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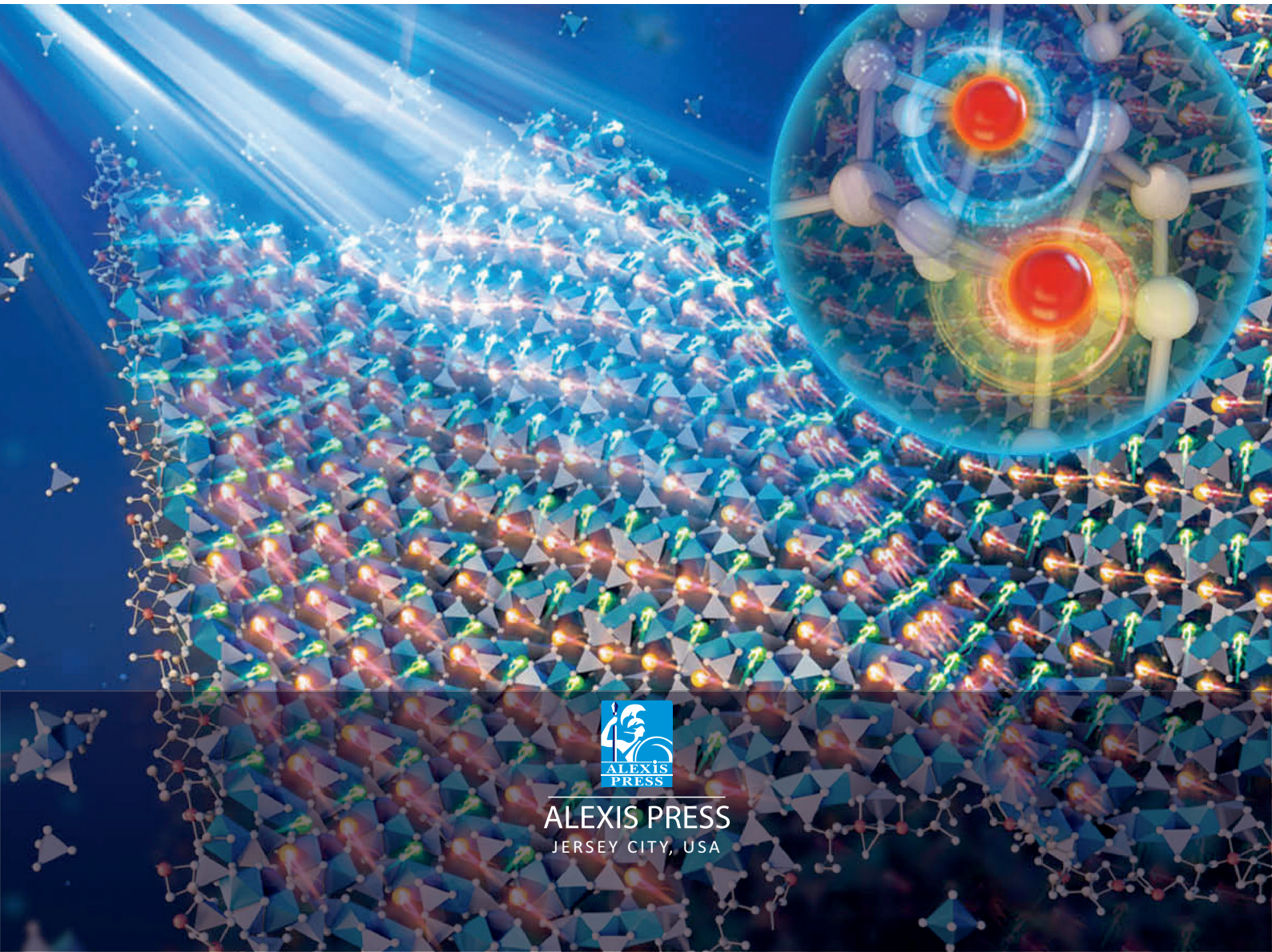
INORGANIC CHEMISTRY, BIO-ORGANIC AND BIO-PHYSICAL CHEMISTRY



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CHAPTER-1

BONDING AND STEREOCHEMISTRY IN MAIN GROUP COMPOUNDS

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This unit's goals are to expose you to key fundamental ideas that will help you comprehend the bonding and structure of inorganic substances. The ideas of valency, dot structures of inorganic compounds, hybridization, and a broad comprehension of structural representation and chemical processes are prerequisites to comprehending the content of this chapter. You will be able to comprehend and explain the relatively complex bonds and structures of inorganic molecules by the conclusion of this chapter. The forms and geometries of molecules are explained by a number of models and ideas. Knowledge of the electronic structures of molecules was supplied by one of G. N. Lewis' key hypotheses. The Lewis hypothesis of molecular electrical structures set the groundwork for many later hypotheses. The shape of a molecule may be predicted using the Valence Shell Electron Pair Repulsion (VSEPR) hypothesis based on the number of electron pairs that surround its core atoms. The idea is also known as the Gillespie-Nyholm hypothesis after its principal proponents, Ronald Gillespie and Ronald Nyholm.

Theory Valence Shell Electron Pair Repulsion

The Lewis model of molecular structures serves as the foundation for the VSEPR model, which describes the forms and geometries of polyatomic compounds. Based on the understanding of Lewis dot structures, this hypothesis forecasts the form of molecules. The VSEPR hypothesis really depends on the valence electron pairs that surround an atom having a propensity to exert repulsion against one another and adopting a geometric layout to reduce this repulsion. Repulsion between two lone pairs is greater than that between a lone pair and a bonding pair of electrons, which is stronger yet than the repulsion between two bonding pairs of electrons, it is crucial to note. As a result, the VSEPR theory uses the locations of several atoms and electrons in relation to a central atom. The exact location of bound and lone electron pairs determines the molecule's structure. By disregarding the location of the lone electron pair of electrons, the final form is inferred. The VSEPR theory is applicable to a wide range of compounds, but it is particularly good at explaining the geometry of the simple halides of the p block elements. It's also vital to remember that steric considerations, or how bulky a substituent is surrounding the core atom, are not taken into account by the VSEPR models.

The main guidelines for calculating the VSEPR geometries of a certain molecule are listed below.

1. Sketch the molecule's Lewis structure for the geometry assessment.
2. Position the electron lone pairs (lp) and bonding pairs (bp) around the main atom.

The following are a few practical examples showing how to distribute electrons in certain compounds to reduce electronic repulsion and the resulting molecular geometries (notice that the bonding pair of electrons, i.e., bp, are shown as solid lines or flying wedges): The composition of

beryllium chloride (BeCl2) Beryllium chloride, which has the chemical formula BeCl2, is a white, hygroscopic solid. According to Figure 1, beryllium chloride contains two bonding pairs and no lone pair of electrons around the beryllium atom. The bonding pairs of electrons are oriented distant from one another in order to reduce mutual repulsion, which gives rise to the molecule's linear structure. The Cl-Be-Cl bond angle is 180 degrees according to VSEPR calculations [1].

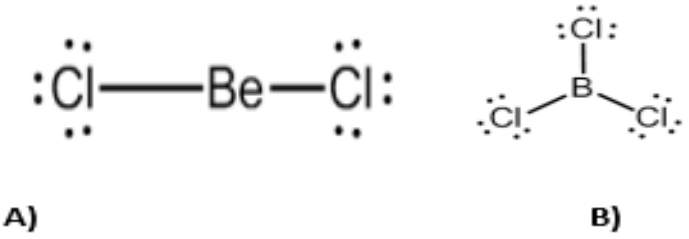

Figure 1: a) The linear geometry of BeCl2 molecule. b) The trigonal planar shape of BCl3 molecule.

Around their respective core atoms, the molecules of water, ammonia, and methane each have four electron pairs. The quantity of lone pairs of electrons and bonded pairs, however, varies. Methane has a tetrahedral shape when it contains four pairs of electrons bonded together (H-C-H bond angle = 109.5°). Trigonal pyramidal shape results from ammonia's three bonding pairs and one electron pair. Since the lp-bp attraction is greater than the bp-bp attraction, the ammonia's H-N-H bond angles are reduced to 107°. In the case of water, the oxygen atom is surrounded by two lone pairs and two bonded pairs of electrons. As a result, the geometry of the molecule becomes bent with a 105° H-O-H bond angle.

Wallace Diagrams

Prof. A.D. Walsh initially developed Walsh diagrams to explain the geometries that polyatomic molecules assume in both their excited and ground states. The computed orbital binding energies of a molecule plotted against bond angles are shown graphically in Walsh diagrams. These illustrations forecast the shapes of tiny molecules and explain why a particular molecule is more stable in one shape than another. According to Walsh's rule, a molecule will choose a structural geometry that gives its highest occupied molecular orbital the maximum stability. (HOMO). In order to describe the regularity in the structures of related molecules with the same amount of valence electrons, a Walsh diagram is utilized. For instance, the structures of water (H2O) and sulfur dioxide (H2S) are comparable. The Walsh diagram also demonstrates how a molecule's shape might alter when its number of electrons or spin state changes [2].

Tri-atomic molecule Walsh diagram

An energy vs bond angle plot, shows a condensed Walsh diagram for a triatomic molecule. It should be noted that the energy levels shown are qualitative and should be determined by a proper simulation for the real system. MO levels for the bent configuration with a 90° bond angle are shown on the left, while those for the linear configuration with a 180° bond angle are shown on the right.

An idealized model AH4 that may take on either a square planar geometry or a tetrahedral shape is appropriate for penta-atomic molecules. The true examples for these groups are methane (CH4) and sulfur tetrafluoride (SF4). For instance, one hydrogen atom from each orbital bonds with one another to produce the methane molecule, which has four 1s orbitals, one 2s orbital, and three 2p orbitals of carbon. Out of the eight orbitals listed above, four bonding orbitals and four antibonding orbitals are produced, with bonding orbitals containing all eight electrons necessary for molecule synthesis. When the orbitals of carbon and hydrogen are arranged in a tetrahedral configuration, there is a chance that their orbitals will overlap significantly, which lowers the energy of bonding orbitals. In contrast, when the orbitals are arranged in a square planar configuration, the extent of overlap is very low, which produces orbitals with a disproportionately high energy, as shown in Figure 1.8. So, instead of the square planar or the intermediate deformed geometries, the CH4 molecule favors the tetrahedral shape [3], [4].

The-p BOND

The presence of d-p bonds is one of many ways that the formation of inorganic molecules differs from that of organic ones. Typically, p orbitals of two atoms like carbon, nitrogen, or oxygen are lateral overlapped to create bonds, as in the case of organic compounds. Inorganic compounds often include connections as a consequence of bonding interactions between two d orbitals. However, the simultaneous employment of suitable d and porbitals is also possible in bonding interactions in inorganic compounds. The term "d-p bond" refers to a link formed by the lateral overlap of p (or p*) and d orbitals on two distinct atoms. Metal complexes like carbonyl and nitrosyl are common examples of compounds where such linkages are seen. An easy case in point is sulfur trioxide. (SO3). D-P linkages may be found in main group compounds such phosphine oxides and disiloxane. D-P bonding interactions often shorten bonds and cause the atoms involved to be in a planar form. The presence of these molecular characteristics should not, however, necessarily be ascribed to d-p bonds since a number of other variables may also be at play. Therefore, it is important to carefully consider both electronic and orbital symmetries.

An example of a d-p bond in a molecule made of nonmetallic components is the phosphate oxide (). In this instance, all of the phosphorous' p orbitals are being used for hybridization and are not accessible for lateral overlapping. A full p orbital that is accessible with an oxygen atom absorbs electron density into its empty d orbital on phosphorus. This d-p bond results in stronger binding of the two atoms involved, which is reflected in the bond's short bond distance (150 pm) and stability (544 kJ/mol bond energy).

Bent's Rule and The Hybridization Energy

The idea of hybridization is the mixing of atomic orbitals of various energies and shapes to create an equal number of new hybrid orbitals. Therefore, hybridization is the linear combination of atomic orbitals that redistributes the energy of atomic orbitals. It is crucial to know the structure of molecules since orbital energy are on the same scale as bond energies. Henry Bent first articulated Bent's rule, which states that "Atomic s character concentrates in orbitals directed toward electropositive substituents," as a relationship between the orbital hybridization of a molecule's core atom and the electronegativities of substituents. The's' orbital has less energy than

the 'p' orbital, students, as you must remember. Additionally, a hybrid orbital with a higher's' character has less energy and a form similar to an's' orbital. On the other side, increased 'p' character causes the hybrid orbitals to have more energy and a 'p' orbital-like form. The lone pair of electrons are stabilized more by the's' orbitals than the 'p' orbitals because they are closer to the atomic nuclei. Therefore, it follows logically that a more stable molecular model would permit orbitals rich in "p" characters for bonding purposes and those rich in "s" characters for tolerating lone electron pairs. Additionally, because the electron density in's' rich orbitals is higher and located nearer the nucleus, there are fewer electrons available for bonding. As a result, electron density would be withdrawn from 'p' rich orbitals rather than's' like orbitals by electronegative substituents. We can demonstrate this using the PCl3F2 structure and bonding. This molecule is created by combining one s, three p, and one d orbitals to create five sp3 d orbitals. The five hybrid orbitals may be divided into two (axial) and three (equatorial) sets, albeit they are not all identical. The equatorial set is produced when the s, px, and py orbitals are mixed, while the axial set is produced when the pz and d orbitals are mixed. The fluorine and chlorine atoms in the PCl3F2 molecule are located in axial and equitorial locations, respectively, according to experimental data, which is consistent with Bent's rule [5].

P, As, and Sb all have atomic sizes that allow three hydrogen atoms to surround them without causing steric crowding. As a result, during the production of their respective hydrides, these elements' atomic orbitals do not undergo energy-intensive hybridization. Since hydrogen atoms' s-orbitals overlap with almost pure p-orbitals, the center lone pair in these hydrides continues to be mostly in the s-orbital. On the other hand, due to its tiny size, nitrogen cannot fit three hydrogen atoms that are bound to it without causing steric crowding. Evidently, it takes more energy for steric reasons to get ammonia to adopt narrower bond angles than what is needed for hybridization. Thus, during the synthesis of ammonia, the atomic orbitals of nitrogen undergo hybridization, resulting in bond angles of 107.2°. Furthermore, the VSEPR hypothesis may be used to explain the reduction in bond angle from its ideal value of 109.5°. Similar justifications may be used to explain group 16 hydrides' bond angle tendency.

Covalently Bonded Molecules: Some Simple Reactions

The structural characteristics of inorganic reactions are only one of the numerous ways in which they vary from organic ones. Organic reactions typically deal with linear, trigonal planar, and tetrahedral geometries since they predominantly include sp, sp2, and sp3 hybridized carbon centers. On the other hand, there is a wide range of structural variation in inorganic compounds. Regarding the structural, configurational, and dynamic changes in the case of inorganic reactions, this raises a lot of questions. Therefore, two transitions involving altered structural properties of inorganic molecules are covered in this section. The impact of subsequent effects on the environment and industry is significant [6], [7].

Nuclear Inversion

Atomic inversion, or the spatial rearranging of atoms to produce mirror images, occurs in molecules. Usually, tri-substituted N and P atom-containing compounds, such as amines and phosphines, exhibit this behavior. It should be emphasized that atomic inversion in non-chiral

compounds results in the same final product as the original. A dissymmetric molecule, on the other hand, results in a product whose molecular configuration is the exact opposite of the parent molecules. The separation of enantiomers is often unaffected by the energy barrier for atomic inversion in the case of amines.

Arnold Pseudo Rotation

Formation of the Lewis acid-Lewis Base Adducts

A Lewis base is a species that possesses an orbital with an electron pair that may be supplied to an electron-deficient species, as opposed to a Lewis acid, which is a chemical species capable of taking an electron pair in its empty orbital. In order to create a Lewis adduct, a Lewis acid may receive an electron pair from a Lewis base. For instance, to create a Lewis adduct, trialkylborane (a Lewis acid) takes an electron pair from amines (a Lewis base). It is possible to think of the covalent link between B and N atoms as a dative bond.

$$R_3B + :NR_3 \rightarrow R_3B{-}NR_3$$

Reaction of nucleophilic substitution

Neucleophilic substitution reactions are a typical part of the hydrolysis or solvolysis of inorganic materials. Figure 2 illustrates the hydrolysis of trimethylchlorosilane to produce trimethylsilanol. Note that a polymeric silicone material is created by hydrolyzing the similar bifunctional chemical dimethyldichlorosilane [8].

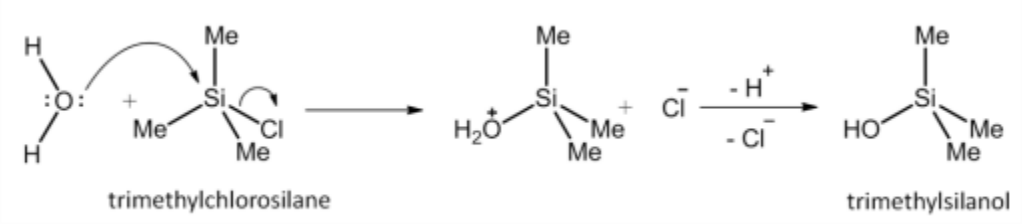

Figure 2: Trimethylsilanol is made by hydrolyzing trimethylchlorosilane.

Nitrogen fixation: The conversion of natural nitrogen, N2 (which contains a triple link between two nitrogen atoms), into ammonia is a crucial process. The Rhizobium bacteria present in the nodules on certain plant roots undergo the reaction at room temperature and 0.8 atm nitrogen pressure. (legumes). The following is a presentation of the response and:

$$N_2 + 6H^+ + 6e^- \rightarrow 2NH_3$$

Enzymatic catalysis is required for the nitrogen fixation process, which is not covered in this book. It should be mentioned, however, that enzymatic processes are chemical reactions that use a lot less energy and use a variety of enzymes as catalysts. It is important to remember that the industrial

Haber process, which produces ammonia, calls for high temperatures, high pressures, and an iron catalyst. You may judge the superiority of enzymatic mechanisms that are still poorly understood by qualitatively contrasting nitrogen fixation to the Haber process. Plants employ the ammonia created in the aforementioned process to create amino acids, one of the fundamental building blocks of life [9], [10].

Some key ideas for comprehending the bonds and structure of inorganic molecules were covered in this chapter. To comprehend the geometry of small molecules, VSEPR theory provides a straightforward yet very helpful notion. In order to fully comprehend the architectures of inorganic molecules, VSEPR theory is complemented with somewhat complex subjects like the Walsh diagram and Bent's rule. Finally, this unit also covered a few significant inorganic compound reactions. The discussion on specific reactions not only describes the chemical changes but also touches on the significance of the same in terms of structure, the environment, and industry.

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CHAPTER-2

COMPOUNDS OF SULFINITROGEN AND PHOSPHORUS-NITROGEN

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This unit's goals are to familiarize you with the synthesis, structure, bonding, and certain uses of inorganic compounds that include chalcogens (O and S), as well as those of group 15 members that are close by. (N and P). The phosphonitrilic (phosphorous-nitrogen), phosphorous-sulfur, and sulfur-nitrogen compounds will be covered in this chapter. It will facilitate developing knowledge of the structure and bonding of these chemicals. Sulfur-nitrogen compounds and phosphazenes (phosphonitriles) are two significant classes of inorganic chemicals with intriguing structure and bonding. They could have cyclic structural patterns that are comparable to inorganic aromatics. These compounds' reaction chemistry is just as fascinating as that of boranes. However, it took more than a century after some of the nitrogen sulfur compounds were discovered before their precise structures were made public.

The polymer SNx was initially found in 1910, and further research showed that it solely contains non-metallic components and exhibits superconductivity at 0.26 K. A finding like this sparked interest in (SN) chemistry. Many theoretical chemists who have attempted to investigate the "aromatic character" of binary S–N systems are still interested in them due to their distinctive structure and features. A minor amount of a compound comprising phosphorous, nitrogen, and chlorine was also produced in the reaction between phosphorous pentachloride and ammonia, which was first documented in 1834. The main reaction result was phospham. Later, the substance was given the name N3P3Cl6. The development of phophazene chemistry was sparked by this finding. They have several uses in the fields of polymer chemistry, organic synthesis, biology, and material chemistry [1], [2].

Phosphazenes (Phosphonitrilic/P-No Compounds)

The compounds with phosphorous and nitrogen atoms connected alternately by single or double bonds are referred to as phosphazene or phosphonitrile. Overall, they might form a ring or chain pattern with trivalent nitrogen and pentavalent phosphorus. After making a few mistakes, the empirical formula for the first phosphazene, N3P3Cl6 (a white, crystalline byproduct of the reaction of ammonia with phosphorous pentachloride), was determined. Initially thought to be NPCl2, it was subsequently shown to be a trimer with a cyclic structure. (proposed by H.N. Stokes). When heated, the trimer produced "inorganic rubber," an elastomer [3].

Cyclophosphazene

The reaction of (NPCl2) resulted in the formation of cross-linked "inorganic rubber."a few traces of water are added. So, if the reaction is conducted in the complete absence of ambient moisture, (NPCl2)n macromolecules that are non-crosslinked and soluble might be created, as shown in

Figure 1. When organic nucleophiles react with (NPCl2)n, the chlorine atom may be replaced, creating stable poly(organo)phosphazenes. If two distinct nucleophiles are utilized on the same molecule, a large variety of polymers with mixed substituents and varying characteristics may be produced. i. Poly(dichloro)phosphazene A crucial precursor in the creation of practically all polymeric phosphazenes is (NPCl2)n.

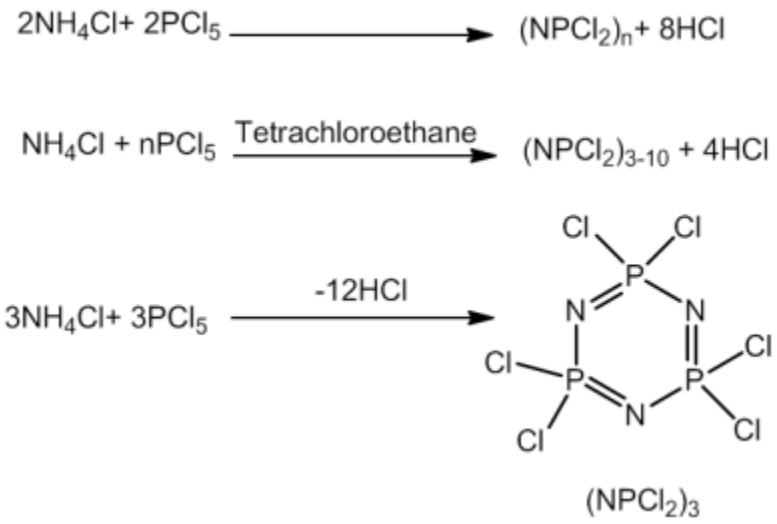

Figure 1: Synthesis of polymeric phosphorene's.

Polyphosphazene Uses

Small modifications to the substituents attached may have a big impact on how the polymer behaves. Due to their flexible chains and great thermal stability, polyphosphazenes are used in a broad variety of products, including high performance elastomers. Because of their limited oxygen indices and side chain activity, they are employed as flame retardants. They are now being researched for a variety of far-reaching applications, including vaccine delivery, fuel cell membranes, tissue engineering matrices, medication and gene delivery, etc. HCCP, or hexachlorotriphosphazene by connecting the rings with multifunctional nucleophiles and employing HCCP, [NPCl2]3, and new materials with high molecular weight, a great amount of work has been done in this area. It is possible to create cyclolinear, cyclomatrix, or dendritic structures using the covalent bond in HCCP. Only two of the six reactive sites in the cyclic $(NPCl2)_3$ unit are employed in the synthesis of cyclolinear compounds. Cross-link or cyclomatrix materials result from reactions involving more than two sites [4].

Compounds of Phosphorus and Sulfur

Significance The synthesis of multidentate ligands with various donor atoms and the idea of hemilability are both receiving a lot of interest. It is possible to safeguard an active site at the metal center by having a molecule with one strong donor (strongly bonding) and one weak donor (weakly bonding) atom. Because these compounds' donor characteristics may be changed by chelation, they provide for intriguing ligand systems. Because the chelate complexes are relatively stable, it is possible to study a metal center's reactivity for a specific reaction—like oxidative addition—

without having to worry about competing ligand replacement processes. The melting temperatures of P-S compounds are lower than those of their oxy-analogues and they are less stable. They are utilized as flotation and vulcanization promoters, lubricating oil additives, and pesticides [5].

Synthesis

Thio-phosphorous compounds may be created by partly or completely substituting oxygen atoms from phosphorous oxides with sulfur atoms. These might have S at terminal places or as a bridge atom. Phosphorous oxides make P4S10 and P4S9 isoelectronic and isostructural, as shown in Figure 2. Using the proper stoichiometric amounts of P and S, P4S3 and P4S7 may be generated.

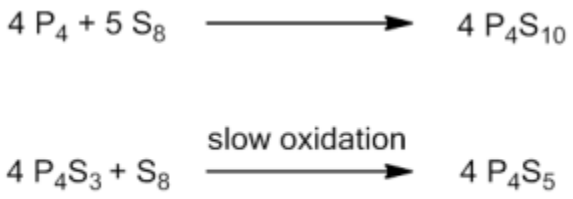

Figure 2: Synthesis of phosphorus-sulfur compounds.

Importance of Sulfur Nitrogen Compounds

Unlike phosphonitriles, the cyclic (SN)X compounds adhere to Hückel's rule of aromaticity, and they may act as donors in charge transfer complexes. These elements have sparked a lot of curiosity in their synthesis, bonds, and chemistry in general. The bonding capabilities of the S-N compounds with transition metals, as well as their magnetic and conducting characteristics, have all been studied. There are several acyclic and cyclic S-N compounds. The smallest homoleptic ring known to exist is S2N2, despite being a strained structure, as seen in Figure 3. It serves as the primary starting material for the production of many polythiazyl (SN)X molecules. The creation, composition, and bonding of a few of these compounds [6], [7].

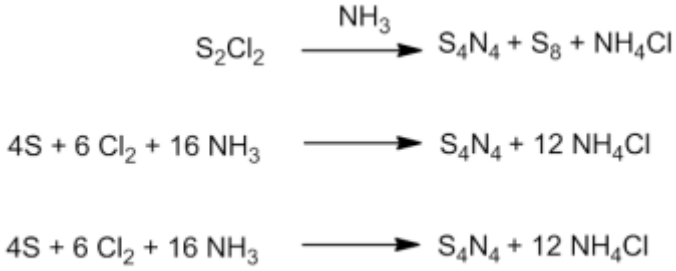

Figure 3: Synthesis of sulfur nitrogen compounds.

When silver metal reacts with S4N4 at a high temperature and low pressure, the remaining S4N4 thermally decomposes and forms silver sulfide, which catalyzes the synthesis of cyclic S2N2 from the remaining S4N4 [8].

Arrangement and Fusion

There are several S-N compounds that have planar rings. They have been discovered to adhere to Hückel's rule of (4n+2) electrons. Sulfur has two electrons and nitrogen has one electron, if we assume that each atom in these planar cyclic S–N compounds contributes one electron to the bond and two electrons to a lone pair. Alternately, the electron distribution may be explained as follows. Two electrons are allotted for sigma bonds at each S–N unit, and two electrons are given to each S and N atom for lone pairs that don't form bonds. Thus, the cyclic -system of the ring may utilise the remaining one electron at N and two electrons at S. Taking into account these electron distributions, we may state that S2N2 has six; S3N3 has ten; S4N3 + has ten; and S5N5 + has fourteen electrons. The S-N compounds stated above, however, contain electrons in the antibonding (*) molecular orbitals, which weakens the S-N bond in contrast to the stable -organic molecules. The following elements contribute to these compounds' stability:

1. Because nitrogen has a stronger electronegativity than sulfur or oxygen, antibonding (*) orbitals with lower energies are drawn closer to the bonding area.
2. The energy of the -system decreases as a result of the longer S–N bonds because they cause fewer electron pairs to repel one another.

The key ideas needed to comprehend the bonds and structures of several intriguing inorganic compounds were covered in this chapter. Here, we discovered that this family of chemicals is crucial to the synthesis of a number of practical polymeric materials. Due to their distinctive chemistry and bonding, the P-N and S-N compounds continue to be a focus of current study. New compounds have been created and their structures have been examined. The S-N compounds can't be compared to the aromatic organic compounds since they follow Hückel's criteria for aromaticity but the P-N compounds do not [9].

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CHAPTER-3

ALKALINE EARTH METALS AND ALKALI ORGANOMETALLIC COMPOUNDS

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This unit's goals are to familiarize you with the synthesis, characteristics, structure, bonding, and applications of organometallic compounds made from alkali metals and alkali earth metals. Each organometallic compound has been discussed, along with its unique reactivity, synthesis process, and applications. Additionally, information on their structural bonding relationships has been given. Students will be able to comprehend their reactivity, structure, and usage at the conclusion of this course. The extensive field of organometallic chemistry of alkali and alkali earth metals is introduced in this chapter. One or more metal carbon bonds may be found in an organometallic molecule. Each compound's stability, reactivity, and structural characteristics are influenced by the periodic characteristics of the corresponding metal.

Li and Na Organometallic Compounds

Organolithium and organosodium compound synthesis Among the group I organometallics, organolithium compounds are particularly important. These compounds may be made by treating an organic halide with lithium or by employing butyllithium in the metallation processes in the presence of a hydrocarbon solvent, such as hexane. Compounds made of organolithium: structure and characteristics.

Both in their solid state and their solution states, alkyl lithium compounds are polymeric. The Li atoms define an octahedron in a (RLi) 6 hexamer whereas they create a tetrahedral unit in a (RLi)4 tetramer's ethers. Weiss et al. demonstrated that the average length of the Li-Li bond in the structure of (MeLi) 4 is 261 pm as opposed to 267 pm in Li2. Additionally, it was determined that only six Li-Li bond lengths in the Li6C6-core of (LiC6H11)6 (C6H11 14 cyclohexyl) are in the 295-298 pm range, while the other six bonds are substantially shorter. (238–241pm). Multinuclear NMR spectroscopy is used to identify the existence of such aggregates in the solution. The polarity of a covalent link between two distinct elements may be identified by the electro negativity difference between them because organolithium compounds have a carbon-metal bond [1].

