. **bonds are formed** between the atoms.
- 2. While joining together, each atom shares one electron in bond formation.
- 3. Thus, a **covalent bond** results in the formation of a molecule.

EXAMPLE



#### **ELECTRONIC CONFIGURATION OF ATOM**

- The electron configuration of an atom is written with the help of subshell labels.
- These labels contain the shell number (given by the principal quantum number), the subshell name (given by the azimuthal quantum number) and the total number of electrons in the subshell in superscript.

#### Aufbau Principle

- This principle is named after the German word 'Aufbeen' which means 'build up'.
- The <u>Aufbau principle</u> dictates that electrons will occupy the orbitals having lower energies before occupying higher energy orbitals.
- The energy of an orbital is calculated by the sum of the principal and the azimuthal quantum numbers.
- According to this principle, electrons are filled in the following order: 1s, 2s, 2p, 3s, 3p, 4s, 3d, 4p, 5s, 4d, 5p, 6s, 4f, 5d, 6p, 7s, 5f, 6d, 7p...

Electronic Configuration S, P, d, + f, d, P, s17 15 25 27 2<u>p 35</u> 3<u>p 45</u> - 6  $3 \rightarrow 3 \underline{4 + p + 55} + \underline{4 + 5 + 65}$   $4 \rightarrow 4 \underline{5 + 54} + \underline{6 + 75} + 5 \underline{6 + 64} + \underline{7 + 85}$   $7 N \rightarrow 15^{2} + 25^{2} + 2p^{3}$ 1-10 4 - 14

#### **EXAMPLE QUESTION:**

List the electron configurations of all the noble gases.

The electronic configurations of the noble gases are listed below.

- Helium (He)  $1s^2$
- Neon (Ne)  $[He]2s^22p^6$
- Argon (Ar) [Ne]3s<sup>2</sup>3p<sup>6</sup>
- Krypton (Kr) [Ar]3d<sup>10</sup>4s<sup>2</sup>4p<sup>6</sup>
- Xenon (Xe)  $[Kr]4d^{10}5s^25p^6$
- Radon (Rn)  $[Xe]4f^{14}5d^{10}6s^{2}6p^{6}$

#### **S &P SHAPES OF ATOMIC ORBITALS**

#### The Shape of s Orbitals

- The boundary surface diagram for the s orbital looks like a sphere having the nucleus as its centre which in two dimensions can be seen as a circle.
- Hence, we can say that s-orbitals are spherically symmetric having the probability of finding the <u>electron</u> at a given distance equal in all the directions.
- The size of the s orbital is also found to increase with the increase in the value of the principal quantum number (n), thus, 4s > 3s > 2s > 1s.



The Shape of p Orbitals

- Each p orbital consists of two sections better known as lobes which lie on either side of the plane passing through the nucleus.
- The three p orbitals differ in the way the lobes are oriented whereas they are identical in terms of size, shape, and energy.
- As the lobes lie along one of the x, y or z-axis, these three orbitals are given the designations  $2p_x$ ,  $2p_y$ , and  $2p_z$ . Thus, we can say that there are three p orbitals whose axes are mutually perpendicular.
- Similar to s orbitals the size, and energy of p orbitals increase with an increase in the principal quantum number (4p > 3p > 2p).



# **Periodic Table**

# What is the Periodic Table? Why is Periodic Table Made?

The periodic table is an arrangement of all the elements known to man in accordance with their increasing atomic number and recurring chemical properties. They are assorted in a tabular arrangement wherein a row is a period and a column is a group. Elements are arranged from left to right and top to bottom in the order of their increasing atomic numbers. Thus,

- Elements in the same group will have the same valence electron configuration and hence, similar chemical properties.
- Whereas, elements in the same period will have an increasing order of valence electrons. Therefore, as the energy level of the atom increases, the number of energy sub-levels per energy level increases.

The first 94 elements of the periodic table are naturally occurring, while the rest from 95 to 118 have only been synthesized in laboratories or nuclear reactors. The <u>modern periodic table</u>, the one we use now, is a new and improved version of certain models put forth by scientists in the 19th and 20th century. Dimitri Mendeleev put forward his periodic table based on the findings of some scientists before him like John Newlands and Antoine-Laurent de Lavoisier. However, Mendeleev is given sole credit for his development of the periodic table.



**The Periodic Classification of Elements** 

All existing matter in our surroundings is made up of basic units known as elements. Initially, in 1800, only 31 chemical elements were discovered. After some advancement in technology in 1865, about 63 more elements were discovered. This created the need for the periodic classification of elements.

Presently, there are *118 elements known to us*. Out of these 118 chemical elements, some elements are man-made.

# **Periodic Classification of Elements Characteristics**

In the long form periodic table the elements are arranged in the order of their atomic numbers. Atomic number of an element is equal to the number of protons inside the nucleus of its atom.

The general features of the long form periodic table are:

- There are in all, 18 vertical columns and 18 groups in the long form periodic table.
- These groups are numbered from 1 to 18 starting from the left.
- There are seven horizontal rows called periods in the long form periodic table. Thus, there are seven periods in the long form periodic table.
- The elements of Groups 1, 2 and 13 to 17 are called the main group elements. These are also called typical or representative or normal elements.
- The elements of Groups 3 to 12 are called transition elements.
- Elements with atomic number 58 to 71 (Ce to Lu) occurring after lanthanum (La) are called lanthanides. Elements with atomic numbers 90 to 103 (Th to Lw) are called actinides. These elements are called f-block elements and also as inner transition elements.

## **TYPES OF CHEMICAL BONDS**

#### What is chemical bonding?

**Chemical bonding** or **chemical bond** is the different types of force that binding together by two common <u>atoms</u> or groups of atoms forming an aggregate of ions or <u>molecules</u> by lowering of <u>energy</u>. The definition and formation of ionic, covalent, metallic, and <u>hydrogen bonding</u> or bonds explain the different types of properties like <u>polarity</u>, <u>dipole moment</u>, <u>electric polarization</u>, <u>oxidation</u> <u>number</u> or state, etc.



#### What is ionic bonding?

The electrostatic forces bind together oppositely charged ions in chemical compounds responsible for the formation of ionic bonds. Therefore, the ionic bonding in the molecule is formed by the transfer of electron or electrons from an electropositive metal to an electronegative non-metal atom.

Electropositive chemical elements have a tendency to lose one or more electrons. But the electronegative elements have a tendency to gain these electrons. As a result of mutual electrostatic attraction between positive and negative ions establishes the formation of ionic bonding in chemical compounds.

<u>Sodium</u> chloride (NaCl), <u>potassium</u> chloride (KCl), <u>magnesium</u> sulfide (MgS), calcium chloride (CaCl<sub>2</sub>), <u>calcium</u> oxide (CaO) are examples of common compounds formed by ionic bonding.

The formation of sodium chloride and calcium oxide is given below the picture,

Ionic bond  $Na + :Cl := Na^+ + :Cl$ Sodium Chlorine  $\mathbf{O} = \mathbf{O} \mathbf{C} \mathbf{a}^{+2} + \mathbf{O}^{-2}$ Ca: Calcium Oxygen

#### What is covalent bonding?

G.N. Lewis in 1916 first proposed the formation of chemical bonds in the molecules by atoms without any transference of electrons from one to another. Lewis suggested that the union of atoms by bonding in molecules,

- 1. Hydrogen, nitrogen, oxygen, chlorine, etc
- 2. Most of the <u>organic compounds</u> like <u>hydrocarbon</u>, <u>alcohols</u>, organic acids, etc.

These types of bonds are formed by the sharing of electrons pair between the atoms. In such a way, the participating atoms complete their octet or form a stable noble gas electronic configuration.

Formation of covalent bond

For example, the carbon atom has four electrons in the outermost shell. Therefore, the carbon atom needs four electrons to complete the octet. If these four are obtained from four chlorine atoms by common sharing, carbon tetrachloride was formed by the covalent chemical bonding.

In each bonding, the chemical atom attains its stable inert <u>gas</u> configuration. In the case of the <u>hydrogen atom</u> and carbon atom in <u>methane</u> molecule where hydrogen atom bonding with <u>carbon</u> by sharing of electrons.

Lewis structure for covalent compounds



Lewis structure explains clearly the formation of covalent bonds through the sharing of electrons and also the most chemical behavior like polarity, dipole moment, or polarization of covalent compounds. But the theory does not provide the mechanism of sharing obtained from the learning of wave mechanics.

#### What is coordinate covalent bond?

The sharing of electrons equal to the partner is not common for the definition of covalent chemical bonds sometimes.

For the formation of the bond between <u>boron</u> trichloride and ammonia, both the electrons come from ammonia. Hence such types of chemical bonding is an example of coordinate covalent bond. Here ammonia acts as <u>Lewis acid</u>, and boron trifluoride acts as Lewis base,

 $NH_3 + BF_3 \rightarrow F_3B \leftarrow :NH_3.$ 

#### What is metallic bonding?

Metals are a good conductor of electricity. The formation of the metallic bonds given crystalline solid with high coordination numbers of 12 or 14.

The atoms in a metal are identical they can not show ionic properties because the ionic compounds are formed between two different atoms. Covalent bonds are also not possible for metal. In covalent compounds, much weak <u>Van der Waals</u> force acts between the two bonding chemical atoms. It can not explain the rigidity of the metal atom.

The metallic chemical bonding may be the collection of positive atomic cores and mobile electrons in the electron sea model. The chemical force that binds the metal and mobile electrons is called a metallic bond. The electron sea model in the metallic bonding can easily explain the <u>conductance</u> and conduction of heat in the metal compounds.

# **CLASSIFICATION OF ORGANIC COMPOUNDS**

#### What are Organic Compounds?

The compounds in solid, liquid or gaseous states which contain carbon in their molecule are known as organic compounds.

There are a large number of organic compounds and therefore a proper systematic classification was required. Organic compounds can be broadly classified as acyclic (open chain) or cyclic (closed chain)



#### 1. Acyclic or Open Chain Compounds:

These compounds are also known as aliphatic compounds, they have branched or straight chains. Following are the examples in this category.



#### 2. Alicyclic or Closed Chain or Ring Compounds:

These are cyclic compounds which contain carbon atoms connected to each other in a ring (homocyclic). When atoms other than carbon are also present then it is called heterocyclic. Examples of this type are as follows:



#### **3. Aromatic Compounds**

They are a special type of compound which contains benzene and other ring related compounds. Similar to alicyclic, they can also have heteroatoms in the ring. Such compounds are called heterocyclic aromatic compounds. Some examples are as follows:



#### 4. Heterocyclic Aromatic Compounds



Organic compounds can also be classified on the basis of functional groups into families or homologous series.

#### **1.** Functional group

The functional group can be defined as an atom or a group of atoms that are joined together in a specific manner, which is responsible for the characteristic chemical properties of organic compounds. Examples, in this case, are the hydroxyl group -OH, aldehyde group -CHO and carboxylic acid group -COOH.

#### 2. Homologous series

A group or a series of organic compounds in which each member contains the same characteristic functional group and differs from each other by a fixed unit form a homologous series and therefore its members are known as homologous. The members of the homologous series can be represented by a general formula and the successive members differ from each other in the molecular formula by a CH<sub>2</sub> unit. There are a number of homologous series in organic chemistry such as alkanes, alkenes, alkynes, haloalkanes, alkanols, amines, etc.

# **Hybridization**

**Hybridization**, in Chemistry, is defined as the concept of mixing two atomic orbitals to give rise to a new type of hybridized orbitals. This intermixing usually results in the formation of hybrid orbitals having entirely different energy, shapes, etc. The atomic orbitals of the same energy level mainly take part in hybridization. However, both fully-filled and half-filled orbitals can also take part in this process, provided they have equal energy.

# **Types of Hybridization**

Based on the **types of orbitals** involved in mixing, the hybridization can be classified as  $sp^3$ ,  $sp^2$ , sp. Let us now discuss the various types of hybridization, along with their examples.

#### sp Hybridization

sp hybridization is observed when one s and one p orbital in the same main shell of an atom mix to form two new equivalent orbitals. The new orbitals formed are called **sp hybridized orbitals.** It forms linear molecules with an angle of 180°.

#### Examples of sp Hybridization:

• All compounds of a carbon-containing triple bond, like C<sub>2</sub>H<sub>2</sub>.



# sp<sup>2</sup> Hybridization

 $sp^2$  hybridization is observed when one s and two p orbitals of the same shell of an atom mix to form 3 equivalent orbitals. The new orbitals formed are called  $sp^2$  hybrid orbitals.

• sp<sup>2</sup> hybridization is also called trigonal hybridization.

- It involves the mixing of one 's' orbital and two 'p' orbitals of equal energy to give a new hybrid orbital known as sp<sup>2</sup>.
- A mixture of s and p orbital formed in trigonal symmetry and is maintained at  $120^{\circ}$ .
- All three hybrid orbitals remain in one plane and make an angle of 120° with one another. Each of the hybrid orbitals formed has a 33.33% 's' character and 66.66% 'p' character.
- The <u>molecules</u> in which the central atom is linked to 3 atoms and is sp2 hybridized have a triangular planar shape.

#### Examples of sp<sup>2</sup> Hybridization

- All the compounds of Boron, i.e., BF<sub>3 and</sub> BH<sub>3</sub>
- All the <u>compounds of carbon</u>, containing a carbon-carbon double bond, Ethylene  $(C_2H_4)$



#### sp<sup>3</sup> Hybridization

When one 's' orbital and 3 'p' orbitals belonging to the same shell of an atom mix together to form four new equivalent orbitals, the type of hybridization is called a **tetrahedral hybridization or sp**<sup>3</sup>. The new orbitals formed are called **sp**<sup>3</sup> **hybrid orbitals**.

- These are directed towards the four corners of a regular <u>tetrahedron</u> and make an angle of 109°28' with one another.
- The angle between the sp3 hybrid orbitals is  $109.28^{\circ}$
- Each sp<sup>3</sup> hybrid orbital has 25% s character and 75% p character.
- Examples of  $sp^3$  hybridization are <u>ethane</u> (C<sub>2</sub>H<sub>6</sub>) and methane.

# 109.5°

Name of the Molecule	Methane
Molecular Formula	CH₄
Hybridization Type	sp <sup>3</sup>
Bond Angle	109.5°

# Hybridization of Methane CH4 (Met

In order to understand the hybridization of  $CH_4$  (methane), we have to take a look at the atomic orbitals which are of different shape and energy that take part in the process. The type of hybridization involved with CH4 is sp<sup>3</sup>. We will discuss in detail how this hybridization occurs below.

Geometry

# Hybridization of Methane

When we talk about CH4 it is basically a combination of 1 carbon and 4 hydrogen atoms. However, to form this compound the central atom carbon which has 4 valence electrons obtain more electrons from 4 hydrogen atoms to complete its octet. When the electrons are shared between carbon and hydrogen there is a formation of a covalent bond or bonds to be more accurate.



Now coming to the <u>hybridization</u> of methane, the central atom carbon is  $sp^3$  hybridized. This is because one 2s orbital and three 2p orbitals in the valence shell of carbon combine to form four  $sp^3$  hybrid orbitals which are of equal energy and shape. Further, four H atoms also use these four  $sp^3$  hybrid orbitals of carbon to form C-H sigma bonds which ultimately leads to the formation of the methane molecule.

#### **HYBRIDIZATION OF ETHANE C2H6**

We will look at the hybridization of C2H6 (Ethane) here on this page and understand the process in detail. Students will also learn about the molecular geometry, bond formation and the bond angles between the different atoms.

Name of the Molecule	Ethane
Molecular Formula	C2H6

Hybridization Type	sp <sup>3</sup>
Bond Angle	109.5°
Geometry	Tetrahedral

#### What is the Hybridization of Ethane?

Before we dive into the hybridization of ethane we will first look at the molecule. Ethane basically consists of two carbon atoms and six hydrogen atoms. However, carbon will be the central atom and its orbitals will take part in hybridization.