An element's ability to attract electron density increases with its electronegativeness. Because of this, partial positive charge continues to function in electropositive elements whereas partial negative charge continues to function in more electronegative elements. The electronegativity difference in organolithium compounds. Mg's Organic Metal Compounds: Synthesis, Characteristics, Structure, Bonding, and Applications. Organomagnesium compound synthesis Victor Grignard, a French scientist, developed organomagnesium halides in 1900. Alkylmagnesium halide solutions may be created by reacting magnesium and alkyl halides in ether solvents to produce Grignard reagents [2].

Arrangement and Fusion

Only a dimer of the Grignard reagent was seen. R2Mg can only be seen when R is bulky, such as when MgC(SiMe3)3 is present.According to crystal structure data, Grignard reagents are often solvated, and the Mg center is typically tetrahedrally located, for instance in EtMgBr.2Et2O. There are instances of 5- and 6-coordination when the macrocyclic ligand forces the greater number of coordination on the metal center. Multiple species, such as RMgX, R2Mg, MgX2, and RMg(m-X)2MgR, may be present in Grignard reagent solutions, which are further complicated by solvation [3].

Compounds of Beryllium and Calcium that are Organometallic

By reacting organopotassium with beryllium chloride in an ether medium, beryllium alkyls and aryls are produced. Water hydrolyzes them, and air causes them to flare up. Me2Be is monomeric in the vapour phase, with a linear C-Be-C unit possessing a Be-C bond distance of 170 pm. Polymers make up the solid-state structure. While a localized bonding scheme may be used to explain the bonding in BeCl2, there aren't enough valence electrons accessible to (Me2Be). For a similar image of connection. Therefore, 3c-2e bonds are anticipated as seen in Figure 1 for BeH2. The tert-butyl derivative is monomeric under all circumstances, whereas higher alkyls gradually polymerize to a lesser amount. When pi-electron rich ligands like cyclopentadiene are combined with beryllium, a sandwich molecule resembling ferrocene results [4].

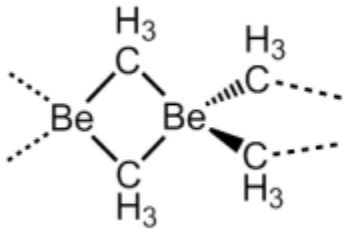

Figure 1: Structure of organ beryllium compounds.

The more electropositive group 2 metals are heavier, and metal-ligand bonding is often thought to be mostly ionic. Cp2Ca, Cp2Sr, and Cp2Ba are polymeric and insoluble in ethers and hydrocarbons, in contrast to Cp2Be and Cp2Mg, which are monomeric and soluble in hydrocarbon solvents. This chapter covered several crucial ideas for understanding the bonding, structure, and applications of Li, Na, Mg, Be, and Ca organometallic compounds. All individual compounds' applications and the bonding between their synthetic structures have been described [5].

Transition Metal Alkyls and Aryls

The goals of this unit are to expose you to the synthesis, characteristics, structure, bonding, and applications of transition metals' organometallic compounds. Each organometallic compound has been discussed, along with its unique reactivity, synthesis process, and applications. You will

comprehend the significance that ligands play in stabilizing organometallic compounds as well as several elements that contribute to their destabilization.

The study of molecules with metal-carbon bonds is known as organometallic chemistry. Because they lack metal-carbon linkages, metal carbonates and metal carboxylates are not considered to be organometallic compounds. Metal cyanides and metal carbides contain a metal-carbon connection, however they are not termed organometallic compounds since they are not organic. The d and f block's organometallic chemistry has just lately been explored. A few d-block organometallic compounds were produced and largely described in the eighteenth century. In 1951, when IR and NMR methods were accessible, the extraordinarily stable organometallic compound ferrocene, Fe(C5H5)2, was discovered.

Within a short period of time, the'sandwich' structure of ferrocene was accurately deduced from its IR spectra and then conclusively established by X-ray crystallography. The following are some general differences between coordination compounds and organometallic compounds: While organometallic compounds are often neutral, have stable d-electron counts, and are soluble in organic solvents like tetrahydrofuran, coordination complexes are typically charged, have variable d-electron counts, and are soluble in water. Many organometallic compounds have low melting points, and the majority of them exhibit characteristics that are far more similar to those of organic molecules than inorganic salts. The most straightforward organometallic compounds are metal alkyls and aryls. Their transition metal compounds were only discovered very recently [6].

Transition Of Metal Alkyls and Aryls

Metal alkyls are created by the bonding of metal atoms with alkyl radicals, while metal aryls are created through the bonding of metal ions with aryl radicals. Alkyls of transition metals are crucial components of various organic synthesis processes. Among organic reagents, lithium alkyl compounds are one of the most often employed. The accidental synthesis of the very unpleasant-smelling Me2As-O-AsMe2 by a cadet using As2O3 and CH3COOK marked the beginning of organometallic chemistry in a pretty spectacular way. In a different instance, Edward Frankland sought to produce free ethyl radicals using ethyl iodide and metallic zinc. He did, however, end up with a colorless liquid that turned out to be diethyl zinc rather than the intended radicals. Frankland is thus regarded as the founder of organometallic chemistry and ZnEt2 is the first synthetically produced organometallic chemical. Alkyl magnesium halide (RMgX) compounds, sometimes known as the Grignard reagent, were later found by Victor Grignard.

Bonding and Sturdiness

The quantity and kind of coordinating ligands affect a metal complex's stability and reactivity. Different bonding mechanisms allow the ligands to attach to metal. If they can make numerous bonds, they may be of the donor/acceptor type or solely the sigma donor type. Alkyl complexes, as Al2Me6, are widely known for their ability to connect two metal centers. Numerous bonding techniques used by metal alkyls. Metal alkyls may be grouped under the following headings and their key characteristics are also examined based on their stability and the process that causes them to decompose [7], [8].

Early transition metal alkyls While the MC bond becomes significantly more secure and less reactive as one moves right and down the periodic table, alkyls of early transition metals like Ti or Zr are very air and moisture sensitive. The intrinsic stability of the alkyl group attached also affects how stable the alkyl compounds are overall. For instance, the lone pair of the anion is stabilized by increasing the "s" character as we proceed from sp3 CH3 - to sp2 C6H5 - to sp hybridized RC-, and as a result, reactivity reduces. In contrast to the main group metal alkyl compounds, the synthesis of stable transition metal complexes with d block metals proved to be much more challenging.

The MC bond in transition metal-alkyls was discovered to be unstable due to the presence of numerous breakdown routes, which caused the challenge. Since the metal-carbon bonds in these compounds are sufficiently strong (E = 30-65 kcal/mol), it is possible that kinetic rather than thermodynamic considerations are to blame for the instability. As a result, if we are aware of the causes of thermodynamic instability, we may take steps to mitigate them by altering the structure of the organometallic complex. If the instability was caused by kinetic causes, handling this is far simpler than increasing the bond strength. Here, we first go over what makes these complexes thermodynamically unstable.

β-Elimination:

The main cause of the breakdown of metal alkyls into hydridometal alkene complex is elimination. The following criteria must be met for -elimination to take place: The complex's -carbon should have a -hydrogen substituent. For the -hydrogen to be close to the metal atom, the orientation of the MCCH should be almost coplanar. The metal must have a free space where it may interact with an atom of hydrogen.

The phrase "vacant site" refers to more than just the opening created by the entering ligand in the coordination sphere of the metal atom. Additionally, the metal has to have an open orbital to take the -H, or more specifically, the pair of electrons that make up the C-H bond. Alkene hydride is therefore produced and has 2e- more than the alkyl starting material. iv) It has been discovered that the phenomena of -elimination occurs more often in the d2 system than in the d0 and primary group metal alkyls.

The Agostic Alkyls

Agostic interaction is the term for intramolecular weak bonding between a C-H proton and a metal center. It would seem that -elimination should take place in certain metal alkyl complexes, however it does not. The Ti(PMe2)2(CH2CH3)Cl3 is one such example. The C-H bond seems to successfully approach the metal in this instance for -elimination, but the reaction does not take place. This occurs because d 0 Ti lacks an electron density that would allow for a back donation into the C-H bond's * orbital. In a manner analogous to the process of oxidative addition, this back donation is crucial for breaking the C–H bond. Additionally, stability is added to the complex with an empty coordination site by the agostic interaction of the C-H proton with the metal center. As a result, we now understand that in order to break the C–H bond, we not only require an unoccupied 2esite on d orbital (an empty d orbital), but also a full d orbital (an accessible electron pair). A bifunctional acidic and basic character is necessary for the majority of frequent organometallic

reactions. These criteria are satisfied by the partly filled d orbitals of transition metals, which makes elimination processes possible.

Reduction and Exclusion

Reductive elimination is a highly frequent breakdown process shown by metal alkyls. As a consequence, the electron count and oxidation state both fall by two. Any metal alkyl (d 0 or 18e) in which the metal may reside in an oxidation state two units lower than that of the initial complex is susceptible to this phenomenon. Due to their thermodynamic stability, metal alkyl complexes with a halide functional group do not undergo reductive elimination since the equilibrium in the reaction is on the left.

Reductive elimination is both thermodynamically and kinetically advantageous if X=H. However, the kinetics of the elimination are not particularly favorable if X=CH3. Because H only contains one 1s electron that is bonded and is capable of forming or breaking bonds in either direction in the transition state, the elimination process is most favorable when X=H. The sp3 orbitals of the CH3 are pointed toward space, however they may not be optimally orientated to provide effective overlap in the transition state, as shown in Figure 2.

Figure 2: An example of reductive elimination.

Halide Removal

Metal alkyls with halide substituents may also experience "elimination of halide," which is similar to "-elimination of H." Due to the strong M–F bond strength, fluoro alkyls of early transition metals, lanthanides, and actinides are not particularly stable and undergo halide -elimination. Late transition metals, on the other hand, create stable fluoro alkyls and have a weaker M–F link. The strength of the M–C bonds is quite strong. For the basic late transition metals, CF3 functions as an acceptor via the C-F bond's * orbitals, strengthening the M-C bond. Eg. With late transition metals, C6F5 creates very stable alkyls. In this case, orbitals serve as electron acceptors.

Stability Against Large Substitutes

Bulky substituents have long been employed to stabilize a variety of organic ligand-based metal complexes, from alkyls to carbenes. Particularly with 16e-metals, decomposition routes that include the interaction of the organometallic complex with a solvent or with another complex molecule are also described. These may be inhibited by adding large coligands. eg. Compared to its p-tolyl equivalent, the diphenyl nickel(II) complex is less stable. This is due to the square planar Ni(II) complex being more open to assault from other species when seen from a 'z' direction

perpendicular to the molecule's plane. Organometallic chemistry often employs bulky alkyl groups as adamantyl, norbornyl, neopentyl (CH2CH3), or trimethylsilylmethyl (CH2Si(CH3)3). Although the aforementioned factors prevent a-elimination, it is sometimes possible. As a result, carbenes with M=C bonds are created. For instance, the first step in the thermal breakdown of Ti(CH2t-Bu)4 is -elimination, which results in the creation of Ti(=CHtBu)(CH2t-Bu)2. Instead, the carbene complex t-Bu(CH)=Ta(CH2t-Bu)3 was created by the synthesis of complex Ta(CH2t-Bu)5.

Metal Alkyl Synthesis

Metathesis

Organomagnesium, organolithium, organotin, organozinc, and organoaluminum reagents react with metal halides. Usually by a nucleophilic assault on the metal, Grignard or organolithium reagents react with a metal halide or cationic metal complex to produce an alkyl. Transmetalation is the process of moving an alkyl group from one transition metal to another.

Organic Synthesis Using Organic Copper Compounds

Copper is bound to the carbon atom in a type of organometallic compounds known as organocopper complexes. Organocopper chemistry may be said to have begun with the isolation of a phenyl copper compound from copper iodide and the phenyl Grignard reagent, notwithstanding the impure nature of the product. Gilman emphasized the significance of organocopper complexes in synthetic organic chemistry in 1936. Grignard reagents and, -unsaturated ketones undergo a reaction in which catalytic concentrations of organocopper reagents prefer 1,4-addition over 1,2-addition. This observation sparked additional research and development of these reagents. Currently, the most often utilized reagents in synthetic organic chemistry are organocuprates. Copper's oxidation states are included in group 11, along with silver and gold. Cu (0) and Cu (IV) species are the least common of the copper oxidation states, which include Cu (I), Cu (II), Cu (III), and Cu (IV). Cu (II) state is the most prevalent in inorganic and coordination chemistry. Cu (II) was reduced to Cu during the production of organocopper compounds (I). As a result, Cu is the oxidation state of copper in organocuprates (I). Organolithium compounds are more reactive than organocuprates in terms of the stability of organocopper compounds.

Compounds made of organocopper are inherently thermally unstable. Organocuprates' R functions as nucleophiles that target different organic electrophiles. Below 0 °C, alkyl copper complexes break down. Alkyl, aryl, alkenyl, and alkynyl are commonly determined to be the stable states of these chemicals.

By (i) replacing the hydrogen atoms in the organic moiety with fluorine, (ii) adding additional ligands like phosphines or amines, and (iii) using substituents with heteroatoms that can provide the metal with extra intramolecular coordination sites, it is possible to increase the thermal stability of organocopper compounds. These complexes may have several conceivable geometries than the linear, trigonal, or T-shaped ones that are often seen in them.

Organocuprate Uses

Cross-coupling processes employ organocopper compounds to create higher alkanes. Cross coupling reactions occur when two distinct alkyls R and R′ join forces to create a brand-new alkane RR′. Alkyl groups may form new CC bonds via this kind of reaction. Organocopper reagents provide quick and easy ways to couple two distinct carbon moieties. The C–Cu bond is less polarized than Li–C or Mg–C bonds because copper has a lower electropositive value than Li and Mg. The following differences in reactivity result from this distinction: (i) Alkylated compounds are produced when organocopper reagents react with alkyl, alkenyl, and aryl halides. (ii) Organocopper reagents are more selective and may be acylated with acid chlorides without harming esters, ketones, or alky halides. (iii) The 1,4-addition of the organocopper reagents is preferred over the 1,2-addition when reacting with, -unsaturated carbonyl compounds.

The importance of ligands in influencing the stability of organometallic compounds cannot be overstated. These complexes may be synthesized using a variety of techniques. The stability of these compounds is primarily regulated by two processes: -elimination and bimolecular breakdown reactions. By changing the substituents and some of the other parameters mentioned above, complexes may be designed in which these effects are minimized. Organocopper complexes have a very important function in synthetic organic chemistry. These complexes may be created using the numerous techniques that have been covered.

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CHAPTER-4

ENZYME USE IN THE FOOD AND DRINKS INDUSTRYBREWING AND MAKING CHEESE

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Enzymes are crucial in the production of many commercial food items. These are only a few examples: vinegar, cheese, beer, and wine. Enzymes are useful for regulating a number of processes, including process time, flavor enrichment, texture improvement, and shelf-life extension. Complex compounds are broken down by enzymes into simpler ones, such as sugar from carbs. They are organic compounds that take part in all biological processes. All living cells generate enzymes, which serve as catalysts in certain chemical processes. Enzymes are very effective, which reduces the actual cost of their respective operations. Below are some examples of how enzymes are utilized in the food, beverage, brewing, and other industries.

In the Food Business, Enzymes

Inorganic life activities including digestion, respiration, and metabolism depend heavily on enzymes. It has a broad range of applications in the food industry and processing because of its outstanding catalytic efficiency, particularly in the production of cheese, bread, beer, and wine. Animal tissues, food plants, edible plant components, and microorganisms including bacteria, yeast, and fungus are all sources of enzyme extraction. Rennet is a naturally occurring enzyme found in the stomachs of domestic animals like calves and goats that is used to make cheese. The baking, drinks, brewing, and dairy industries may also see revolutionary expansion in the enzyme business.

Drinking and Brewing Industries Use Enzymes

In the beverage business, enzymes are cutting-edge alternatives to chemical or mechanical techniques for increasing output and quality. Pectinases, amylases, cellulases, and xylanases are a few of the enzymes that are used in the extraction and clarifying of fruit juices. Alcohol is produced from sugar during the brewing of beer. Enzymes from malt, which is barley that has been germinated, interact with the starch of other grains during mashing to create sugars. By skipping this step, energy and farmland will be saved. Malting needs grains and heat for drying. B. subtilis proteases are used in the preparation of wort to solubilize proteins from barley adjuncts. Microbial proteases also hydrolyze the proteinaceous components in beer that cause haze to appear. Here are a few of the enzymes utilized in the beverage and brewing industries [1], [2].

Making cheese with Enzymes

Using cheese, milk may be kept fresh for a very long time. In order to preserve milk proteins and fat, bacteria, enzymes, and naturally occurring acids are used throughout the lengthy and complex process of creating cheese. Milk may be kept for many months or even years after being made into

cheese. The key preservatives that give cheese its life are acids and salts. Four different kinds of enzymes are utilized to make cheese, including: Rennet 1. In order to make cheese, milk must first be infected with rennet and lactic acid bacteria. An enzyme called rennin, which is present in rennet, aids in the modification of milk proteins. Rennin specifically transforms caseinogen, a prevalent protein in milk that does not dissolve in water, into casein. Curd is what forms when the casein precipitates out as a gel-like material. The majority of the milk's fat and calcium are also absorbed by the casein gel. As a result, the milk begins to curdle and separate into curds and whey due to the lactic acid and rennet. Proteases 2. Whey protein, which is broken down by an enzyme called a protease, is present in cow's milk. Therefore, suggests assistance in the dissolution of these proteins and peptide linkages. The whey protein is removed from the milk after curdling in order to make soft cheese. Catalase 3. This enzyme aids in the conversion of hydrogen peroxide into water and hydrogen. In order to maintain the natural milk enzymes that are helpful for the cheese product's flavor development, this is utilized while manufacturing cheese. 4. Lipases Lipases aid in the digestion of milk fatty acids for creating cheese. Lipases are used to create cheeses with richer flavors. These flavors are derived from the fatty acids created during the hydrolysis of milk lipids.

Made from Corn Starch Syrups

One of the foods created from maize starch is corn syrup. This is the umbrella term for a wide range of nutritional sweeteners made from maize starch. A concentrated and refined mixture of the saccharides produced by the hydrolysis of maize starch is known as corn syrup. A relatively large number of sugars, including glucose, maltose, and some higher oligosaccharides, are present in maize starch. Practically speaking, corn syrup is the liquid hydrolysate of mono-, di-, and higher saccharides and is made from starch, such as that found in potatoes, wheat, tapioca, and starch. It is also known as glucose syrup and is often used to improve flavor, prevent sugar from crystallizing, and soften textural volume. High fructose corn syrup (HFCS) is a liquid substitute for sucrose as a sweetener.

Making of Corn Syrups

Corn starch is primarily used as a raw material in the manufacturing of corn syrup. In certain businesses, corn syrup is produced straight from maize powder. However, maize starch works best for making high-quality corn syrup while making corn syrup. The following is a quick description of the manufacture of corn syrup:

Preparation of the Raw Materials

The "yellow dent corn" kind of corn is the main ingredient used to make corn syrup. In the midwestern region of the United States and other parts of the globe, it is one of the common varieties grown. Other ingredients used in the process of turning maize into corn syrup include water, hydrochloric acid, sulfur dioxide, or other enzymes. The corn starch should have a significant level of corn starch for the processing of raw materials. The ideal specification would be as follows: starch content (85.4%), moisture (14%), fat (0.1%), protein (0.4%), and ash (0.1%).

Mixing Technique

The liquefaction conditions for corn starch or starch milk are adjusted during the mixing process. This procedure must be carried out in a controlled environment with a pH between 5.3 and 5.6. To achieve the desired concentration of the medium, the appropriate quantity of water should be supplied. 8.6.1.3 Liquefaction The starch milk completely contacts steam via the injection port, quickly warms up, and the starch is totally liquefied before being inactivated by a high temperature and high pressure jet [3], [4].

Saccharification

The pH level is lowered to between 4.2 and 4.5 following liquefaction, and the solution is cooled to 60 °C. Under the influence of the enzyme, the liquefied substance continues to react for a while. The needed glucose's dextrose equivalent (DE) value should be between 15% and 20%. Depending on how quickly an enzyme reacts, the reaction time for saccharification is typically between 24 and 48 hours. The glucoamylase enzyme assists in this phase by releasing individual glucose units from the ends of the dextrin molecule. Using this method, syrups with a glucose content of 95% or more may be produced.

Filtration and Color Removal

After passing through the filter to remove protein and other impurities, glucose flows through active carbon to decolorize it at the proper temperature before being sent through filters to remove the activated carbon and continuing to the next phase.

Evaporation

The glucose is thoroughly cleaned using a safety filter machine before being delivered to an evaporator for concentration to produce the desired DS. A drum or spray drier is used to remove 97% of the water from corn syrup powder, also known as corn syrup solids. Corn syrup powder with crystals is the result of this [5].

The Uses of Corn Starch

Corn syrups are widely used in the food industry to prepare the following foods: 1. It is commonly used in meals, beverages, cigarettes, cold drinks, fruit juices, preserve foods, and wines, among other things. Commercial goods including breads, cereals, yogurts, soups, and sauces, among others, benefit from its thickening, sweetening, and humectant properties. 3. It preserves food goods' freshness and moisture. 4. HFCS is created using corn syrup, and products containing it include baked goods, drinks, yogurt, and sauces. HFCS improves a product's sweetness, texture, and flavor, stabilizes its color, and lowers its cost. 5. HFCS works well to improve the texture and sparsity of dairy goods like chocolate milk and ice cream. 6. With a comparable concentration, it may take the place of cane sugar. While tasting somewhat like natural juice. 7. The applicability in other industries, such as agriculture, pharmaceuticals, animal feed, and poultry feed, has not yet been described [6].

Enzymes as a Drug Design Target

Numerous kinds of biological reactions have been recognized to be catalyzed by enzymes. They serve as biological targets for medications, which are intended to have the desired therapeutic impact. In contrast to cell surface receptors, nuclear hormone receptors, ion channels, and transporters, enzymes provide novel potential for drug creation. Drugs may affect enzymes in two different ways: first, by inhibiting them (inhibitors), and second, by inactivating them (inactivators). The first one is more typical in this regard. The medications that operate as enzyme-inhibitors or inactivators do so either by noncovalent binding or covalent interaction with nucleophilic enzyme residues. These medications work by blocking the contact between the enzyme and substrate via competitive, non-competitive, or uncompetitive interactions. Microsomal enzymes in newborn jaundice and Cushing's syndrome are a few examples of these targeted enzymes, as are transmembrane receptors like receptor tyrosine kinases, receptor JAK-STAT receptors, receptor Serine-Threonine Kinases, receptor Toll-like receptors, and receptor TNF- receptors.

Drugs' mechanism of Enzyme Inhibition

It is well knowledge that enzymes and substrates react. Here, the enzyme and substrate combine to create an enzyme-substrate (ES) complex, which ultimately leads to the synthesis of the final products. Using competitive, non-competitive, or uncompetitive inhibition of the enzyme-substrate interaction, drugs that inhibit enzymes stop the production of the product. As a result, the drug's kind of inhibition is categorized appropriately [7].

Drug-Induced Competitive Enzyme Inhibition

Compounds that have chemical structures and molecular geometries similar to the substrate molecule's produce competitive inhibition. The inhibitor just binds to the enzyme in this kind of inhibition; it does not also bind to the complex of the enzyme and substrate. Competitive inhibition is often known to be overcome if enough substrate molecules are eventually available because the inhibitor becomes tightly bonded to the enzyme and prevents any substrate molecules from further interacting with the enzyme.

Drug-Induced Non-Competitive Inhibition

A chemical interacts with the enzyme at the allosteric site to inhibit the enzyme non-competitively. It has an identical affinity for both the ES complex and the enzyme. Drugs don't always need to resemble the structure of the enzyme's substrate. This kind of restriction cannot be overcome. The substrate can no longer interact with the enzyme to produce a reaction since the active site's shape has changed. Non-competitive inhibition is often irreversible, however in a few instances, such as when acetazolamide inhibits carbonic anhydrase, reversible inhibition has been seen. Aldehyde dehydrogenase is inhibited non-competitively by disulfiram. It produces diethylthiomethyl carbamate (DETMC), an active metabolite. Acetaldehyde cannot be converted to acetic acid anymore. Acetaldehyde buildup produces flushing, nausea, vomiting, and other symptoms that are regarded as a positive aspect in the process of overcoming an alcohol addiction. In addition to disulfiram, other medications that inhibit aldehyde dehydrogenase include metronidazole,

schlorpropamide, glibenclamide, tolbutamide, griseofluvin, cefotetan, cefoperazone, etacrynic acid, and urinary antiseptics like nitrofurantoin.

Anti-Suicide Medications

It creates an irreversible kind of enzyme inhibition when an enzyme contacts an inhibitor and forms an irreversible complex with the inhibitor. Suicide inhibition is also known as suicide inactivation or mechanism-based inhibition.

For instance, -lactams are administered with -lactamase inhibitors to block the -lactamase enzyme and so prevent the breakdown of -lactam medications like penicillins. Clavulanic acid undergoes structural change as a consequence of a covalent connection with a serine residue found in the active site of -lactamase. Drug targets for microsomal enzymes Hepatocytes' endoplasmic reticulum is the normal location for microsomal enzymes. They are crucial in the metabolism of several endogenous substrates and medications. specific medications have the ability to activate or inhibit these enzymes in order to change how specific endogenous substrates or medications are metabolized [8].

Connected to intracellular enzymes via transmembrane receptors Transmembrane receptors function in cell signaling by interacting with external substances. When ligands bind to membrane receptors, a process known as signal transduction occurs via membrane receptors that includes both equivalent internal and exterior events that set off an intracellular response. There are many different types of Transmembrane receptors linked to intracellular enzymes, such as receptor tyrosine kinases, JAKSTAT receptor, receptor serine-threonine kinases, toll-like receptors (TLR), TNF- receptors (Tumor necrosis factor alpha receptors), etc.

The majority of enzyme-linked receptors are protein kinases or are associated with it [9].

Applications

Pharmaceutical companies employ enzymes as pharmacological targets to create medications, such as theophylline, methotrexate, and other dihydrofolate reductase inhibitors. The therapeutic role of enzymes has further expanded to include things like tissue plasminogen activators, which work as fibrinolytics, -lactamases for penicillin allergies, and serratiopeptidases as anti-inflammatory agents. To treat malignant disorders, a variety of anti-cancer medications have been developed.

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CHAPTER-5

MOLECULAR -COMPLEXES

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This chapter will examine the synthesis, bonding, structure, reactions, and different structural characteristics of organometallic compounds with diverse donor/acceptor ligands. Alkenyl, allyl, aryl, akynyl, diene, cyclopentadiene, etc. are examples of these ligand classes. The terminology and fundamental ideas of organometallic chemistry will be introduced in this chapter before moving on to organometallic complexes, their synthesis, reactions, and characteristics. The chapter seeks to give information on the structure and interactions of metal atoms with their organic ligands' molecular orbitals, including carbene, carbyne, and carbide, as well as some other pertinent topics [1], [2].

The research focuses on organometallic compounds. These compounds have mostly covalent metal element bonds. It incorporates both inorganic and organic chemistry. Organometallic compounds are mixtures of metal ions and organic ligands in which the metal is connected to the ligand through a metal-carbon link. The contact between one or more carbon atoms of an organic group or molecule and a transition, lanthanide, actinide, or main group metal atom must be "ionic or covalent, localized or delocalized" in order for these complexes to form a bond. This MC bond (MC, MC, M C) may be single, double, or triple bound. One of the first studies on metal carbon single bonds dates back to the late nineteenth century, when substances like the Grignard reagent came under scrutiny. Organic and inorganic chemistry have been brought together by organometallic compounds. These complexes have a broad variety of uses in the catalysis industry. This chapter will address the synthesis, stability, chemical reactivity, nomenclature, applications, and other characteristics of metal alkenyl, allyl, aryl, akynyl, diene, and cyclopentadiene complexes as well as certain arene and alicyclic ligand complexes.

Hapticity

The process through which a ligand's group of adjacent atoms is coordinated to the metal center is known as hapticity. The Greek character eta () denotes it. The number of adjacent ligand atoms that are coordinated to the metal is denoted by the symbol x, where x is represented by the letter x. The phrase is often used to describe ligands with prolonged -conjugation. Complexes of transition metals with carbon (structure, synthesis and reactions).

A ligand in carbido complexes is atomic carbon. Carbido complexes are carbon-only bonds to metal atoms. These complexes are thus not particularly reactive, but if one or more metal atoms are taken out to reveal the carbon atom, the complex changes into a highly reactive species. They may be used to create more intricate carbides. Two Fe2+ ions are removed from [Fe6C(CO)16] by 2-oxidation, exposing the carbon atom, which may interact with nucleophiles like carbon monoxide. The production of carbides and other organic compounds uses the carbido complexes as precursors. A terminal carbide complex with a Ru-C distance that is close to a metal carbon

triple bond is RuC(PCy3)2Cl2. PCy is the tricyclohexylphosphine ligand in this instance. Below are a few examples of metal carbide complexes [1], [2].

Complexes in Transition Metal

Alkene, allyl, diene, and arene ligands are often used to create transition metal complexes. These ligands are unsaturated and hence abundant in electrons, which may engage in donation, donation, or back bonding, among other forms of bonding. These unsaturated ligands undergo significant property changes when metal ligand bonds are formed, which is critical for their key synthetic uses. On the basis of their capacity to serve as electron donors, metal complexes may be classified into a number of different categories. i. Alkene and alkyne are two electron donors; alkenyl and alkynyl complexes. Complexes made out of allyl, a three-electron donor. Diene is a four-electron donor in dienyl complexes. Comparing Arene complexes with Aryl, a six-electron donor, to cyclopentadienyl complexes with five electron donors [3].

Arrangement and Fusion

Alkenes are two electron donors, and their bond bonds to the metal in a specific way. The Dewar Chatt model accounts for two electron donations that are in opposition to one another. One sigma is donated from C=C -electrons to an empty metal d orbital, and then a full metal d orbital is donated back into an empty C=C * orbital. It follows that it is clear that metal in the d0 configuration won't combine with olefins. The olefinic moiety coupled to metal experiences the above-mentioned form of electron donation, which alters the C=C bond and alters the CC bond distance. The quantity of back bonding relies on the metal center's electron density and whether or not an alkene has electron withdrawing groups to boost its capacity to absorb electrons. For instance, the complex below is a superior acceptor since it has electron-withdrawing fluorine groups. The C=C bond is weakened as a consequence, whereas the alkene metal bond is strengthened.

The C-C bond in the metal-bound olefin moiety lengthens when there is less of a metal to ligand back donation than a ligand to metal donation. This occurs because the alkene to metal donation takes the C=C electrons out of the olefin moiety's C=C bond and transports them toward the metal center, reducing the bond order and lengthening the C=C bond in the process. Additionally, the electron donation from the filled metal d orbital to the metal that is attached to the olefin moiety rose as the metal to ligand "back donation" increased. The length of the C=C bond increases as a consequence of this. This elongation of the C=C bond in the metal-bound olefin may be linked to the metal's basicity. For instance, C=C bond lengthening is anticipated to be minimal for weak basic metals while being large for strong basic metals. One may see a shift in hybridization at the olefinic carbon as a consequence of ligand-metal back donation.

When there is metal to ligand back donation, the sp2 olefinic carbon that is present in complexes without it converts to sp3 carbon. Both 1H and 13C NMR spectroscopy are capable of quickly identifying this shift in hybridization. IR spectroscopy may be used to quickly monitor electronic effects in alkenes. The C=C double bond becomes weaker and the C=C stretching frequency in the IR decreases as back bonding increases. Both donating and back bonding, it should be noted, weaken the C=C link and reduce the stretching frequency, but back bonding has a stronger impact.

Stronger binding of strained olefin systems to the metal center, as shown in the case of cyclopropane and norbornene, is also caused by the metal to ligand "back donation." These systems' stronger bonds are a result of the strain alleviation they get when they attach to the metal. The chemical reactivity of the olefin attached to the metal is opposite to the free olefin in metal-olefin complexes with little back bonding. Due to the abundance of electrons in its outermost valence orbital, a free olefin is vulnerable to electrophilic assault. But when an olefin is attached to a metal (an "olefin-metal complex"), there is a considerable electron donation from the metal to the ligand, which causes the olefinic C to become positively charged and be attacked by a nucleophile.

Umpolung character describes this reversal of olefin reactivity's nature [4]. Complexes of transition metals with alkyls (structure, synthesis and reactions). Alkynes have an additional pair of pi electrons compared to alkenes. Depending on the requirements of the metal concerned, they may function as two or four electron donors. They produce good bridging ligands thanks to the additional pair of pi electrons.

Arrangement and Fusion

Alkynes may interact through sigma bonding (sigma 1) and/or beta bonding (sigma 2) to produce a variety of coordination states. It is possible to think of transition-metal alkynyl complexes as complexes of the HC-C ligand, which has an isoelectronic bond to CN, CO, and N2. Alkynes are classified as strong-field ligands in the spectrochemical series and, in comparison to the other ligands in the series, are excellent donors and acceptors and poor acceptors. For steric and electrical reasons, alkynes are better donors than alkenes and coordinate to metal more easily. In addition, they are more responsive to reactions such as C-C coupling. Alkynes are often used as bridging ligands because they virtually invariably form bonds parallel to the M–M axis. In cluster compounds, they can bridge more than two metals [5].

Complexes of Transition Metal Allyls

Allyl (-C3H5) complexes, allyl (-C3H5) complexes, and allyl bridged (-C3H5) complexes are the three types of metal allyl complexes. The allyl radical (CH2=CHCH2) donates only one electron to the metal-allyl bond in allyl complexes (1, monohapto form), resulting in a typical carbon-metal electron-pair connection. While the allyl radical provides three electrons to the metal-allyl bond in allyl complexes (3, trihapto form). In complexes, this leads to a stronger metal-allyl connection. According to some accounts, the allyl ligand may bridge bonds.

Complexes of Transition Metal Butadiene (Structure, Synthesis and Reactions)

Arrangement and Fusion

The four (hapticity) electron donors that are diene ligands are covered below. Complexes with the 4-electron donor 1,3-butadiene are the most researched. It forms a trans bond with the metal. According to the Dewar-Chatt model, the ligand may attach to metal as either an L2 (2) donor type (for example, (butadiene) Fe (CO)3), which is analogous to an alkene, or as an LX2 (2) donor type. Bonding of the L2 type is less frequent than LX2 type. Because of the LX2 type of bonding, the length of the C2-C3 bond, which was previously 1.45, is now 1.40, as shown in Figure 1.

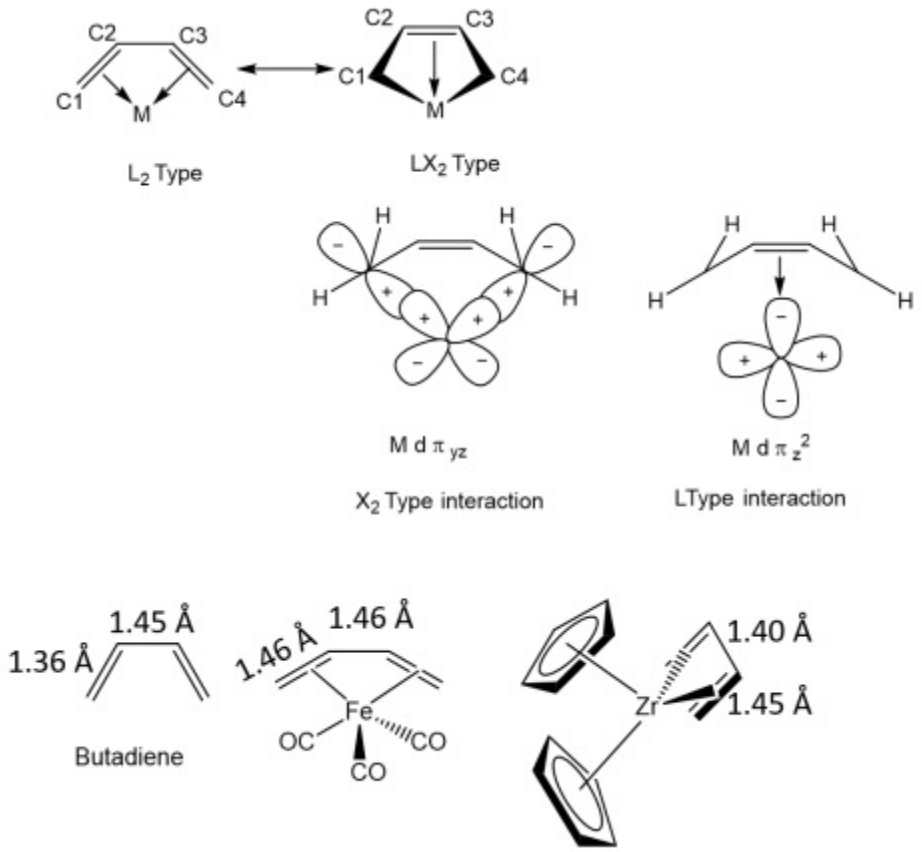

Figure 1: Transition Metal Butadiene Complexes.

Cyclopentadiene Transition Metal Complexes

The formal contribution of dienyl ligands to the bonding of transition metals is five electrons. Cp, also known as cyclopentadienyl (C5H5), is the most prevalent dienyl. This ligand is made up of several different organometallic substances. It stabilizes the organometallic complexes and is inert to the majority of nucleophiles and electrophiles. They might be bent metallocene Cp2MXn (n=1, 2, or 3), metallocene Cp2M type, or "piano-stool" CpMLn (n=2, 3, or 4). The Cp ring serves as the "seat" of the stool in the "piano-stool" structure, while the other ligands serve as its legs.

Other metallocenes are referred to as "sandwich" compounds because the metal atom is sandwiched between two carbocyclic rings in these compounds. The most frequent binding form to metal is the 5 form, although other rarer hapticities are also seen, such as 3 in (5 -Cp) (3 -Cp)W(CO)2 and 1 (monohapto) in (5 -Cp)(1 -Cp)Fe(CO)2. The 1H NMR spectroscopy may also be used to determine the binding mechanisms of Cp. For Cp-protons, a singlet is seen between 5.5 and 3.5 ppm. Other related transition metal complexes are known under names that are trivially similar to ferrocene, such the complex (-C5H5)2Fe. They took part in reactions like those of aromatic chemicals, thus the name. Only ferrocene has good thermal stability up to 5000 C and does not oxidize in air among the several metallocenes. The list below includes a few known metallocene instances [6].

Ferrocene's Structure and Bonding

Two anionic cyclopentadienyl (Cp) rings that are sandwiched together and each donate six electrons to the Fe2+ cation were discovered to form the sandwich structure of ferrocene in 1952 by G. Wilkinson and R. B. Woodward. Single crystal X-ray diffraction investigations on the structure of ferrocene have shown that iron is positioned between two cyclopentadiene rings. The placement of these rings resembles an eclipse. The range of C–C lengths is 1.40–0.02. The hexagonal ring of benzene with sp2 hybridized carbon is comparable to the pentagonal ring of Cp. Six electrons, of which three are in the five -bonding orbitals and the other two are unoccupied, are contributed by five electrons from five carbons and one electron from the creation of Cp. Fe(II) is d2 sp3 hybridized in the Fe complex ferrocene, with each Cpcoordinate providing three electron pairs.

Interaction of cyclopentadienyl with metal in Ferrocene

Five orbitals (numbered 1 through 5) are present in the cyclopentadienyl ligand's frontier molecular orbitals (FMO), which are dispersed across three energy levels. Since the lowest energy state (1) has no nodes, it is known as an a1 state. The next higher energy levels after a1 are the doubly degenerate e1 states, which are 2 and 3. The primary axis is contained in a single nodal plane for them. Double degenerate 4 and 5, also known as e2 states, which have two nodal planes and are much more energetic, are located above them. Until the number of molecular orbitals equals the number of atomic p orbitals, which is the number of carbon atoms in the ring, this pattern of doubly degenerate orbitals of increasing energy and nodal planes continues. The highest antibonding orbital is degenerate if this number is odd, while it is not degenerate if this number is even. Ligand group orbitals are created when two ligands interact in addition to or in subtraction via their orbitals. (LGO).

The linear combination of the five p-atomic orbitals' wave functions for the C5H5 ring yields the wave functions () of these five molecular orbitals. The molecular orbitals are created by combining them with atomic orbitals on the metal that have the same symmetry. (MO). Consider the ligand bonding orbital with the lowest energy for a better understanding. A gerade ligand group orbital with symmetry (a1g) identical to the atomic s orbital is created when the wave function of this orbital from the two ligand metallocene rings is joined. On the other hand, if the two wave functions are subtracted, an ungerade LGO with the same symmetry as an atomic p orbital is created. (a2u). Other LGOs may thus be created in a similar way by combining or combining the upper MOs of the two rings. The orbitals interact with the metal orbitals to produce the overall molecular correlation diagram of Cp2M type complexes, as illustrated below.

From Sc through Zn, the first row of transition metal ions forms the Cp2M type complexes. The quantity of unpaired electrons matches the quantity of unpaired electrons found in the metal's valence orbitals. Manganocene is one of two types of transition metallocenes in the first row. The first is a low spin form with one unpaired electron like Cp2 *Mn, where Cp* has a stronger field, while the second is a high spin form with five unpaired electrons like Cp2Mn. The cobaltocene compound Cp2Co, which has 19 valence electrons, is oxidized to produce the diamagnetic

Cp2Co+ compound, which now has 18 valence electrons. Similar to this, Cp2Fe has 18 valence electrons and is likewise diamagnetic. The ferrocene MO diagram is seen below. Fe(II) (6 electrons) and two C5H5 rings (2x6=12) combine to occupy a total of 18 electrons. With 19 and 20 electrons, respectively, Fe(C5H5)2 is more stable than Co(C5H5)2 and Ni(C5H5)2, respectively. This is caused by the absence of electrons in antibonding molecular orbitals (ABMO) in ferrocene, compared to the presence of one ABMO electron in cobaltocene and two ABMO electrons in nickelocene. Cobaltocene and nickelocene are quickly oxidized since these electrons may be withdrawn so easily. Similar to Cr(C5H5)2 and V(C5H5)2, which contain vacant bonding molecular orbitals and nonbonding molecular orbitals due to having 16 and 15 electrons, respectively, making them vulnerable to reduction [7].

Organometallic chemistry, a crucial topic of inorganic chemistry, is explained in this chapter. The notion of synthesis, bonding, and chemical reactivity of organometallic complexes is developed in this course. It establishes a link between inorganic and organic chemistry. The feature of many organometallic complexes is the idea of -bonding and -back donation. These substances need extensive investigation since they are key catalysts in several organic synthesis processes [8].

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CHAPTER-6

THE ROLE OF METAL SCUFFS

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The chapter discusses isopoly and heteropoly acids, as well as boranes, carboranes, metalloboranes, and metallocarboranes. With regard to their synthesis, structure, and characteristics, metal cluster compounds are the focus of this chapter. We will concentrate on different boranes and carboranes, their synthesis, and different characteristics of bonding in this family of molecules. Multiple metal atoms with a diverse coordination environment are seen in metal clusters. It brings the reader's attention to how the chemistry of these materials differs from that of the bulk metal.

Clusters are groups of atoms or molecules that are between a molecule and a bulk solid in size. They serve as a bridge between atoms, molecules, and bulk material and may have a variety of nuclearities and stoichiometry. Cluster characteristics vary with cluster size. Metal-metal connections exist in metal clusters. This chapter begins with boron compounds before moving on to clusters such isopoly-heteropoly acids, carboranes, metalloboranes, and metallocarboranes. These complicated materials have a variety of uses in both industry and the production of different organic derivatives.

Boron

Natural forms of the element include kernite ($Na_2B_4O_5(OH)_4.2H_2O$) and borax ($Na_2B_4O_5(OH)_4.8H_2O$). Colemanite, Urexite, and Kernite are a few more ores containing boron. Tetrahedral or trigonal BO_3 units may be found in borate minerals. There are two stable isotopes of boron: $^5B^{10}$ (19.6% abundance), which has a relatively high neutron absorption cross section, and $^5B^{11}$ (80.4% abundance). While the other elements in group 13 (III A) exhibit metallic qualities, boron is a non-metal and is a member of this group. As a result, boron's chemistry is quite distinct from that of the other group members. Because of its propensity to use its sp^2 hybridized orbitals to generate covalent compounds, boron is similar to carbon and silicon. The high energy of ionization prevents the formation of any ionic compounds containing B^{3+} cations. All BX_3 compounds exhibit Lewis acid behavior and are coordinatively unsaturated, with Lewis bases often forming adducts [1].

Boranes or Boron Hydrides

Since just boron and hydrogen bonds are involved, boron creates a number of hydrides known as boranes, which may either be neutral or ionic. They are electron deficient species because they don't have enough valence electrons to form a confined bonding pattern. Alfred Stock was the first to research their chemistry. B_2H_6, B_4H_{10}, B_9H_{15}, $B_{10}H_{14}$, and $B_{20}H_{16}$ are examples of typical boranes.

Many mistakes and discrepancies were made in the early phases of deciphering the structure of diborane, which eventually led to the development of the structure we currently know. There cannot be normal 2c-2e (two center-two electron, two electrons are shared between two atoms) links because of the impending electron shortage in their structural formula. Thus, the first theories of multicenter bonding were proposed in an attempt to justify the structure of boranes. The 3c-2e (three center-two electron) bond hypothesis put out by Languet-Higgins made a significant contribution to our knowledge of bonding in boranes. This suggests that more than two atomic centers may be shared by a pair of electrons.

When compared to its electron-precise homologue C2H6, the simplest borane, diborane B2H6, has two more electrons available for bonding. Diborane falls two electrons short of the usual 2c-2e bonding, hence. It has been suggested that BH3 may exist as a dimer to create B2H6. X-ray diffraction research subsequently verified this. These investigations identified hydrogen atoms that were both terminal and bridging. Each boron atom has two terminal hydrogen atoms that combine to produce the traditional 2c-2e bonds, using eight of the 12 available electrons. The last two H atoms are bridge-like in their structure. The two boron cores are connected by them. (B-H-B). Only 4 electrons are used by the electron-deficient bridging bridges, which result in 3c-2e bonds. Thus, the creation of the electron-deficient B-H-B bridging bridges makes up for the deficit of two electrons. The higher boranes formed several 3c-2e bonds and gained a deltahedral structure[2], [3].

Carboranes

Carboranes are a broad class of boron and carbon atom-containing clusters. They are mixed hydrides of carbon and boron with a molecular structure that lacks electrons. The carboranes are thought to be formed from BnHn2 by substituting the BH unit(s) with isoelectronic and isostructural CH unit(s). Each C-H group is thought to be contributing three electrons to the framework electrons since it has one more electron than the B atom. Therefore, a neutral molecule with the general formula Bn-2C2Hn will result from the substitution of two BH. Carboranes with n ranging from 5 to 12 are known. In the carbon-containing boron framework, the electrons have been delocalized. High boron concentration carboranes predominate. Since B10H10 2- and B12H12 2- are the most researched boranes, C2B10H12, which is isoelectronic with [B12H12] 2-, is the most researched system for carboranes. Below is a list of more boranes and the associated carboranes:

Wade's Law

Kenneth Wade established a set of guidelines to forecast the geometry of boron clusters. These principles connect the number of skeletal electron pairs to the skeletal structures of boranes, carboranes, heteroboranes, and their anions (closo, nido, arachno, and hypho). The rule states that if a cluster comprises n+1 skeletal bonding electron pairs and has, let's say, 'n' skeletal atoms (the vertices), it will adopt a closo structure. Similar results are obtained for the skeletal bonding electron pairs nido if n+2, arachno if n+3, hypho if n+4, and so on [4].

Metallacarboranes

Metal complexes known as metallacarboranes or metallacarboboranes include at least one metal atom as part of the cage structure and function as ligands for carboranes or heteroboranes. They are inorganic polyhedral clusters that include various ratios of carbon, boron, hydrogen, and metal ions. Midway through the 1960s, Hawthorne and colleagues produced the first synthetic metallacarborane. The [C2B9H11] 2 (dicarbollide) cluster, which has a metal atom wedged between two dicarbollide units, is a typical example of metallacarborane. The cyclopentadienyl ligand, which is fairly akin to ferrocene in this case, and the dicarbollide bind as 5 and are thus thought to be isolobal. According to Hawthrone, [C2B9H11] 2 is isoelectronic with C5H5 and as a result, it should be able to serve as the ligand in compounds that are comparable to metallocenes.

Compounds Containing Multiple Metal-Metal Bonds

Compounds with metal-metal bonding are referred to as metal clusters. As ancient as chemistry itself, they are. We shall talk about the halide and oxide metal clusters here. These clusters usually include transition metals on the left side of the periodic table and have metal ions in higher formal oxidation states (+2 to +3). (Early second row and third row of transition metals). Zr, Nb, Tc, Ru, Rh, Hf, Ta, W, Re, Os, Ir, and Pt are a few examples. Since efficient d orbital overlap is critical for the stability of metal clusters, the d orbitals are important in the creation of these clusters. The cluster will become unstable when the d orbitals contract. These factors account for the first-row transition metals' inability to expand their d orbitals enough for effective overlap, even in +2 or +3 oxidation states.

These compounds have two fascinating structural characteristics. First off, the compound's Re-Re distance, at 224 pm, is less than the typical Re-Re distance in rhenium metal (275 pm) or in Re3Cl9. (248 pm). Second, at 330 pm from Re, the chlorine atoms are in an eclipsed configuration, which is smaller than the total of their van der Waals radii. (340-360 pm). Therefore, a staggered shape would be preferred in this circumstance. F described both of the aforementioned traits. By suggesting a quadruple bond, A. Cotton. According to Cotton, each Re atom was connected to four chlorine atoms in an almost square planar configuration, and the metal-metal linkages were centered on the z axis. The dx2 -y 2 orbitals are used to dsp2 hybridize the Re-Cl bonds. He suggested that the metal's dz2 and pz orbitals may combine and lay along the bond axis. The rhenium atom is directly in the path of one of the matching hybridized orbitals, whereas the other orbital is pointed in the other direction.

While the later hybridized orbital produces an almost nonbonding orbital, the former establishes a bond with the orbital of comparable symmetry on the second rhenium atom. Each metal atom's dxz and dyz orbitals point obliquely in the direction of the corresponding orbital on the other rhenium atom. Two bonds are created when these orbitals come together, one in the xz plane and the other in the yz plane. The two dxy orbitals on each rhenium atom side by side overlap to produce the fourth bond, which is a bond. Only when the chlorine atoms are eclipsed is it feasible for the dxy orbitals to overlap. The metal dxy orbitals will also be staggered if they are, resulting in 0% overlap. The Re-Cl bonds between the Re3+ and Clions are thought of as dative bonds. The total quadruple bond is made up of the eight d electrons from two metal atoms that are engaged in

a bond, two bonds, and a bond. The compound is hence diamagnetic. The small metal-metal distance and eclipsed orientation of chlorine atoms are also explained by this hypothesis [5], [6].

Triatomic Clusters

[(ReCl3)3] and its variants are a common illustration of a noncarbonyl cluster containing three metal atoms. There is a d 4 configuration for each Re (III). Instead of being paramagnetic, as would have happened if each Re atom had just a single link with another Re atom, the complexes are diamagnetic. The complexes are paramagnetic because the metal atoms are linked by double bonds to their nearby metal atoms.

Clumps of Tétranuclei

The dimer W4(O-i-Pr)12 of W2(O-i-Pr)6, whose structure is seen above, is one of the usual instances. It has also been possible to create WW single bonds in W4(OR)16. It may be thought of as W4(OR)12's saturated counterpart. Tetranuclear clusters may be created by dimerizing substances with quadruply linked dinuclear bonds [7].

Clusters of Hexanuclei

It is well known that rhenium and transition metals like molybdenum, niobium, and tantalum may form large metal clusters with many metal-metal connections. Eg. [Mo6Cl8]Cl4 is an octahedron having six metal atoms and eight chloride ions on each face. Each Mo(II) atom has four available electrons, which it may employ to create four connections with nearby metal atoms and four dative bonds with the four chloride ions.

Polyoxometalates (Isopoly And Heteropoly Acids)

One significant field of heterogeneous catalysis is acid catalysis. Polyoxometalates (POM), also known as heteropoly acids (HPAs), occupy a significant place among various acid catalysts as a result of their catalytic capabilities. Due to their excellent solubility in polar solvents and thermal stability, HPAs are utilized as catalysts in a variety of processes as acid, redox, and bifunctional catalysts in homogeneous and heterogeneous reaction systems. Additionally, they are used in medicine as homogeneous and heterogeneous catalysts as antiviral and anticancer drugs. A vast number of nanosized anionic clusters made of transition metal oxoanions connected by shared oxide ions are collectively referred to as polyoxometallates. Transition metal polyoxoanions like V, Mo, and W make up the majority of polyoxometalates. Based on their composition, the POMs may be divided into two broad categories of anions: isopolyoxometalates and heteropolyoxometalates. The isopolyoxometalates have the generic formula [MmOy] p- and are composed of metal-oxide clusters containing d0 metal ions like Mo6+, W6+, or V5+. These don't have any extra heteroatoms. The metal-oxide framework is combined with extra p, d, or f block components in heteropolyoxometalates. Here, x m, and they have the general formula[8].

Tri chromates (Cr3O10) and tetra chromates (Cr4O13) are two examples of polymerization reports. The polymerization process stops at (Cr4O13)-2. Corner sharing between CrO4 2- tetrahedra produces both these anions and the dichromate ion. There is a limited propensity for Cr to produce many polyacids. Evidently, the tiny size of Cr6+ prevents it from coordinating with

oxygen on an octahedral rather than tetrahedral scale. In a highly alkaline solution, the vanadate anion VO4 3- exists. Protonation takes place when the pH is lowered. As the pH is lowered from 13 to 8 in increasingly concentrated solutions, protonation and dehydration take place, creating [V2O7] 4- and higher vanadates. Low pH promotes polymerization, which leads to the precipitation of hydrous V2O5. Decavanadate [V10O28] 6- is produced at a pH about 6. As the pH is decreased to 3.5, the ion protonates to [HV10O28] 5 - and [[H2V10O28] 4-. Isopolyvanadate alkali salts may be colored or colorless. Salts with an alkali metal to vanadium ratio of at least one are typically colorless, whereas salts with a ratio of one or less are often colored. The dissolution of molybdate trioxide in aqueous alkali yields tetrahedral [MoO4]-2. Yellow molybdic acid MoO3.2H2O precipitates are produced at pH values that are very acidic. [Mo7O24] 6-, also known as heptamolybdate or paramolybdate, is the first stable isopolymolybdate. The octamolybdate ion [Mo8O26]-4 is produced when this solution is further acidified to a pH of between 1.8 and 2.9.

Vanadate, molybdate, and tungstate ions polymerize to create isopoly anions, with the coordination number of the metal ion ranging from four to six. Six oxygen atoms forming an octahedron around each metal ion make up the fundamental building block. The octahedra may connect by sharing an edge or an apex but not often a face. The stronger octahedral pattern allows the electrostatic repulsions to be relaxed. [V10O28] 6-, [Mo8O26] 4-, [W6O19] 2-, [W7O24] 6-, [Nb6O19] 8-, and [Ta6O19] 8- are a few examples of typical edge-sharing polyanions. Edge sharing is changed to apex sharing to create bigger polyanions. The isopoly anions might be thought of as a tightly packed array of oxide ions with metal ions residing in the octahedral holes. Ten octahedral are layered in an edge-sharing fashion in the [V10O28] 6- array. The metal ions repel one another because to the sharing of edges between MO6 octahedra, which is somewhat alleviated by the displacement of M from the octahedron's center.

It is interesting that isopoly anions cause the polymerization to stop. It has an answer that may be found in the arrangement of oxygen atoms. Strong bonds are formed between a terminal oxygen atom and a transition metal (such Mo (VI) or W(VI)). Because these terminal oxygen atoms are never in close proximity to one another, they cannot compete for the same open t2g orbital. Instead, they are found in opposition to an internal or bridging oxygen. This causes the metal ion to be shifted away from the oxygen next to it and towards the terminal oxygen, which is what we experience as the trans effect. Metal ions, on the other hand, are poor acceptors. Examples are Ga (III) and Al (III). They cannot stabilize their terminal oxygen atoms as a consequence, which allows them to attack neighboring units and cause further polymerization [9].

They generally have the formula [XxMmOy] n- (x m); M is typically Mo or W and sometimes V, Nb, or Ta. The heteroatom X could be present in the polyanion's center. Any element on the periodic table, including P5+, As5+, Si4+, Ge4+, B3+, and others, may serve as the heteroatom. Heteropolyanions are extensively explored since they are crucial for catalysis and other uses. Because their d orbitals are accessible for building metal-oxygen bonds, molybdenum and tungsten polyoxometalates have received the most attention and are the easiest to make. The 1934 determination of the structure of the associated phosphotungstate anion led to the common naming of the structure after its discoverer, Keggin. Other basic structures, such as the Wells-Dawson ion, were later identified, and their chemistry and potential uses as catalysts were elucidated.

Structure-based classification of polyoxometalates

Ammonium phosphomolybdate, which contains the [PMo12O40] 3 ion, is the first instance of POM. A few extremely symmetrical "parent" polyanions are taken into consideration when classifying the polyoxometalates, and several additional polyoxometalate structures may be seen as their derived forms as a result. These three parent structures may be thought of broadly as a tetrahedron, an octahedron, and an icosahedron polyhedron XOn (n = 4, 6, or 12) positioned in the middle. Below are the structures that are covered. A full structure has forty oxygen atoms of four distinct types: four internal X-O-M atoms, twelve terminal M=O atoms, twelve edge-bridging angular M-O-M atoms shared by the octahedra within an M3O13 group, and twelve corner-bridging quasi-linear M-O-M atoms joining two separate M3O13 groups. The 17O NMR spectroscopy was used to identify these various sorts of oxygen atoms. The geometric isomers are created when M3O13 groups are rotated by 600 degrees around the three-fold axis. Lacunary derivatives of Keggin anions are created when one or more metal atoms are taken out.

Additional Structure:

The secondary structure of HPAs is a general three-dimensional structure made up of massive polyanions, cations, crystallization water, and other molecules. In the solid state, heteropoly anions have counterprotons or cations in their acid form. These are crucial in tying together the nearby heteropoly anions. For instance, the protons in H3PW12O40.6H2O form H5O2 + species, which form hydrogen bonds with the terminal WOd to connect the four nearby heteropoly anions. Organic molecules may also be present in secondary structure.

Third-Level Structure:

The tertiary structure of the heteropoly acid (HPA) is its fully completed structure. In other words, it takes into account the distribution of protons, pore structure, and particle size. acids' characteristics the following list summarizes the general properties of heteropoly ions: Heteropoly acids often have a high acidity. They are often extremely soluble in organic solvents and very soluble in water. Because heteropoly compounds have low lattice energies, heteropolyanions likewise have low solvation energies. The solvation energy of the cation affects how soluble HPAs are. They are stable in aqueous medium at lower pH levels but hydrolyze at higher pH levels. Multi-electron oxidants include heteropoly anions. The oxidants with Mo and V are comparatively more potent. Strong oxidizers, heteropolymolybdates easily transform into the reduced form known as "heteropoly blues." Heteropoly acids' acidic characteristics Heteropoly acids act as strong acids in aqueous solution. They are frequently referred to as "super-acids" due to the fact that they are more potent than the typical mineral acids like H2SO4, HCl, HNO3, etc. This is explained by the existence of "mobile protons" in HPAs' secondary structure. Additionally, compared to mineral acids, the negative charge of HPAs is distributed across significantly bigger anions. Dissociation constants and the Hammet acidity function are often used to determine acidity. The polyanion's structure, its component elements, level of hydration, and level of reduction all affect how strong the acid is. Crystalline heteropoly acids' acidity weakens with increasing order [10].