Molecular orbital picture of ethane

During the formation of C2H6, 1 s orbital and px, py, and pz orbitals undergo  $sp^3$  hybridization. This results in the formation of four hybridized orbitals for each carbon atom. The molecular hybrid orbitals now form different bonds between the electrons.

Among the four  $sp^3$  hybrid orbitals, one hybrid orbital of one carbon atom will overlap with 1 s-orbital of the hydrogen atom to produce 3 sigma bonds. In addition, the last orbital will overlap with one  $sp^3$  orbital of another carbon atom forming a sigma bond between two C-atoms.

#### HYBRIDIZATION OF ETHYNE C2H2

Hybridization of  $C_2H_2$  (ethyne) on this page. The type of hybridization that exists in this chemical compound is sp type. To understand the process we have to learn about the bonding and the orbitals. We will discuss everything in detail below.

Name of the Molecule

Acetylene or Ethyne

Molecular Formula	C <sub>2</sub> H <sub>2</sub>
Hybridization Type	sp
Bond Angle	180°
Geometry	Linear

#### What is the Hybridization of Ethyne?

When we break down ethyne molecules it basically consists of 2 CH molecules. However, we will take first take both carbon and hydrogen molecule separately and draw their orbital diagrams. When we do this we will see that carbon has 6 electrons and hydrogen has one electron.



Now, if we see the electronic configuration of carbon in its ground state it will be represented as  $1s^2 2s^2 2p^2$ . When it gets into an excited state, one of the electron from 2s orbital will move or jump to the 2pz orbital and the electronic configuration will change to  $1s^2 2s^1 2px^1 2py^1 2pz^1$ . Meanwhile, the CH molecule has only 1 hydrogen atom, therefore the  $2s^1$  and the  $2pz^1$  orbitals get hybridised. This further leads to the formation of 4 sp hybridized orbitals wherein each CH molecule will form 2 hybridized sp orbitals.

During <u>hybridization</u>, C-C sigma bond is formed when one sp orbital overlaps from each of the carbons and two C-H bonds are created when second sp orbital on each carbon overlaps with 1s orbital of hydrogen. In this, the carbon atom will have two half-filled 2p orbitals. These two pairs of p orbitals do not participate in the hybridization and instead form two pi bonds resulting in the creation of a triple bond.

#### HYBRIDIZATION OF BENZENE

The hybridization of benzene is said to be  $sp^2$  type. Benzene consists of 6 carbon and 6 hydrogen atoms where the central atom usually is hybridized. Here, carbon is the central atom. Students will understand all the mechanisms involved in the occurrence of hybridization in this lesson. We will look at the details below.

Name of the Molecule	Benzene
Molecular Formula	C <sub>6</sub> H <sub>6</sub>
Hybridization Type	sp <sup>2</sup>
Bond Angle	120°
Geometry	Trigonal Planar

#### What is the Hybridization of Benzene?

Before we talk about the <u>hybridization</u> of  $C_6H_6$  let us first understand the structure of benzene. This chemical compound is made from several carbon and hydrogen atoms. However, to form benzene, the carbon atoms will need one hydrogen and two carbons to form bonds. Further, the carbon atom lacks the required number of unpaired electrons to form the bonds. At this stage its electronic configuration will be  $1s^2$ ,  $2s^2$ ,  $2px^1$ ,  $2py^1$ . What happens next is the promotion of one  $2s^2$  electron pair to the empty 2pz orbital.



During this, the carbon atom will enter into an excited state and the electron configuration will also change to become  $1s^2$ ,  $2s^1$ ,  $2px^1$ ,  $2py^1$ ,  $2pz^1$ . Now when the electron is promoted from the 2s to the empty 2p orbital, we will get 4 unpaired electrons. These electrons will be used in the formation of the bonds. For, hybridisation to occur the outer orbitals are used. Three of the carbon orbitals are used rather than all four. In this, 1 s orbital and two p orbitals are hybridized and form three  $sp^2$  hybridized orbitals. Each of the carbon atoms will form sigma bonds with two other carbons and one hydrogen atom.

# <u>Definition with example – Electrophile, nucleophile and</u> <u>free radical</u>

Electrophile and nucleophile are the chemical species that *donate or accept electrons* to form a new chemical bond. A nucleophile is a chemical species which, in relation to a response, gives an electron pair to form a chemical bond. Any molecule, ion or atom that is in some manner deficient in electron can act as an electrophile.

A nucleophile is usually negatively charged or neutral with a lone pair of electrons.  $H_2O$ , -OMe or -OtBu are some examples. Overall, the *electron-rich species is a nucleophile*. Electrophiles are generally positively charged or neutral species with empty orbitals attracted to a centre rich in electrons.

The <u>chemical reactions</u> happening between electron donors and acceptors are described by concepts like *electrophile and nucleophile*. These are the most important concepts in organic

chemistry. They have replaced cationoid and anionoid terms and were introduced in the year 1933.

# What is Electrophile?

Positively charged or neutral species are called electrophiles that are deficient in electrons and can accept a pair of electrons. These are also called species that love electrons (philic).

- The term electrophile can be split into "electro" derived from electron and "phile" which means loving.
- They are electron deficient and hence love to accept electrons (electrons loving).
- They are positively charged or neutral.
- They attract electrons. The movement of electrons depends on the density.
- They move from high-density area to low density area.
- They undergo electrophilic addition and <u>electrophilic substitution</u> reactions.
- An electrophile is also called Lewis acid.

#### What is Nucleophile?

A nucleophile is a reagent comprising an negative charge or lone pair of electrons. As a nucleophile is rich in electron, it looks for electron-deficient locations. Nucleophiles act as Lewis bases, i.e, species which can donate a pair of electrons.

- The term nucleophile can be split into "nucleo" derived from the nucleus and "phile" which means loving.
- They are electron-rich and hence nucleus loving. They are negatively charged or neutral.
- They donate electrons.
- The movement of electrons depends on the density.
- They move from low-density area to high-density area.
- They undergo nucleophilic addition and nucleophilic substitution reactions.
- A nucleophile is also called a Lewis base.

For example, as nitrogen is less electronegative than oxygen, ammonia is a <u>stronger</u> <u>nucleophile</u> than water. The lone pair of electrons on nitrogen in ammonia can be more easily given than the lone pair of electrons on oxygen in the water.

To make you understand how **electrophile and nucleophile** are different from each other, here are some major **differences between atom and ion:** 

# **Difference between Electrophile and Nucleophile**

ELECTROPHILE	NUCLEOPHILE
Also called Lewis acid	Also called <u>Lewis base</u>
They are positively charged / neutral	They are negatively charged / neutral
They undergo electrophilic addition and electrophilic substitution reactions	They undergo nucleophilic addition and nucleophilic substitution reactions
Electron-deficient	Electron-rich
It accepts a pair of an electron to form a covalent bond	It donates a pair of an electron to form a covalent bond
All carbocations are electrophiles.	All carbanions are nucleophiles.
Example: Hydronium Ion, methyl carbocation.	Example: Chloride Ion, methyl carbanion.

#### What are Free Radicals?

A free radical is termed as a molecular species which can contain an unpaired electron in its atomic orbital and can exist independently.

All the radicals share some common properties due to the *unpaired electron*.

Generally, molecules bear bonding electron pairs and lone pairs a nonbonding electron pair or un-shared electron pair. Each bonding or nonbonding electron pair has two electrons which are in opposite in spin orientation, +1/2 and -1/2 in one orbital based on <u>Pauli's exclusion</u> <u>principle</u>, whereas an unpaired electron is a single electron, alone in one orbital. A molecule that has an unpaired electron is called a free radical and is a paramagnetic species.

# **OXIDATIVE STRESS**







Cell

Free Radicals Attacking Cell

Oxidative Stress



The antioxidant donates an electron to the free radical's unpaired electron.



#### **Sources of Free Radicals**

Free radicals are generated internally through the following sources.

- Mitochondria
- Inflammation
- Exercise
- Phagocytosis
- Peroxisomes

Free radicals are found externally in the following sources

- Environmental pollution
- Cigarette smoke
- Radiation
- Drugs and pesticides
- Ozone layer

# UNIT II

# What are Acids and Bases?

Acids are chemical substances which are characterized by a sour taste in an aqueous medium. They have the tendency to turn blue litmus red. On the other hand, bases are chemical substances which are characterized by a bitter taste and are slippery to touch. Some bases are soluble in water, while others are not.

Water soluble bases are known as alkalis. They have the tendency to turn red litmus blue. Acids and bases react with a wide range of chemical compounds to form salts.



# **Physical Properties of Acids and Bases**

The physical properties of acids and bases are listed in the table below.

Properties	Acids	Bases
Colour	Mineral acids are colourless liquids but sometimes sulphuric acid becomes yellow due to impurities. Some organic acids are white-coloured solids. <b>Examples:</b> benzoic acid	Bases are colourless except for the hydroxides of iron and copper.
Taste	Sour	Bitter

Touch	_	Slippery
Solubility	Soluble in water	Some bases are soluble in water. They are called alkalis.

# **Physical Properties of Acid**

- 1. The word "acid" comes from the Latin word 'acere' which means sour. This distinguishable property helps identify acids from other compounds such as salt and bases. Many acids can be hazardous if ingested and shouldn't be tasted.
- 2. Once the acid binds to the base, it becomes a neutral substance. Often this reaction can lead to water and salt. This is often seen when strong acids react with strong bases.
- 3. Acids in an aqueous solution produce hydrogen ions which are responsible for the conductivity of the solution. The acid that conducts electricity strongly is a strong acid, and the acid that conducts electricity weakly is a weak acid.

# **Chemical Properties of Acid and Bases**

#### 1. Reactions of Acids and Bases with Metals

When a metal reacts with an acid, it generally displaces hydrogen from the acids. This leads to the evolution of <u>hydrogen gas</u>. The metals combine with the remaining part of acids to form a salt. For example, the reaction of sulphuric acid with zinc.

Alkalis (bases that are soluble in water) react with metals to produce salt and hydrogen gas. For example, reaction of zinc with sodium hydroxide.

#### 2. The Reaction of Metal Carbonates/Metal Bicarbonates with Acids

Metal carbonates/metal bicarbonates react with acids to produce salt, carbon dioxide and water. For example the reaction of sodium carbonate/sodium bicarbonate with hydrochloric acid.

#### 3. The Reaction of Metal Oxide with Acids

Metal oxides react with acids to produce salt and water. For example reaction of copper oxide and dilute hydrochloric acid.

#### 4. The Reaction of Non-metal Oxide with Bases

<u>Non-metal</u> oxides react with bases to produce salt and water. For example the reaction of carbon dioxide and lime water (calcium hydroxide)

#### 5. The Reaction between Acids and Bases

Acids react with bases to produce salt and water. The reaction between acids and bases to give salts is known as <u>neutralization</u> reactions. For example the reaction of sodium hydroxide with hydrochloric acid.

#### Neutralization of Acid and Base

The reaction between an acid and a base invariably gives salt and water and is called neutralization. In a neutralization reaction, one  $H^+$  ion of acid is neutralized by one  $OH^-$  ion of the base. When all the  $H^+$  ions in the acidic solution are neutralized by the same number of  $OH^-$  ions of the basic solution, it is called complete neutralization. The relative amounts of acid and base required for complete neutralization depend upon the total number of  $H^+$  and  $OH^-$  ions produced by the respective acid and base.

#### **Comparative Study of Properties of Acids and Bases**

A comparative study of properties of acids and bases is given below in table.

Corrosive action on skin: All acids and some alkalies show corrosive action on skin as they form painful blisters when they come in contact with the skin.

Reactions taking place between acids and bases: All acids react with alkalis (metal hydroxides) to form salt and water. The reaction of an acid with a base to form salt and water as the products is called neutralization. H<sub>2</sub>SO<sub>4</sub> absorbs water from skin tissues. HNO<sub>3</sub> reacts with skin proteins to form a pulp like mass. NaOH and KOH are called caustic soda and caustic potash, respectively due to their causticizing action on the skin.

 $2KOH + H_2SO_4 \rightarrow K_2SO_4 + 2H_2O$ 

$$Ca(OH)_2 + 2HNO_3 \rightarrow Ca(NO_3)_2 + 2H_2O$$

## Acid vs Base

To give you a more clear understanding of the differences between <u>acids and bases</u> here is a comparison chart that you can refer to.

Basis	Acid	Base
Definition	An acid is any chemical compound once dissolved in water produces a solution with hydrogen ion activity more than purified water	A base is an aqueous substance that could absorb hydrogen ions.
Strength	Relies on the concentration of the hydronium ions	Relies on the concentration of the hydroxide ions
Examples	Acetic acid CH3COOH and sulphuric acid	Sodium Hydroxide (NaOH) and Ammonia
Characteristics (Physical)	Acids would look solid, liquid or in the form of gas. It would also have a sour taste.	Bases would feel slippery and solid in nature (except for ammonia, which is gaseous). It would have a bitter taste.
Disassociation	Acids would release hydrogen ions (H+) when mixed with water	Bases would release hydroxide ions(OH-) when mixed with water
Test with Litmus	Would turn blue litmus red	Would turn red litmus blue



# **Difference between Acids and Bases**

Acids	Bases
Acid gives off hydrogen ions when dissolved in water.	Bases give off hydroxyl ion when dissolved in water.
It turns blue colour litmus paper into red.	It turns red colour litmus paper into blue.
It has a sour taste.	It has bitter taste and soapy to touch.
Its pH value ranges from 1 to 7.	Its pH value ranges from 7 to 14.
Example: HCl, H <sub>2</sub> SO <sub>4</sub> etc.	Example: NaOH, KOH etc.

# **Concepts of acids and base**

#### **Arrhenius theory**

The **Arrhenius theory** was first introduced by the Swedish scientist Svante Arrhenius in the year 1887. To conduct electricity, one must have free-moving ions. Svante Arrhenius noticed that the solution of acid conducts electricity by dissolving the substance in the solution, which dissociates into ions. This theory is known as "Electrolytic dissociation." This concept is well-known these days, but during those days, it was controversial.

Water is a neutral substance which does not conduct electricity. By dissolving some substance in water, it conducts electricity. These substances are called electrolytes, and the process is known as "electrolytic dissociation."

# **Arrhenius Theory of Acid and Base**

According to Arrhenius theory, acid is a substance that gives  $H^+$  ions on dissolving in the aqueous solution. It increases the concentration of  $H^+$  ions in the solution. The base is a substance that ionises  $OH^-$  ion by dissolving in the aqueous solution. The concentration of  $OH^-$  ions is high in the solution.

Acid	Base
Acidic in nature	Basic in nature
The concentration of H <sup>+</sup> ion is high	The concentration of OH <sup>-</sup> ion is high
Taste sour	Taste bitter
Are red on blue litmus paper	Are blue on red litmus paper
Have PH<7	Have PH>7

The general properties of acid and base

Common examples: Lemons, oranges, vinegar, urine, sulphuric acid, hydrochloric acid

Common examples: Soap, toothpaste, bleach, cleaning agents, limewater, ammonia, water, sodium hydroxide

Arrhenius acid in the aqueous solution increases the concentration of protons or  $H^+$  ions. For example, hydrochloric acid in the water. HCl undergoes a dissociation reaction to produce an  $H^+$  ion and a Cl<sup>-</sup> ion, as explained below. The concentration of the H+ ions is increased by forming hydronium ions.

 $HCl_{(aq)} \rightarrow H^{\scriptscriptstyle +}_{(aq)} + Cl^{\scriptscriptstyle -}_{(aq)}$ 

 $HCl_{\scriptscriptstyle (aq)} + H_2O_{\scriptscriptstyle (l)} \longrightarrow H_3O^{\scriptscriptstyle +}_{\scriptscriptstyle (aq)} + Cl^{\scriptscriptstyle -}_{\scriptscriptstyle (aq)}$ 

Other examples of Arrhenius acids are listed below:

 $NHO_{3(aq)} + H_2O_{(l)} \rightarrow H_3O^{+}_{(aq)} + No_3^{-}$ 

In this reaction, nitric acid dissolves in aqueous water to give hydrogen and nitrate ions.

**Arrhenius Acids** 

Hydrochloric acid (HCl)

Nitric acid (HNO<sub>3</sub>)

Sulphuric acid (H<sub>2</sub>SO<sub>4</sub>)

Phosphoric acid (H<sub>3</sub>PO<sub>4</sub>)

Carbonic acid (H<sub>2</sub>CO3)

Acetic acid (CH<sub>3</sub>COOH)

#### Arrhenius Base

An Arrhenius base is a substrate that increases the concentration of hydroxide ions in the aqueous solution. The example for Arrhenius base is a highly soluble sodium hydroxide compound in water, which dissociates to give sodium ion and hydroxide ion.

In an aqueous solution, NaOH completely dissolves to give hydroxide ions and sodium ions, to increase the concentration of hydroxide ions.

 $NaOH_{(aq)} \rightarrow Na^{+}_{(aq)} + OH^{-}_{(aq)}$ 

Some other examples of Arrhenius bases are 1st and 2nd group hydroxides, like LiOH and Ba(OH)2.

In the above reaction, lithium hydroxide dissolves in water to give lithium ion and hydroxide ion.

Examples of an Arrhenius base are listed below:

Name	Formula
Sodium hydroxide	NaOH
Potassium hydroxide	КОН
Calcium hydroxide	Ca(OH) <sub>2</sub>
Magnesium hydroxide	Mg(OH) <sub>2</sub>

#### Limitations of Arrhenius theory

The Arrhenius theory is applicable only in aqueous solution; for example, according to the theory, HCl is an acid in the aqueous solution but not in benzene, even though it donates the H+ ion to the benzene. Also, under Arrhenius's definition, the solution of sodium amide in liquid ammonia is not alkaline, even though the amide ion deprotonates the ammonia.
## **Bronsted-Lowry theory**

The **Bronsted-Lowry theory** (Proton theory of acid and base) is an acid-base reaction theory, introduced by Johannes Nicolaus Bronsted (Danish Chemist) and Thomas Martin Lowry (English Chemist) in 1923. According to the theory, acid and base react with each other and by an exchange of proton acid, forms its conjugate base and the base forms its conjugated acid.

The Bronsted-Lowry theory is an extended version of an Arrhenius theory of acid-base.

According to the Arrhenius theory, in aqueous solution, acid increases the concentration of  $H^+$  ions and base increases the concentration of  $OH^-$  ions. The limitations of Arrhenius theory were that it identifies the reaction of an acid and base only in the aqueous medium.

# **Bronsted-Lowry Theory of Acid and Base**

According to Bronsted-Lowry theory, acid is a substance which donates an  $H^+$  ion or a proton and forms its conjugate base and the base is a substance which accepts an  $H^+$  ion or a proton and forms its conjugate acid.

## **Bronsted-Lowry Acid**

The Bronsted-Lowry acid is a substance which donates a proton or H<sup>+</sup> ion to another compound.



### **Bronsted-Lowry Base**

The Bronsted-Lowry base is a substance which accepts a proton or H+ ion from other compounds.



The Bronsted-Lowry Acids and their Conjugated Bases

The strength of the acid decreases as it descends and the strength of their corresponding conjugate base increases.

Acids	Conjugated base
Perchloric acid (HCIO <sub>4</sub> )	Perchlorate ion (CIO <sub>4</sub> <sup>-</sup> )
Hydroiodic acid (HI)	Iodide ion (I <sup>-</sup> )
Hydrobromic acid (HBr)	Bromide ion (Br)
Hydrochloric acid (HCl)	Chloride ion (Cl <sup>-</sup> )

Sulphuric acid (H <sub>2</sub> SO <sub>4</sub> )	Hydrogen sulphate ion (HSO <sub>4</sub> <sup>-</sup> )
Nitric acid (HNO <sub>3</sub> )	Nitrate ion (NO <sub>3</sub> <sup>-</sup> )
Hydronium ion $(H_3O^+)$	Water (H <sub>2</sub> O)
Hydrogen sulfate ion (HSO <sub>4</sub> <sup>-</sup> )	Sulfate ion $(SO_4^{2})$
Nitrous acid (HNO <sub>2</sub> )	Nitrite ion (NO <sub>2</sub> <sup>-</sup> )
Acetic acid (CH <sub>3</sub> COOH)	Acetate ion (CH <sub>3</sub> COO <sup>-</sup> )
Carbonic acid (H <sub>2</sub> CO <sub>3</sub> )	Hydrogen carbonate ion (HCO₃ <sup>-</sup> )
Ammonium ion (NH <sub>4</sub> <sup>+</sup> )	Ammonia (NH <sub>3</sub> )
Hydrogen carbonate ion (HCO <sub>3</sub> <sup>-</sup> )	Carbonate ion $(CO_3^2)$
Water (H <sub>2</sub> O)	Hydroxide ion (OH <sup>-</sup> )
Methanol (CH <sub>3</sub> OH)	Methoxide ion (CH <sub>3</sub> O <sup>-</sup> )
Ammonia (NH <sub>3</sub> )	Amide ion (NH <sub>2</sub> -)

## Lewis acids

Lewis acids and bases are described by the Lewis theory of acid-base reactions as electronpair acceptors and electron pair donors respectively. Therefore, a Lewis base can donate a pair of electrons to a Lewis acid to form a product containing a coordinate covalent bond. This product is also referred to as a Lewis adduct. An illustration detailing the reaction between a Lewis acid and base leading to the formation of a coordinate covalent bond between them is given below.



Lewis acids and bases are named after the American chemist Gilbert Newton Lewis, who also made invaluable contributions in the fields of <u>thermodynamics</u> and photochemistry.

# Lewis Acid

Lewis Acids are the chemical species which have empty orbitals and are able to accept electron pairs from Lewis bases. This term was classically used to describe chemical species with a trigonal planar structure and an empty p-orbital. An example of such a Lewis acid would be BR<sub>3</sub> (where R can be a halide or an organic substituent).

Water and some other compounds are considered as both Lewis acids and bases since they can accept and donate electron pairs based on the reaction.

# **Examples of Lewis Acids**

Some common examples of Lewis acids which can accept electron pairs include:

- $H^+$  ions (or <u>protons</u>) can be considered as Lewis acids along with onium ions like  $H_3O^+$ .
- The cations of d block elements which display high oxidation states can act as electron pair acceptors. An example of such a cation is  $Fe^{3+}$ .
- Cations of metals such as Mg<sup>2+</sup> and Li<sup>+</sup> can form coordination compounds with water acting as the ligand. These aquo complexes can accept electron pairs and behave as Lewis acids.
- Carbocations given by  $H_3C^+$  and other trigonal planar species tend to accept electron pairs.
- The Pentahalides of the following group 15 elements can act as Lewis acids Antimony, Arsenic, and Phosphorus.

Apart from these chemical compounds listed above, any electron-deficient  $\pi$  system can act as an acceptor of electron pairs – enones, for example.

## Lewis Base

Atomic or molecular chemical species having a highly localized HOMO (The Highest Occupied Molecular Orbital) act as Lewis bases. These chemical species have the ability to donate an electron pair to a given Lewis acid in order to form an adduct, as discussed earlier.

The most common Lewis bases are <u>ammonia</u>, alkyl amines, and other conventional amines. Commonly, Lewis bases are anionic in nature and their base strength generally depends on the  $pK_a$  of the corresponding parent acid. Since Lewis bases are electron-rich species that have the ability to donate electron-pairs, they can be classified as nucleophiles. Similarly, Lewis acids can be classified as electrophiles (since they behave as electron-pair acceptors).

# **Examples of Lewis Bases**

Examples of Lewis bases which have an ability to donate an electron pair are listed below.

- Pyridine and the derivatives of pyridine have the ability to act as electron pair donors. Thus, these compounds can be classified as Lewis bases.
- The compounds in which Oxygen, Sulphur, Selenium, and Tellurium (which belong to group 16 of the Periodic Table) exhibit an oxidation state of -2 are generally Lewis bases. Examples of such compounds include water and ketones.
- The simple anions which have an electron pair can also act as Lewis bases by donating these electrons. Examples of such anions include H<sup>-</sup> and F<sup>-</sup>. Even some complex anions, such as the sulfate anion ( $SO_4^{2^\circ}$ ) can donate pairs of electrons.
- The  $\pi$ -systems which are rich in electrons (such as benzene, ethyne, and ethene) exhibit great electron pair donating capabilities.

Weak Lewis acids have strong conjugate Lewis bases. Apart from this, many chemical species having a lone pair of electrons such as  $CH_3^-$  and  $OH^-$  are identified as Lewis bases due to their electron pair donating capabilities.

# **Chemical Reactions Between Lewis Acids and Bases**

### Reactions with the H<sup>+</sup> ion

The H<sup>+</sup> ion acts as a Lewis acid and H<sub>2</sub>O acts as a Lewis base. The reaction between the water molecule and the proton yields a hydronium ion (H<sub>3</sub>O<sup>+</sup>), as illustrated below.



Here, the oxygen atom donates an electron pair to the proton, forming a coordinate covalent bond in the process. The resulting Lewis acid has a +1 charge associated with it. Another example of a reaction in which the  $H^+$  ion acts as a Lewis acid is its reaction with ammonia (NH<sub>3</sub>) to form an ammonium ion (NH<sub>4</sub><sup>+</sup>).



In this reaction, the proton receives an electron pair from the nitrogen atom (belonging to the ammonia molecule). The formation of a coordinate covalent bond between the two results in the formation of a Lewis adduct (the ammonium cation).

### Reaction Between Ag<sup>+</sup> and Ammonia

In this reaction, two Lewis bases form an adduct with one Lewis acid, as illustrated below.



Here, ammonia acts as a Lewis base and the silver ion acts as a Lewis acid. Each nitrogen atom donates an electron pair to  $Ag^+$ , resulting in two separate coordinate covalent bonds. The adduct formed from the Lewis acid and base has the chemical formula  $Ag(NH_3)_2^+$ .

### Reaction Between the Fluoride Ion and Boron Trifluoride

This reaction features the formation of a coordinate bond between the fluoride anion ( $F^-$ ) and boron trifluoride ( $BF_3$ ).



Here,  $F^-$  acts as an electron pair donor whereas  $BF_3$  accepts the electron pair. The reaction between the Lewis acid and base results in the formation of an adduct with the chemical formula  $BF_4^-$ .

## **Applications of Lewis Acids and Bases**

Some important applications of Lewis acids and bases are provided below.

Lewis acids play a vital role as a catalyst in the <u>Friedel-Crafts reaction</u> – AlCl<sub>3</sub> accepts a lone pair of electrons belonging to the chloride ion leading to the formation of  $AlCl_4^-$  in the Friedel-Crafts alkylation process.

This also leads to the formation of the highly electrophilic carbonium ion which acts as a strong Lewis Acid. The chemical reaction can be written as follows.

### $\mathbf{RCl} + \mathbf{AlCl}_3 \longrightarrow \mathbf{R}^{\scriptscriptstyle +} + \mathbf{AlCl}_{4^{\scriptscriptstyle -}}$

In the field of organic chemistry, Lewis acids are widely used to encourage many cationic or pseudo-cationic chemical reactions.

Lewis bases have immense applications in the modification of the selectivity and the activity of metallic catalysts. For the production of pharmaceuticals, asymmetric <u>catalysis</u> is an

important part of enantioselective synthesis. In order to enable asymmetric catalysis, chiral Lewis bases are often used to confer chirality on catalysts.

Several Lewis bases have the ability to form many bonds with Lewis acids. These compounds are also called 'multidentate Lewis bases' or 'chelating agents' and have a wide range of industrial and agricultural applications.

## **CONCENTRATION OF SOLUTION**

# Concentration

It is the amount of solute present in one litre of solution. It is denoted by C or S.

# 1. Concentration in Parts Per Million (ppm)

The parts of a component per million parts (10<sup>6</sup>) of the solution.



# 2. Mass Percentage (w/w):

When the concentration is expressed as the percent of one component in the solution by mass it is called mass percentage (w/w). Suppose we have a solution containing component A as the solute and B as the solvent, then its mass percentage is expressed as:

Mass % =  $\frac{\text{Mass of solute}}{\text{Mass of solution}} X 100\%$ 

## 3. Volume Percentage (V/V):

Sometimes we express the concentration as a percent of one component in the solution by volume, it is then called as volume percentage and is given as:

Volume % = volume of Solute volume of Solution X 100%

For example, if a solution of NaCl in water is said to be 10 % by volume that means a 100 ml solution will contain 10 ml NaCl.

## 4. Mass by Volume Percentage (w/V):

This unit is majorly used in the pharmaceutical industry. It is defined as the mass of a solute dissolved per 100mL of the solution.

% w/V = (Mass of component A in the solution/ Total Volume of the Solution)x 100

## Mass/Volume Percent = Mass of Solute (g) Volume of Solution (mL) X 100

## 5. Molarity (M):

One of the most commonly used methods for expressing the concentrations is molarity. It is the number of moles of solute dissolved in one litre of a solution. Suppose a solution of <u>ethanol</u> is marked 0.25 M, this means that in one litre of the given solution 0.25 moles of ethanol is dissolved.

Molarity (M) = Moles of Solute/Volume of Solution in litres

$$M = \frac{n \text{ (moles of solute)}}{V \text{ (volume of solution)}}$$

## 6. Molality (m):

<u>Molality</u> represents the concentration regarding moles of solute and the mass of solvent. It is given by moles of solute dissolved per kg of the solvent. The molality formula is as given-

 $Molality = m = \frac{moles \, of \, solute}{kg \, of \, solvent}$  $m = \frac{mol}{kg}$ 

## 7. Normality

It is the number of gram equivalents of solute present in one litre of the solution and it is denoted by N.

The relation between normality and molarity.

- N x Eq.Wt = Molarity x Molar mass
- N = Molarity x Valency
- $N = Molarity x Number of H^+ or OH^-ion.$

 $Normality(N) = \frac{number \ of \ gram \ equivalent \ of solute}{volume of the solution in litre}$ 

$$N = \frac{n}{v}$$

## 8. Formality

It is the number of gram formula units present in one litre of solution. It is denoted by F.

It is applicable in the case of ionic solids like NaCl.

Formality (F) =  $\frac{\text{No. of formula weight of solute (fw)}}{\text{Volume of solution in liters (V)}}$ 

### 9. Mole Fraction:

If the solution has a solvent and the solute, a mole fraction gives a concentration as the ratio of moles of one component to the total moles present in the solution. It is denoted by x. Suppose we have a solution containing A as a solute and B as the solvent. Let  $n_A$  and  $n_B$  be the number of moles of A and B present in the solution respectively. So, mole fractions of A and B are given as:

The above-mentioned methods are commonly used ways of expressing the concentration of solutions. All the methods describe the same thing that is, the concentration of a solution, each of them has its own advantages and disadvantages. <u>Molarity</u> depends on temperature while mole fraction and molality are independent of temperature. All these methods are used on the basis of the requirement of expressing the concentrations.

# Mole Fraction (X)

X<sub>Solute</sub> = <u>Moles of solute</u> Total moles of solution

X<sub>Solvent</sub> = <u>Moles of solvent</u> Total moles of solution Where:

 $X_{\text{solute}} + X_{\text{Solvent}} = 1$ 

#### UNIT II

#### **pH SOLUTION**

pH ("potential of hydrogen" or "power of hydrogen") of a solution, we are basically discussing the measure of hydrogen ion concentration in a solution. pH, in other words, is a scale that is used to specify the acidity or basicity of an aqueous solution. Acidic solutions which contain higher concentrations of H+ ions are generally measured to have lower pH values than basic or alkaline solutions.