Uses of heteropoly acids in catalysis

Numerous variables, including size, mass, electron and proton transport and storage capacity, thermal stability, oxygen mobility in the lattice, and Bronsted acidity, influence the use of HPAs as catalysts. Both homogeneous and heterogeneous systems (gas-solid, liquid-solid, or biphasic liquid-liquid) are capable of supporting catalytic processes. As a result of the following characteristics, HPAs may function as effective catalysts. Their structural mobility and multifunctionality. They display quick, reversible multi-electron redox conversions under favorable circumstances and are powerful Bronsted acids as well as effective oxidants. By adjusting their chemical makeup, their acid-base characteristics may be tailored. Unlike the network of zeolites or metal oxides, solid heteropoly compounds have separate solid state ionic structures. When substituted or after going through oxidation or reduction, the structure of heteropoly compounds is not altered, and they have excellent proton mobility. The HPAs have a good thermal stability in the solid state and are highly soluble in polar solvents. The dehydrogenation of alcohols, aldehydes, and carboxylic acids to generate C=C and C=O bonds, as well as the synthesis of carboxylic acids from their corresponding aldehydes, have all been processes in which HPAs have been utilized as catalysts. For the oxidation of methacrolein to methacrylic acid, the hydration of olefins like propene and butene, the polymerization of tetrahydrofuran, and other processes, HPAs have been developed and commercialized. Molybdovanadates are used as catalysts in the Wacker process, which oxidizes alkenes and couples aromatics. In the hydrodesulfurization and hydrodenitrification of fossil fuels, polyoxomolybdates are often utilized [11].

The information in this chapter is helpful for comprehending metal clusters that include boron hydrides and their transition metal derivatives, such as metalloboranes, carboranes, and metallacarboranes. An essential knowledge of metal clusters may be gained from their synthesis, naming, and structural aspects. The distinctive numerous bonds between metal atoms in certain transition metal clusters are another feature of metal clusters. The chapter's discussion of polyoxometallates puts the spotlight on the isopoly and heteropoly acids of chromium, molybdenum, and tungsten that may be used in catalysis.

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CHAPTER-7

IN SOLUTION FOR METAL-LIGAND EQUILIBRIA

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Complexes are created when metal ions are added to an aqueous solution that also contains other species, such as ligands, with which the metal ions may interact. These complexes include both weak and strong intramolecular interactions as well as metal ligand connections. The system achieves equilibrium between the reactants and newly generated species after a certain amount of time. Because these metalligand systems and their equilibrium are crucial to bio-organic, bio-inorganic, industrial, and other processes, it is necessary to investigate them. It is important to be aware of the equilibrium constants in order to comprehend the chemical behavior of systems in solution when the assumption is that the system is in equilibrium (equilibrium occurs between different chemical species in the system). These are known as stability constants or formation constants in a system where complexes form in metal ligand solution.

Constants of Stepwise and General Formation, and Relationship between Them

When a compound is said to be stable, it means that it may be kept in storage for a significant amount of time and exists in a stable state under appropriate circumstances. A measure of the strength of the interaction between metal and ligands that results in the creation of the complex is the stability constant (also known as the formation constant or binding constant). When viewed in terms of kinetic and thermodynamic stability, the production of complexes in solution may be understood qualitatively [1], [2].

Stable Thermodynamics

It is a measurement of the degree to which complex creation or degree of transformation happens under a certain set of conditions at equilibrium. The strength of the connection between the metal and the ligand determines the thermodynamic stability. There is a wide range in the strength of the binding between the metal and the ligand. For instance, the connection between the metal and the thiocyanate is exceedingly weak in [Co(SCN)4] 2+ and instantly breaks in aqueous solution. In contrast, the link between the ferric ion and the nitrile anions in [Fe(CN)6]-3 is very strong and does not dissolve in water. Therefore, metal ligand bond energy and other thermodynamic characteristics are relevant to thermodynamic stability. Hexa amine cobalt(III) cation [Co(NH3)6] 3+ in acid solution is kinetically inert and thermodynamically unstable, while tetracyanonickelate(II) [K2Ni(CN)4] ion is an excellent example of a thermodynamically stable complex yet kinetically labile [3], [4].

$$[Co\ (NH3)6]\ 3+ + 6H3O + \rightarrow [Co\ (H2O)\ 6]\ 3+ + 6NH4 +$$

Stability and inertness can be expressed thermodynamically in terms of free energies of reaction $\Delta G°$. A stable complex has large negative $\Delta G°$. The following relation relates the standard enthalpy change $\Delta H\ °$ for the reaction to equilibrium constant βn:

$$\Delta G^\circ = -RT \ln \beta n \quad \Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

Similar complexes of metal ions from a certain transition series with a specific ligand will not have substantially different S° values, and as a result, H° value will be connected to n values. As a result, the order of H°'s values will match the order of n values.

Kinetic Constancy

In general, reactivity or ligand substitution is referred to as kinetic stability. The quickness with which reactants change is what allows equilibrium to be reached. As a result, whereas substitution may proceed slowly with certain ligands, it may proceed quickly with others. Labile ligands are the first kind, while inert ligands are the second. The stability of the compound is mostly determined by time in kinetic experiments. It discusses the process and pace of complex creation. Formation constants that are cumulative and overall. When a complex forms, the competing species Mn+ ion, ligand (L), and H+ ions are in an acid-base equilibrium of some kind. Thus, two equilibria must be taken into account [5].

$$H + L \rightleftharpoons HL$$

$$M + L \rightleftharpoons ML$$

Moreover, to consider stability constant for complex formation the equation can be represented as:

$$M + nL \rightleftharpoons ML_n$$

Stepwise Formation Constant

Complex creation is thought to be a process that happens in phases and proceeds sequentially. The stepwise formation constant of MLn, for instance, may be written as.

Based on The Nature of Metal Ion and Ligand, Factors Affecting the Stability of Metal Complexes.

Chemical Reaction

Chelates are formed when a ligand is attached to a metal ion at two different sites, forming a closed ring in an inorganic metal complex. For a chelate to form, a bidentate ligand is the bare minimum. Alternately, we may state that multidentate ligands create chelate complexes. The term "chelate" comes from the Greek word "chela," which means "lobster or crab claw." A number of tests showed that inorganic chelate metal complexes were more stable than those whose structures lacked chelating ligands. However, there are a number of other elements that should be taken into account when determining the stability of complexes, as detailed below. Ethylene diamine (en) and cupric ion may combine to generate the complex ion [Cu(NH2CH2NH2)2] 2+. Consider, for instance, a reaction vessel with cupric ions, NH3, and en (ethylene diamine), assuming that the ligands are both equally accessible to the cupric ions and that the concentration of NH3 is double

that of the en ligand. The copper chelate complex created by the bidentate en ligand results in a five-membered ring, but in the copper complex formed by the NH3 ligand, the two en ligands are swapped out for four NH3 ligands. It is discovered that complex 1 has a higher concentration than complex 2 under the specified circumstances. This is explained by the extra stability offered by the chelation of a ligand in complex 1.

$$Cu^{2+} + 2en \rightleftharpoons [Cu(en)_2]^{2+} \quad 1$$

$$Cu^{2+} + 4NH_3 \rightleftharpoons [Cu(NH_3)_4]^{2+} \quad 2$$

Factors affecting chelation's stability Size of the ring

The size of the ring affects a chelate complex's stability. That is the quantity of atoms that make up the ring. A four-membered ring, for instance, is unstable, but complexes with five and six members are more stable. Due of the tiny inter-bond angle in the ring, internal strain is thought to be the source of the four membered chelate's instability. The broad description of the order is Five members followed by six and then seven By increasing the chelate size, metal chelates become less stable, as shown in Figure 1. This is because less entropy is lost during the creation of bigger rings since they are less rigid. Other multidentate ligands that form chelate complexes besides ethylenediamine (en) include diethylenetriamine (dien), EDTA (ethylenediaminetetraacetic acid), and DTPA. (Diethylenetriaminepentaacetic acid).

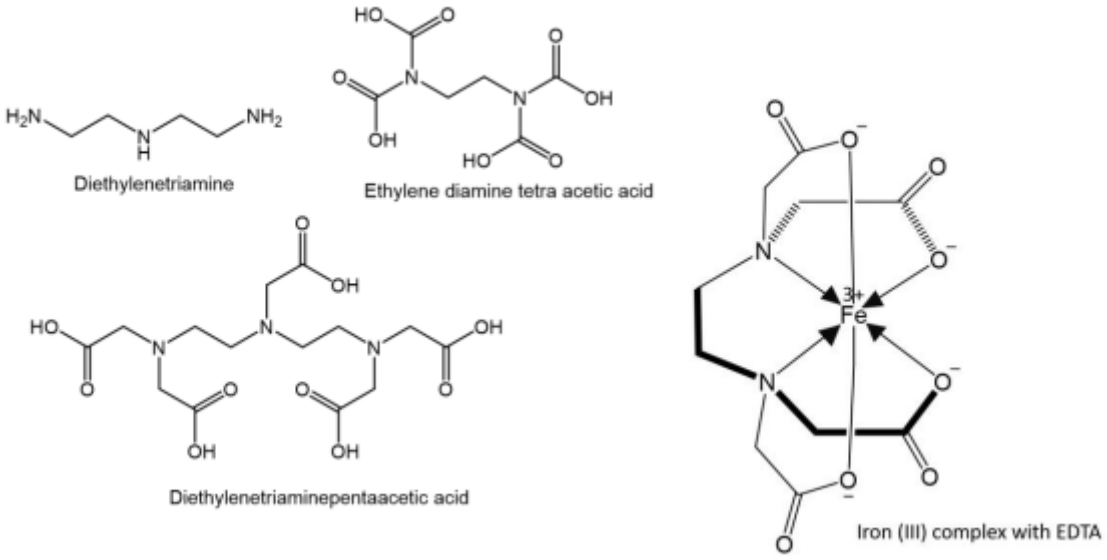

Figure 1: Illustrate the non-protonated version of EDTA creates a hexacoordinate complex.

When combined with iron-containing five-membered chelates. Because DTPA contains eight donor atoms, it may form complexes with large-atomic-size metals like actinide or lanthanide, which can have 8 or 9 coordinates [6].

Amount of Rings

In general, it has been shown that as the number of donor atoms accessible for coordination grows, so does the stability of the complex. The stability of the compound rises as the number of rings increases. A compound with no chelation, such as [Ni(NH3)6] 2+, is about 1010 times less stable than [Ni(en)3] 2+, which has three chelate rings. The chelate effect is the name Schwarzenbach gave to this rise in stability caused by the ligand's dentate nature. The transition metal ions have a stronger impact on this.

Stratic Impact

This phenomenon occurs when the groups on coordinating ligands interfere with one another, distorting bond angles and causing stability to diminish. The F-strain phenomenon is thus named. Complex stability rises as steric impact declines. In contrast to complexes with 8-hydroxy quinoline, Ni(II) complexes with 2-methyl 8-hydroxy quinoline are less stable. Ethylene diamine complexes are also more stable than their tetramethyl derivatives. The latter compounds contain more methyl groups, which results in increased steric repulsion. The thermodynamics of the chelate action We are aware that the chelate effect is what gives chelate complexes their increased stability. The thermodynamic elements of this phenomena may be used to explain the extra stability brought on by chelation. Entropy is thought to vary between complicated processes using chelates and those involving non-chelates. Because there are more free particles formed when chelate complexes are formed than when equivalent nonchelate complexes are formed, there is higher disorder as a consequence of the production of chelate complexes. The following instance will help to explain this fact. In comparison to a complex of the same metal ion with monodentate ligands possessing a similar donor ability, such as ammonia, the stability of a complex with a bidentate ligand, such as ethylenediamine, is noticeably higher.

Cyclical Impact

It has been shown that complexes generated with macrocyclic ligands exhibit greater stability than equivalent complexes created with open chain ligands. Entropy and enthalpy changes are taken into account for the phenomenon, which is known as the "macrocyclic effect." The fact that macrocyclic ligands can only bind to certain metal ions depending on the size of the cavity in them is an essential aspect. They exhibit selectivity with metal ions as a result, in contrast to open chain (chelating) ligands. For instance, the potassium ion, K+, and the crown ether 18-crown-6 form significantly stronger complexes than the sodium ion, Na+, which is much smaller.

Central Metal Ion's Nature

A and B class metals

Ahrland, Chatt, and Davies state that metal complexes may be classified as class A if they create stronger complexes with ligands that have N, O, or F as donor atoms, whereas class B can be

applied to those that form stable complexes with ligands that have P, S, or Cl as donor atoms. For instance, Pt(II) produces stable complexes with phosphine ligands when the donor atom is phosphorous, but Ni(II) creates stable complexes with amine ligands. Later, metals were divided into hard and soft categories according to Pearson's Hard and Soft Acid Base Theory (HSAB), with class a metal being hard acids and class B metals being soft acids. Hard bases and hard acids often combine to generate stronger complexes. While soft-soft interactions are mostly covalent in nature, hard-hard interactions are primarily electrostatic in nature. As the oxidation state rises, metal ions get harder. Fe3+ forms stable complexes with O donor ligands but Fe2+ does not, as can be shown from the fact that Fe2+ forms stable complexes with N donor ligands.

Determination of the Binary Formation/Stability Constants Methods

In the past few decades, the focus of research on the formation of metal complexes in aqueous solutions has shifted from more fundamental goals of understanding the mechanism of formation and correlating stability constant data to a wide range of practical applications, including the formation of complexes in biological fluids and the treatment of sewage. Finding the toxicity of cadmium to the grass shrimp (Palaemonetes pugio) in the presence of the chelating agent nitrilotriacetic acid and the chloride ion is an intriguing example of how these findings were put to use. (NTA). It was discovered via research on the metal ion's chloride and NTA complexes that the level of toxicity was closely correlated with the activity of the free cadmium ion. Stability data are utilized in instances like the ones above as tools to research systems or processes or to comprehend the workings of biological and other responses. Measuring the equilibrium constants (K) for the complex-forming process is often used to calculate the stability constant of the complex in the solution. Understanding the stability constant is essential for rationalizing our understanding of how metal complexes behave in solutions. Additionally, the majority of the complexes' features and usefulness rely on the research of stability or formation constants. To find complexes forming in solutions and estimate stability constants, several physical and chemical parameters may be used. The identification of complexes and the calculation of stability constants are closely connected processes. The next section discusses a few techniques for finding binary stability constants [7].

Potentiometric Technique

The connection between the ligand as an anion of the weak acid HnL and the metal ion Mm+ is investigated in this approach. Here, it is necessary to identify the type and concentration of every species present in the solution, including the pH of the buffer solution containing the metal ion often employed as perchlorate salt, base (NaOH), and HnL. (generalized here as MXm). We need equations on the mass balance and charge balance conditions in order to determine the stability constants using potentiometric pH titration data.

Method of Irving-Rossotti

The technique developed by Bjerrum is the foundation of the Irving and Rossotti approach. They demonstrated how, without knowledge of the hydrogen ion concentration or activity, the formation curve of a system of metal ligand complex could be estimated simply from pH-meter data during a titration. They arrived at straightforward generic equations that may be applied to any ligands

that are conjugate bases or weak acids, and they provided examples of how to employ those equations in particular situations. The ligand production curve on the Irving-Rossotti titration curves for the identical quantities of alkali is positioned in relation to the acid curve in two distinct pH ranges. The ligand titration curve has greater pH values at low pH than the acid titration curve, which suggests that it has less titrable hydrogen ions. Due to the dissociation of the -COOH group, it presents a lower pH value than the acid titration curve at higher pH levels and acts as an acid. nH may be computed from the displacement of these two curves.

The metal + ligand solution includes some titrable hydrogen ions as a result of the ligand's release of H+ ions upon coordination with the metal, which is why the metal titration curve has a lower pH value for the same quantity of alkali than the ligand curve. As a result, the difference in the volume of alkali needed to create the same pH in the metal and ligand titration may be used to calculate the n factor. The curves of formationThe Irving-Rossotti technique includes measuring the pH of the following three sets of mixes (while maintaining a fixed total volume) in comparison to a carbonate-free reference alkali. Method using spectrophotometry Methods using spectroscopes are quite sensitive. The species involved in chemical equilibria must absorb light and produce a distinct spectral response in order for this approach to work. As a result, UV-visible spectra may be used to directly assess the concentration of species engaged in equilibria and newly created species [8].

The approach is based on the Beer-Lambert Law, which states that log (I0/I) = cd (where I0/I is the ratio of incoming light to transmitted light, c is the molar concentration of the absorbing solute, d is the light path length in centimeters, and is the absorptivity) and that d is the light path length in meters. While measuring absorbance, several safety measures must be taken into account, such as guarding against contamination of the solution or cell faces. Additionally, because the spectrophotometer's precision in measuring absorbance is little, it should be utilized to capture minute variations in optical density. When just two species are involved, as in the ionization of monobasic acids, the equilibrium constant may be determined by measuring the absorbance as a function of wavelength at various pH levels. Since absorptivities are often great enough to enable analysis of solutions with concentrations up to l0-5 mol dm-3, this may be relevant for substances whose solubility is poor. A compound that is excessively stable or weak cannot have its K value calculated spectrophotometrically. Additionally, the obtained absorbances must be rectified if the ligand or metal absorbs at the selected wavelength.

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CHAPTER-8

STORAGE AND TRANSPORT OF METAL

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Transition metals are stored and transported by living things in order to maintain the proper concentrations for use as metalloproteins or cofactors as well as to safeguard themselves from the toxic effects of metal excesses. Metal cofactors and metalloproteins can be found in plants, animals, and microorganisms. Each metal has a certain normal concentration range in biological systems, and both deficits and excesses may result in pathological alterations. In multicellular creatures made up of a variety of specialized cell types, the storage of transition metals and the production of transporter molecules are not carried out by all kinds of cells, but rather by specific cells that specialize in these tasks. Metals are always ionic, but depending on biological requirements, their oxidation states may alter.

The transition metals iron, zinc, copper, molybdenum, cobalt, chromium, vanadium, and nickel are significant for biological storage and movement, in decreasing order of abundance in living things. Although zinc isn't strictly a transition metal, it does possess numerous bioinorganic traits and is treated as one in this chapter. More than any other metal in the group, iron storage and transportation are well known. Using chemical principles to describe biological structure and function is the aim of biochemistry. Since biomolecules are carbon-based compounds with a variety of functional groups, carbon occupies a central role in the chemistry of living things. More over half of a cell's dry weight is made up of carbon. The other five most common elements are hydrogen, oxygen, nitrogen, phosphorus, and sulfur. Metal ions and inorganic elements are equally important in biological processes, despite the fact that organic chemistry is more often associated with molecular biology.

The significance of metalloproteins, mettaloenzymes, and platinum in anticancer medications, as well as metals as inherent components of proteins, cannot be overstated. Alkali and alkaline earth ions, in particular Na+, K+, and Ca2+, have a function in biology in the induction of biological responses. The quick influx of sodium ions across the cell membrane to excite neurons and the regulation of intracellular activity by calcium-binding proteins like calmodulin are two of their crucial functions. Blood coagulation, acid-base balance, fluid balance, bone calcification, and osmatic regulation are further processes essential for the organism's existence. Around 70% of the inorganic material in the human body is made up of the seven primary elements calcium, phosphorus, magnesium, sodium, potassium, chloride, and sulfur. Important trace elements include iron, copper, iodine, manganese, zinc, molybdenum, cobalt, fluorine, selenium, and chromium. Other trace elements including barium, nickel, and vanadium may also be crucial for biological processes [1], [2].

External Parts of Living Systems

There are Six elements carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur make up all living matter and account for over 90% of the dry weight of the human body. The following elements are also important physiologically: Ca, K, Na, Cl, Mg, Cu, Co, I, Zn, F, Mo, and Se. They have quite different bodily compositions; for instance, Ca makes up around 2% of body weight whereas Co just makes up 0.00004 percent.

The Porphyrin Ring

A porphyrin is a big ring heterocyclic compound made up of four pyrroles (smaller rings made up of four carbons and one nitrogen). A massive ring is formed when these pyrrole molecules are connected by a string of single and double bonds, as shown in Figure 1.

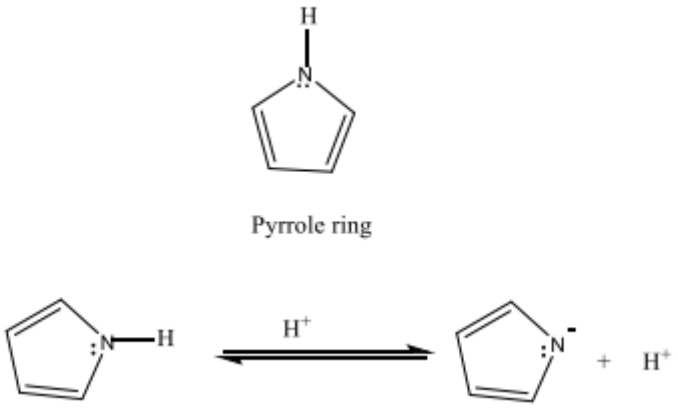

Figure 1: Illustrate the Pyrrole ring.

The scientific name for four connected pyrroles is a tetrapyrrole. The ring is flat in space, and the distribution of electrons along its circumference is rather uniform. A porphyrin is thus categorized as an aromatic compound. In this configuration, a porphyrin molecule is very stable. The prototype of a universal porphyrin is called porphin [3]. All across the biological world, the porphyrin pathway serves as an assembly line for the most common hues in both plants and animals. Porphyrins are ring-shaped molecules that bind various metal ions, each of which performs a specific biological function. Magnesium is bound by chlorophylls and is necessary for photosynthesis. Heme supports the electron transport chains necessary for cellular respiration, binds iron to coordinate molecular oxygen and carbon dioxide transport, and supports the catalysis of several enzymes.

Figure 2 illustrates how porphyrins bind nickel to create coenzyme F430, which is essential for bacterial methane metabolism. When cobalt binds to a porphyrin derivative, vitamin B12 is created; a vitamin B12 shortage may lead to pernicious anemia and impair brain and nervous system function. The "colors of life" might be referred to as these porphyrin-derived pigments since they are necessary for maintaining vital activities in almost all organisms. Heme, also known as protoporphyrin, is an iron-containing molecule that is essential to numerous biological functions by attaching oxygen to its iron ion. The ability of certain proteins, referred to as hemeproteins, to

connect to hememolecules is necessary for their ability to function. The amazing heme-iron interaction with certain amino acids or gas molecules is what gives heme its natural function[4], [5]. The prevalence of protoporphyrins containing other metals is lower than that of protoporphyrin containing iron. Despite the fact that there are several unique hemeprotein types with a wide range of activities, including hemoglobins, myoglobins, cytochromes, and peroxidases. The two most famous electron transfer (ET) chain mechanisms in nature, the aerobic respiration system of our mitochondria and the photosynthetic system of chloroplasts, both require hemeproteins. In ET activities, the Fe ion in heme (Fe2+, Fe3+) transports electrons, and its redox potential is highly dependent on the protein's heme-binding site [6], [7].

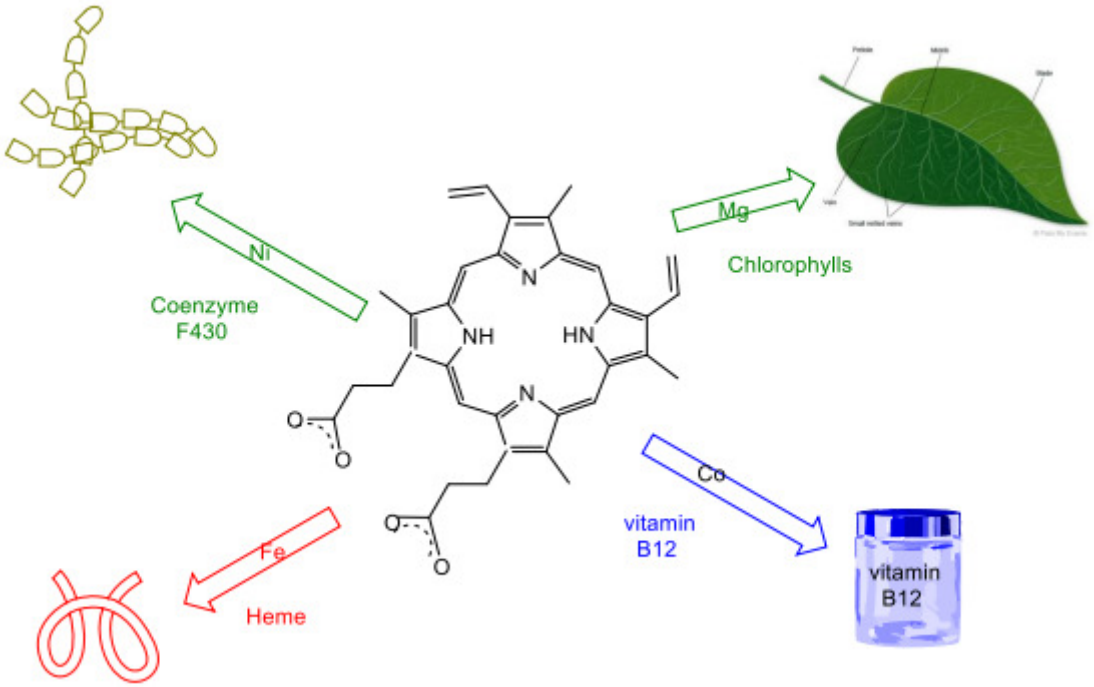

Figure 2: combination of several metal ions with the porphyrin ring.

Metalloporphyrin

The molecules bearing the heme group and the chlorophyll molecule are two significant types of the metalloporphyrins. The porphyrin ring's conjugated polyene structure is connected to chlorophyll's capacity to absorb light.

There are at least two purposes for the magnesium ions that are coordinated to the nitrogen atoms of the four pyrrole rings. They provide the required structural stiffness and accelerate the pace at which the singlet-excited state produced by photon absorption transforms into the triplet state, allowing the excitation energy to be transferred into the redox chain.

Transporting oxygen and mediating electron transfer processes are the two primary roles of heme iron-containing proteins. A protein molecule, such as hemoglobin, myoglobin, cytochromes, or an enzyme like catalase or peroxidase, is always linked to the heme group [8].

Observations made on metalloporphyrin include:

Metalloproteases are microcyclic compounds with cyclic structures or closed ring structures. Metal ions that are the right size for the cavity and can fit within it. iii. The number of conjugated double bonds in the matelloporphyrin ring is 11. The mattelloporphyrin ring is planar, stiff, conjugative, and follows the Huckel rule, making it an aromatic compound.

Iron's Impact on The Living System

Every living thing, including plants, bacteria, animals, and people, needs iron to carry oxygen via the hemoglobin in humans and animals and to generate energy. through electron transfer in the mitochondrial respiratory chain. The following categories of substances include iron in biological systems.

1. A substance containing one or more heme groups, such as cytochromes, cytochrome P450, myoglobin, and hemoglobin.
2. Iron-sulfur protein, such as nitrogenase, ferridoxin, and rubredoxin.
3. A chemical with a di-iron oxo bridge, such as haemerythrene or ribonucleotides.

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CHAPTER-9

TRANSPORT OF METAL FOR STORAGE AND BIOMINIRALISATION TRANSFERRIN, FERRITIN AND SIDERROPHORES

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Minerals with specific forms and compositions are synthesized in living organisms on specific organic surfaces of proteins and/or lipids. The natural process of biomineralization takes occurring everywhere, including the ocean. (Ca is involved in shell formation). Another example is the creation of the ferritin core. The main non-haem protein that stores iron in animals is ferritin. Keep in mind that myoglobin and hemoglobin contain the lion's share of Fe. When fully loaded, ferritin contains around 20% Fe in terms of mass. Once the ferritin is saturated, no more iron can enter the cell. In living things, there are methods for not only storing and accumulating metal ions but also using them afterwards.

Different complexion agents are used by the organisms to transfer iron. Higher animals' bloodstreams carry iron thanks to the iron-binding protein transferrins. Transferrins transport iron to the porphyrin ring, where it is inserted by enzymes, from the location where other iron-containing molecules, such hemoglobin and chromosomes, are produced. Because cells need and consume large quantities of iron, iron storage is crucial. Inorganic iron is stored in gut mucousal cells coupled to the intracellular protein ferritin.

Iron-Ferritin Storage

Ferritin's Function

In 1937, the French researcher Laufberger isolated a unique protein from horse spleen that contained up to 23% iron by dry weight. This protein turned out to be ferritin. Ferritin, an iron storage protein, is where the majority of iron is kept. Ferritin release tron is necessary for the synthesis of cytochrome, myoglobin, and hemoglobin. This is critical because unbound free iron is very poisonous and encourages the creation of free radicals, which harms cells. Ferritin plays a crucial role in the storage of iron in mammalian tissues such the liver, spleen, and bone marrow.

Ferritin Structure

Ferritin is an iron-binding protein that exists both within and outside of cells. As shown in Figure 1, apoferritin forms a roughly spherical container inside which ferric iron, the ferrihydrite mineral, is maintained. (Apoferritin refers to the iron-free form of the protein; the iron-containing form is termed holoferritin or simply ferritin). The apoferritin shell consists of 24 subunits in total, as shown in Figure 1.

H and L are the two categories of subunits. The ratio of these subunits varies significantly depending on the kind of tissue and is highly susceptible to inflammatory and viral conditions. L-subunit-rich tissue ferritins to H-subunit-rich tissue ferritins, which are mostly found in the heart

and kidney. The diameter of an apoprotein molecule is about 450,000 d. The L monomer has a molecular weight of 174 and is composed of 174 amino acids. The H monomer is composed of 182 amino acids and has a molecular mass of 21,000 d [1], [2].

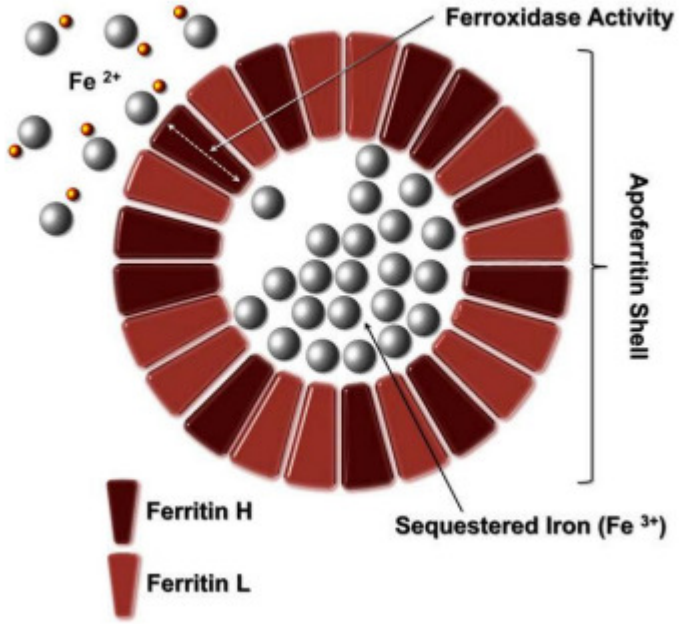

Figure 1: Illustrate the Structure of ferritin.

Iron-Transferrin Transport

Transferrins are a family of related and structurally significant glycoproteins called Fe-protrins. Their molar masses (molecular weights) are around 80 k Da. Old red cells are eliminated in the spleen and liver, while new haemoglobin is generated in the bone marrow. Transferrins are iron-binding proteins that transport iron in higher animals via the bloodstream to the site of synthesis of other iron-containing compounds such as hemoglobin, cytochrome, and others, where it is inserted into the porphyrin ring via enzyme. Transferrins include serum protein, lactoferrin (found in milk), and ovatransferrin (found in eggs).

Siderophores

Iron is required for microbial development even though it is weakly soluble in its ferric state. In order to allow iron to enter their cells, most bacteria create and release siderophores, which serve as highaffinity chelators. One of bacteria, fungi, and plants' most prevalent tactics is the generation of siderophores. (from the Greek: "iron carriers"). Low molecular weight natural iron chelators are known as siderophores (400–2000 Da). They are created when there is a deficiency in iron to scavenge iron and create soluble iron (III) complexes. Because they make it possible for organisms to acquire insoluble iron forms, they play a role in pathogenic bacteria stealing iron from host proteins. Low molecular weight natural iron chelators are known as siderophores (400–2000 Da).

They are created when there is a deficiency in iron to scavenge iron and create soluble iron (III) complexes. Because they make it possible for organisms to acquire insoluble iron forms, they play a role in pathogenic bacteria stealing iron from host proteins. A nearly universal element for microbes is iron. Iron is bound and transported by the serum proteins ferritin and transferrin in animals. Microorganisms collect iron from their environment via siderophores, solubilize and transport iron (III) by building very stable octahedral complexes with Fe(III), and then transport iron across the cell membrane since they are unable to bisynthesize high-molecular-weight complex proteins [3], [4].

The human body contains 5.0 103% iron, which is the most prevalent transition metal in biological systems by weight. It follows that the abundance and diversity of iron-containing proteins and enzymes in all living species are not unexpected. First, iron-containing species might be divided into two groups: those with a porphyrin ligand system and an iron-containing heme moiety, and those without porphyrin ligands and non-heme iron-containing proteins.

Heamoglobin

Animals' hemoglobin, which has a molecular weight of 645000, serves as an oxygen transporter. The majority of animals' blood color comes from pigment. When oxygen and hemoglobin are present, the color of the blood is red. Blue is the color of blood when haemoglobin has no oxygen. It results from an electron transfer between the iron atom's ring's and * orbitals. The average human body contains close to 4 g of iron. Haemoglobin uses around 0.8 g of thin to generate the red color in RBCs. The remaining iron is stored as ferretin. An excellent example of a protein's quaternary structure is hemoglobin. (association of two or more peptide chains in the complete protein).

Four heme units, one for each protein chain, are combined to form hemoglobin. Hemoglobin consists of two slightly distinct peptide chains in each of its four subunits. These are joined by hydrogen bonds, electrostatic forces, and van der Waals forces. The imidazole of histidine in the globin protein chain, exactly as in myoglobin by a coordinating histidine nitrogen atom, holds the heme prosthetic group in position in each subunit of hemoglobin [5], [6].

Hemoglobin has the molecular formula C34H32N4O4Fe. The hemoglobin molecule has two carboxylic and two ethylenic groups. The (-CH=) group on methine connects each of the four pyrrole rings in heme to one another. Hemeglobin contains iron that is located in the center of each of the four pyrrole rings, each of which includes one methyl group.

Each of the four subunits that make up hemoglobin has a polypeptide chain and a heme group. The iron protoporphyrin IX prosthetic heme group is present in all hemoglobins, and it is linked to a polypeptide chain with residues of 141 (alpha) and 146 (beta) amino acids. The N of a histidine is connected to the ferrous ion of the heme. A phenylalanine in its polypeptide chain wedges the porphyrin ring into its pocket.

Adult hemoglobin is made up of two types of polypeptide chains called alpha and beta chains that are identical in length but different in the order of their amino acids. Both embryonic and adult human hemoglobins have the same alpha chain. A larger look at the heme group shows that it is made up of a porphyrin ring and a ferrous iron atom (Fe2+). (four nitrogen-containing pyrrole

molecules). One molecule of oxygen and the iron atom may reversibly attach to each other. (O2). By absorbing dioxygen from the air in the lungs and transferring it to Mb in tissues, hemoglobin (Hb) delivers oxygen in the blood. A protein with several subunits, hemoglobin has two a and two p polypeptide chains.The hemoglobin molecule has a lifespan of around 16 weeks [7].

Myoglobin (MB)

An iron- and oxygen-binding protein called myoglobin, abbreviated as Mb or MB, is present in almost all mammalian skeletal muscle tissue. The same pigment as hemoglobin is myoglobin. It is made up of globin and heme. With 153 amino acids, it is alpha halical neuclear protein. Myoglobin has a molecular weight of 17000. When oxygen is needed, myoglobin releases its stored oxygen from the muscle tissue. Hemoglobin's monomer, myoglobin, has a Fe2+ ion in its active site. Myoglobin has a stronger affinity for oxygen than hemoglobin and does not cooperate with oxygen in the same way that hemoglobin does. However, it is fundamentally an oxygen-binding protein found in red blood cells. Myoglobin is only detected in the bloodstream of humans following a muscle damage. To bind oxygen, iron in the heme group must be in the Fe+2 form. Met myoglobin is produced when iron is oxidized to the Fe+3 state. Myoglobin concentration in muscle, which differs across muscle types, body weight, level of muscular growth, and overall quantity of myoglobin in an animal are all related. (red muscle is rich in myoglobin and white muscle is myoglobin poor).

Hb and Mb have likely undergone the most extensive research into metalloproteins due to the amount of spectroscopic, thermodynamic, and kinetic investigations that have been performed on their dioxygen-binding reactions. Their optical spectra are characterized by strong Soret, a, and bands in the 400–600 nm range, which are sensitive to the oxygenation level and are known as porphyrin ring to * transitions. An O-O stretching band at - 1105 cm-1 has been discovered via resonant Raman spectroscopy investigations of the coordinated dioxygen molecule and its '80-substituted analogs. This result indicates that MbO and HbO adducts are most appropriately categorized as coordinated superoxide (O2-) ion iron (II1) complexes. A diamagnetic ground state with S = 0 is produced by magnetic interaction between these ions. As a result, when dioxygen is coordinated to deoxy Hb or Mb, electron transfer takes place to create a superoxide ion, which is then stabilized by hydrogen bonding to the distal imidazole proton, as was mentioned before[8].

Collaborative Impact

Cooperative effect refers to the phenomenon in which the binding of one O2 molecule to one subunit promotes the binding of another O2 molecule to another subunit.The cooperative effect defines the conformational flexibility of the four identical haemoglobin subunits. The uptake or release of an O2 molecule by one of the subunits causes this alteration because it makes the other haemoglobin domains more capable of accepting or releasing oxygen.

The exquisitely complex bioinorganic system designed by nature in which dioxygen attaches to Hb in the lungs and is transferred to Mb in tissues or is transmitted to fetal Hb in the uterus is of great relevance to the physiological activities of Hb and Mb. When deoxy Hb turns into oxy Hb, iron moves toward the plane of the porphyrin ring. This mobility acts as a signal to the multisubunit hemoglobin protein to bind dioxygen cooperatively. It is assumed that the protein has two distinct

quaternary structures, R for relaxed and T for tense. While the latter, tense state, has a lower affinity for O2, the former has a high affinity for O2, comparable to that of isolated subunits. There is an equilibrium between these two conformational states. Inter sub unit interactions are thought to hold the proximal histidine back from moving into the porphyrin-ring plane and reduce the O2 binding constant in the T state, which occurs when all four sub units are a ligated.

Bohr's Impact

The Danish scientist Christian Bohr initially identified the Bohr effect in 1904. The Bohr effect is a broad term used to explain how pH affects blood-O2 binding affinity. Hemoglobin's (Hb) affinity for oxygen depends on the pH. With a drop in pH, Hb's affinity for that substance diminishes. Myoglobin's (Mb) affinity for oxygen is pH independent. Hemoglobin and oxygen (O2) attach to one another in a competitive and irreversible manner, with the affinity of this interaction depending on environmental factors.

Hemoglobin has a predisposition for positive cooperativity, which is shown by the sigmoidal shape of the oxygen dissociation curve. Hemoglobin undergoes conformational modifications to improve its affinity for oxygen as molecules gradually attach to each of its four accessible binding sites. The Bohr effect explains hemoglobin's reduced affinity for oxygen as a result of rising carbon dioxide partial pressure and/or falling blood pH. In order to fulfill the tissue's need for oxygen, this decreased affinity accelerates the unloading of oxygen into tissues [9].

Model HEME

One study found that myoglobin and hem group I hemoglobin had the remarkable capacity to bind oxygen molecules and release them later without irreversibly oxidizing the iron atom to the Fe(III) state. The following details are crucial: The Fe(II) center is thought to be substantially off of the porphyrin unit's plane prior to O2 binding; this location is known as the doming effect. As a consequence, the iron atom and the protein's globin domain are constrained. When oxygen binds to the iron atom in the heme group, it advances toward the plane of the heme, acting as a trigger and causing significant structural changes in the other hemogobin subunits.

The protein mass in both myoglobin and hemoglobin folds around the heme units.(s). This distinctive protein folding and structure surrounding the heme unit causes steric hindrance, which prevents the approach of two iron porphyrin moieties and prevents the creation of any hematin. To prevent access to the reactive iron centers, mass (like protein structure) has been introduced to sample iron porphyrin complexes in the synthetic models. The following considerations should be noted: In biological systems, imidazole and its derivatives serve as effective mimics for the protein histidine residue.

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CHAPTER-10

ROLE OF THE PHOTOSYNTHESIS IN BIO-ORGANIC

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Thanks to a process known as photosynthesis, plants can manufacture their own sustenance. They transform light energy into chemical energy. With the aid of this chemical energy, CO2 from the atmosphere and water are incorporated into organic molecules. It is frequently referred to as CO2 assimilation rather than photosynthesis. Not just in terms of quantity, but also in terms of quality, photosynthesis is an essential activity. Every year, photosynthesis changes 200 to 500 billion tonnes of carbon. Photosynthesis is thus a quantitatively significant process as well. The light response of photosynthesis results in the production of energy-dense NADPH and ATP at the cost of solar energy. These items are used in the carbon-assimilation process, which may take place in either light or darkness and lowers CO2 to make carbohydrates. Through the process of photosynthesis, green plants, algae, and photosynthetic microbes use solar energy to create carbohydrates from carbon dioxide and water.

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$$6CO_2 + 6H_2O \xrightarrow[\text{CHLOROPHYLL}]{\text{SUNLIGHT}} C_6H_{12}O_6 + 6O_2$$

Figure 1: Synthesis of carbohydrates from carbon dioxide and water.

Phase of Photosynthesis

There are two phases to the photosynthesis reaction: The light process, which produces NADPH and ATP using light energy. A carbon-assimilation or carbon-fixation process in which NADPH and ATP are used to synthesise carbohydrate from CO2 and H2O.These reactions are frequently referred to as "dark reactions", as shown in Figure 2 [1].

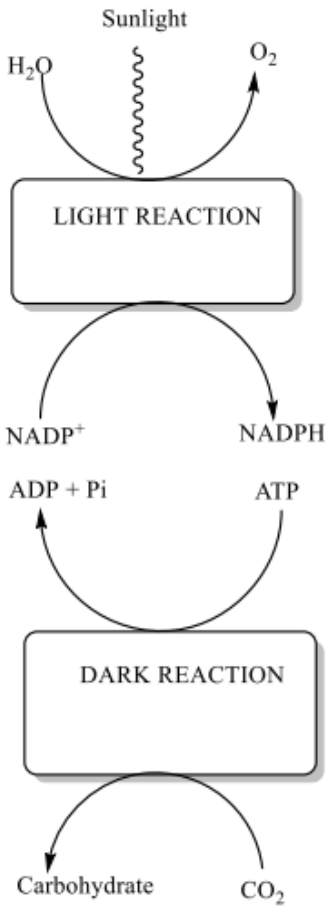

Figure 2: Illustrate the Light reaction and Dark reactions.

Function of photosystems I and II

Green plants and algae utilise two different kinds of photosystems: photosystem I (PSI) and photosystem II (PSII). (PSII). P stands for pigment, and P700 refers to the reaction center chlorophyll in PSI, whereas P680 refers to the reaction center chlorophyll in PSII. PSI's reaction center chlorophyll has an absorption maximum of 700 nm. The two photosystems are connected by additional electron carriers, notably the cytochrome bf complex. The many elements of the so-called Z scheme (Fig. 1.20) are arranged in accordance with their redox potential because the overall shape of the redox diagram gives the appearance of z. These activities make use of plastoquinone, plastocyanin, ferredoxin, and other highly mobile electron carriers [2].

Light-Dependent Reduction Mechanism

Electron transport routes from H2O to NADP+ are established during photosynthesis. This endergonic process is made possible by the light absorption properties of PSII and PSII. A PSII chlorophyll in a PSII reaction center has no tendency to give up an electron while it is in its ground, unexcited state. It becomes excited when a photon's energy passes through the antenna chlorophyll, and it has a strong propensity to transmit that excitement to its excited electron. Actually, it functions as a reducing agent. A mobile quinone in the thylakoid membrane with a structure like

ubiquinone in the mitochondrial electron transport chain, plastoquinone (Q) receives the high-energy electron after being delivered there. As a consequence, P680 becomes the P680+ cation. By absorbing two electrons and two H+ ions, plastoquinone is transformed into plastoquinol(QH2). The following should be noted: i. A protein complex containing Mn catalyzes the light-driven splitting of H2O, producing O2 in the process. (Fig. 1.21). This potent reductant creates NADPH by transferring its electron to NADP+. ii. The four electrons that have been removed from the water do not get immediately to P680+ since this atom can only take in one electron at a time. Instead, the water splitting complex, a unique molecular apparatus, transfers each of the four electrons to P680+ one at a time. iii.Now that PSII has reduced plastoquinone, it now transfers one electron to the cytochrome bf complex. A copper-containing protein called PC accepts electrons by cycling between the Cu2+ and Cu+ states of copper [3].

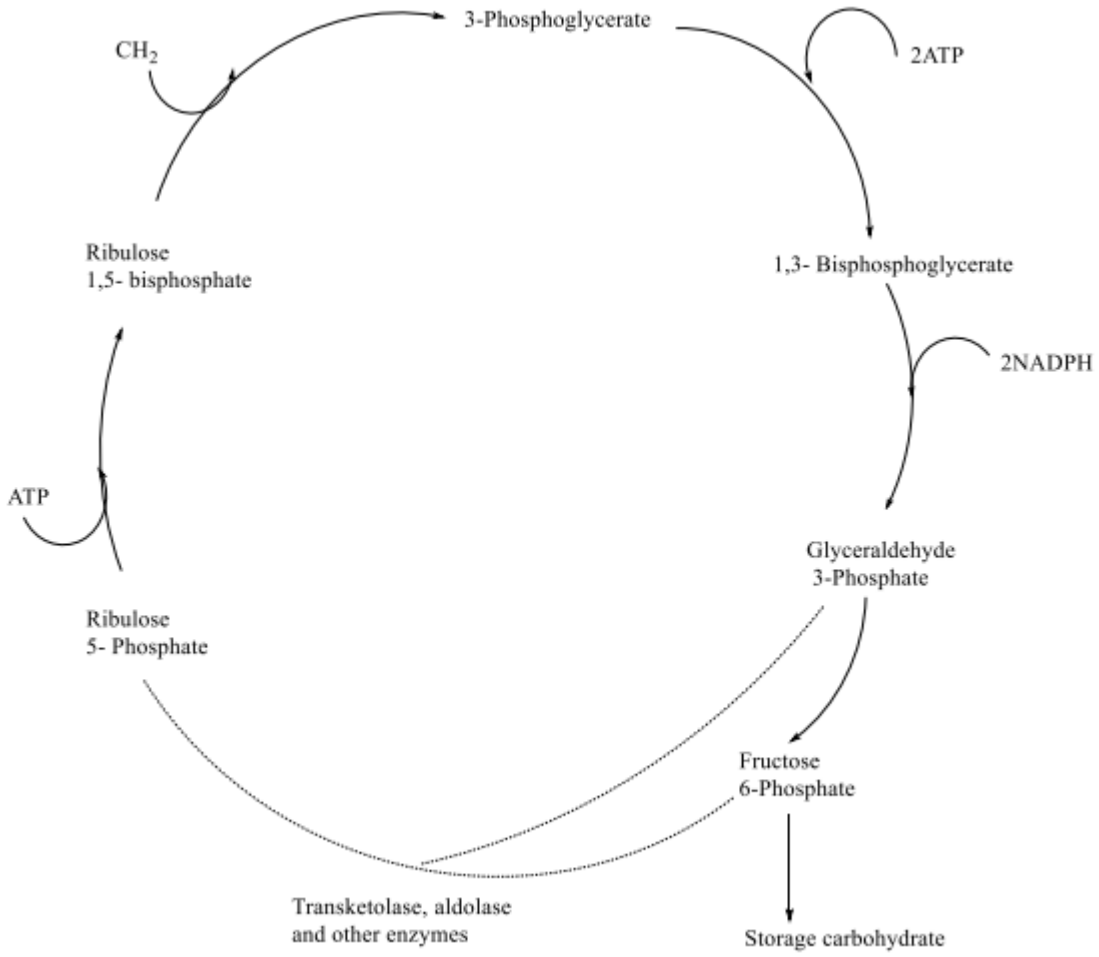

Figure 3: The Calvin Cycle.

NADP was reduced in PSI as a consequence of an electron being stimulated out of P700+ and transferred to ferredoxin. On the other side, P700+ has now changed to P700+, an oxidizing agent, after losing one electron. It returns to the unexcited state after stealing one electron from the reduced form of plastocyanin (Pc). Remember how the PSII reaction center pigment P680 had one

electron stimulated out of it by light? This left P680+, which required its electron to be restored in order to transition to the ground state and be available for another photon to begin another cycle of reaction. The electron's source is water.

The enzyme ribulose bidphosphate carboxylase, the most prevalent protein on the earth, catalyzes the primary carbon fixation process. Three-phosphoglycerate is produced using CO2. The interaction of CO2 with ribulose 1,5-bisphosphate, which results in the production of two molecules of 3-phosphoglycerate, initiates the calvin cycle (dark phase of photosynthesis). Similar to gluconeogenesis, the conversion of 3-phosphoglycerate to fructose and glucose 6-phosphate requires enzymes, although glyceraldehyde 3-phosphate deglydrygenase in chloroplasts is selective for NADPH rather than NADH. Fructose 6-phosphate, glyceraldehyde 3-phosphate, and dihydroxoacetone phosphate are utilized to regenerate ribulose 1, 5-bisphosphate via a series of intricate processes [4]. The pentose phosphate pathway and the regeneration of ribulose 1, 5-bisphosphate share certain steps, as shown in Figure 3.

Three ATP and two NADPH are needed for every unit of CO2 that is converted into hexose. Four photons are absorbed by photosystem I, and four more are absorbed by photosystem II, producing two NADPH and a proton gradient high enough to produce three ATP. Starch in the chloroplast and sucrose in the cytosol are the main carbohydrate stores in plants. Under normal air circumstances, Rubisco reacts with ribose 1, 5 bisphosphate to add CO2. If the CO2 content is low, it may then add O2.

As a consequence of this procedure, phosphoglycolate and 3-phosphoglycerate are created. Despite the fact that the phosphoglycerate may be retrieved and used in biosynthetic processes, this process results in CO2 and NH4+ wastage of metabolic energy. It is known as photorespiration because the overall consequence of this process is to absorb O2 and release CO2. Bipyridine Ru(II) complexes, which resemble green leaves and function as a photochemical device, are used to harvest solar energy [5].

Fixation of Nitrogen

When it comes to regular chemical reactions, elemental nitrogen is rather unreliable. Nitrogen fixation is the process by which atmospheric nitrogen is changed into a form of nitrogen, such as ammonia, either naturally or artificially. In the natural world, microorganisms consume atmospheric nitrogen to produce plant-useable ammonia nitrites and nitrates. Nitrogen fixation is necessary for the production of all nitrogen-containing organic compounds, including amino acids and nucleic acids. It is necessary for agriculture and the creation of fertilizer since it is a component of the nitrogen cycle. Additionally, it is helpful in the production of all nitrogen chemical compounds, including certain explosives, medications, and colors [6].

N2 Fixation Process Type

There are two methods of fixing nitrogen:

1. Fixation of nitrogen physically
2. The biological fixation of nitrogen

Industrial Nitrogen Fixation:

On a large-scale Nitrogen and hydrogen are directly combined at high pressure and temperature to make ammonia. Additionally, it is transformed into a variety of fertilizers, including urea and others.

Nitrogen fixing by living things

Biological nitrogen fixation is the process by which living organisms transform atmospheric nitrogen into a nitrogenous molecule. Microorganisms that dwell in tight symbiotic relationship with other plants and those that are free living or non-symbiotic often carry out the procedure. A- Free-living, nitrogen-fixing bacteria: These include the saprophytic bacteria Azotobacter, Beijerinckia, and Clostridium. These bacteria contribute around 10 to 25 kg of nitrogen per hectare each year. Numerous blue-green algae that are free-living also fix nitrogen. They annually inject 20–30 kg of nitrogen per hectare. B- Symbiotic Nitrogen Fixing Bacteria: Although some rhizobiota species exist in the soil, they are unable to fix nitrogen on their own. They only participate in nitrogen fixing when associated with legume roots as symbionts. A constant supply of ATP, coenzyme and cofactor like CoA, inorganic phosphate and Mg+2, cobalt and molybdenum, protective mechanisms against oxygen-leghemoglobin, ferrotoxins, hydrogen releasing systems, and nitrogenase enzyme complex are essential for nitrogen fixation [7].

General structural feature: The highly conserved protein complex known as the nitrogenase complex is in charge of biological nitrogen fixing. The three types of nitrogenase found in various nitrogen-fixing bacteria are molybdnum nitrogenase, vanadium nitrogenase, and iron-only nitrogenase. Figure 4 illustrates more thorough exploration and characterization of molybdnum nitrogenase. Fe protein dinitrogenase reductase and Mo-Fe protein dinitrogenase reductase are the two proteins that make up all nitrogenases. In component II, catalysis occurs when an electron moves from a pair of ATP molecules to the Fe-S cluster, where N2 is reduced to NH3.

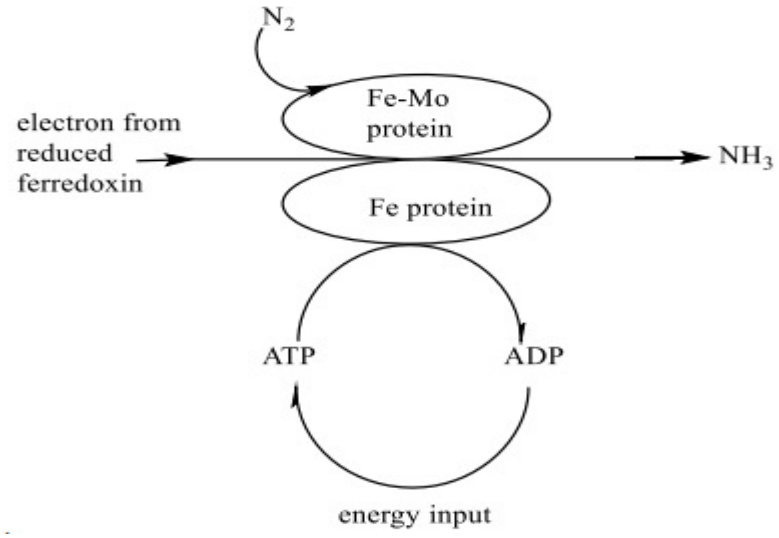

Figure 4: Illustrate the Nitrogenase Complex.

The smaller protein, which is also known as iron protein, has a molecular weight of 60000. Reductase is the name of the Fe4S4 cluster that it includes. The other protein is known as the Mo-Fe protein and has a molecular weight of 240.000. The two molybdenum atoms, around 30 iron atoms, and about 30 inorganic/labile sulfur atoms in this 2-2-2 tetramer. The cluster of iron and sulfur seems to function as redox centers. Iron and molybdenum are found in a soluble protein-free cofactor that has been discovered. Both proteins are inactive when taken alone, but when combined, the activity is restored.

Detail of the structure:

Two identical subunits make up the Fe-protein, which also has a single Fe4S4 center that is connected to each subunit by Fe-S interactions with two cystein residues in each subunit. Additionally, the sole point of any meaningful interaction between the two subunits is the solitary Fe4S4 center, which is situated at one end of the molecule. These iron-sulfur clusters, which serve as redox centers, catalyze the hydrolysis of ATP [8].

The immediate cause of substrate reduction is thought to be the Fe-Mo protein.The active region of this bigger protein, the FeMo protein, is where the actual conversion of N2 to NH3 takes place.In actuality, the nitrogenous FeMo protein contains two different types of centers, referred to as P cluster and Fe-Mo center. Unlike Fe4S4, FeMo protein contains four P clusters, but lacks the ferredoxin cluster. There is a double cubane structure in the P cluster. with every cystein ligand coupled to one of the two iron atoms in the bound Fe4S4 cluster that are not bridged. The presence of iron in a Fe4S4 is not unusual.

Two cystein ligands and two sets of fe atoms form a face-sharing arrangement that links the two Fe4S4 clusters. The two clusters are connected by a disulphide unit. This arrangement may be redox active throughout the nitrogenase cycle. A brand-new iron-molybdenum cofactor is called Fe-Mo. This cofactor has 2Mo, 6-8 Fe and 6S atoms and is very insoluble and air sensitive.

FeMo is posited as the location of substrate binding and for converting N2 to NH3 actually taking place. The structure of the molybdenum iron protein nitrogenase, Fe-Mo, was recently determined using X-ray crystallography. The cluster core, composed of Fe3MoS8, is represented by two cuboidal pieces. One of these parts has five iron atoms, while the other contains three iron atoms and one molybdenum atom.

The two pieces of the cluster are connected by two S-2 ions and an unidentified ligand. The idea that dinitrogen is bonded and activated for reduction at the cluster's core by two or more iron atoms is based on the fact that molybdenum is octahedrally coordinated whereas the iron atom at the interface is not. This suggests that dinitrogen is not directly coordinated to molybdenum.

The process of nitrogen fixation, which requires eight electrons (six for N2 reduction and two for the production of one molecule of H_2), is carried out by a greatly reduced form of the Fe-Mo protein. This protein is thus involved in the binding and reduction of dinitrogens, and figure 6 illustrates the involvement of multiple other iron-sulfur clusters in the protein in electron transport. The molybdenum site in FeMo is unquestionably distinctive when compared to other molybdenum-containing enzymes.

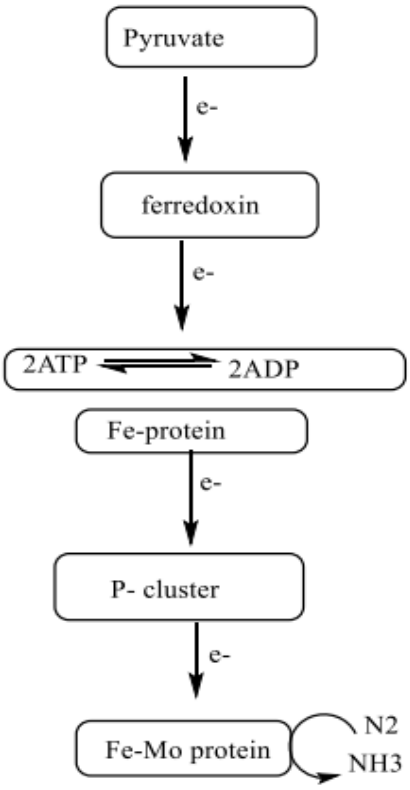

Figure 6: Nitrogen fixation by nitrogenase.