If the temperature is 25 °C and the solution has a pH of less than 7, then it is acidic. Likewise, solutions with a pH greater than 7 are basic. If a solution has a pH of 7 at the temperature, they are neutral; for example, pure water, which tends to dissociate slightly into equal concentrations of hydrogen and hydroxyl (OH–) ions. The concentration of the dissociated hydrogen ions in pure water is 10-7 moles per litre. Solutions are categorised as acidic or basic based on their hydrogen ion (H+) concentration compared to pure water.

The pH of an aqueous solution is based on the pH scale, which typically ranges from 0 to 14 in water. In any case, students can keep these points in mind.

- Acidic solutions have lower hydroxide concentrations and high hydronium concentrations. Acidic solutions have a hydrogen ion concentration greater than 10-7 moles per litre.
- Basic solutions have high hydroxide concentrations and lower hydronium concentrations. Alkaline (basic) solution has a lower concentration of H+ ion that is less than 10-7 moles per litre.
- The concentration of hydrogen ions in a solution is expressed in terms of pH.

Additionally, some indicators (universal indicator paper, etc.) may be used to measure pH. It is solely based on the fact that the indicator's colour changes with pH. A visual comparison of the colour of a test solution with a defined colour chart helps to determine the pH accurately to the nearest whole number. pH can also be measured using an electronic pH metre.

### Ph scale :

The pH of a substance can be measured using a pH meter which measures the voltage difference between two electrodes and converts it into a pH value, or with pH paper which changes color according to the acidity or alkalinity of the substance it is dipped in.

- The pH scale is a precise way of classifying the acidity, basicity, or neutrality of any solution.
- The pH scale is a numerical and a visual scale, that can be represented by numbers, graphics, and colors.
- The numerical scale has values ranging from 0 (the most acidic) to 14 (the most basic).
- Pure water has a pH value of 7. This value is considered neutral (neither acidic nor basic).

# The pH Scale



### Measurement of ph:

pH is a measure of the acidity or alkalinity of a solution. It indicates the concentration of hydrogen ions (H $\square$ ) in the solution. The pH scale ranges from 0 to 14, where:

- A pH of 0 is highly acidic.
- A pH of 7 is neutral.

- A pH greater than 7 is alkaline (basic).

The pH scale is logarithmic, meaning that each whole pH value represents a tenfold change in acidity or alkalinity. For example, a solution with a pH of 4 is ten times more acidic than a solution with a pH of 5.

To measure pH, various methods and devices are used:

1. **\*\*pH Meter\*\*:** This is one of the most common methods. A pH meter is an electronic device that consists of a pH-sensitive electrode and a reference electrode. When the pH-sensitive electrode comes into contact with the solution, it generates a voltage proportional to the pH of the solution. The pH meter then converts this voltage into a pH reading.

2. **\*\*pH Test Strips\*\*:** These are paper strips impregnated with pH-indicating dyes. When the strip is dipped into a solution, it changes color according to the pH of the solution. The color is then compared to a color chart provided with the strips to determine the pH.

3. **\*\*pH Indicator Solution\*\*:** pH indicator solutions are chemical substances that change color based on the pH of a solution. They are added drop by drop to the solution until a color change occurs. The pH can then be determined by comparing the color to a reference chart.

4. **\*\*Universal pH Indicator\*\*:** This is a solution that changes color across the entire pH scale. It's often used in educational settings to demonstrate the concept of pH changes.

5. **\*\*pH Probes\*\*:** These are specialized electrodes that can be used with various types of instruments, such as pH meters and portable testers. They can be immersed directly into the solution to measure the pH.

6. **\*\*pH Capsules\*\*:** These are small capsules containing a pH-sensitive dye. They are dissolved in the solution, and the resulting color is compared to a chart to determine the pH.

When measuring pH, it's important to properly calibrate the measurement device using buffer solutions with known pH values to ensure accurate readings. Additionally, the temperature of the solution can affect pH measurements, so some pH meters and probes come with automatic temperature compensation.

Remember that accurate pH measurements are crucial in various fields, including chemistry, biology, environmental science, food and beverage production, and more.

### **BUFFER SOLUTION**

### What is Buffer in Chemistry?

A solution whose pH is not altered to any great extent by the addition of small quantities of either an acid or base is called buffer solution.

Buffer is also defined as the solution of reserve acidity or alkalinity which resists change of pH upon the addition of a small amount of acid or alkali.

Many chemical reactions are carried out at a constant pH. In nature, there are many systems that use buffering for pH regulation. For example, the bicarbonate buffering system is used to regulate the pH of blood, and bicarbonate also acts as a buffer in the ocean.

### **Characteristics of buffer solution**

(i) It has a definite pH.

(ii) Its pH does not change on standing for long periods of time.

(iii) Its pH does not change on dilution.

(iv) Its pH is slightly changed by the addition of small quantity of an acid or base.

### **Types of buffer solutions**

### (a) Acidic Buffer:

It is formed by the mixture of weak acid and its salt with a strong base.

Examples: (i) CH<sub>3</sub>COOH + CH<sub>3</sub>COONa, (ii) HCN + NaCN, (iii) Boric acid + Borax etc.

### (b) Basic Buffer:

It is formed by the mixture of a weak base and its salt with strong acid.

Examples: (i) NH<sub>4</sub>OH + NH<sub>4</sub>Cl, (ii) NH<sub>4</sub>OH + NH<sub>4</sub>NO3, (iii) Glycine + Glycine hydrochloride

### (c) Simple Buffer:

It is formed by a mixture of acid salt and normal salt of a polybasic acid,

example  $Na_2HPO_4 + Na_3PO_4$ 

Or a salt of weak acid and a weak base. Example: CH<sub>3</sub>COONH<sub>4</sub>

### (a) Acidic Buffer:

It is the mixture of CH<sub>3</sub>COOH and CH<sub>3</sub>COONa in aqueous solution.

 $CH_3COOH \rightleftharpoons CH_3COO^- + H^+$  (incomplete dissociation)

 $CH_3COONa \rightarrow CH_3COO^- + Na^+$  (complete dissociation)

 $H_2O \rightleftharpoons H^+ + OH^-$  (incomplete dissociation)

Action of acid: when a drop of stong acid (HCl) is added in the above buffer solution H+ ions combine with CH3COO- ions to form feebly ionised CH3COOH. Whose ionisation is further suppressed due to common ion effect. So pH of the solution unaltered.

Action of base: when a drop of strong base (NaOH) is added to the above buffer solution it react with free acid to form undissociated water molecules. So pH of the solution unaltered.

 $CH_3COOH + OH^- \leftrightarrows CH_3COO^- + H_2O$ 

(b) Basic Buffer:

It is the mixture of NH<sub>4</sub>OH and NH<sub>4</sub>Cl in aqueous solution.

 $NH_4OH \rightleftharpoons NH_4^+ + OH^-$  (incomplete dissociation)

 $NH_4Cl \rightarrow NH_4^+ + Cl^-$  (complete dissociation)

 $H_2O \rightleftharpoons H^+ + OH^-$  (incomplete dissociation)

Action of acid: when a drop of HCl is added, the added H+ ions combine with NH4OH to form undissociated water molecules. So the pH of buffer is unaffected.

 $NH_4OH + OH^- \rightleftharpoons NH_4^+ + H_2O$ 

Action of base: when a drop of NaOH is added, the added  $OH^-$  ions combine with  $NH_4^+$  ions to form feebly ionised  $NH_4OH$ . It is further suppressed due to common ion effect. So the pH of buffer is unaffected.

## Hendersion's Equation (pH of buffer)

(a) Acidic Buffer:

It is a mixture of CH<sub>3</sub>COOH and CH<sub>3</sub>COONa

#### $\mathrm{CH_3COOH}\leftrightarrows\mathrm{CH_3COO^-}+\mathrm{H^+}$

#### $CH_3COONa \rightarrow CH_3COO^- + Na^+$

By the law of chemical equilibrium,  $K_a = \{[CH_3COO^-] [H^+]\} / [CH_3COOH]$ 

 $\therefore [H^{\scriptscriptstyle +}] = \{K_a [CH_3COOH]\} / [CH_3COO^{\scriptscriptstyle -}]$ 

 $[H^+] = \{K_a [Acid]\} / [salt]$ 

Taking negative log both sides, we obtain that

 $-\log[H^{\scriptscriptstyle +}] = -\log K_{\scriptscriptstyle a} - \log K_{\scriptscriptstyle a} [Acid] \} / [salt]$ 

 $pH = pK_a + \log \{ \{ salt ] / [acid] \}$ 

 $pH = pK_a + log \{[salt] / [acid]\}$ 

This equation is known as Hendersion's Equation

Where,  $K_a = dissociation constant$ 

 $[CH_3COO^-]$  = initial concentration of salt

[CH<sub>3</sub>COOH] = initial concentration of acid

(b) Basic Buffer:

It is a mixture of NH<sub>4</sub>OH and NH<sub>4</sub>Cl

 $NH_4OH \leftrightarrows NH_4^+ + OH^-$ 

 $NH_4Cl \rightarrow NH_4^{_+} + Cl^-$ 

By the law of chemical equilibrium,  $K_b = \{[NH_4^+] [OH^-]\} / [NH_4OH]$ 

 $\therefore [OH^{\scriptscriptstyle -}] = \left\{ K_{\scriptscriptstyle b} \left[ NH_4 OH \right] \right\} / \left[ NH_4^{\scriptscriptstyle +} \right]$ 

Taking negative log both sides, we obtain that

 $-\log [OH^{-}] = -\log K_{b} - \log \{[base] / [salt]\}$ 

 $pOH = pK_b + log \{ [salt] / [base] \}$ 

 $pOH = pK_b + log \{[salt] / [base]\}$ This equation is known as **Hendersion's Equation**  Where,  $K_{b} = dissociation constant$ 

 $[NH_4^+]$  = initial concentration of salt  $[NH_4OH]$  = initial concentration of base

### pH + pOH = 14

# **Buffer capacity**

Buffer capacity is defined as the number of moles of acid or base added in one litre of solution as to change the pH by unity.

Buffer capacity ( $\Phi$ ) = No. of moles of acid or base added to 1 litre solution/change in pH

```
\Phi = \partial b / \partial (pH)
```

Where  $\partial b$  – No. of moles of acid or base added to 1 litre

 $\partial(pH)$  – change in pH

## **Applications of Buffer in chemistry**

(i) Buffers are used in industrial processes such as manufacture of paper, dyes, inks, paints, drugs, etc.

(ii) Buffers are also employed in agriculture, dairy products and preservation of various types of foods and fruits.

(iii) It is used to determine the pH with the help of indicators.

(iv) Blood is the natural buffer, it maintenance of pH is essential to sustain life because enzyme catalysis is pH sensitive process. The normal pH of blood plasma is 7.4.

(v) For the removal of phosphate ion in the qualitative inorganic analysis after the second group using  $CH_3COOH + CH_3COONa$  buffer.

### **Buffer action**

**Buffer action,** in general, is defined as the ability of the buffer solution to resist the changes in pH value when a small amount of an acid or a base is added to it.

### **Mechanism of Buffering Action**

To understand the mechanism of buffer action, we can take the example of an acidic buffer that is made up of a weak acid like <u>acetic acid</u> and its sodium salt, sodium acetate. In this acidic buffer, the solution contains equimolar amounts of acetic acid and sodium acetate. Usually, a large number of sodium ions (Na<sup>+</sup>), acetate ions (CH<sub>3</sub>COO<sup>-</sup>) and undissociated acetic acid molecules are present.

The salt exists completely as ions.



Here, the buffer will consist of both acid (CH<sub>3</sub>COOH) and its conjugate base (CH<sub>3</sub>COO<sup>-</sup>). If we add a small quantity of acid, the hydrogen ions will be removed by the conjugate base (CH<sub>3</sub>COO<sup>-</sup>). It is represented as follows:

### $H+(aq) + CH3COO-(aq) \leftrightarrow CH3COOH(aq)$

Here, the ethanoic acid will only be slightly dissociated in the form of CH<sub>3</sub>COOH, which means that it will not contribute any H+ ions. Therefore, the pH of the resulting solution will remain more or less constant. The added H+ ions are also removed, due to which there is no appreciable decrease in pH

The reaction comes to a completion as  $CH_3COOH$  is a weak acid whose ions have a strong tendency to form non-ionised  $CH_3COOH$  molecules. On the other hand, if we add a strong base, the  $OH^-$  ion gets neutralised by the reaction with the acid in the buffer,

### $CH_3COOH (aq) + OH- (aq) \rightarrow CH_3COO- (aq) + H_2O (l).$

We can also consider that the  $OH^-$  ion can react with the  $H^+$  ion in order to form water. The  $OH^-$  ions that are added are removed, wherein the acid equilibrium shifts to the right to replace the  $H^+$  ions that are exhausted. This results in a minor change in the pH value.

Alternatively, if we add a drop of NaOH, the OH<sup>-</sup> ions react with the free acid to give undissociated water molecules. The extra OH<sup>-</sup> ions of the base are neutralised. As a result, the pH of the solution remains the same. This condition, or the resistance offered by the pH when a base is added, is known as reserve acidity. This is mainly due to  $CH_3COOH$ .

If we add a strong base, the acid present in the buffer neutralises the hydroxide ions (OH<sup>-</sup>).

So, we can say that when acid or base is added, its effect is practically balanced, and the pH of the solution is always constant.

### Key Points to Remember

If we take a solution, the salt will be completely ionised, and the weak acid will be partly ionised.

- $CH_3COONa \rightleftharpoons Na++CH_3COO-$
- $CH_3COOH \rightleftharpoons H++CH_3COO-$

### On Addition of Acid and Base

1. When acid is added, the protons of acid that are released will be removed by the acetate ions to form an acetic acid molecule.

 $H^+ + CH_3COO^-$  (from added acid)  $\rightleftharpoons CH_3COOH$  (from buffer solution)

2. When a base is added, the hydroxide that is released by the base will be removed by the hydrogen ions to form water.

HO- + H+ (from added base)  $\rightleftharpoons$  H<sub>2</sub>O (from buffer solution)

### UNIT 4

### What are Lipids?

These organic compounds are nonpolar molecules, which are soluble only in nonpolar solvents and insoluble in water because water is a polar molecule. In the human body, these molecules can be synthesized in the liver and are found in oil, butter, whole milk, cheese, fried foods and also in some red meats.



### **Properties of Lipids**

Lipids are a family of organic compounds, composed of fats and oils. These molecules yield high energy and are responsible for different functions within the human body. Listed below are some important characteristics of Lipids.

- 1. Lipids are oily or greasy nonpolar molecules, stored in the adipose tissue of the body.
- 2. Lipids are a heterogeneous group of compounds, mainly composed of hydrocarbon chains.
- 3. Lipids are energy-rich organic molecules, which provide energy for different life processes.
- 4. Lipids are a class of compounds characterised by their solubility in nonpolar solvents and insolubility in water.
- 5. Lipids are significant in biological systems as they form a mechanical barrier dividing a cell from the external environment known as the cell membrane.

### **Lipid Structure**

Lipids are the polymers of fatty acids that contain a long, non-polar hydrocarbon chain with a small polar region containing oxygen. The lipid structure is explained in the diagram below:



Lipid Structure - Saturated and Unsaturated Fatty Acids

### **Classification of Lipids**

Lipids can be classified into two main classes:

- Nonsaponifiable lipids
- Saponifiable lipids

Nonsaponifiable Lipids

A nonsaponifiable lipid cannot be disintegrated into smaller molecules through hydrolysis. Nonsaponifiable lipids include cholesterol, prostaglandins, etc

Saponifiable Lipids

A saponifiable lipid comprises one or more ester groups, enabling it to undergo hydrolysis in the presence of a base, acid, or <u>enzymes</u>, including waxes, triglycerides, sphingolipids and phospholipids.