The iron protein and nitrogenase component go through cyclic association and dissociation while converting N2 to NH3. The nitrogenase component is referred to as Fe-Mo protein. The two teo proteins cannot fix nitrogen on their own, but they may be divided and combined to do so. A reduced Fe-Protein then binds to the Fe-Mo protein and transfers a single electron as a consequence. Then, in a cycle of replication, the oxidized Fe-protein separates from the Fe-Mo protein. Each cycle requires the hydrolysis of two ATP molecules. The function of ATP is to provide chemical energy, and the structural changes that result from ATP hydrolysis in proteins aid in lowering the activation energy of the nitrogen fixation process. When two ATP molecules bind to the Fe reduction protein, its potential is changed from 300 to 420 mV. As a consequence, the reducing power of the Fe-protein rises, which facilitates the transfer of electrons to the FeMo protein. Since mutants of this protein with a damaged Fe-Mo cluster co-factor can reduce acetylene quite well but N2 only somewhat, it is hypothesized that this protein is the true site of N2 coordination.

Four pyrroles make up the big ring molecule known as a porphyrin. (smaller rings made up of four carbons and one nitrogen, which is a heterocyclic compound). A massive ring is created when these pyrrole molecules are connected by a string of single and double bonds. The transfer of electrons between the and * orbitals of the ring and the iron atom causes the blood's color to become blue in the absence of oxygen in hemoglobin. The scientific name for four connected pyrroles is a tetrapyrrole. The electrons around its circumference are distributed rather evenly, and

it is flat in space. Animals' hemoglobin, which has a molecular weight of 645000, serves as an oxygen transporter. The majority of animals' blood color comes from pigment. A protein called myoglobin, which binds iron and oxygen, is present in almost all mammalian skeletal muscle tissue as well as in the tissue of other vertebrates.

The same pigment as hemoglobin is myoglobin. It is made up of globin and heme. With 153 amino acids, it is alpha halical neuclear protein. Myoglobin has a molecular weight of 17000. Thanks to a process known as photosynthesis, plants can manufacture their own sustenance. They transform light energy into chemical energy. With the aid of this chemical energy, CO2 from the atmosphere and water are incorporated into organic molecules. It is frequently referred to as CO2 assimilation rather than photosynthesis.Nitrogen in its elemental form has very little role in typical chemical reactions. Nitrogen fixation is the process by which atmospheric nitrogen is changed into a form of nitrogen, such as ammonia, either naturally or artificially. In the natural world, microorganisms consume atmospheric nitrogen to produce plant-useable ammonia nitrites and nitrates.

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CHAPTER-11

ROLE OF METALLOENZYMES IN INORGANIC CHEMISTRY

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In the first unit, we spoke about the roles that myglobin and hemoglobin play in humans and other living things. We also talked about various oxygen storage and transport systems. In this unit, we also discussed nitrogen fixation, the enzymes involved, the process of photosynthesis in plants, and the many types of photosynthesis. We wish to talk about metalloenzymes and their roles in the second unit. In metalloenzymes, metal ions (metal cofactors) are directly attached to the protein or to nonproteins that bind to the enzyme. (prosthetic groups). A third of all enzymes so far found are metaloenzymes. In addition to enzymes, other metalloproteins (cytochromes) participate in non-enzyme electron transfer activities and may operate as storage (for instance, ferritin for iron) or transport proteins. (e.g., transferrin for iron). In the later protein groups, metal storage is reversible, and the metal is simply a temporary component.

In a broader sense, ribozymes, or RNA molecules with enzyme activity, may include structurally and/or functionally important metal ions (often divalent metal ions like Mg2+). For this reason, metalloenzymes are sometimes referred to be ribozymes. Well-known proteins called natural metalloenzymes contain one or more transition metal ions such Fe, Cu, Zn, Ni, and Co. Numerous biosynthetic and metabolic processes may be catalyzed by these metalloenzymes. Most of the time, these metal ions behave as Lewis acids or redox-active sites. Several enzymes have also been used in industrial- and laboratory-scale processes to produce significant chemical compounds. In one well-known instance, acrylamide has been produced in large amounts commercially by nitrile hydratase, which contains a Co (III) ion at the reaction site. On the other hand, metal complexes including pricey metals like Ru, Rh, or Pd have served as catalysts in the production of a variety of compounds and drug precursors. Numerous research teams have investigated how to modify these metal complexes to enhance their stereo-, regio-, and substrate selectivity in addition to their unique catalytic reactivities.

A Carboxypeptidase (Zinc Enzyme)

The zinc enzyme carboxypeptidase A has a tetrahedral structure and sp3 hybridization. It has Zn2+ in its active site. Carboxypeptidase A hydrolyzes the C-terminal peptide link in proteins and peptides, releasing the C-terminal amino acid. In relation to carboxypeptidase A, it's important to remember that: Zn2+ is found in the carboxypeptidase A active site. Function facilitates the hydrolysis of proteins' or peptide bonds' C-terminal ends. Tetrahedral structure hybridized with sp3. The pancreas secretes the carboxypeptidase A enzyme, which has a molecular mass of 34,800 and is employed to quicken the hydrolysis step. A single 307-amino acid chain that makes up this enzyme folds into a tight, globular shape with helices and pleated sheet regions [1], [2].

Peroxidases and Catalases

Ascorbate, ferrocynide, and cytochrome C are only a few of the substrates that are oxidized by hydrogen peroxide with the help of the heme protein peroxide. The catalase enzyme is found in almost all living things. Catalases were used to catalyze the disproportionation of organic peroxides and hydrogen peroxide. They also facilitate the oxidation of substrates by hydrogen peroxide. One catalyse molecule converts millions of H2O2 molecules into water and oxygen per second, having the highest turnover rate of any enzyme. Peroxide and catalysts have comparable chemical structures and reaction mechanisms. The imidazole nitrogen of the residue resides in the fifth coordination site, and both have an active Fe (III) heme with a high spin. The sixth coordination site is occupied by a water ligaand in the enzyme while it is at rest.

Mechanism and Architectural Elements

The structures of horseradish b peroxidase and beef liver catalase have been determined, among other things. Both enzymes feature a high spin iron group at their active sites. The majority of in vivo circumstances favor the peroxidase activity of catalase. Among other sites, catalase may be found in the blood, bone marrow, mucous membranes, kidneys, and liver. It participates in the oxidation of H2O that oxidases create. As a consequence, enzymes that produce H2O2 and those that break it down are combined. Phenolate, which is the deprotonated phenolic oxygen atom of tyrosine, and most likely a water molecule are the catalase axial ligands. It is believed that the water molecule attached to the heme is kept in the sixth-position cavity of the enzyme's active site. The phenolate moiety from a protein's tyrosyl residue is linked to the heme on the active side and maintained far from the cavity. (which holds water at the sixth position on the heme). H2O2 replaces water in the cavity at the enzyme's active site during catalytic activity. The axial ligand of horse radish peroxidase is an imidazole derived from a histidyl residue on the protein. Additionally, both enzymes include histidine and asparagine or arginine side chains close to their active sites that are orientated properly to participate in the enzyme's catalytic cleavage of O-O when H2O2 takes the place of water [3].

After hydrogen peroxide attaches to the ferric core, the O-O bond undergoes heterolysis. Positive and negative charge separation in the transition state is necessary beforehand. Near the active site, the amino acid side chains histidine and asparagine or arginine play this function. While the arginine residue aids in stabilizing the growing negative charge on the leaving oxygen atom, the basic imidazole group of histidine aids in the proton transfer from the oxygen atom of H2O2 coupled with the iron to the departing oxygen atom. As a consequence, the O-O bond breaks, creating compound 1, a typical high valent oxo intermediate. The capacity of compound 1 to oxidize other substances by two electrons.

Cytochrome P-450's Structural Makeup

A physiologically active protein that takes part in several oxidation processes is cytochrome P-450. A protein with the prosthetic group Fe(III) protoporphyrin IX is cytochrome P-450 (heme B type).Similar to myoglobin, cytochrome P-450 possesses an oxygen-binding heme unit, but it has a cystein thiolate residue rather than the axial histidine that is found in myoglobin. Cytochrome P-450 is a single polypeptide (-halical) chain. Between two helices of two axial ligands, one of which

is a cystein ligand from a protein and the other of which is a water molecule, is a heme group b molecule. The CYPs are hemoproteins with 400–500 amino acid residues and a single haem prosthetic group in the active site, as shown in figure 1. The two spin states of iron in the ferric form (Fe3+) are low spin (LS), where the five 3d electrons are maximally paired, and high spin (HS), where the five 3d electrons are maximum unpaired. Evidence from spectroscopy, NMR, and crystallography suggests that a water molecule makes the Fe3+'s sixth axial ligand in the substrate-free form, retaining the ion's LS state. The iron-water molecule is moved when substrates attach to the enzyme, altering the coordination state of the iron ions from six to five, which causes the iron ions to move out of the haem ring plane [3]–[5].

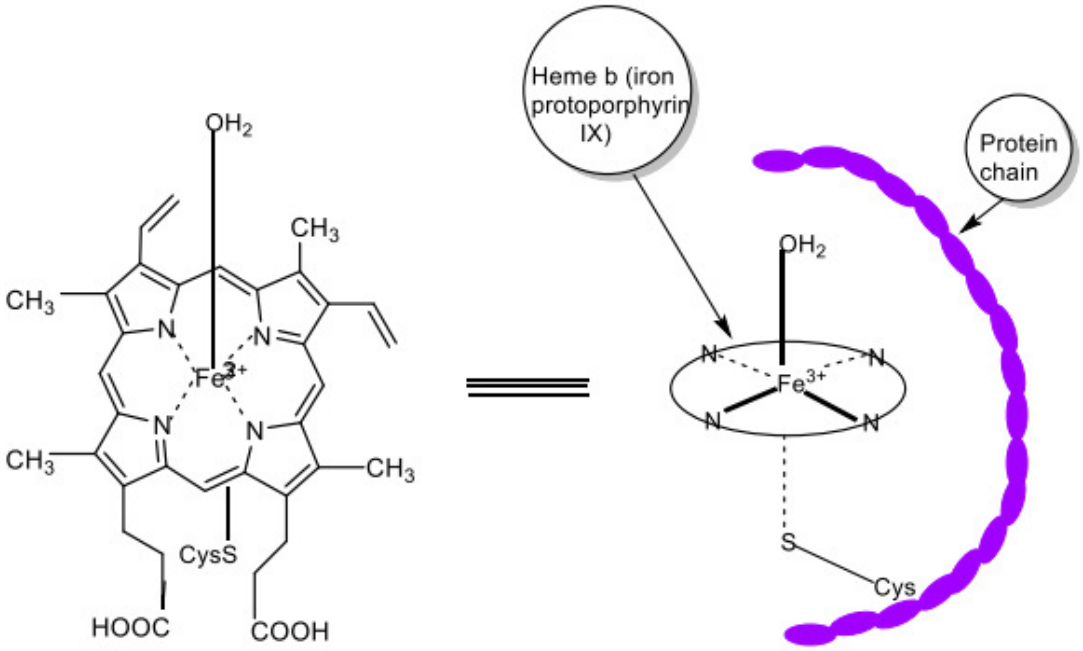

Figure 1: Structure of cytochrome P-450.

The majority of the knowledge about P-450 is based on research done on an enzyme called P-450 that was derived from the bacteria Pseudomonas putida. Camphor is the sole carbon source used by this source (organism), at this stage. The cytochrome P-450 enzyme has a molar mass of around 50,000. The cytochrome P-450 enzyme's catalytic cycle is shown in Figure 2 for reference. The organic substrate enters a hydrophobic pocket of the protein at the iron axial coordination site, driving water molecules out to form Fe(III) complexes, which are then reduced by a different enzyme system to form high-spin Fe(II) complexes. Similar to hemoglobin and myoglobin, a dioxygen molecule bonds with a Fe(II) center in the third stage, causing one electron to be transferred from Fe(II) to dioxygen and the creation of a Fe(III)-superoxo complex.The Fe(III)-peroxo complex is created in step four by the addition of an additional electron.In step five, the Fe(III)-peroxo complex is protonated, leading in the elimination of one oxide ion as water and the formation of an oxyferryl complex [6].

Copper Enzyme

Copper is crucial for iron absorption, energy production, and oxidative stress defense in yeast. Three crucial copper enzymes in yeast a multicopper oxidase, a copper heme oxidase, and a superoxide dismutase explain the majority of the phenotypes seen during copper deficiency.

Copper Enzyme Superoxide Dismutase (SOD)

A catalytic enzyme called superoxide dismutase helps the body get rid of the dangerous superoxide anion, or O2 -, which is a consequence of oxidative metabolism. This enzyme breaks down superoxide into hydrogen peroxide and molecular oxygen. Hydrogen peroxide is subsequently eliminated by the actions of enzymes like catalase, which is a potentially dangerous molecule. SOD and catalase work together to protect organisms that use dioxygen from potentially harmful consequences of O2 metabolism [7].

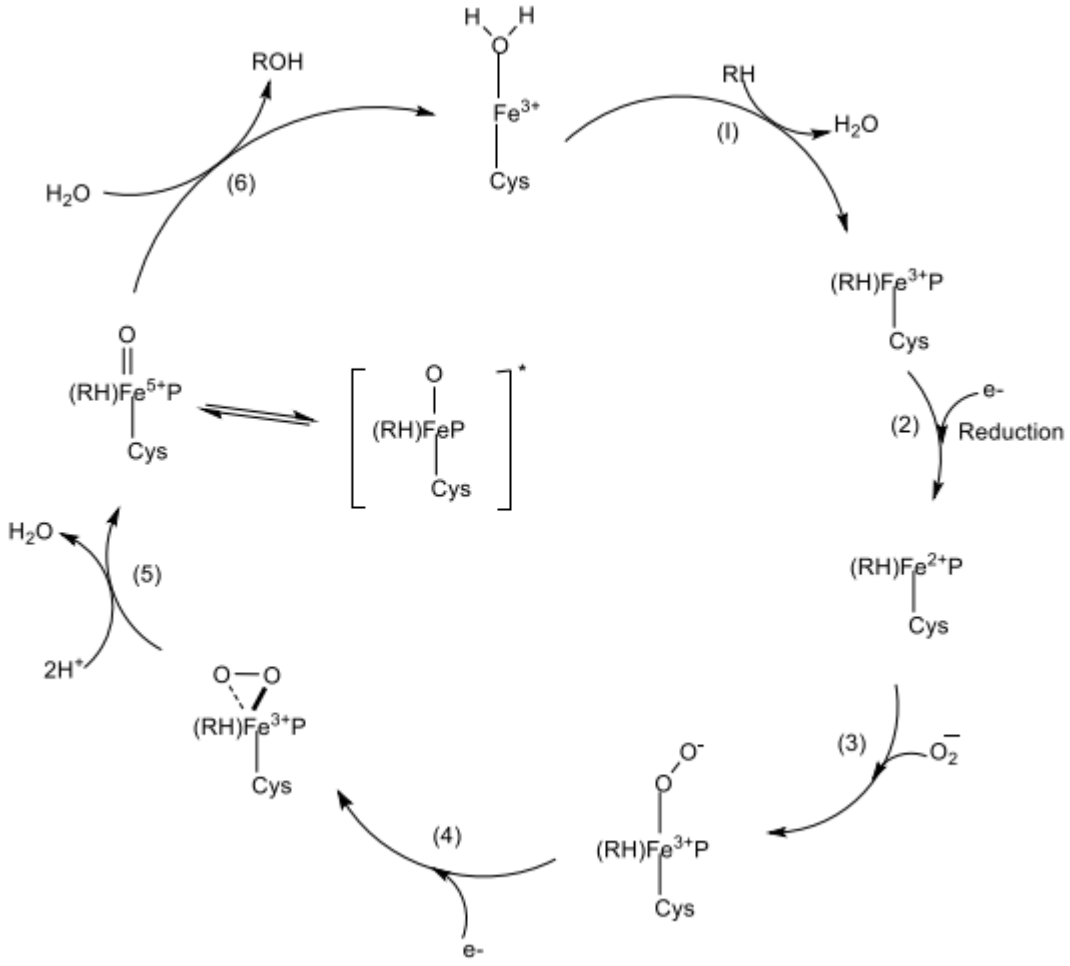

Figure 2: Cyclic mechanism of cytochrome P-450.

In all Mo enzymes, a ligand known as molybdopterin normally coordinates the metal. Metal donors are a pair of S atoms from a ditholene group covalently bound to a pterin. The phosphate group is joined to a nucleoside base R, such guanosine 5'-diphosphate. Through its role as an electron

channel, the pterin group may help redox processes. The following factors may be taken into account while studying the reaction's mechanism: The oxidized version of the enzyme is characterized by one terminal molybdenum oxo (Mo=O) group, two thiolate-type sulphur ligands (pterin dithiolene side chain), and one terminal sulphido group (Mo=S). While one oxygen atom is transported from the Mo(VI)=O unit to the reactant xanthine, the terminally connected sulphido group acts as a base to remove hydrogen. Direct O atom transfer from the Mo enzyme to the substrate (xanthine). Thus, the O atom is not transferred to the substrate by a solvent attack from water or hydroxide that is favored by Mo. The related deprotonation and electron activities at the Mo center repair the oxo group from the water molecule.

Direct O atom transfer from the Mo enzyme to the substrate (xanthine). Thus, the O atom is not transferred to the substrate by a solvent attack from water or hydroxide that is favored by Mo. The related deprotonation and electron activities at the Mo center repair the oxo group from the water molecule. The oxo group carried by Mo enzymes is created from water rather than molecular oxygen, which is an important distinction between this oxygenation process and that of other Fe and Cu enzymes.

Xanthine oxidase catalyzes the two-electron oxidation of xanthine to uric acid, which is subsequently reduced to Mo, at the Mo(VI) site (Mo cofactor, molybdepterin). (IV). Mo(VI) species are renewed when electrons are lost (one at a time) to the Fe2S2 and FAD sites. Although the enzyme's Fe2S2 sites are not directly engaged in the interaction with the substrate, they are essential to the enzyme's overall operation. Similar to the straightforward electron transfer function of Fe2S2 ferrodoxine during photosynthesis, the enzyme's Fe2S2 core does this duty.

B12 Vitamin

Only coenzyme B12 and vitamin B12 are found in nature as organometallic substances. Originally derived from liver extracts, vitamin B12 was later shown to be deficient in either B12 or B12 coenzyme, which is what causes permicious anemia in humans. In vitamin B12, the Co(III) ion is joined to four N-atoms of a corrin ring. The porphyrin ring is changed into the corrin ring, which has one less =CH- bridge linking the two pyrrole rings. Corrin rings are thus less symmetric and saturated than porphyrin rings. The fifth and sixth positions are occupied by an imidazole nitrogen and a cyanide ion, respectively. On the other hand, the cyanide ion is missing in vivo, and a loosely bound water molecule takes up the sixth position. The integration of Co (III) into the corrin ring changes the reduction potential of cobalt, allowing it to be reduced by one electron to produce vitamin B12 [Co (II) complex] or by two electrons to produce vitamin B12 [Co (I) complex]. These reductions may be carried out in vivo through reduced ferredoxin. It is readily alkylated because it is very nucleophilic [8].

Utilizing vitamin B12

A water-soluble vitamin called vitamin B12 is included in dairy, fish, and meat items. Additionally, it is usually blended with other B12 vitamins and is produced in a lab.The growth and effective functioning of several bodily organs, including the brain, neurons, and blood cells, depend on vitamin B12. Methylcobalamin is the vitamin B12's active form. The kind that appears most often in supplements is cyanocobalamin, which the body must convert into the active form.

The treatment of vitamin B12 deficiency, cyanide poisoning, and high blood homocysteine levels is common. It's also claimed to cure a range of other conditions, including fatigue, cataracts, Alzheimer's disease, osteoporosis, and canker sores, albeit the majority of these claims lack supporting evidence. Enzymes carry out the following operations that need for coenzyme B12.

B12 vitamin

It may become more difficult to absorb this vitamin as we age. Additionally, it may occur if you regularly consume alcohol or have surgery for weight reduction or another procedure that included the removal of a portion of your stomach.Additionally, the following conditions may increase your risk of vitamin B12 deficiency: Pernicious anemia makes it difficult for your body to absorb vitamin B12; atrophic gastritis, which causes the lining of your stomach to thin; Crohn's disease, celiac disease, bacterial growth, or a parasite that affects your small intestine. Abusing alcohol or drinking excessively might hinder you from consuming enough calories or make it tougher for your body to absorb nutrients. Glossitis, or a swollen, irritated tongue, may be one indication if you don't get enough B12. Immune system problems, such as Lupus or Graves' illness Been using medicines that prevent B12 absorption. Proton pump inhibitors (PPIs) like esomeprazole (Nexium), lansoprazole (Prevacid), omeprazole (PrilosecOTC), pantoprazole (Protonix), and rabeprazole (Aciphex), H2 Blockers like cimetidine (Tagamet), famotidine (Pepcid AC), and certain diabetes medications like metformin are among the medications mentioned here. (Glucophage) [9].

Sources of vitamin B12 in food

Animal foods, which naturally contain vitamin B12, as well as those that have been fortified with it, are both sources of this vitamin.Dairy, eggs, fish, meat, and poultry are examples of items derived from animals. Look at the Nutrition Facts label of the product to see whether it has B12 added. The aforementioned section discusses the several crucial elements of enzymes. The unit's synopsis is as follows: The zinc enzyme carboxypeptidase A has a tetrahedral structure and sp3 hybridization. Carbon dioxide (CO2) is converted to carbonic acid by the enzyme carbonic anhydrase. As a monooxygenase, cytochrome P-450 assists in the cleavage of oxygen and makes it easier for oxygen atoms to enter the substrate. Copper is crucial for iron absorption, energy production, and defense against oxidative stress in yeast. Three important copper enzymes in yeast account for the majority of the phenotypes seen after copper deficiency.

A catalytic enzyme called superoxide dismutase helps the body get rid of the superoxide anion, or O2, which is a consequence of oxidative metabolism. Organisms that use dioxygen are protected from potentially harmful byproducts of O2 metabolism by SOD and catalase. Uric acid is produced from xanthine oxidase. Xanthine oxidase inhibitors may be used to treat gout, which is brought on by the body producing too much uric acid. Only coenzyme B12 and vitamin B12 are found in nature as organometallic substances. It was established that human permicious anemia is brought on by a deficiency in vitamin B12 or B12 Coenzyme, which was first isolated from liver extracts. The corrin ring, a modified porphyrin ring with one less =CH- bridge linking the two pyrrole rings than the porphyrin ring, is coupled to four N-atoms of the Co(III) ion. It may be

reduced in vitro using reduced ferredoxin because it is readily alkylated due to its nucleophilic nature.

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CHAPTER-12

METAL-NUCLEIC ACID INTERACTIONS

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There are a lot of literature available on DNA, RNA, and the function of metal ions in living things. This helps us comprehend how metal ions are used in the medical profession. the negative impact metal ions have on our surroundings. Many biological processes need metal ions to act as catalysts. (enzyme). the parts of our body Think about the components that make up the composition of the ordinary healthy individual. (weighing 70 kg). More over half of a typical man's weight is made up of oxygen. the variety of components that make up human bodies.

DNA (DEOXYRIBOSE NUCLEIC ACID)

DNA is a very large macromolecule that contains the genetic code necessary for all known living things to grow and operate. It is made of of information that may be handed down across generations in the form of a special genetic code. Chromosomes, which are thread-like structures that encircle certain protein complexes, are made up of tightly twisted bundles of DNA molecules. Figure 1. In eukaryotes (cells with a nucleus), chromosomes are housed in the membrane-bound nucleus, but in prokaryotes, they are found in the cytoplasm of the cell. (cells without a nucleus). Nucleotides, which are branched linear chains of monomeric units, are the building blocks of DNA, a polymeric biomolecule. The phosphate, pentose, and nitrogenous base are the three components that make up a nucleotide. The sugar in DNA is always 2'-deoxyribose [1], [2].

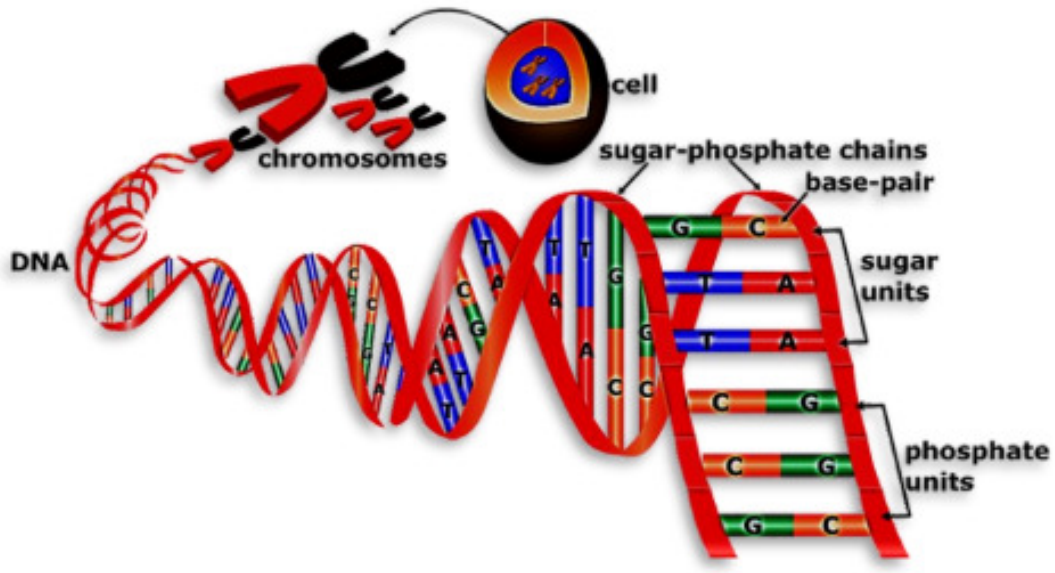

Figure 1: Diagram displaying a cell, chromosome, gene, and DNA.

Deoxyribonucleic Acid

Nucleotide bases come in two different varieties: pyrimidine and purine. Pyrimidines contain a six-membered heterocyclic conjugated ring, while purines have a five-membered imidazole ring fused to a six-membered ring. DNA contains the pyrimidine nucleotides cytosine (C) and thymine (T). The pyridine bases are joined to pentose by N1 [3].

DNA's Basic Structure

A single polynucleotide chain makes up the core of DNA. A polynucleotide chain is created when a phosphodiester bond is formed between the phosphate group on one nucleotide's 5' carbon and the hydroxyl (OH) group on another nucleotide's 3' carbon. The polynucleotide chain's sugar phosphate backbone is produced via the phosphodiester linkage. The chain has a free 5' phosphate group at one end and a free 3' OH group at the other. DNA's basic structure is as follows: Erwin Chargaff and other biochemists showed in the 1940s that nucleic acids do not contain equal amounts of each nucleotide. DNA was isolated from many animals by Chargaff, who then hydrolyzed it to create individual nucleotides. After that, the nucleotides were separated using paper chromatography. Based on his research, Chargaff asserted that for each given species:

Polymerization of DNA

DNA replication, which entails creating two identical copies of a double-stranded DNA molecule, is the most important biological process in all living things.The most crucial biological activity in all living things is called DNA replication, which involves copying a double-stranded DNA molecule into two identical duplicates. The enzyme in charge of DNA replication is called DNA polymerase, as shown in Figure 2. By sequentially adding nucleotides made from deoxynucleoside triphosphates, this enzyme catalyzes the creation of polynucleotide strands. To divide a single DNA molecule into two identical DNA strands, it often works in pairs [4], [5]. For replication, a DNA polymerase needs the following elements.

Four nucleotides have triphosphate forms: ATP, GTP, TTP, and CTP.

1. As a template, single-stranded DNA is used.
2. A primer is an existing nucleic acid strand with a free 3' end.
3. A nucleic acid strand that already exists and has a free 3' end.

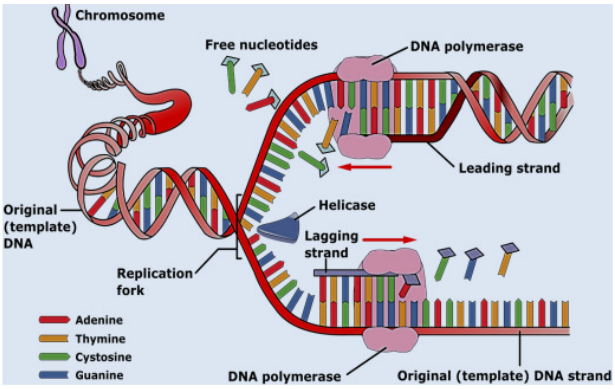

Figure 2: DNA replication process.

A thorough explanation of the DNA polymerization process the following are the stages involved in DNA replication: DNA replication starts when an enzyme called helicase breaks the hydrogen bonds between each nucleotide, releasing the two strands of the DNA molecule. The opening of a brief segment of the DNA helix, which gives rise to the Replication Fork structure, marks the beginning of replication. The unwound single strands of DNA are subsequently bound by SSB proteins, preventing them from breaking and reannealing [6], [7].

Elongation

However, when the helicase separates the strands, RNA primase briefly binds to each strand and produces an RNA primer that acts as the foundation for DNA synthesis. After the primer is in place, DNA polymerase III starts generating a new complementary strand by adding the reciprocal sequences of the DNA to a single unwinding polynucleotide strand. This procedure takes place the other way since DNA polymerase can only add nucleotides in the 5' (prime) to 3' (prime) orientation.In other words, DNA is replicated on the lagging strand in the opposite direction of fork movement whereas bases are added on the leading strand in the direction of the origin of replication. The consequence is short, Okazaki-like bits of the lagging strand. Following the removal of the primer RNA fragments from both strands by the RNase enzyme, DNA polymerase fills in the gaps with the necessary nucleotides. A single nick on the leading strand and multiple nicks on the lagging strand are produced by DNA Ligase activity, which are then filled to make two continuous double strands of DNA [8].

Termination: The last stage of DNA replication, known as termination, takes place when the enzyme DNA polymerase reaches the ends of the strands, where further replication is impossible. The last section of the lagging strand, which is not replicated, has the RNA primer deleted. A repeating non-coding nucleotide sequence is found in the genome's telomeres. Each time a replication cycle is completed, a piece of the telomere is lost, resulting in shorter strands. The new double helix structures were then "proofread" by enzymes like nucleases, which eliminated any decreased nucleotides that happened during DNA replication. The holes left by the deleted nucleotides are subsequently filled up by DNA Polymerase I [9], [10].