Further, these categories can be divided into non-polar and polar lipids.

Nonpolar lipids, namely triglycerides, are utilized as fuel and to store energy.

Polar lipids, that could form a barrier with an external water environment, are utilized in membranes. Polar lipids comprise sphingolipids and glycerophospholipids.

Fatty acids are pivotal components of all these lipids.



### **Types of Lipids**

Within these two major classes of lipids, there are numerous specific types of lipids, which are important to life, including fatty acids, triglycerides, glycerophospholipids, sphingolipids and steroids. These are broadly classified as simple lipids and complex lipids.

Simple Lipids

Esters of fatty acids with various alcohols.

- 1. Fats: Esters of fatty acids with glycerol. Oils are fats in the liquid state
- 2. Waxes: Esters of fatty acids with higher molecular weight monohydric alcohols

### Complex Lipids

Esters of fatty acids containing groups in addition to alcohol and fatty acid.

- 1. **Phospholipids**: These are lipids containing, in addition to fatty acids and alcohol, phosphate group. They frequently have nitrogen-containing bases and other substituents, eg, in glycerophospholipids the alcohol is glycerol and in sphingophospholipids the alcohol is sphingosine.
- 2. Glycolipids (glycosphingolipids): Lipids containing a fatty acid, sphingosine and carbohydrate.
- 3. **Other complex lipids**: Lipids such as sulfolipids and amino lipids. Lipoproteins may also be placed in this category.

### Precursor and Derived Lipids

These include fatty acids, glycerol, steroids, other alcohols, fatty aldehydes, and ketone bodies, hydrocarbons, lipid-soluble vitamins, and hormones. Because they are uncharged, acylglycerols (glycerides), cholesterol, and cholesteryl esters are termed neutral lipids. These compounds are produced by the hydrolysis of simple and complex lipids.

Some of the different types of lipids are described below in detail.

### Fatty Acids

Fatty acids are carboxylic acids (or organic acid), usually with long aliphatic tails (long chains), either unsaturated or saturated.

### • Saturated fatty acids

Lack of carbon-carbon double bonds indicate that the fatty acid is saturated. The saturated fatty acids have higher melting points compared to unsaturated acids of the corresponding size due to their ability to pack their molecules together thus leading to a straight rod-like shape.

### • Unsaturated fatty acids

Unsaturated fatty acid is indicated when a fatty acid has more than one double bond.

"Often, naturally occurring fatty acids possesses an even number of carbon atoms and are unbranched."

On the other hand, unsaturated fatty acids contain a cis-double bond(s) which create a structural kink that disables them to group their molecules in straight rod-like shape.

### Role of Fats

Fats play several major roles in our body. Some of the important roles of fats are mentioned below:

- Fats in the correct amounts are necessary for the proper functioning of our body.
- Many fat-soluble vitamins need to be associated with fats in order to be effectively absorbed by the body.
- They also provide insulation to the body.
- They are an efficient way to store energy for longer periods

### **Examples of Lipids**

There are different types of lipids. Some examples of lipids include butter, ghee, vegetable oil, cheese, cholesterol and other steroids, waxes, phospholipids, and fat-soluble vitamins. All these compounds have similar features, i.e. insoluble in water and soluble in organic solvents, etc.

#### Waxes

Waxes are "esters" (an organic compound made by replacing the hydrogen with acid by an alkyl or another organic group) formed from long-alcohols and long-chain carboxylic acids.

Waxes are found almost everywhere. The fruits and leaves of many plants possess waxy coatings, that can safeguard them from small predators and dehydration.

Fur of a few animals and the feathers of birds possess the same coatings serving as water repellants.

Carnauba wax is known for its water resistance and toughness (significant for car wax).

### Phospholipids



Membranes are primarily composed of phospholipids that are Phosphoacylglycerols.

Triacylglycerols and phosphoacylglycerols are the same, but, the terminal OH group of the phosphoacylglycerol is esterified with phosphoric acid in place of fatty acid which results in the formation of phosphatidic acid.

The name phospholipid is derived from the fact that phosphoacylglycerols are lipids containing a phosphate group.

### Steroids

Our bodies possess chemical messengers known as **hormones**, which are basically organic compounds synthesized in glands and transported by the bloodstream to various tissues in order to trigger or hinder the desired process.

Steroids are a kind of hormone that is typically recognized by their tetracyclic skeleton, composed of three fused six-membered and one five-membered ring, as seen above. The four rings are assigned as A, B, C & D as observed in the shade blue, while the numbers in red indicate the carbons.

### Cholesterol

- Cholesterol is a wax-like substance, found only in animal source foods. Triglycerides, LDL, HDL, VLDL are different types of cholesterol found in the blood cells.
- Cholesterol is an important lipid found in the cell membrane. It is a sterol, which means that cholesterol is a combination of steroid and alcohol. In the human body, cholesterol is synthesized in the liver.
- These compounds are biosynthesized by all living cells and are essential for the structural component of the cell membrane.
- In the cell membrane, the steroid ring structure of cholesterol provides a rigid hydrophobic structure that helps boost the rigidity of the cell membrane. Without cholesterol, the cell membrane would be too fluid.
- It is an important component of cell membranes and is also the basis for the synthesis of other steroids, including the sex hormones estradiol and testosterone, as well as other steroids such as cortisone and vitamin D.

What is Fatty Acid Metabolism?

Fatty acids are long-chain hydrocarbon molecules that serve as a major source of energy for cells. They can be obtained through the diet or synthesized endogenously. The metabolism of fatty acids involves several interconnected pathways, including fatty acid oxidation (beta-oxidation), fatty acid synthesis (lipogenesis), and the synthesis and degradation of complex lipids such as triglycerides and phospholipids.



(a) Fatty acid chains. (b) Lipid molecules. (Halimet al., 2012)

#### **Fatty Acid Oxidation**

Activation and Transport: In the cytoplasm, fatty acids are activated by conjugating with coenzyme A (CoA) to generate fatty acyl-CoA. Carnitine and the enzyme carnitine palmitoyltransferase I (CPT1) then help transport the fatty acyl-CoA through the mitochondrial membrane.

**Beta-Oxidation Steps:** Once inside the mitochondria, fatty acyl-CoA undergoes a series of four enzymatic reactions, collectively known as beta-oxidation. In each cycle of beta-oxidation, two carbon units are sequentially removed from the fatty acyl-CoA molecule. These steps include oxidation, hydration, oxidation, and thiolysis, resulting in the generation of acetyl-CoA, NADH, and FADH2.

**Acetyl-CoA Utilization:** Acetyl-CoA generated during beta-oxidation enters the tricarboxylic acid (TCA) cycle, also known as the Krebs cycle, where it undergoes further oxidation to produce additional NADH, FADH2, and ATP. The NADH and FADH2 molecules subsequently participate in the electron transport chain (ETC) to generate ATP through oxidative phosphorylation.

**Regulation:** Fatty acid oxidation is tightly regulated by various factors to ensure a balanced energy supply. The key regulatory enzyme, carnitine palmitoyltransferase I (CPT1), controls the entry of fatty acids into the mitochondria. Hormones such as glucagon and epinephrine stimulate fatty acid oxidation, whereas insulin inhibits it, favoring other metabolic pathways.

#### **Fatty Acid Synthesis**

Fatty acid synthesis, or lipogenesis, is the process by which excess carbohydrates are converted into fatty acids. It predominantly occurs in the cytoplasm and involves several enzymatic steps.

Acetyl-CoA Carboxylation: The first committed step in fatty acid synthesis is the conversion of acetyl-CoA to malonyl-CoA. This reaction is catalyzed by the enzyme acetyl-CoA carboxylase (ACC), which adds a bicarbonate molecule to acetyl-CoA in the presence of ATP and biotin as a cofactor. Malonyl-CoA is the building block for fatty acid synthesis. Fatty Acid Synthase (FAS) Complex: Fatty acid synthase is a large, multifunctional enzyme complex responsible for the synthesis of long-chain fatty acids. The FAS complex consists of multiple enzymatic domains, including acyl carrier protein (ACP), ketoacyl synthase (KS), ketoacyl reductase (KR), and enoyl reductase (ER).

**Fatty Acid Elongation:** The FAS complex catalyzes a series of reactions to sequentially add two-carbon units from malonyl-CoA to the growing fatty acid chain. These reactions include condensation, reduction, dehydration, and reduction again, leading to the formation of a saturated fatty acid chain.

**Desaturation:** If unsaturated fatty acids are required, additional enzymatic steps are involved. Desaturases introduce double bonds into the fatty acid chain at specific positions. These enzymes are responsible for the synthesis of important polyunsaturated fatty acids, such as omega-3 and omega-6 fatty acids, which cannot be synthesized by the human body and must be obtained from the diet.

### **Regulation of Fatty Acid Metabolism**

Fatty acid metabolism is tightly regulated to maintain energy homeostasis and adapt to different nutritional conditions. Various enzymes, signaling pathways, and hormones play critical roles in controlling fatty acid oxidation and synthesis.

**Hormonal Regulation:** Insulin, which is released in response to high blood glucose levels, increases lipogenesis by activating important fatty acid synthesis enzymes such as ACC and FAS. Insulin also inhibits fatty acid oxidation by reducing the activity of beta-oxidation enzymes.

Glucagon, on the other hand, increases fatty acid oxidation when released during fasting or low blood glucose levels. It inhibits lipogenesis by inactivating ACC and FAS and stimulates beta-oxidation enzymes, boosting fatty acid breakdown for energy production.

Leptin is a hormone produced by adipose tissue that controls hunger and energy expenditure. It regulates food intake and modulates fatty acid metabolism via acting on the hypothalamus.

AMP-Activated Protein Kinase (AMPK): AMPK acts as a sensor of cellular energy status and is activated under conditions of low energy availability, such as during fasting or exercise. AMPK phosphorylates and inhibits ACC, the key enzyme in fatty acid synthesis, reducing malonyl-CoA levels and inhibiting lipogenesis. Simultaneously, AMPK activates enzymes involved in fatty acid oxidation, enhancing energy production from fatty acids. **Transcriptional Regulation:** A number of transcription factors are important in regulating fatty acid metabolism. Peroxisome proliferator-activated receptors (PPARs), for example, are ligand-activated transcription factors that regulate the expression of fatty acid oxidation genes. Sterol regulatory element-binding proteins (SREBPs) regulate gene expression in fatty acid production and absorption.

### **Applications of Fatty Acid Metabolism**

Fatty acid metabolism has important implications in various aspects of human health and disease. Here are some notable applications:

Obesity and Weight Management: Understanding the regulation of fatty acid metabolism is crucial for developing strategies to manage obesity and promote weight loss. Targeting enzymes and signaling pathways involved in fatty acid synthesis and oxidation can potentially modulate energy balance and promote fat utilization.

Diabetes and Metabolic Syndrome: Dysregulation of fatty acid metabolism is closely linked to insulin resistance and the development of type 2 diabetes. Studying the intricate mechanisms of fatty acid metabolism can help identify therapeutic targets for managing glucose and lipid metabolism and improving insulin sensitivity.

Cardiovascular Diseases: Abnormal fatty acid metabolism contributes to the development of cardiovascular diseases, including atherosclerosis and coronary artery disease. Understanding the underlying mechanisms can aid in identifying novel therapeutic approaches to prevent or treat these conditions.

Cancer Metabolism: Altered fatty acid metabolism is a hallmark of many cancer types. Cancer cells often exhibit enhanced lipogenesis and increased fatty acid uptake to meet their high energy demands. Targeting specific enzymes and transporters involved in fatty acid metabolism holds promise for developing novel anticancer therapies.



### **Detection of Fatty Acid Metabolism**

The detection and quantification of fatty acid metabolism rely heavily on mass spectrometry (MS). It has a high sensitivity, specificity, and can evaluate a wide variety of fatty acid species. Here are some examples of mass spectrometry-based approaches used to study fatty acid metabolism:

**Lipidomics:** MS-based lipidomics enables the identification and quantification of individual fatty acid species, including saturated, monounsaturated, and polyunsaturated fatty acids. Various MS techniques, such as electrospray ionization (ESI) and matrix-assisted laser desorption/ionization (MALDI), coupled with different mass analyzers, are employed for lipidomic analysis.

**Stable Isotope Tracer Experiments:** Stable isotope-labeled fatty acids combined with mass spectrometry allow for the investigation of fatty acid metabolism in vivo and in vitro. By administering labeled fatty acids and analyzing their incorporation into lipid pools or metabolic intermediates, researchers can track fatty acid uptake, oxidation, and synthesis. Isotope labeling combined with MS can provide quantitative insights into the kinetics and fluxes of fatty acid metabolism.

**Metabolomics:** MS-based metabolomics techniques, such as liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS), enable the profiling and quantification of fatty acid-related metabolites, such as acylcarnitines, acyl-CoAs, and other lipid-derived molecules. These metabolites serve as important indicators of fatty acid metabolism and its dysregulation in various diseases.

**Imaging Mass Spectrometry:** Imaging mass spectrometry (IMS) allows for the spatial visualization of fatty acids and their metabolites within tissue sections. Techniques such as MALDI imaging mass spectrometry (MALDI-IMS) enable the direct analysis and mapping of lipid distributions in biological samples. This approach provides valuable insights into the localization and changes in lipid metabolism in specific tissues or regions of interest.

Triglyceride Metabolism: Structure, Regulation, and Role in Metabolic Diseases

Triglycerides, commonly referred to as triacylglycerols, are a vital class of lipids present in living things. In numerous cells and tissues, they act as the main energy storage molecules. Glycerol and three fatty acids combine to produce triglycerides, which are hydrophobic and insoluble in water due to the ester linkages that result from their composition. Triglycerides' structure and chemical makeup, importance in lipid metabolism, metabolic pathways, and connection to metabolic illnesses will all be covered in detail in this extensive essay.

### **Structure and Chemical Properties of Triglycerides**

#### Composition of Triglyceride Molecules

Triglycerides consist of a glycerol backbone and three fatty acid chains. The glycerol molecule is a trihydric alcohol with three hydroxyl groups (-OH), and the fatty acids are long hydrocarbon chains with a carboxyl group (-COOH) at one end. The fatty acids are covalently bonded to the glycerol through ester linkages, resulting in the formation of triglycerides. The specific fatty acids attached to the glycerol backbone can vary, leading to a wide diversity of triglyceride molecules in biological systems.



molecule.

#### Importance in Lipid Metabolism

Triglycerides serve as the primary storage form of fatty acids in adipose tissue, allowing for efficient energy storage. When energy demands increase, such as during periods of fasting or physical activity, triglycerides are broken down into glycerol and fatty acids through a process called lipolysis. These released fatty acids can then be used as an energy source by various tissues, including skeletal muscles and the liver.

Triglycerides also play a crucial role in lipid transportation. They are packaged into lipoprotein particles in the liver and intestine for transport through the bloodstream. These lipoproteins, such as chylomicrons and very low-density lipoproteins (VLDL), facilitate the transport of triglycerides to peripheral tissues, where they are either stored or utilized as an energy source.

### **Triglyceride Metabolism Pathways**

### Synthesis, Degradation, and Transport of Triglycerides

Triglyceride synthesis predominantly occurs in the liver and adipose tissue. In the liver, excess dietary carbohydrates and proteins undergo de novo lipogenesis, a process that converts these substrates into fatty acids. These fatty acids, along with those obtained from the diet, subsequently combine with glycerol to form triglycerides. The newly synthesized triglycerides are incorporated into VLDL particles and released into the bloodstream for transportation to peripheral tissues.

In adipose tissue, triglycerides are synthesized using glycerol and fatty acids obtained from the bloodstream. These triglycerides serve as a vital energy storage reserve, accessible during periods of energy deficit or heightened energy demands.

The breakdown of triglycerides into glycerol and fatty acids is known as lipolysis. This process is primarily regulated by hormones like glucagon and adrenaline, which stimulate lipolysis during fasting or stressful situations. The released glycerol and fatty acids can then be utilized as an energy source by various tissues.

Key Enzymes and Regulation of Fatty Acid Synthesis and Breakdown

The synthesis and breakdown of triglycerides are tightly regulated by a series of enzymes and signaling pathways. Key enzymes involved in fatty acid synthesis include acetyl-CoA carboxylase (ACC), fatty acid synthase (FAS), and acyl-CoA synthetase. These enzymes catalyze the stepwise addition of carbon atoms to form long-chain fatty acids.

On the other hand, lipolysis, or triglyceride breakdown, is regulated by enzymes such as hormone-sensitive lipase (HSL) and adipose triglyceride lipase (ATGL). These enzymes hydrolyze triglycerides into glycerol and free fatty acids, which can then be released into the bloodstream.

The regulation of triglyceride metabolism is influenced by various factors, including nutritional status, hormonal signaling, and genetic factors. Dysregulation of these processes can lead to metabolic disorders such as obesity and type 2 diabetes.

### Lipid Metabolism and Metabolic Diseases

### Triglycerides and Metabolic Disorders

Hypertriglyceridemia, characterized by elevated levels of triglycerides in the bloodstream, is frequently associated with metabolic disorders. Among these, obesity stands out as one of the most prevalent conditions linked to high triglyceride levels. Obesity is characterized by the excessive accumulation of adipose tissue due to an imbalance between energy intake and expenditure. In individuals with obesity, adipose tissue becomes insulin resistant, which subsequently leads to increased lipolysis. As a result, free fatty acids and glycerol are released into the bloodstream, contributing to the development of hypertriglyceridemia.



Cholesterol and triglyceride metabolism, and molecular mechanisms of lipid-lowering drugs (Zodda et al., 2018).

### Triglycerides and Cardiovascular Disease

High triglyceride levels are also linked to an increased risk of cardiovascular conditions such as atherosclerosis, coronary heart disease, and stroke. The development of atherosclerotic plaques and inflammation inside artery walls have both been associated with high triglyceride levels. Triglyceride-rich lipoproteins, like VLDL, have also been proven to encourage atherosclerosis and contribute to the emergence of cardiovascular problems.

### **Measurement and Analysis Techniques**

Accurate <u>cmeasurement and analysis of triglyceride levels</u> are essential for understanding lipid metabolism and its implications in health and disease. Various laboratory techniques and instruments are commonly used for measuring triglyceride levels in biological samples.

### Gas Chromatography (GC)

Gas chromatography (GC) is an effective analytical method for determining the concentration of specific fatty acids inside triglyceride molecules. Triglycerides are first transmethylated into fatty acid methyl esters (FAMEs) in this process. Gas chromatography is then used to separate the FAMEs depending on physical parameters such as boiling temperatures and polarity. A flame ionization detector (FID) is often used for detection.

Individual fatty acids may be identified and quantified by GC, providing useful information on the fatty acid composition of triglycerides in a sample. It is frequently employed in research investigations and specialist lipid analysis.

### High-Performance Liquid Chromatography (HPLC)

High-performance liquid chromatography (HPLC) is another versatile technique used for triglyceride analysis. HPLC separates components in a mixture based on their interactions with a stationary phase and a mobile phase. For triglyceride analysis, the triglycerides are typically extracted from the sample and separated on an HPLC column. Detection is often done using ultraviolet (UV) or refractive index detectors.

HPLC provides excellent sensitivity and resolution, allowing for the identification and quantification of triglycerides in complex mixtures. It is commonly used in research and clinical settings for lipid analysis.

### Mass Spectrometry (MS)

Mass spectrometry (MS) is a strong method for analyzing triglycerides and their fatty acid content. Triglycerides are ionized and broken into charged ions in MS, and then separated depending on their mass-to-charge ratios.

Tandem mass spectrometry (MS/MS) is a popular technique for lipid research since it permits the identification of specific fatty acids inside triglyceride molecules. MS/MS may also be utilized to explore lipid metabolic pathways using stable isotope-labeled tracers.

MS methods, such as liquid chromatography-mass spectrometry (LC-MS), are commonly employed in <u>lipidomics research</u> because they provide useful insights into complicated lipid profiles and metabolic pathways.

### Data Analysis Methods

Data analysis in triglyceride research involves statistical methods to interpret experimental results and draw meaningful conclusions. Various statistical tools, such as t-tests, ANOVA (analysis of variance), and regression analysis, are commonly used to assess differences between groups and correlations between variables.

Graphical representations, such as bar charts, line graphs, scatter plots, and heatmaps, are employed to visualize data and trends effectively. Data visualization helps researchers and clinicians to better understand the relationships between triglyceride levels and other parameters, such as age, body mass index (BMI), or disease status.

Advanced bioinformatics tools and software are also utilized for lipidomics data analysis, enabling the identification of specific lipid species and metabolic pathways associated with triglyceride metabolism.

### **Regulation Mechanisms of Triglyceride Metabolism**

### Gene Expression Regulation

The control of gene expression is a fundamental mechanism in triglyceride metabolism regulation. Transcription factors play a pivotal role in this process by modulating the expression of genes involved in triglyceride synthesis, storage, and breakdown.

### **Transcription Factors in Triglyceride Metabolism**

Several transcription factors are central players in regulating triglyceride metabolism:

- SREBPs (sterol regulatory element-binding proteins): SREBPs are important lipid biosynthesis regulators. SREBPs are activated and translocate to the nucleus when cellular lipid levels are low, where they bind to sterol regulatory elements (SREs) in the promoters of lipid metabolism genes. This promotes lipid storage by upregulating genes involved in fatty acid and triglyceride production.
- PPARs (peroxisome proliferator-activated receptors): PPARs are a transcription factor family that regulates lipid metabolism and energy homeostasis. Fatty acids and their derivatives activate PPARs, which govern the activation of genes involved in fatty acid absorption, storage, and oxidation.

### Non-coding RNAs in Triglyceride Metabolism

Non-coding RNAs, such as microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), also contribute to the regulation of triglyceride metabolism. These small RNAs can interact with mRNA and modulate gene expression.

- miRNAs: miRNAs can target specific mRNAs and inhibit their translation or induce their degradation. Some miRNAs are involved in the post-transcriptional regulation of lipid metabolism genes, affecting processes like lipogenesis and lipolysis.
- lncRNAs: lncRNAs play a role in gene regulation by interacting with chromatinmodifying proteins and transcription factors. Some lncRNAs have been implicated in the regulation of lipid metabolism genes and pathways.

Signaling Pathways in Triglyceride Metabolism

Various signaling pathways respond to cellular and environmental cues, regulating triglyceride metabolism to match the body's metabolic needs.

### **Insulin Signaling Pathway**

A key factor in controlling triglyceride metabolism is the hormone insulin, which is secreted in reaction to high blood glucose levels. Insulin encourages fatty acid and glucose absorption in adipose tissue, which facilitates the production and storage of triglycerides. Inhibiting lipolysis, which stops triglycerides from being broken down into fatty acids, is another effect. Insulin helps the liver absorb more glucose and fatty acids, which helps to synthesize triglycerides and slows down the oxidation of fatty acids. Hepatic lipid buildup is subsequently elevated as a result.

### **Glucagon Signaling Pathway**

Glucagon, a hormone released in response to low blood glucose levels, opposes the actions of insulin. It stimulates lipolysis in adipose tissue, breaking down triglycerides into fatty acids and glycerol, which are released into the bloodstream for energy production in other tissues. In the liver, glucagon promotes the breakdown of stored glycogen into glucose and stimulates gluconeogenesis, leading to increased fatty acid oxidation and energy production.

### AMP-activated Protein Kinase (AMPK) Pathway

AMPK is a master regulator of cellular energy homeostasis. It is activated in response to low cellular energy levels, indicated by a high AMP/ATP ratio. Activated AMPK stimulates fatty acid oxidation and inhibits lipogenesis, promoting energy production and conservation.

Role of Triglyceride Metabolism Regulation at the Cellular and Organ Levels

The regulation of triglyceride metabolism plays a crucial role at both the cellular and organ levels.

### **Cellular Level**

At the cellular level, triglyceride metabolism regulation ensures that lipid synthesis and breakdown are well-balanced to match the cell's energy demands and nutrient availability. Transcription factors, such as SREBPs and PPARs, coordinate the expression of genes involved in lipid metabolism, tailoring cellular triglyceride levels to meet metabolic requirements.

AMPK acts as a cellular energy sensor, adjusting triglyceride metabolism based on the cellular energy status. When energy levels are low, AMPK is activated, promoting fatty acid oxidation to generate energy while inhibiting fatty acid and triglyceride synthesis to conserve energy.

### **Organ Level**

At the organ level, the regulation of triglyceride metabolism ensures the harmonious coordination of lipid storage and utilization among different tissues.

In adipose tissue, triglycerides are stored during periods of energy excess and mobilized during energy demand. Hormones like insulin and glucagon modulate lipolysis and lipogenesis to regulate triglyceride storage and release. In the liver, triglycerides are synthesized from excess glucose and fatty acids and transported in lipoproteins to other tissues for energy utilization. The liver also plays a critical role in lipid metabolism regulation and cholesterol synthesis.

### **Cholesterol Metabolism**

Lipid and Lipoprotein Metabolism (Rosensen, 2009)

Lipids = cholesterol and triglyceride - are insoluble in plasma and are transported in lipoproteins.
Functions = energy utilization, steroid hormone production, bile acid production, lipid deposition.

Lipoprotein consists of esterified and unesterified cholesterol, triglycerides, phospholipids and apolipoproteins. The proteins function as cofactors and ligands for receptors.



Major lipoproteins include:

- 1. Chylomicrons large particles that carry dietary lipid
- 2. Very low density lipoprotein carry endogenous triglyceride and some cholesterol
- 3. Intermediate density lipoprotein carry cholesterol esters and triglycerides
- 4. Low density lipoprotein carry cholesterol esters
- 5. High density lipoprotein carry cholesterol esters

Exogenous pathway for lipid metabolism:

- 1. Dietary cholesterol and fatty acids are absorbed.
- 2. Triglycerides are formed in the intestinal cell from free fatty acids and glycerol and cholesterol is esterified.
- 3. Triglycerides and cholesterol combine to form chylomicrons.
- 4. Chylomicrons enter the circulation and travel to peripheral sites.
- 5. In peripheral tissues, free fatty acids are released from the chylomicrons to be used as energy, converted to triglyceride or stored in adipose.
- 6. Remnants are used in the formation of HDL.

Endogenous pathway for lipid metabolism:

- 1. VLDL is formed in the liver from triglycerides and cholesterol esters.
- 2. These can be hydrolyzed by lipoprotein lipase to form IDL or VLDL remnants.
- 3. VLDL remnants are cleared from the circulation or incorporated into LDL.
- 4. LDL particles contain a core of cholesterol esters and a smaller amount of triglyceride.
- 5. LDL is internalized by hepatic and nonhepatic tissues.
- 6. In the liver, LDL is converted into bile acids and secreted into the intestines.

- 7. In non hepatic tissues, LDL is used in hormone production, cell membrane synthesis, or stored.
- 8. LDL is also taken up by macrophages and other cells which can lead to excess accumulation and the formation of foam cells which are important in plaque formation.

### What does HDL do?

HDL is a small particle composed of phospholipid and apolipoproteins and produced in hepatic and intestinal cells.

### Why is HDL good?

Incidence of coronary heart disease events in a normal population is inversely related to the serum HDL-cholesterol concentration - low levels carry an increased coronary risk

HDL is thought to be anti-atherogenic and high HDL levels are cardioprotective.

This effect may be mediated by reverse cholesterol transport, a process whereby excess cholesterol in cells and in atherosclerotic plaques is removed and transported back to the liver.

Risk for myocardial infarction increases by about 25 percent for every 5 mg/dL decrement in serum HDL-cholesterol below median values for men and women.

Low HDL-cholesterol is a component of the metabolic syndrome that is characterized by obesity, insulin resistance, dyslipidemia, and hypertension

Patients considered high risk for cardiovascular disease based on HDL levels include:

- Patients with HDL less than 40 mg/dL
- Patients with the metabolic syndrome gender adjusted HDL-cholesterol levels of less than 40 mg/dL in men and 50 mg/dL in women.

Exercise, weight loss (in overweight subjects), smoking cessation, and changes in diet (specifically substitution of monounsaturated for saturated fatty acids) all can raise HDL-cholesterol.

Medical treatment for low HDL includes niacin and fibrates.

## **Beta Oxidation of Fatty Acid**

Beta-oxidation is the catabolic process by which <u>fatty acid</u> molecules are broken down in the cytosol in prokaryotes and in the mitochondria in eukaryotes to generate acetyl-CoA. Acetyl-CoA enters the <u>citric acid cycle</u> while NADH and FADH<sub>2</sub>, which are coenzymes, are used in the electron transport chain. It is referred as "beta oxidation" because the beta carbon of the fatty acid undergoes oxidation to a carbonyl group.



## **BETA-OXIDATION OF FATTY ACID**



A key metabolic process that breaks down fatty acids and produces ATP and other compounds rich in energy is beta-oxidation. This activity takes place in cells' mitochondria and is crucial for maintaining energy balance, especially during fasting or vigorous exercise. We shall investigate the mechanism, control, and relevance of beta-oxidation in this article, focusing on its role in energy generation and metabolic diseases. The majority of the molecules that make up the human body's stores of energy are fatty acids. They are typically produced in the liver from dietary fats. Long hydrocarbon chains with a carboxyl group at one end make up fatty acids.

They can have one or more double bonds or be saturated (no double bonds). A large energy reserve known as adipose tissue contains triglycerides, which are fatty acids. The triglycerides that have been stored are converted into fatty acids and glycerol when energy demands rise, such as during fasting or physical activity. Energy generation depends on the following breakdown of fatty acids via beta-oxidation.

Mechanism of Beta-oxidation of Fatty Acid

Beta-oxidation of fatty acids occurs in several stages, with each stage taking place in specific tissues within the body. Let's explore the stages and tissues involved in the beta-oxidation process.

Stage 1: Activation and Transport of Fatty Acids

The first stage of beta-oxidation involves the activation and transport of fatty acids. This step occurs in the cytoplasm of cells.

### 1. Activation

- Fatty acids, whether derived from dietary intake or adipose tissue mobilization, undergo activation before entering the mitochondria.
- In this process, fatty acyl-CoA synthetase enzymes activate fatty acids by coupling them with coenzyme A (CoA).
- This reaction requires the hydrolysis of ATP, resulting in the formation of fatty acyl-CoA molecules.

### 2. Transport

- The activated fatty acyl-CoA molecules are transported across the mitochondrial membrane to enter the mitochondrial matrix, where beta-oxidation takes place.
- This transport is facilitated by a specific transport protein called carnitine palmitoyltransferase I (CPT-I), located in the outer mitochondrial membrane.
- CPT-I catalyzes the exchange of CoA with carnitine, allowing the fatty acyl-carnitine to traverse the mitochondrial membrane.
- Once inside the mitochondrial matrix, another enzyme, carnitine palmitoyltransferase II (CPT-II), converts the fatty acyl-carnitine back into fatty acyl-CoA, ready for beta-oxidation.

Stage 2: Beta-Oxidation Cycle

The second stage involves the actual beta-oxidation cycle, where fatty acids undergo a series of reactions to generate acetyl-CoA units. This stage occurs within the mitochondrial matrix.

**1. Oxidation:** The fatty acyl-CoA undergoes a series of oxidation reactions, resulting in the removal of two carbon atoms in the form of acetyl-CoA. The first step involves the oxidation of the fatty acyl-CoA by acyl-CoA dehydrogenase, which introduces a double bond between the alpha and beta carbons of the fatty acid chain. This generates trans-enoyl-CoA.