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CHAPTER-13

CLASSIFICATION OF ELEMENTS IN ACCORDANCE WITH THEIR ACTIVITIES IN THE BIOLOGICAL SYSTEM

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Out of the more than 100 discovered components, only roughly seven are known to be essential for the effective operation of the human body. Na, K, Mg, Ca, P, Fe, Mn, S, Zn, Cu, Co, Cr, Mo, Cl, F, I and Se are a few examples of essential elements. They are considered essential since the organism could not survive without them. Based on the absolute amounts of each essential component in the body, two categories may be made:

1. Macronutrients
2. Micronutrients

The remaining substances are referred to as micronutrients since the body only needs them in trace quantities. Because the body only requires tiny amounts of these substances, they are sometimes referred to as trace elements.

i. Sodium

The main electrolyte detected in extracellular fluid at high quantities (140 mmol/L) is sodium. The primary is Na+. It controls the osmotic pressure throughout the body. Most sodium in the body is found as bicarbonate (NaHCO3) and chloride (NaCl), respectively. Every day, adults need between 1 and 3.5 grams of salt. It improves the absorption of glucose and amino acids. It maintains the acid-base equilibrium together with chloride and bicarbonate. It has a role in regulating membrane potential. Table salt (NaCl) is the most used source of sodium in cooking. Among the other sources are bread, cheese, carrots, cauliflower, egg nuts, spinach, and other foods. Headaches and cramps in the abdomen muscles are symptoms of low sodium. On the other side, consuming a lot of table salt raises blood pressure [1].

The main cation in the intracellular fluid is potassium K +. It makes heart muscles work harder. It helps to keep the body's osmotic pressure stable together with Na+. In addition, it maintains the acid-base equilibrium. It makes enzymes like pyruvate kinase more active. It also has a significant impact on ribosome synthesis and blood coagulation.

ii. Magnesium

A macronutrient that the body requires in large amounts is magnesium. There are around 25 gms of magnesium in an adult. The bones and teeth contain 70% of the body's mg. Mg2+ has a crucial role as an intracellular cation and as an enzyme activator for the phosphatase enzyme. A complex salt of bones is created when phosphorus, calcium, and magnesium are combined. It is a crucial component of chlorophyll. Additionally, it takes part in the hydrolysis of ATP, the body's primary

source of energy. Like calcium, magnesium supports blood clotting, lung function, muscle contraction, and blood pressure control. It participates in several life-sustaining processes. Magnesium's role in DNA synthesis, energy generation, nerve transmission, muscle protein synthesis, and the activity of enzymes. Magnesium may be found in good amounts in nuts, soybeans, and shellfish. Neuromuscular dysfunction comes from magnesium insufficiency.

iii. Calcium

The mineral calcium is the most prevalent in the human body. It is a key component of bones and teeth. The skeleton contains the majority of the body's calcium, which is preserved as calcium phosphate deposits. The main minerals in bone and teeth are calcium and phosphorus, which are present as the double salt of calcium and phosphate, CaCO3. nCa3(PO4)2 (n range from 2 to 3). These minerals provide these tissues their strength and hardness. In soft tissue, including muscles and organs, there are little calcium deposits. Calcium aids in the coagulation of blood. It is important for the contraction of muscles. Many enzymes, including protein kinase, lipase, adenylate cyclase, etc., need calcium as a cofactor. It supports nerve function as well. The main calcium-rich foods are milk, eggs, almonds, beans, cabbage, cauliflower, and others. Osteoporosis in adults and rickets in children are diseases caused by calcium deficiency. But too much calcium may have negative effects on the body, leading to the development of stones [2].

iv. Phosphorus

The body contains phosphate, which is phosphorous. About 700 g of phosphate make up the whole body. More than 85% of it is present in bones, whereas only 15% and 1%, respectively, are in soft tissues and extracellular fluid. 90% of the daily absorption of phosphate from food In combination with calcium, it is present in bone and teeth. It is also a part of DNA and RNA, the building blocks of life and development. Additionally, it is necessary for the control of enzyme activity through phosphorylation. The expression of the Na-P co-transporter in the small intestine is increased by vitamin D, which increases intestinal phosphate absorption. Phosphorus reabsorption in the kidney is decreased by the parathyroid hormone (PTH), which increases urine excretion. The absorption and excretion of phosphorus are influenced by the Ca:P ratio in the diet. The excretion of the other is enhanced if one is consumed in excess. The phospholipid found in bone and teeth is crucial. Additionally, it is a component of lipoprotein, phospholipid, and nucleic acids. It supports different enzymatic reactions and plays significant roles in biological processes [3].

v. Iron

A crucial trace element for the human body is iron. A typical person's body has 2.4 grams of iron. It may be found in metalloenzymes like nitrogenase, reductase, and hydrogenase as well as in the active sites of proteins that transport electrons and oxygen, such as cytochromes and the active centers of proteins like haemoglobin and myoglobin. The two forms of iron that are present in the human body are essential (or function) iron and store iron.

Heme Protein

Myoglobin and hemoglobin are two heme proteins that are connected to the globin protein by an iron porphyrin prosthetic group. They both participate in the transfer of dioxygen. Catalases and

peroxidases are additional heme proteins. The catalase enzyme, which has four heme groups, is present in the liver, kidney, mucous membrane, bone marrow, and blood. It helps hydrogen peroxide turn into water and molecular oxygen via catalysis [4].

Another heme protein called peroxidase is present in milk, erythrocytes, leucocytes, and lens fibers. Cytochromes: Cytochromes are a different group of substances that include iron. The majority of cytochromes are located in mitochondria. Enzymes that include iron: Some enzymes, such as succinate dehydrogenase, aconitase, ribonucleotide reductase, etc., also employ iron as a co-factor. Hemosiderin and ferritin are storage proteins for iron. Iron that is not linked to ferritin is hazardous whereas free iron is not. The iron-storing protein ferritin is present in the colon, liver, spleen, bone marrow, and blood. Ferritin is the source of hemosiderin. Compared to ferritin, it has a higher percentage of iron. sources of iron in food Cereals, legumes, molasses, eggs, meat, fish, and other foods are among the foods high in iron. Foods fried on iron skillets are another non-food source of iron. Anaemia is a result of iron deficiency. It takes a year for iron deficiency symptoms to manifest, which include exhaustion, weakness, and shortness of breath.

Zinc:

Average clothing materials include Zn, the second-most abundant metal. The body contains around 2g of zinc.It is dispersed throughout the body in places including the bones, teeth, skin, kidneys, and muscular tissue.For healthy human body development, wood healing, and tissue regeneration, it is crucial. It controls how insulin works and keeps vitamin A levels in a normal range. It is a crucial part of a number of enzymes. Superoxide dismutase, carbonic anhydrase, and carboxypeptidase are vital zinc-containing enzymes. Superoxide dismutase is an enzyme that contains two Zn^{2+} atoms per Cu-Zn protein molecule.Red blood cells, brain cells, and epithelial cells all contain it. Each enzyme molecule of carbonic anhydrase includes one Zn^{2+} ion. Red blood cells, parietal cells, and epithelial cells all contain it. The hydrolytic enzyme found in pancreatic juice is called carboxypeptidase. Alcohol dehydrogenase alkaline phosphate, lactate dehydrogenase, glutamate dehydrogenase, DNA, and RNA polymerase are further zinc-containing enzymes [5], [6].

Copper:

Copper is essential to both plants and animals, although its functions are less clear-cut than those of iron. 100 to 150 mg of copper are dispersed throughout the liver, muscles, and bones. About 32% of dietary copper may be absorbed under typical circumstances. The mucosal cells absorb the copper. Copper is the third most prevalent element in the human body, after Fe and Zn. Dietary excesses of either Zn or Mo prevents the absorption of Cu. Cu enters the plasma after being absorbed and is bound to serum proteins there. Numerous proteins, metalloenzymes, and naturally occurring pigments include it. Tyrosinase, catalase, ascorbic acid oxidase, superoxide dismutase, and other enzymes all include copper. Hemocyanin, a copper protein, is used as an oxygen transporter by many invertebrates. Additionally, copper contributes to the coloring of skin and hair as well as the formation of a barrier around nerve fibers. The finest copper sources are whole grains and legumes.

Effect of too much Copper Fever, high blood pressure, diarrhea, disorientation, depression, weariness, irritability, joint and muscle pain, nausea, rapid aging, vomiting, skin wrinkles, headache, etc. are all symptoms of an excess of copper. A high level of copper in the body causes Wilson disease sickness. It is a hereditary condition. Because Wilson's disease patients have low amounts of the copper storage protein ceruloplasmin, copper is poisonous even at physiological levels. Wilson disease is characterized by brown or green rings on the eye, liver damage, and neurological dysfunction. Many chelating ligands may be used to remove extra copper, however D-penicillamine is one of the best. The chemical formula of this chelating ligand's combination with copper ions (Cu+ and Cu2+) is [Cu8 + Cu6 2+(penicillamine)12Cl], and it exhibits a strong purple color. D-penicillamine's sulfhydryl groups have an impact on copper's elimination as a Cu+ complex. Additionally, the symptoms are eliminated with EDTA chelating treatment [7].

Cobalt

Cobalt is one of the most significant trace metals. It is one of the oldest types of biocatalysts. The average person's body has just around 1.5 mg of cobalt, and the bulk of it is in the form of cobalamin, or vitamin B12. Cobalamins are benzimidazoles that have been covalently bonded to the corrin ring in the unique macrocycle known as corrin, which complexes cobalt in B12. Cobalamins are cofactors in enzymes that catalyze various radical-based rearrangements as well as alkyl transfer reactions. Cobalamin-containing enzymes have significant UV-visible absorption bands, and EPR spectra for Co(II) have been reported. Neither plants nor animals are able to synthesize vitamin B12. It can really only be produced by a few number of bacteria. All of the vitamin B12 that humans consume comes from meat and other animal products. Vitamin B12 insufficiency is rare since it just needs to be present in minimal levels. Vegans, who do not consume any animal products, have been shown to be vitamin B12 deficient. Insufficient absorption of vitamin B12 in the stomach leads to an increase in the excretion of methyl malonic acid, which the body cannot convert to succinic acid, which is the root cause of vitamin B12 deficiency. The lack of cobalt results in pernicious anemia. In addition to being an important part of vitamin B12, cobalt is required for the activity of several enzymes, including coenzyme A, methyl malonyl oxidoreductase, and others. Skin rashes, diarrhea, vomiting, and nausea are all symptoms of having too much cobalt in the body.

Sulphur

The oxidized form of sulfur, sulphate, is found in the body as a component of several proteins. Along with coenzyme A and lipoic acid, it is also present. It is a crucial part of the structure of several proteins, including insulin. Specific sulfhydryl groups are required for catalytic activity in various enzymes. It is crucial in the production of S-acetyl lipoate and acetyl coenzyme A. The body needs sulphates in order to function, which are provided by foods high in protein, such as meat, fish, eggs, and milk.

Manganese

The body also needs manganese, a trace mineral that is mostly concentrated in the kidneys and liver. Many enzymes, including enolase, arginase, isocitrate dehydrogenase, cholinesterase, etc., use it as a cofactor or an activator. In the case of several of the enzymes, manganese and

magnesium may stand in for one another. It aids in bone development and is crucial for the metabolism of fat and carbohydrates. The main sources of manganese include leafy green vegetables, tea, nuts, whole grains, and cereals [8].

Fluorine

Human teeth contain trace levels of fluorine, which aids in dental enamel hardening, regular maintenance, and tooth formation. Additionally, necessary for healthy bone growth, fluorine also improves calcium and phosphate absorption and protects against osteoporosis in old life. Humans mostly get their fluoride from drinking water. Fish, tea, salmon, and other foods are additional sources of fluoride. In places where drinking water has less than 0.5 ppm of fluorine, tooth decay and dental enamel erosion are common in both adults and children. However, too much fluoride in the food or water, as well as its inhalation, is dangerous and is thought to be the primary cause of the fluorosis condition.

Chlorine

The fluid and electrolytic equilibrium are maintained by the chloride ion. It is crucial in the control of osmatic pressure, too. The chloride ion plays a significant role in the creation of HCl in gastric juice, aiding in food digestion. It serves to maintain the balance of the acid-base. Table salt helps to maintain the acid-base balance and is a significant source. Table salt, processed foods, and soy sauce are significant sources. The moderate sources include milk, eggs, and meat.

Iodine

Iodine's involvement in thyroid function, which helps to control growth and development, is its main function. Seafood, bread, and dairy products are excellent dietary sources of iodine in addition to iodized salt. Iodine deficiency causes thyroid enlargement. xv. Chromium The body has a large amount of chromium. The metabolism of proteins, lipids, and carbohydrates all benefit from chromium. Chromium improves the function of insulin and aids in keeping insulin levels stable. Having too little chromium may lead to diabetes and other conditions. Me/at, brewer's yeast, whole grains, etc. are excellent sources of chromium.

Molybdenum

The primary use of molybdenum is in the biological fixation of nitrogen. Additionally, it is found in a number of flavoproteins, including xanthine oxidase and NADH nitrate reductase. All of these enzymes engage in internal transfers during oxido-reductions, including molybdenum. Molybdenum, even in trace concentrations, aids in the usage of copper. High molybdenum intake, on the other hand, results in copper insufficiency. Legumes, grains, and nuts are important sources of Mo.

Selenium

The heart needs the trace metal selenium, which is also a vital component. It is present in all bodily tissues and is particularly concentrated in the liver, kidneys, and fingernails. Selenium levels are low in adipose tissues, blood, muscles, and bones. The enzyme glutathione peroxidase, which is found in mitochondria and cell cystol and has the job of reducing hydroperoxide, has selenium as

its prosthetic group. It controls thyroid gland functioning. Additionally, it is necessary for healthy pancreatic operation. Whole grains, fruits, and vegetables are the main sources of selenium. Selenium deficiency results in cardiac failure, pancreatic degeneration, infertility, failure of growth, and necrosis of liver cells.

ATPASE, Na+-K+

In 1957, Jens Skou discovered the transmembrane protein known as Na+K + -ATPase. This enzyme is also known as the Na+ -K + pump because it pumps three Na+ out and two K+ into the cell while hydrolyzing intracellular ATP. The Na+-K+ pump controls the extracellular K+ concentration while keeping the cell's Na+ content low in animal cells. Ion transport produces the transmembrane electric potential. The Na+ -K + -ATPase has two conformations, E1 and E2. The E1 conformation enzyme binds three Na* from the inside of the cell. E has a high affinity Na+ binding site, while E2 has a high affinity K+ binding site. After E1, 3Na+ attaches to ATP, which is hydrolyzed, the phosphate group is transferred to the aspartic acid residue of the transport protein. This aspartyl phosphate changes the structure of the tranet protein from E to E. Low affinity for Na+ and high affinity for K+ are characteristics of the Na+ - K + -ATPase E1 conformation. The transporter then releases 3Na+ into the environment while binding 2K+ from the media around it. The phosphate group is hydrolyzed, and the enzyme changes back to its E1 structure. The transporter delivers 2K+ to the interior of the cell because the E1 conformation of the enzyme has a high affinity for Na but a low affinity for K+. The movement of 2K+ ions into the cell and 3Na+ ions out of the cell results in a trans membrane potential of -50 to -70 mV. Due to the production of an electric potential, this ion movement is known as electrogenic.

Sites for Biological Metal-Coordination

Metal-containing substances that are not present in biological systems seem to have a special function. Because they avoid the stress and hazards involved with injection, oral medicines are recommended. To detect disease or damage, inorganic chemicals like radioactive technetium are also used. Treatment for Fe overload involves the sequestration of Fe by ligands derived from or inspired by siderophores. The phrase "iron overload" describes a number of serious health issues that affect a sizable portion of the global population.

Due to its significance, it is crucial to keep in mind that Fe is a potentially hazardous element. This is particularly true given that it may combine with oxygen to produce harmful radicals, and its concentrations are often subject to stringent regulation. A hereditary disorder causes a failure in this control in many individuals. Proteins, nucleic acids, lipids, and a variety of other compounds may all coordinate with metal ions. The weak coordination of K+ and Mg2+ to the phosphate groups in DNA stabilizes it, but the binding of soft metal ions like Cu+ to the bases destabilizes it.

For membrane stabilization, Mg2+ binding to phospholipid head groups is crucial. Aside from water and free amino acids, there are a number of significant tiny ligands. These include organic acids like citrate that form rather robust polydentate complexes with Fe3+ as well as sulphide, sulphate, carbonate, cyanide, carbon monoxide, and nitrogen monoxide. A protein is a polymer made up of a particular sequence of amino acids connected by peptide bonds, as learned in basic chemistry. On a unique assembly known as a ribosome, the genetic information conveyed by DNA

is translated to create proteins. By changing the protein structure by post-translational modification, which involves the binding of cofactors such metal ions, a protein may be processed further.

Metalloproteins, or proteins with one or more metal ions, carry out a variety of specialized tasks. These processes include DNA processing (Zn), radical-based rearrangement events and methyl-group transfer (Co), hydrolysis (Zn, Fe, Mg, Mn, and Ni), and oxidation and reduction (for which Fe, Mn, Cu, and Mo are the most crucial elements). Different metal atoms need certain proteins for transit and storage. The activity of Ca2+ is to modify a protein's conformation, or shape, as a stage in cell signaling, which is the word used to describe the movement of information between and within cells. Metal ion-activated proteins are a common name for these proteins.

Medical Uses of Metal Complexes

Cisplatin: Cancer Treatment

In 1969, B. The anticancer properties of cisplatin, [Pt(NH3)2Cl2], a simple square planar Pt(II)complex were first identified by Rosenberg and colleagues. This substance is used as a chemotherapeutic treatment to slow down the multiplication of tumor cells, which would otherwise divide quickly. Chemotherapy is the use of anticancer drugs intended to slow the body's naturally occurring cancer cells from rapidly proliferating. This complex's precise mechanism of operation is unknown. Chelation or at least coordination to donor atoms at cisposition is a crucial component of activity since the trans-isomer is inactive. According to proton NMR experiments, platinum attaches to the N-7 atom of two nearby quinine bases in a rapidly growing tumor, with the chloride ligands initially being replaced by water molecules and later by DNA bases.

The N atoms of two neighboring guanine bases N-7 on DNA connect with cis-platin most often inside the same strand (intrastrand linking) or sporadically between the strands. Guanine base's N7 position is far more basic than adenine's, and as a result, it offers a greater target for platinum's assault. Recent X-ray research on a 12-base pair double-stranded DNA fragment fragment has revealed that Pt binding alters the local DNA structure and prevents the cell division necessary for the growth of cancer cells. Cisplatin causes neurotoxicity and renal damage as adverse effects. To prevent these harmful side effects, other Platinum compounds have been created. The most significant of them is carboplatin, which substitutes O chelate cyclobutanedicarboxylate for the right Cis Chloride ligands.

Wilson Illness

Wilson illness is brought on by the body having too much copper. Wilson disease is a hereditary disorder in which individuals have low quantities of the copper storage protein ceruloplasmin, making copper intolerance even at normal levels possible. Brown or green rings in the cornea of the eyes and neurological impairment are all symptoms of the Wilson illness.

One of the best chelating ligands for removing excess copper is D-penicillamine, which has the chemical formula Cu8 ICu6 II (penicillamine)12Cl. This chelating ligand forms a complex with copper ions (Cu+ and Cu2+) and has a strong purple color. The D-penicillamine's sulfhydryl group removes copper as the Cu+ complex [9].

Magnetic Resonance Imaging (MRI)

Because of the variations in water proton relaxation times typically caused by paramagnetic metal ions, nuclear magnetic resonance spectroscopy can be used to image specific tissues of biological systems. The useful metal ions for magnetic resonance imaging in humans are Gd(III), Fe(III), and Mn(II) ions. A benefit of paramagnetic MRI over radio isotopic imaging agents is that there is no possibility of radiation damage. The removal of excess metal ions from the body is known as chelate therapy. The paramagnetic character of these ions alters the relaxation rate of nearby water proton, allowing the normal and diseased tissue to be distinguished.

The Chelate Therapy Are Toxic Metals for Hg, Cd, Pb, As

Chelate treatment refers to the removal of hazardous metal cations or other extra cations that act as chelating ligands.

Lead

Lead is a relatively toxic element that accumulates over time in both plant and human tissues. Lead compounds, in particular organolead compounds like Pb(C2H5)4, are particularly hazardous. Organolead compounds may be ingested, inhaled, or come into contact with the skin. Similar to Hg(II), lead's high toxicity is caused by its strong affinity for the sulfhydryl groups SH of cysteine residue in proteins and enzymes. Lead's toxicity is also caused by its ability to produce oxidative stress, OH radicals, and peroxides, which can cause damage to DNA and nerve cells.

Lead poisoning symptoms Anaemia, lack of appetite, headaches, mental disorders, brain damage, liver damage, kidney damage, cholestasis, and skin illnesses are all signs of lead poisoning. Treatment of lead poisoning Lead poisoning may be treated by complexing and sequestering the lead using chelating ligands as British anti-lewisite BAL penicillamine or ethylene diamine tetra acetate CaNa2(EDTA).

In many Zn(II) enzymes and proteins, the Zn(II) binding sites may be occupied by mercury Hg(II), which is a congener of Zn(II). However, since Hg(II) is significantly bigger than Zn(II), any Hg(II) proteins that are produced may not function as well as their Zn(II) counterparts, if at all. Enzymes whose active sites include cysteine are inhibited by Hg(II), which binds specifically to cysteine residue. The strong affinity of Hg(II) and CH3Hg+ for the sulfhydryl group (SH) of cysteine residue in proteins, which inhibits the function of enzymes and other proteins, is the cause of Hg(II) toxicity. Once within an organism, inorganicHg(II) molecules are biotically changed to CH3Hg+ (monomethyl mercury), which is less ionic and has some attraction for cell membrane due to the methyl group, allowing for relatively simple absorption via membrane.

Mercury is exceedingly poisonous and has a sizable vapour pressure. These organomercury compounds are more easily absorbed in the gastrointestinal system than Hg2+ salts because they have a better capacity to cross bio membranes, making them more hazardous than metallic mercury itself and inorganic compounds like HgCl2. They attach to the -SH group of cysteine residues in proteins, which causes them to concentrate in the blood and have an instant and lasting impact on the brain and central nervous system [10].

Toxicity Treatment with Mercury

More The injection of chelating agents such 2, 3-dimercaptopropane-1-ol, HSCH2CH(SH)CH2OH, and N-acetyl penicillamine is necessary for the rapid removal of cadmium, mercury, and lead. Mercury-resistant bacteria have been shown to have a very unusual natural detoxifying process. Bacteria have evolved a resistance to heavy metals, and metalloregulator proteins, which can specifically recognize metal ions, start and regulate the detoxification process. It is a little DNA-binding protein that regulates the mer genes' transcription. Cadmium is a very hazardous metal because, like mercury, it may replace many zirconium-containing enzymes and proteins. However, since Cd(II) is much bigger than Zn(II), the proteins made from Cd(II) may not operate as effectively as the comparable zinc enzyme or their activity may be completely lost. Because Cd(II) is a soft acid and has a large affinity for, it is similar to Hg(II). The enzymes and proteins become inactive when Cd(II) firmly coordinates to deprotonated sulfhydryl groups of cysteine residue in zinc tablet-dependent proteins, leading to protein denaturation and the formation of insoluble CdS.

Arsenic

For most creatures, arsenic is an extremely poisonous element. The body converts inorganic compounds of arsenic to methylarsenic compounds, which are traditionally produced from arsenate and arsenite by substituting up to three OH-/Ofunctions for methyl groups. The most prevalent form of arsenate is AsO4-3, which glutathione can easily decrease in living things. Thus, it decreases glutathione's availability as an antioxidant. Chromel damage, mutagenesis, cancer, and oxidative stress are all results of arsenic poisoning.

DNA is a sophisticated molecule that contains the genetic information required for the growth and operation of every known living species. One of the most well-known discoveries of all time was the double helix structure of DNA, which Watson and Crick discovered in 1953. When they suggested the double helix model of DNA, Watson and Crick also offered a likely path for DNA replication. A double-stranded DNA makes a duplicate of itself to generate two identical copies via the process of DNA replication. Since then, the conservative, semi-conservative, and dispersive models of DNA replication have all been put forward. Four classes of elements—essential, trace, non-essential, and toxic—have been established. No common element is toxic at normal concentrations, but almost everything may be deadly at extremely high concentrations. The amount of metal ions in a person's system is carefully regulated. Metal ion excess or shortfall results in disruption, which may cause a number of illnesses.

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CHAPTER-14

THE BIOORGANIC CHEMISTRY

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A branch of science known as "bioorganic chemistry" combines biology with organic chemistry. Structure design, synthesis, and kinetics are the topics covered in organic chemistry. Biochemistry is the study of biological processes using biochemical methods. To create biological molecules, analyze their structure, and study biochemical processes, organic chemistry techniques are applied. According to one definition, bioorganic chemistry is a field of chemistry or, more generally, a field of science that applies the concepts, methods, and tools of organic chemistry to the study of biochemical and biophysical processes.

The goal of this subject was to provide students a fundamental grasp of the chemistry behind biomolecules. Learners will be exposed to biomolecules such nucleic acids, proteins, carbohydrates, and lipids as part of this unit. Learners will be able to:

1. Recognize and identify several categories of biomolecules at the conclusion of this lesson.
2. Describe the key structural and functional characteristics of biomolecules.
3. Recognize, group, and identify proteins, lipids, nucleic acids, and carbohydrates based on their makeup and intended uses.
4. Recognize the chemistry principles behind biological compounds and their biochemical characteristics.
5. Describe the makeup of nucleic acids and clarify the distinction between DNA and RNA.

The Chemistry of Biomolecules

All living things have chemicals called biomolecules that are essential to their upkeep and metabolic functions. Biomolecules are huge macromolecules consisting of carbon and hydrogen, such as proteins, polysaccharides, lipids, and nucleic acids. These biomolecules are typically thought of as hydrocarbon derivatives, with some hydrogen atoms substituted by different functional groups like hydroxyl, methyl, carbonyl, carboxyl, amino, phosphate, and sulfhydryl to form various bioorganic molecules or biological molecules. Many biomolecules have two or more functional groups that may interact to affect each other's reactivity, making them polyfunctional. The basic building blocks of biomolecules are carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur. These biomolecules also have a number of heterocyclic and homocyclic rings, such as the indol ring in the amino acid tryptophan and the phenanthrene ring in steroids. While the thiophene ring is a component of the vitamin biotin, pyrole is the fundamental unit of porphyrins, which are present in many biomolecules, including hemoglobin, chlorophyll, and others. Imodazole's ring structure is included in the amino acid histadine. The fundamental components of nucleic acids are pyrimidines and purines [1], [2].

Typically, biomolecules are bigger than organic molecules. Small biomolecules have molecular weights of over 100, but the majority of biomolecules have molecular weights in the thousands, millions, or even billions. Due to their size, most biomolecules have distinct 3-dimensional forms with carefully calculated atom placements in space. Numerous non-covalent connections between the atoms in the molecule maintain its 3-dimensional form. Due to the weak nature of the majority of noncovalent bonds and interactions between the biomolecule and the solvent, the structure of a biomolecule is flexible rather than static. The stereochemistry of organic substances is also present in biomolecules. When a molecule contains stereogenic (or chiral, or asymmetric) carbon, it may exist in two distinct isomeric enantiomers, or diastereomers, with different spatial configurations and unique characteristics.

Carbohydrates

One significant class of naturally occurring chemical molecules is the carbohydrates. They are naturally created by photosynthetic processes in plants. Plants absorb water via their roots and utilize carbon dioxide from the atmosphere to create glucose and oxygen during photosynthesis. Plants need energy to carry out photosynthesis since it is the opposite of the process that creatures utilize to get energy the oxidation of glucose to carbon dioxide and water. Originally, the term "carbohydrate" applied to substances with the generic formula Cn (H_2O) n. Where n is the molecule's representation of carbohydrates' number of carbons. In the molecules of carbohydrates, carbon, hydrogen, and oxygen are distributed in a 1:2:1 ratio. Only simple sugars, or monosaccharides, however, perfectly match this formula. The overall formula for the other two forms of carbohydrates, oligosaccharides and polysaccharides, which are based on monosaccharide units, is somewhat different. In Greek, the word "saccharides" for carbohydrates means "sugar." Sugars and starches are types of carbohydrates. Many creatures use them as their main energy source, energy storage mechanism, and structural element. The most prevalent sort of biomolecule is the carbohydrate due to its extensive spread.

The molecules that make up carbohydrates are polyfunctional and include the functional groups hydroxyl (-OH), aldehyde (-CHO), and ketone (>C=O). Therefore, polyhydroxyaldehydes like D-glucose, polyhydroxy ketones like D-fructose, and big molecules like sucrose that form these chemicals on hydrolysis may all be referred to as carbohydrates. We are aware that Hemiacetal or acetal is created when an alcohol (alcoholic -OH) and a carbonyl molecule (aldehyde or ketone) interact. An internal hemiacetal is produced when an aldehyde group in carbohydrates combines with an alcoholic -OH of the same molecule. We'll also observe that removing the H2O molecule from between two sugar molecules' hemiacetal OH groups results in the formation of larger carbohydrate molecules. A better definition of a carbohydrate would be polyhydoxy molecules having an aldehyde or ketone function, either free or as hemiacetal or acetal, in light of the aforementioned information [3].

Carbohydrate Classification and Nomenclature

The three main categories of carbohydrates are monosaccharides, oligosaccharides, and polysaccharides based on whether or not they undergo hydrolysis and, if so, how many products are produced. Monosaccharides: The polyhydroxy aldehydes (aldose) and polyhydroxy ketones

(ketose), which are the monosaccharides, cannot be broken down by hydrolysis to produce simpler carbs. Example: Galactose, fructose, and glucose. The classification of monosaccharides into trioses, tetroses, pentoses, hexoses, and heptoses is based on the number of carbon atoms in the main chain [4].