**2. Hydration:** The trans-enoyl-CoA molecule undergoes hydration catalyzed by enoyl-CoA hydratase, also known as crotonase. This step adds a water molecule across the double bond, resulting in the formation of L-3-hydroxyacyl-CoA.

3. Dehydrogenation: The L-3-hydroxyacyl-CoA is further oxidized by L-3-hydroxyacyl-

CoA dehydrogenase, generating 3-ketoacyl-CoA. This step involves the transfer of electrons to NAD+, producing NADH.

**4. Thiolytic Cleavage:** The final step of the beta-oxidation cycle involves the cleavage of the 3-ketoacyl-CoA by beta-keto thiolase. This cleavage generates acetyl-CoA and a shorter fatty

acyl-CoA chain, which is two carbons shorter than the original fatty acid. The shorter fatty acyl-CoA then re-enters the beta-oxidation cycle, repeating the series of reactions until the entire fatty acid is oxidized.

Stage 3: Generation of ATP and Metabolic Intermediates

- The acetyl-CoA molecules generated through beta-oxidation can enter the citric acid cycle (also known as the Krebs cycle or TCA cycle) to produce ATP through oxidative phosphorylation.
- This stage occurs in the mitochondrial matrix. The acetyl-CoA molecules derived from beta-oxidation enter the citric acid cycle, where they undergo a series of reactions, producing reducing equivalents (NADH and FADH2) and GTP (which can be converted to ATP).
- These reducing equivalents are utilized in the electron transport chain to generate ATP through oxidative phosphorylation.

**Tissues Involved in Beta-Oxidation** 

Beta-oxidation occurs in various tissues within the body, depending on the specific energy demands and metabolic states.

**1. Liver:** The liver is a significant site of fatty acid oxidation, particularly during fasting. It plays a crucial role in mobilizing fatty acids from stored triglycerides in response to energy needs and producing ketone bodies as an alternative fuel source.

**2. Skeletal Muscle:** Skeletal muscle is another important tissue for beta-oxidation. During periods of exercise or increased energy demands, skeletal muscle utilizes fatty acids as a source of fuel for ATP production.

**3.** Adipose Tissue: Adipose tissue primarily functions as a storage site for triglycerides. However, during energy deficit or fasting, adipose tissue releases stored fatty acids through lipolysis, which can be taken up and oxidized by other tissues for energy production.

**4. Cardiac Muscle:** The heart relies heavily on fatty acid oxidation for energy production, as it has a high energy demand. Beta-oxidation provides a significant portion of ATP to support the continuous contraction and relaxation of the cardiac muscle.

Beta-oxidation of fatty acids occurs in multiple stages, starting with the activation and transport of fatty acids, followed by the beta-oxidation cycle within the mitochondria. This process generates acetyl-CoA units, which can be further metabolized in the citric acid cycle to produce ATP. Different tissues, including the liver, skeletal muscle, adipose tissue, and cardiac muscle, contribute to the overall beta-oxidation process, depending on energy demands and metabolic requirements.

### **Role of Fatty Acids in Regulation of Beta-Oxidation**

The supply of fatty acids plays a significant role in regulating fatty acid beta-oxidation. The availability of fatty acids for oxidation depends on various factors, including dietary intake, adipose tissue mobilization, and de novo lipogenesis. The regulation of fatty acid supply ensures the appropriate balance between energy utilization and storage in the body.

- 1. Dietary Intake
  - The consumption of dietary fats provides a source of exogenous fatty acids for betaoxidation.
  - The composition of the diet, particularly the types of fatty acids consumed, can influence the regulation of beta-oxidation.
  - Saturated fatty acids, which lack double bonds, are more easily metabolized compared to unsaturated fatty acids with one or more double bonds.
  - Additionally, the length of the fatty acid chain affects its oxidation rate, with shorterchain fatty acids being oxidized more readily.
- 2. Adipose Tissue Mobilization
  - During periods of energy deficit or fasting, adipose tissue serves as a crucial reservoir of stored triglycerides.
  - Hormonal signals, such as glucagon and adrenaline, stimulate the mobilization of fatty acids from adipose tissue through lipolysis.
  - Hormone-sensitive lipase (HSL) and adipose triglyceride lipase (ATGL) are key enzymes involved in the breakdown of triglycerides into fatty acids and glycerol.
  - The released fatty acids can then be taken up by peripheral tissues, including muscle and liver, for beta-oxidation.
- 3. De Novo Lipogenesis
  - In addition to dietary intake and adipose tissue mobilization, the de novo synthesis of fatty acids, known as **de novo lipogenesis (DNL)**, can also influence the supply of fatty acids for beta-oxidation.
  - DNL primarily occurs in the liver and is regulated by nutritional and hormonal factors.
  - When dietary carbohydrate intake is high, excess glucose is converted into acetyl-CoA, which serves as a precursor for fatty acid synthesis.
  - Under conditions of energy surplus, DNL can contribute to an increase in fatty acid supply for storage or oxidation, depending on the metabolic needs of the body.
  - The supply of fatty acids for beta-oxidation is tightly regulated to ensure metabolic efficiency and energy homeostasis.
  - Several factors influence this regulation, including hormonal signals and metabolic intermediates.

### **1. Hormonal Regulation**

- Hormones such as insulin, glucagon, and adrenaline play crucial roles in regulating fatty acid supply and beta-oxidation.
- **Insulin**, released in response to high blood glucose levels, promotes glucose uptake and utilization, inhibiting lipolysis and fatty acid release from adipose tissue.
- In contrast, **glucagon and adrenaline**, released during fasting or exercise, stimulate lipolysis and increase the availability of fatty acids for oxidation.

### 2. Metabolic Intermediates

- Metabolic intermediates within the beta-oxidation pathway can feedback and regulate the supply of fatty acids.
- For instance, malonyl-CoA, an intermediate in fatty acid synthesis, inhibits the entry of fatty acids into mitochondria for beta-oxidation.

- This ensures that fatty acids are channeled toward storage when energy needs are met.
- Conversely, during conditions of energy deficit, malonyl-CoA levels decrease, relieving this inhibition and promoting the transport of fatty acids into the mitochondria for oxidation.

The regulation of fatty acid supply is essential for maintaining energy balance and metabolic flexibility. Dysregulation in this process can contribute to metabolic disorders such as obesity, insulin resistance, and fatty acid oxidation disorders. Understanding the intricate mechanisms that control the supply of fatty acids and their integration with beta-oxidation provides insights into the pathophysiology of metabolic diseases and can help develop targeted therapeutic strategies.

### Significance of Beta-Oxidation

- The body's ability to produce energy and maintain its energy balance depends heavily on beta-oxidation.
- When glucose levels are low by prolonged fasting or strenuous activity and fatty acids are the body's main fuel source, this is very crucial.
- Acetyl-CoA, which may join the citric acid cycle and create the reducing equivalents (NADH and FADH2), is produced by the beta-oxidation of fatty acids.
- The electron transport chain uses these reducing equivalents after that to produce ATP by oxidative phosphorylation.
- Therefore, beta-oxidation makes a considerable contribution to ATP synthesis and the body's overall energy balance.
- Additionally, beta-oxidation plays a role in a number of metabolic diseases.
- Fatty acid oxidation disorders (FAODs), a group of metabolic illnesses, can be caused by flaws in the beta-oxidation-related enzymes.
- Inefficient fatty acid breakdown causes a buildup of fatty acyl-CoA intermediates, which is a hallmark of several illnesses.
- Severe metabolic crises, such as **hypoglycemia**, liver failure, muscular weakness, and cardiomyopathy, can be caused by FAODs.
- Beta-oxidation has also drawn attention in relation to metabolic syndrome and obesity.
- The buildup of fatty acids in non-adipose tissues including the liver and skeletal muscles can cause insulin resistance, inflammation, and the emergence of metabolic diseases.
- This accumulation can be attributed to dysregulation of fatty acid metabolism and defective beta-oxidation.

### What are Nucleic Acids?

Nucleic acids are long-chain polymeric molecules, the monomer (the repeating unit) is known as the nucleotides and hence sometimes nucleic acids are referred to as polynucleotides.

Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are two major types of nucleic acids. DNA and RNA are responsible for the inheritance and transmission of specific characteristics from one generation to the other. There are prominently two types of nucleic acids known to us.

### Deoxyribonucleic Acid (DNA)

Chemically, DNA is composed of a pentose sugar, phosphoric acid and some cyclic bases containing nitrogen. The sugar moiety present in DNA molecules is  $\beta$ -D-2-deoxyribose. The cyclic bases that have nitrogen in them are adenine (A), guanine (G), cytosine(C) and thymine (T). These bases and their arrangement in the molecules of DNA play an important role in the storage of information from one generation to the next one. DNA has a double-strand helical structure in which the strands are complementary to each other.

### **Ribonucleic Acid (RNA)**

The RNA molecule is also composed of phosphoric acid, a pentose sugar and some cyclic bases containing <u>nitrogen</u>. RNA has  $\beta$ -D-ribose in it as the sugar moiety. The heterocyclic bases present in RNA are adenine (A), guanine (G), cytosine(C) and uracil (U). In RNA the fourth base is different from that of DNA. The RNA generally consists of a single strand which sometimes folds back; that results in a double helix structure. There are three types of RNA molecules, each having a specific function:

- 1. messenger RNA (m-RNA)
- 2. ribosomal RNA (r-RNA)
- 3. transfer RNA (t-RNA)



- <u>Nucleic acids</u> are responsible for the transmission of inherent characters from parent to offspring.
- They are responsible for the synthesis of protein in our body
- DNA fingerprinting is a method used by forensic experts to determine paternity. It is also used for the identification of criminals. It has also played a major role in studies regarding biological evolution and genetics.

### **Purines and Pyrimidines**

Purines and pyrimidines are both organic compounds that take part in the synthesis of DNA and RNA, therefore they are called as the building blocks of the genetic material – DNA and RNA. They are nitrogenous bases that make up the two different nucleotides in DNA and RNA.

Purines (adenine and guanine) are two-carbon nitrogen ring bases while pyrimidines (cytosine and thymine) are one-carbon nitrogen ring bases.



### **Purine vs Pyrimidine**

Purines Pyrimidines

Purine is a heterocyclic aromatic organic compound composed of a pyrimidine ring fused with imidazole ring.	Pyrimidine is a heterocyclic aromatic organic compound that is composed of carbon and hydrogen.
It comprises adenine and guanine as nucleobases.	It comprises cytosine, thymine, uracil as nucleobases
It consists of two hydrogen-carbon rings and four nitrogen atoms	It consists of one hydrogen-carbon ring and two nitrogen atoms
The melting point of purine is 214 °C	The melting point of pyrimidine is 20-22 °C
Catabolism results in the production of uric acid	Catabolism produces carbon dioxide, beta- amino acids and ammonia

Both purine and pyrimidine have similar functions. They are vital for the production of DNA and RNA, starch and **proteins**. They also serve as a form of energy for cells. They regulate enzymes and are necessary for cell signalling.

### **CLASSIFICATION OF DNA & RNA**



	idenine phospha	ribosyl transfe	rase
Adenine	PRPP	PPI	AMP
Guanine	Hype xanthin phosphoribosy	e guanine I transferase	GMP
	PRPP	PPI	
typoxanthir	phosphoribo	syl transferase	IMP

### UNIT 5

### What is an Amino acid?

"Amino Acids are the organic compounds that combine to form proteins; hence they are referred to as the building components of proteins. These biomolecules are involved in several biological and chemical functions in the human body and are the necessary ingredients for the growth and development of human beings. There are about 300 amino acids that occur in nature."

Amino acids are organic compounds containing the basic amino groups (-NH2) and carboxyl groups (-COOH). The ingredients present in proteins are amino acids. Both peptides and proteins are long chains of amino acids. Altogether, there are twenty amino acids, which are involved in the construction of proteins.

### List of 20 Amino acids with the chemical formula

Listed below are the names of twenty amino acids along with their chemical formula.

Alanine	СЗН7NO2	Leucine	C6H13NO2
Aspartic Acid	C4H7NO4	Lysine	C6H14N2O2
Asparagine	C4H8N2O3	Methionine	C5H11NO2S

Arginine	C6H14N4O2	Proline	C5H9NO2
Cytosine	C4H5N3O	Phenylalanine	C9H11NO2
Cysteine	C3H7NO2S	Serine	C3H7NO3
Glycine	C2H5NO2	Tyrosine	C9H11NO3
Glutamine	C5H10N2O3	Threonine	C4H9NO3
Histidine	C6H9N3O2	Tryptophan	C11H12N2O2
Isoleucine	C6H13NO2	Valine	C5H11NO2

### General properties of Amino acids

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- They have a very high melting and boiling point.
- Amino acids are white crystalline solid substances.
- In taste, few Amino acids are sweet, tasteless, and bitter.
- Most of the amino acids are soluble in water and are insoluble in organic solvents.

### **Essential and Non-essential Amino acids**

Out of 20 amino acids, our body can easily synthesize a few on its own, which are called nonessential amino acids. These include alanine, asparagine, arginine, aspartic acid, glutamic acid, **cysteine**, glutamine, proline, glycine, serine, and tyrosine.

Apart from these, there are other nine amino acids, which are very much essential as they cannot be synthesized by our body. They are called essential amino acids, and they include

isoleucine, histidine, lysine, leucine, phenylalanine, tryptophan, methionine, threonine, and valine.

Also read about Proteins

### **Structure of Amino acids**



The general structure of Amino acids is H2NCH RCOOH, and it can be written as:



There are 20 naturally occurring amino acids and all have common structural features – an amino group (-NH3+), a carboxylate (-COO-) group and a hydrogen-bonded to the same carbon atom. They differ from each other in their side-chain called the R group. Each amino acid has 4 different groups attached to  $\alpha$ - carbon.

These 4 groups are:

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- Amino group,
- COOH,
- Hydrogen atom,
- Sidechain (R).

Structure of 20 Amino acids with their chemical formula

Here is the structure of twenty amino acids with their chemical formula.



Sources of Amino acids



Amino acids play an important role in performing several biological and chemical functions in different parts of our body, including building and repairing the tissues, the formation and function of <u>enzymes</u>, food digestion, the transportation of molecules, etc. Our body can synthesize only certain amino acids and the rest of the amino acids which are called essential amino acids should be supplied through protein-rich foods in our daily diet.

Foods rich in amino acids include plant-based products like broccoli, beans, beetroots, pumpkin, cabbage, nuts, dry fruits, chia seeds, oats, peas, carrots, cucumber, green leafy vegetables, onions, soybeans, whole grain, peanuts legumes, lentils, etc. Fruits rich in amino acids are apples, bananas, berries, figs, grapes, melons, oranges, papaya, pineapple, and pomegranates. Other animal products include dairy products, eggs, seafood, chicken, meat, pork etc.

## **Protein Structure**

Protein structures are made by condensation of amino acids forming peptide bonds. The sequence of amino acids in a protein is called its primary structure. The secondary structure is determined by the dihedral angles of the peptide bonds, the tertiary structure by the folding of protein chains in space. Association of folded polypeptide molecules to complex functional proteins results in quaternary structure.



## **Define Protein Structure**

Protein structure is defined as a polymer of amino acids joined by peptide bonds.

Let us see how a peptide bond is established from the following reaction:



Formation of Peptide Bond

We can thus see that the <u>peptide bond</u> (-CO-NH) is formed between the amine group of one molecule and the carboxyl group of the adjacent molecule followed by the elimination of a water molecule. This bond is otherwise an amide linkage. When peptide bonds are established among more than ten amino acids, they together form a polypeptide chain. Very often, when a polypeptide chain has a mass exceeding 10000u and the number of amino acids in the chain exceeding 100, we get a protein.

## **Classification of Proteins**

Based on the molecular shape, proteins can be classified into two types.

### 1. Fibrous Proteins:

When the polypeptide chains run *parallel* and are held together by hydrogen and disulfide bonds, then the fiber-like structure is formed. Such proteins are generally insoluble in water. These are water-insoluble proteins.

*Example* – keratin (present in hair, wool, and silk) and myosin (present in muscles), etc.

### 2. Globular Proteins:

This structure results when the chains of polypeptides *coil around* to give a spherical shape. These are usually soluble in water.

*Example* – Insulin and albumins are common examples of globular proteins.

## Levels of Protein Structure

## **1. Primary Structure of Protein**

- The Primary structure of proteins is the exact ordering of amino acids forming their chains.
- The exact sequence of the proteins is very important as it determines the final fold and therefore the function of the protein.
- The number of polypeptide chains together form proteins. These chains have amino acids arranged in a particular sequence which is characteristic of the specific protein. Any change in the sequence changes the entire protein.

The following picture represents the primary protein structure (an amino acid chain). As you might expect, the amino acid sequence within the polypeptide chain is crucial for the protein's proper functioning. This sequence is encrypted in the DNA genetic code. If mutation is present in the DNA and the amino acid sequence is changed, the protein function may be affected.

## PRIMARY STRUCTURE



BYJU'S

The protein 's primary structure is the <u>amino acid</u> sequence in its polypeptide chain. If proteins were popcorn stringers designed to decorate a Christmas tree, a protein 's primary structure is the sequence in which various shapes and varieties of popped maize are strung together.

Covalent, peptide bonds which connect the amino acids together maintain the primary structure of a protein.

All documented genetic disorders, such as cystic fibrosis, sickle cell anemia, albinism, etc., are caused by mutations resulting in alterations in the primary protein structures, which in turn lead to alterations in the secondary, tertiary and probably quarterly structure.

Amino acids are small organic molecules consisting of a chiral carbon with four substituents. Of those only the fourth the side chain is different among amino acids.

## 2. Secondary Structure of Protein

### Secondary structure of protein refers to local folded structures that form within a

polypeptide due to interactions between atoms of the backbone.

- The proteins do not exist in just simple chains of polypeptides.
- These polypeptide chains usually fold due to the interaction between the amine and carboxyl group of the peptide link.
- The structure refers to the shape in which a long polypeptide chain can exist.
- They are found to exist in two different types of structures  $\alpha$  helix and  $\beta$  pleated sheet structures.
- This structure arises due to the regular folding of the backbone of the polypeptide chain due to hydrogen bonding between -CO group and -NH groups of the peptide bond.
- However, segments of the protein chain may acquire their own local fold, which is much simpler and usually takes the shape of a spiral an extended shape or a loop. These local folds are termed secondary elements and form the proteins secondary structure.

## SECONDARY STRUCTURE



## (a) $\alpha$ – Helix:

 $\alpha$  – Helix is one of the most common ways in which a polypeptide chain forms all possible hydrogen bonds by twisting into a right-handed screw with the -NH group of each amino acid residue hydrogen-bonded to the -CO of the adjacent turn of the helix. The polypeptide chains twisted into a right-handed screw.

## (b) $\beta$ – pleated sheet:

In this arrangement, the polypeptide chains are stretched out beside one another and then bonded by intermolecular H-bonds. In this structure, all peptide chains are stretched out to nearly maximum extension and then laid side by side which is held together by intermolecular hydrogen bonds. The structure resembles the pleated folds of drapery and therefore is known as  $\beta$  – pleated sheet

## 3. Tertiary Structure of Protein

- This structure arises from further folding of the secondary structure of the protein.
- H-bonds, electrostatic forces, disulphide linkages, and Vander Waals forces stabilize this structure.
- The tertiary structure of proteins represents overall folding of the polypeptide chains, further folding of the secondary structure.
- It gives rise to two major molecular shapes called fibrous and globular.
- The main forces which stabilize the secondary and tertiary structures of proteins are hydrogen bonds, disulphide linkages, van der Waals and electrostatic forces of attraction.

### **TERTIARY STRUCTURE**





## 4. Quaternary Structure of Protein

The spatial arrangement of various tertiary structures gives rise to the quaternary structure. Some of the proteins are composed of two or more polypeptide chains referred to as subunits. The spatial arrangement of these subunits with respect to each other is known as quaternary structure.

## QUATERNARY STRUCTURE





The exact amino acid sequence of each protein drives it to fold into its own unique and biologically active three-dimensional fold also known as the tertiary structure. Proteins consist of different combinations of secondary elements some of which are simple whereas others are more complex. Parts of the protein chain, which have their own three-dimensional fold and can be attributed to some function are called *"domains"*. These are considered today as the evolutionary and functional building blocks of proteins.

Many proteins, most of which are enzymes contain organic or elemental components needed for their activity and stability. Thus the study of protein evolution not only gives structural insight but also connects proteins of quite different parts of the metabolism.

## **Classification of Proteins**

Protein molecules are large, complex molecules formed by one or more twisted and folded strands of amino acids. Each amino acid is connected to the next amino acid by covalent bonds.

- 1. **Primary (first level)** Protein structure is a sequence of amino acids in a chain.
- 2. Secondary (secondary level) Protein structure is formed by folding and twisting of the amino acid chain.
- 3. **Tertiary (third level)** Protein structure is formed when the twists and folds of the secondary structure fold again to form a larger three dimensional structure.
- 4. **Quaternary (fourth level)** Protein structure is a protein consisting of more than one folded amino acid chain.

Proteins can bond with other organic compounds and form "mixed" molecules. For example, glycoproteins embedded in cell membranes are proteins with sugars attached. Lipoproteins are lipid-protein combinations.

## **Nucleic Acids**

The two forms of nucleic acid are deoxyribonucleic acid and ribonucleic acid. The basic building blocks of <u>nucleic acids</u> are called nucleotides. Each nucleotide consists of a phosphate unit, a sugar and a nitrogen base. DNA nucleotide bases include adenine, thymine, guanine and cytosine. RNA uses the same set of bases, except for the substitution of unit cells for thymine.

Nucleotides bind to one another to form strands or other structures. In the DNA molecule, nucleotides are arranged and twisted, and a double strand called a double helix. The sequence of different nucleotides along the DNA double helix is the "master code" for assembling proteins and other nucleic acids.

## Amino Acids Degradation

The liver is the principal site of amino acid metabolism, but other tissues, such as the kidney, the small intestine, muscles, and adipose tissue, take part. Generally, the first step in the breakdown of amino acids is the separation of the amino group from the carbon skeleton, usually by a **transamination reaction**. The carbon skeletons resulting from the deaminated amino acids are used to form either glucose or fats, or they are converted to a metabolic intermediate that can be oxidized by the citric acid cycle. The latter alternative, amino acid catabolism, is more likely to occur when glucose levels are low—for example, when a person is fasting or starving.

### Transamination

Transamination is an exchange of functional groups between any amino acid (except lysine, proline, and threonine) and an  $\alpha$ -keto acid. The amino group is usually transferred to the keto carbon atom of  $\alpha$ -ketoglutarate, converting the  $\alpha$ -keto acid to glutamate. Transamination reactions are catalyzed by specific transaminases (also called aminotransferases), which require pyridoxal phosphate as a coenzyme.



In an  $\alpha$ -keto acid, the carbonyl or keto group is located on the carbon atom adjacent to the carboxyl group of the acid.



Figure 10.2.110.2.1: Two Transamination Reactions. In both reactions, the final acceptor of the amino group is  $\alpha$ -ketoglutarate, and the final product is glutamate.

Another important example of a transamination reaction is the formation of aspartate, which is used during urea formation. In this case, the acceptor of the amino group is oxaloacetate. For example, aspartate can be obtained from another amino acid such as alanine:



Figure 10.2.210.2.2: A transamination reactions in which aspartate is formed. In this case, oxaloacetate is the amino group acceptor

### **Oxidative Deamination**

In the breakdown of amino acids for energy, the final acceptor of the  $\alpha$ -amino group is  $\alpha$ -ketoglutarate, forming glutamate. Glutamate can then undergo oxidative deamination, in which it loses its amino group as an ammonium (NH<sub>4</sub><sup>+</sup>) ion and is oxidized back to  $\alpha$ -ketoglutarate (ready to accept another amino group):



This reaction occurs primarily in liver mitochondria. Most of the  $NH_4^+$  ion formed by oxidative deamination of glutamate is converted to urea and excreted in the urine in a series of reactions known as the **urea cycle**.

$$H_2N - C - NH_2$$
  
urea

The synthesis of glutamate occurs in animal cells by reversing the reaction catalyzed by glutamate dehydrogenase. For this reaction nicotinamide adenine dinucleotide phosphate (NADPH) acts as the reducing agent. The synthesis of glutamate is significant because it is one of the few reactions in animals that can incorporate inorganic nitrogen ( $NH_4^+$ ) into an  $\alpha$ -keto acid to form an amino acid. The amino group can then be passed on through transamination reactions, to produce other amino acids from the appropriate  $\alpha$ -keto acids.

## The Fate of the Carbon Skeleton

Any amino acid can be converted into an intermediate of the citric acid cycle. Once the amino group is removed, usually by transamination, the  $\alpha$ -keto acid that remains is catabolized by a pathway unique to that acid and consisting of one or more reactions. For example, phenylalanine undergoes a series of six reactions before it splits into fumarate and acetoacetate. Fumarate is an intermediate in the citric acid cycle, while acetoacetate must be converted to acetoacetyl-coenzyme A (CoA) and then to acetyl-CoA before it enters the citric acid cycle.



Figure 10.2.310.2.3: Fates of the Carbon Skeletons of Amino Acids

Those amino acids that can form any of the intermediates of carbohydrate metabolism can subsequently be converted to glucose via a metabolic pathway known as gluconeogenesis. These amino acids are called **glucogenic amino acids**. Amino acids that are converted to acetoacetyl-CoA or acetyl-CoA, which can be used for the synthesis of ketone bodies but not glucose, are called **ketogenic amino acids**. Some amino acids fall into both categories. Leucine and lysine are the only amino acids that are exclusively ketogenic. Figure 10.2.210.2.2 summarizes the ultimate fates of the carbon skeletons of the 20 amino acids. The table below summarizes the Glucogenic and Ketogenic Amino Acids.

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Glucogenic	Both Glucogenic and Ketogenic	Ketogenic
Aspartate	Isoleucine	Leucine
Asparagine	Phenylalanine	Lysine
Alanine	Tryptophan	
Glycine	Tyrosine	
Serine		
Threonine		
Cysteine		
Glutamate		
Glutamine		
Arginine		
Proline		
Histidine		
Valine		
Methionine		

### **Glucogenic and Ketogenic Amino Acids**

## What is the Urea Cycle?

The conversion of ammonia into urea through a series of biochemical reactions is known as the urea cycle or ornithine cycle. It takes place in the liver with the help of mitochondrial and cytosolic enzymes. It is an important pathway in amphibians and mammals as they help in disposing highly toxic ammonia by converting it into urea. The animals that excrete in the form of urea are called ureotelic.

The urea cycle was discovered by Hans Krebs and Kurt Henseleit in 1932. Ammonia is produced in our bodies by amino acid catabolism, deaminations and prolonged starvations. All animals need to excrete ammonia in one way or another. Animals that directly excrete ammonia, such as aquatic organisms are called ammonotelic.

Mammals and amphibians cannot excrete ammonia directly, so they convert it into a simpler form of urea. The urea converted in the liver is transported to the kidney via the bloodstream and then finally excreted in the form of urine. This process is important because, if the nitrogenous waste is not excreted, it starts building up in the body and can be detrimental. Urea is inert in nature, soluble in water and can be easily excreted in urine, whereas ammonia is highly toxic.

## Steps

The urea cycle starts in the mitochondria of hepatocytes (liver cells) and the final step takes place in the cytoplasm. The final product formed is then transported to the kidney, where it is excreted out of the body.

## Entry into the Urea Cycle

Ammonia and carbon monoxide are converted into carbamoyl phosphate in this rate limiting step by the enzyme carbamoyl phosphate synthetase I (CPS I). Two ATP molecules are utilised in this step.

Ammonia becomes the source of the first amine group in urea. The CPS I requires an obligate activator, namely, N-acetyl glutamate (NAG). NAG is formed by a reaction between glutamate and acetyl-CoA in the presence of NAG synthase.

## First Step

In the first step, carbamoyl phosphate enters the urea cycle and combines with ornithine to form citrulline in the presence of enzyme ornithine transcarbamylase (OTC). The citrulline formed is then transported out of the mitochondria into the cytoplasm by ornithine translocase.

## Second Step

Citrulline and aspartate undergo a condensation reaction to form argininosuccinate in the presence of the enzyme argininosuccinate synthetase. Here, aspartate becomes the source of the second amine group on urea. This reaction utilises one ATP molecule.

## Third Step

Argininosuccinate is cleaved off to make arginine and fumarate in the presence of enzyme argininosuccinate lyase. The fumarate is used up in the production of NADH in the TCA cycle, and the arginine moves forward for the next step of the urea cycle.

## Fourth Step

Arginine undergoes hydrolysis to yield urea and ornithine in the presence of arginase. Ornithine is transported back to the mitochondria, which is used up in the second step of the cycle to form citrulline by combining with carbamoyl phosphate.

The overall reaction equation of the urea cycle is:

# $NH_3 + CO_2 + aspartate + 3 ATP + 3 H_2O \rightarrow urea + fumarate + 2 ADP + 2 P_i + AMP + PP_i + H_2O$

## **Regulation of the Urea Cycle**

- **N-acetyl glutamate (NAG):** In the urea cycle, the enzyme CPS I is allosterically activated by NAG. It is an obligate activator of carbamoyl phosphate synthase. NAG is produced by the reaction of acetyl CoA and glutamate in the presence of NAG synthase, and the reaction is stimulated by both arginine (Arg) and glutamic acid (Glu). Therefore, Glu is both a substrate and activator for the urea cycle.
- **Substrate Concentrations:** All the enzymes in the urea cycle work based on the concentrations of their substrates except arginase.

## **Disorders of the Urea Cycle**

- 1. **Ornithine Transcarbamylase (OTC) Deficiency:** It is the only X-linked recessive enzyme deficiency disorder in the urea cycle. The deficiency of the enzyme leads to an increased concentration of carbamoyl phosphate in the mitochondria. The carbamoyl phosphate is rechanneled to the pyrimidine synthesis pathway in the cytoplasm. It is then converted into orotic acid. Orotic acid is built up in the blood and urine, and appears as orange crystals in the diapers of infants.
- 2. Argininosuccinate Synthetase Deficiency: Argininosuccinate synthetase deficiency, also known as citrullinemia type I, is an autosomal recessive disorder of the urea cycle. This disorder is associated with build up of citrulline and, ultimately, ammonia. In infants, the disease is represented by seizures, lethargy, anorexia and respiratory distress. In adulthood, it appears in milder forms and symptoms include vomiting, ataxia and lethargy.
- 3. **Carbamoyl Phosphate Synthetase I (CPS I) Deficiency:** It is an autosomal recessive metabolic disorder that is commonly seen in infants. It makes the child lethargic, unwilling to eat, altered body temperature and respiratory rate. In other affected individuals, it shows symptoms only later in life.

### HORMONE AND VITAMIN

The **main difference between hormone and vitamin** is that hormone is an organic compound a particular tissue secretes into the bloodstream to induce a specific physiological response in another tissue, whereas vitamin is an essential micronutrient included in the diet and required for proper metabolism.

Hormones and vitamins are two organic substances important in different functions of the body. Their function is generally away from the production site.

# HORMONE

VERSUS

## VITAMIN

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VIIAMIN	
Any of a group of organic compounds which are essential for normal growth and nutrition and are required in small quantities in the diet because they cannot be synthesized by the body	
Plants produce vitamins	
Catalyze enzymatic reactions	
Have effects on the metabolism	
Have nutritive functions	
Examples: Vitamin A, B, C, D, E, and K	

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