Carbohydrate Structure and Stereochemistry

Fischer projections or wedge-and-dash structures are often used to depict the chemical structures of carbohydrates, as shown in Figure 1. Numerous stereocenters exist for carbohydrates. For instance, glyceraldehyde only has one. However, you'll see a rise in stereocenters when you consume more complex carbs. A glucose molecule has four chiral carbons. This suggests that the glucose molecule has a total of 16 stereoisomers. Where "n" is the number of chiral centers, the number of stereoisomers is equal to 2 n.

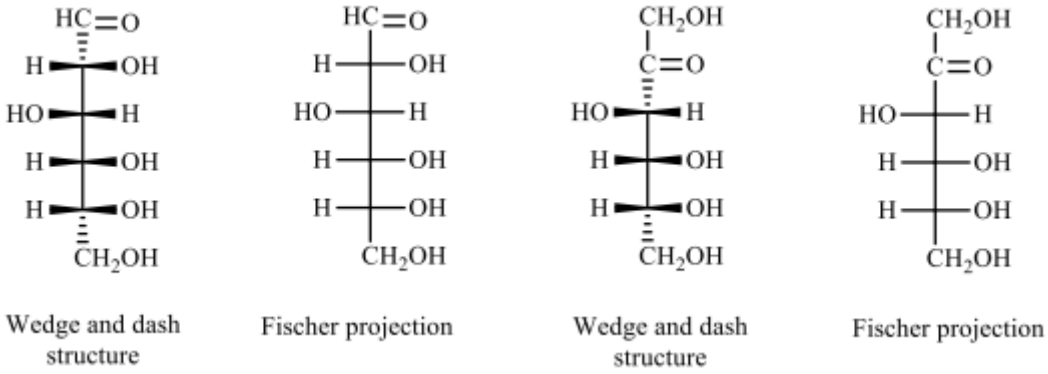

Figure 1: Wedge -dash structures and Fischer projections of carbohydrates.

Carbohydrates with an Open Chain

The D and L notation, which describes the arrangement of the last chiral carbon in the chain, is used to explain the stereochemistry of carbohydrates. By connecting the molecule to glyceraldehyde, it is utilized to provide the name of the molecule. To discriminate between D and L carbohydrates, utilize Fischer's projection.

The carbohydrates are assigned the D configuration if the hydroxyl group is positioned to the right of the final stereocenter in the Fischer's projection, and the L configuration if it is positioned to the left of the last stereocenter carbon. The only information provided is the configuration of carbohydrates; nothing about the direction of rotation of plane-polarized light is specified.

Asymmetrical molecules are those in which the atoms are arranged differently from symmetrical molecules. The D and L configuration cannot identify absolute stereochemistry, but the anomeric carbon center may by comparing its orientation to the glyceraldehyde.

The D-L system is significant because it provides the molecules' relative configuration. For example, the D- and L- notation is a convenient shorthand for distinguishing enantiomers. The enantiomer of L-glucose is D-glucose.

Types of Carbs That Cycle

Carbohydrates may generate intramolecular (cyclic) hemiacetals because they have carbonyl and alcohol functional groups. To achieve it, a carbohydrate must be at least a tetrose, therefore lesser carbohydrates lack intramolecular cyclic forms. A 5-membered ring results from the cyclization of the -OH on the fourth carbon. A 6-membered ring results when the -OH is provided by the fifth carbon. The 5-membered rings are referred to as furanoses, while the 6-membered rings are referred to as pyranoses, since they are analogous to the common heterocyclic compound's furan and pyran, which contain oxygen. Here is an illustration of how the ubiquitous sugar D-galactose may take on two distinct cyclic forms.

Carbs in The Shape of Chairs

The six membered pyranoses really assume a non-planar ring conformation similar to that of cyclohexane, which differs significantly from the shape predicted by the planar Haworth projection formulas. The sugar in solution most often cycles into rings in the chair form. There are two possible conformations for the chair. Changes in the axial vs equatorial orientations of the carbon functional groups are the main result of the different conformations. If equatorial rather than axial hydroxyl groups is preferred, the pyranoses assume a non-planar ring shape, and the chair form has the maximum amount of hydroxyl groups. It should be observed that axial hydroxyl groups are present in -D-glucopyranose, as opposed to -D-glucopyranose. The hydroxyl group linked to C-1 is below the ring plane in the -form, while it is above the ring plane in the form [5].

Glucosyl Binds

Disaccharides, oligosaccharides, and polysaccharides may be created by joining monosaccharides. Lactose (galactose + glucose), sucrose (glucose + fructose), and maltose (glucose + glucose) are all significant disaccharides. Glycosidic bonds are the bonds that bind sugar molecules together, as shown in Figure 2. These are created by enzymes called glycosyltransferases using the substrates nucleotide sugars like UDP-glucose.

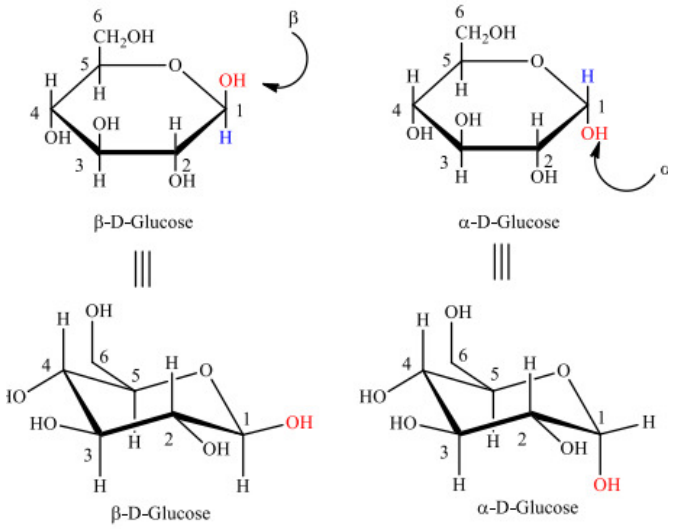

Figure 2: Illustrate the Chair form of α and β-D-Glucose.

Epimer

Isomers are substances with the same chemical formula but distinct structures. For instance, the isomers of fructose, glucose, mannose, and galactose all have the same molecular formula, C6H12O6. Epimers of each other are defined as carbohydrate isomers that vary from each other only in the configuration of a single carbon atom. For instance, just the location of the -OH group at carbon 4 distinguishes the structures of glucose and galactose, which are both C4 epimers. The carbons in sugars are numbered starting with the carbonyl carbon, also known as the aldehyde or keto group, at the end. C-2 epimers of glucose and mannose exist. Galactose and mannose, on the other hand, are only referred to as isomers because of the different positions of the -OH groups at their two carbons (2 and 4) [6].

Mutarotation

When the material is present in the crystallized anhydrous form, the two potential orientations of the hydroxyl group result in different optical characteristics. -D-glucose has a specific rotation of +113°, whereas that of -D-glucose is +19.7°. However, both forms produce an equilibrium mixture in aqueous solution that has a specific rotation of +52.5°, with around 36% in the form and 64% in the -form and just a tiny amount of free aldehyde. Any standard glucose solution for use with a particular enzyme assay (for example, glucose by the glucose oxidase which is specific for -D-glucose) should be allowed to achieve equilibrium before use in order to ensure that the proportions of each isomer in the standard and test solutions are the same. It takes several hours for this equilibrium to be established at room temperature. Mutarotation is the interconversion of the and forms of D-glucose to an equilibrium mixture, which results in changes in the specific optical rotation. Mutarotases are enzymes that hasten the achievement of this equilibrium and may be added to test reagents to hasten the creation of equilibrium. When the matching stereocenters interconvert, the equilibrium between two anomers changes, causing the optical rotation to alter. This is known as mutarotation. The interconversion of the and anomeric forms causes the rotation of cyclic sugars.

Sir Dubrunfaut, a French scientist, noted that the precise rotation of an aqueous sugar solution changed with time and made the discovery of mutarotation in 1846. [Dubrunfaut subsequently identified the organic fructose molecule in 1847]. There are two possible states for sugars in the ring form: one in which the C-1 hydroxy group is above the plane of the ring (), and the other in which it is below (). The hemi acetal structure breaks apart in aqueous solution and then reforms, allowing for continual transitions between the several conformations [7].

Lipids

Fats and oils are lipids. Lipids are a category of compounds that may be removed from cells using organic solvents and are soluble in nonpolar solvents but insoluble in water. They are chemically more varied than other groupings of biomolecules since they are categorized according to solubility characteristics. Lipids fall into a number of diverse classes. The majority of lipids serve as molecules that store energy or as parts of the structural makeup of membranes. Some are furthermore pigments, vitamins, and harmones. Major functions of lipids in human biology include: They save their energy in fat cells. Glycogen is a source of energy that is stored in the

body for when we need instant energy. However, burning fat produces more than double the amount of energy as burning an equivalent amount of carbs. They are a component of the membranes that divide up spaces into compartments. The majority of substances that make up the body, such proteins and carbohydrates, are water soluble. The body requires insoluble substances for the membranes that divide compartments containing aqueous liquids. These membranes are made of lipids. As chemical messengers, they serve. Signals are sent from one region of the body to another portion of the body through primary messengers, such as steroid hormones. The hormonal response is mediated by auxiliary messengers including prostaglandins and thromboxanes.

Lipid classification and Chemistry

Oleic Acid

Long hydrocarbon chains make up the carboxylic acids known as fatty acids.There are two types of lengthy hydrocarbon chains: saturated and unsaturated. Since the production of fatty acids involves the concatenation of C2 units, the majority of naturally occurring fatty acids have an even number of carbon atoms. Fatty acids are most often found with carbon atoms between 14 and 20. Half of the fatty acids in higher plants and animals are polyunsaturated. Saturated fatty acids with the highest concentrations may be found in palmitic acid (C16), stearic acid (C18), and arachidic acid (C20). Unsaturated fatty acids are denoted by the formula C: n, where C stands for the number of carbon atoms and n for the number of double bonds. Oleic acid (18:1), linoleic acid (18:2), linolenic acid (18:3), and arachidonic acid (20:4) are examples of commonly occurring unsaturated fatty acids. The double bonds are always present in the cis orientation in unsaturated fatty acids. Unsaturated fatty acids have a lower melting point than their saturated counterparts as a result of the hard 300 bend that this cis arrangement across the double bonds imposes into the structure, interfering with its efficient packing.

Sterols

The fourth type of lipids is called sterols, which are structural lipids as opposed to the membrane lipids previously addressed. The steroid nucleus of their distinctive structure is made up of four fused rings. The fourth ring has five carbons, whereas the other three rings contain six. It is a rather stiff planar ring structure. The C-C bonds in this arrangement prevent any movement around them. Due to the polar hydroxyl group connected to the third carbon atom and the lengthy non-polar aliphatic chain attached to the 17th carbon atom, cholesterol is mildly amphipathic in nature. The primary sterol that plays a crucial structural role in biological cell membranes and acts as a precursor to many of the body's key steroid hormones is cholesterol. The body's vital physiological systems, including glucose metabolism, are controlled by steroids. The steroid ring system, which consists of four fused rings, different side groups, and a hydroxyl group, is present in sterols. Another kind of steroid has a carbonyl group. They cannot be saponified because they lack a fatty acid. They are amphipathic, with the oxygen group serving as the molecule's polar head. Steroids are lipids that cannot be hydrolyzed. Compounds called steroids have four joined carbocyclic rings. The described lipids' structure is entirely different from those of steroids. Although some of them

are, in general, they are not esters. Although their functions are quite different, steroids have very similar structural similarities [8].

Protein

A protein is a molecule with biological activity that is made up of one or more polypeptides. More than half of the dry mass of most cells is made up of proteins. The support of structural integrity, storage, mobility, cellular communication, and defense against external chemicals are all activities of proteins. A protein's stable structure heavily influences how well it performs. There are four layers in this structure: primary, secondary, tertiary, and quaternary. Multiple weak interactions work together to maintain protein structure. The sequence of amino acids connected by peptide bonds makes up the primary structure. The local folding of a polypeptide's secondary structure. The tertiary structure, which is the next level, combines -helixes and -sheets. While a protein's quaternary structure is its subunit structure. We will get greater understanding of the protein structure and its many levels in this session.

Acids Amino

Although there are many different types of proteins, they all generally share the same structure: they are made up of chains of amino acids. A chemical molecule known as an amino acid has both an amino and a carboxylic group as shown in Figure 3. Alpha amino acids are the 20 amino acids that are often present in proteins. All the amino acids in all the proteins in the human body, with the exception of glycine, which is an achiral amino acid, are L-isomers.

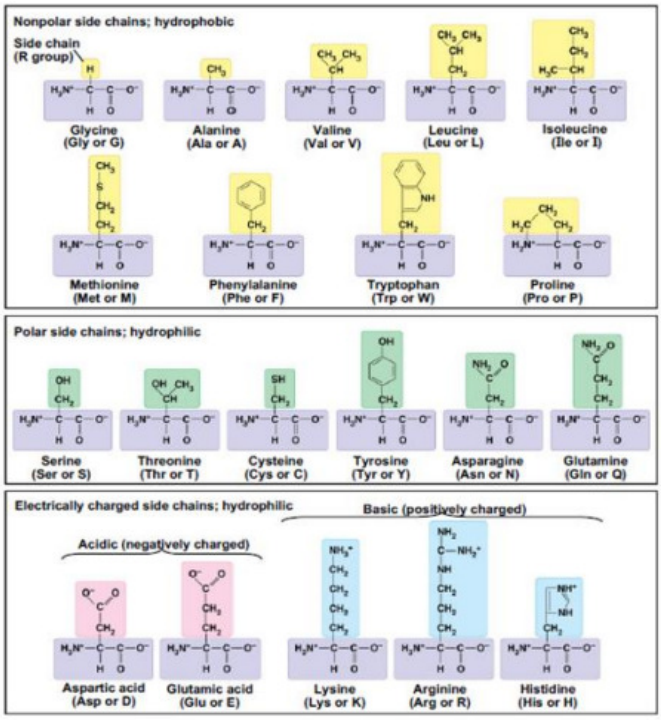

Figure 3: Illustrate the General structure of an amino acid.

The polarity of the R groups is what matters most. Amino acids are divided into four classes based on this classification: nonpolar, polar but neutral, acidic, and basic. While polar side chains that are neutral, acidic, or basic are hydrophilic (attracted to water), nonpolar side chains are hydrophobic (repel water). An amino acid is a molecule that contains both -COOH and -NH2 groups. As a result, an amino acid truly possesses the structure of the internal salt when it is in a water solution because the -COOH contributes a proton to the -NH2. Zwitterions are substances that contain an atom with a positive charge on it and an atom with a negative charge on it. The term zwitter is a German word that means "hybrid." Both in the solid form and in aqueous solutions, amino acids are zwitterions. Robert Corey and Linus Pauling studied the peptide bond. They discovered that the peptide bond is planar as a result of the shorter C-N bond than in an amine. They discovered resonance between the peptide bond's carbonyl carbon and amide nitrogen components (OC-NH). The hydrogen (H) and oxygen (O) in the peptide bond are both in the trans position. Due to the double bond nature of the peptide, no free rotation was seen around it. It is hard and flat as a result. Additionally, the nitrogen and oxygen in carbonyl carbon each have a little positive and negative charge. The little electric dipole is created by this. N-C and C-C bonds are the two types of bonds where rotation is allowed. When a C-C bond rotates, the bond angle is known as the psi angle, but when an N-C bond rotates, the bond angle is known as the phi angle. Angles for psi and phi should range from -180° to +180° G.N. Ramachandran graphically illustrated the allowable rotations around the N-C bond (phi angle) and C-C bond (psi angle).

Basic Structure

A protein's distinctive amino acid sequence makes up its main structural component. Each peptide or protein has a specific amino acid sequence. The locations of the amino acids in the sequence are assigned starting at the N-terminal end, much as with peptide naming. For instance, Frederick Sanger identified the first amino acid sequence of the protein bovine insulin in 1953. Since severe diabetics need insulin injections, insulin is required for the correct utilisation of carbohydrates. As illustrated in figure 4, the 51 amino acids of bovine insulin are made up of two polypeptide chains, A (21 amino acids) and B (30 amino acids), which are connected by intra- and inter-chain disulphide linkages.

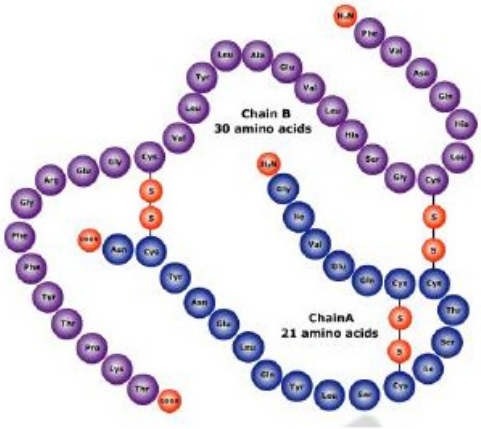

Figure 4: Primary Structure of bovine insulin.

Second-Level Architecture

The secondary structure of a protein refers to the geometric configurations created by the groupings of amino acid residues. Two notable secondary protein structures are -helixes and -sheets. Random coils are protein conformations that don't show a recurring pattern. i) The protein keratin has the helix structure. A protein may take several conformations by rotating around single bonds and stiff peptide bonds. The -helix is the most basic configuration for a polypeptide chain. The side groups of the polypeptide stick out from the helix as it coils around a hypothetical axis. The repeating unit of the -helix is a single turn, which has a diameter of 5.4 Angstrom. The intra-hydrogen bonds maintain the -helix's stability. The first amino acid and the fourth amino acid combine to create this connection. The side chains' charge has the potential to make the helix unstable. The development of the -helix is hampered by nearby Glu, Arg, or Lys that are charged at pH neutral. Similar to how pro, which has a ring structure, causes the helix to bend and become unstable. In the a-helix form, a single protein chain twists until it becomes the shape of a helix, or a right-handed coiled spring. Numerous intramolecular hydrogen bonds between the backbone -C=O and H-N- groups help to maintain the helix's form. Each -N-H and C=O are almost parallel to the helix's axis, pointing upward for each and downward for each. The side chains of every amino acid face away from the helix [9].

A polypeptide's stretched zigzag shape is known as a -sheet. Within a polypeptide, neighboring segments create an intramolecular hydrogen bond. Both parallel and antiparallel orientations are possible for the neighboring segments. Aside from -sheets, -turns are crucial parts of the protein structure. By forming a hydrogen bond between the first and fourth amino acids, -turns link the two adjacent segments of the antiparallel sheet.

The -pleated sheet is another significant ordered structure seen in proteins. In this instance, intermolecular or intramolecular hydrogen bonds are responsible for preserving the regular alignment of protein chains. When polypeptide chains are antiparallel (neighboring N-terminal ends on opposing sides) or parallel (all N-terminal ends on one side), the -sheet structure may form between molecules. The formation of antiparallel pleated sheets, which result from the polypeptide chain making a U-turn and producing a hairpin shape, may also happen intramolecularly. The -pleated sheet is another significant ordered structure seen in proteins. In this instance, intermolecular or intramolecular hydrogen bonds are responsible for preserving the regular alignment of protein chains. The hydrogen bonding in all secondary structures is between the H-N groups and the backbone -C=O.

An Ancient Building

When two or more polypeptide chains combine to produce one macromolecule, quaternary structure is the outcome. The quaternary structure, which is applicable to proteins having more than one polypeptide chain, is the highest degree of protein organization. The same factors that hold together tertiary structures hydrogen bonds, salt bridges, and hydrophobic interactions are used to pack and hold the subunits together. Adult humans have four chains (referred to as globins) that make up their hemoglobin: two identical -chains with 141 amino acid residues each and two identical -chains with 146 residues each. The four polypeptides that make up hemoglobin, the

blood's oxygen transport, form a quaternary structure with the formula 2 and 2. The structures of polypeptides and myoglobin are similar. Each globin chain in hemoglobin encircles a heme unit that contains iron. Conjugated proteins are proteins that include non-amino acid segments. A prosthetic group is the name for the non-amino acid part of a conjugated protein. The globins in hemoglobin are the sections made up of amino acids, whereas the heme units are the prosthetic groups.

Protein Denaturation

Denaturation is the process by which a chemical or physical substance destroys the secondary, tertiary, and quaternary structures of a protein while maintaining the fundamental structure. For instance, boiling a protein solution breaks the a-helical and -pleated sheet structure because heat cleaves hydrogen bonds. Heat induces the polypeptide chains in globular proteins to unfold; as a result of subsequent protein-protein interactions, precipitation or coagulation occurs. When we boil an egg, that is what occurs.

Secondary, tertiary, and quaternary structures are altered by denaturation. Primary structures, or the arrangement of amino acids that make up a chain, are unaffected. Denaturation may be stopped if these changes take place just little. For instance, a denatured protein often regains its secondary and tertiary structures when we take it from a urea solution and add it to water. The term "reversible denaturation" refers to this phenomenon. Chaperones can stop certain heat-induced denaturation in live cells. These proteins aid in restoring the secondary, tertiary, and quaternary structures of a partly heat-denatured protein. However, some denaturation is irreversible. A hard-boiled egg cannot be re-boiled.

Atomic Acid

Biopolymers and macromolecules called nucleic acids are necessary for all known forms of life. Purines and pyrimidines are a combination of organic bases that may be produced when nucleic acid, a naturally occurring chemical molecule, is broken down. Because they control the creation of proteins, nucleic acids the primary information-carrying molecules of the cell determine the inherited traits of every living creature. They are constructed of monomers called nucleotides, which are comprised of a nitrogenous base, a phosphate group, and a 5-carbon sugar. Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are the two primary types of nucleic acids. All free-living creatures and the majority of viruses have genetic material made up of DNA, which is the ultimate life-plan. RNA is the genetic material of certain viruses, but it is also present in all living cells and is crucial to many biological activities, including the synthesis of proteins.

Chemistry of Nucleic Acids

Polynucleotides, or long, chain-like molecules made of a number of virtually identical nucleotides, are what constitute nucleic acids. Each nucleotide is made up of a pentose (five-carbon) sugar connected to a phosphate group, which is then bonded to an aromatic base with nitrogen. Adenine (A), guanine (G), cytosine (C), thymine (T), and uracil (U) are the four nitrogen-containing bases found in each nucleic acid, out of a potential five. While C, T, and U are collectively referred to as pyrimidines, A and G are classified as purines. The nucleotides A, C, and G are present in all

nucleic acids; T, on the other hand, is only present in DNA, while U is only present in RNA. The lack of a hydroxyl group (OH) on the 2′ carbon of the sugar ring distinguishes the pentose sugar in DNA (2′-deoxyribose) from the sugar in RNA (ribose). A nucleoside is a sugar that is joined to one of the bases but does not have a phosphate group. The phosphate group joins the next sugar residues in the chain by forming a bridge between the 5′-hydroxyl group on one sugar and the 3′-hydroxyl group on the following sugar. Both RNA and DNA include these phosphodiester bonds, which are nucleoside connections [10].

Nutrient-Rich Bases

Single-ringed or two-ringed nitrogenous bases make up nucleotides. The two-ringed nitrogenous base is known as purine, whereas the one-ringed nitrogenous base is known as pyrimidine. Basic purine or pyrimidine structure. Pyrimidines are aromatic six-membered rings with two N-atoms. Pyrimidine rings and five-membered imidazole rings make up the structure of purines.

Nucleoside

By establishing a -N-glycosidic connection between a sugar and a nitrogenous base, nucleosides are created. Purine nitrogenous bases are connected to the sugar by their N-9 atom, while pyrimidine nitrogenous bases are linked via their N-1 atom. 'Osine' is added to nucleosides that have purine as their base. Adenosine and guanosine, for instance. While 'idine' is added to nucleosides that use pyrimidine as their base. Cytidine, uridine, and thymidine are a few examples. Deoxyribonucleosides are the term given to nucleosides whose sugar is 2-deoxy ribose.such include deoxyadenosine and deoxyguanosine.

DNA's Secondary Structure

In this session, we learned about the basic makeup of nucleic acids. While RNA is made up of ribonucleotides with uracil in place of thymine, adenine, cytosine, and guanine, DNA is made up of deoxyribonucleotides with these bases. RNA typically exists as a single strand, while DNA typically exists as a double strand. Adenine and thymine invariably bind with guanine and cytosine in double stranded DNA. Inside a cell, DNA may exist in a variety of shapes. They are DNA forms A, B, and Z that are determined by various humidity levels. Deoxyribonucleic acid (DNA) is made up of the four nucleotides A, C, G, and T. These nucleotides are linked together by a backbone made up of alternating phosphate and deoxyribose sugar residues. These bases with nitrogen occur in complimentary pairs based on their capacity to create hydrogen bonds with one another. via two hydrogen bonds, A and T are always paired, and via three hydrogen bonds, G and C are always paired. A:T and G:C hydrogenbonded pairs may bridge the sugar-phosphate chains evenly since their spans are almost equal. DNA is the best genetic material because of its structure and chemical stability. Additionally, the bonding of complementary nucleotides offers a mechanism for DNA replication and genetic information transfer.

Ribonucleic acid (RNA) is a single-stranded nucleic acid polymer made up of the nucleotides A, C, G, and U that are connected by an alternating backbone of phosphate and ribose sugar residues (Fig. 4.28). It is the initial step in translating DNA information into proteins that are necessary for a cell to function. Some RNAs have direct functions in cellular metabolism as well. A fragment of

single-stranded nucleic acid is used to replicate the base sequence of a gene, a portion of double-stranded DNA. RNA has several functions and is chemically far more reactive than DNA, which gives the cell's genetic instructions and is by nature fairly stable. RNA is susceptible to oxidizing substances like periodate that cause the 3′-terminal ribose ring to open. Because the presence of alkali causes the phosphodiester bond between the ribose and phosphate groups to rapidly cleave, the 2′-hydroxyl group on the ribose ring is a key contributor to the instability of RNA. Due to the continual synthesis and degradation of RNA, this instability often poses little threat to the cell.

Connection Effect

Figure 5 illustrates how an enzyme must combine with its substrate to create an enzyme-substrate complex in order to catalyze a chemical reaction. By stabilizing the transition state of the process, the enzyme makes it simpler for the bound substrate to create the transition state and transform into product. The resultant enzyme-product complex then separates, liberating the free product and rejuvenating the free enzyme, allowing it to perform more catalytic cycles. Through proximity in enzyme-substrate interactions, the reactive chemical groups may be aligned and brought together in the optimum orientation and spatial connection for a reaction to occur. Once the substrates are thus fixed, the enzymatic reaction behaves kinetically like an intramolecular process. Certain theories contend that molecules behave most reactivity when their orbitals are designed to lower the electronic energy of the transition state.

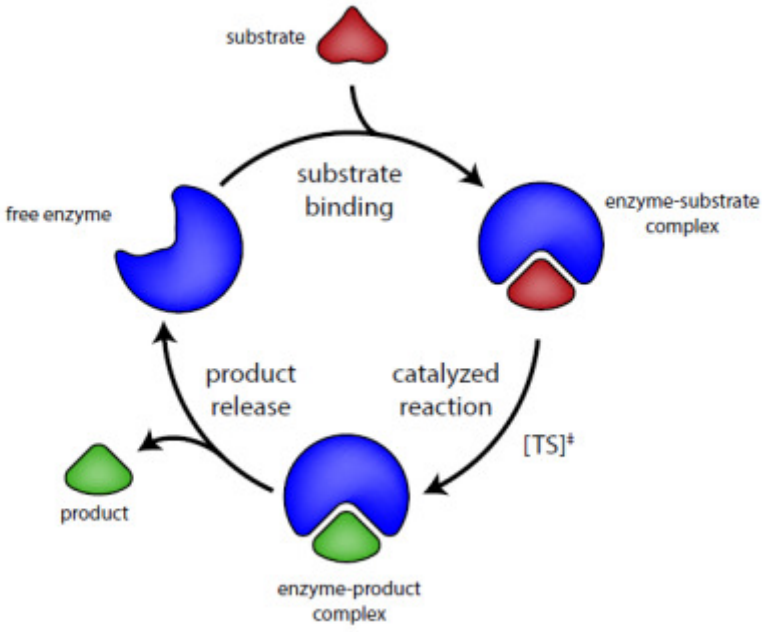

Figure 5: For chemical processes, enzymes attach to their substrates and catalyze them.

The orientation and mobility of the substrate molecules inside the enzyme's active site results in the proximity effect, which brings the reactants considerably closer together than they would be in solution. The reaction will go more quickly if the reactants are closer together since this will enhance the frequency of their collisions. This closeness and orientation impact gives the reaction an intramolecular character and a significant rate increase, similar to an effective rise in reagent

concentration. The equivalent intermolecular processes between two distinct molecules go more slowly than intramolecular reactions between groups that are bound together in a single molecule. Think about the two hypothetical reactions' rates as an illustration of the proximity effect in catalysis. The random collision between the two substrates, which brings A and B near enough to react, is what triggers the reaction at the top. In contrast, if A and B are already connected, there is a significantly higher chance that they will come into contact in the reaction at the bottom.

Mechanical Adaptation

The molecule's shape impacts whether it may be identified by a receptor and exhibit the same biological activity as a bioactive molecule. Similar-looking substances could compete for the same biological target. The creation of novel medications by molecular alteration may greatly benefit from this knowledge. Examples are given to illustrate these truths. Genetic information is stored in nucleic acids (DNA and RNA) by all living systems. Therefore, any substance that prevents the production of these essential components is hazardous to all living things. These harmful substances are referred to as antimetabolites, and one such antimetabolite is 5-fluorouracil (5-Fu), which prevents DNA synthesis. This uracil derivative blocks the enzyme that uses methylation to convert uracil into thymine. A methyl group is the sole difference between thymine and uracil; thymine is 5-methyluracil. One is aware that hydrogen and fluorine are about the same size. Thus, it may be said that 5-fluorouracil mimics uracil in size and form, which causes the enzyme to adapt and consequently block the production of dTMP, which in turn inhibits DNA synthesis.

5-fluorocytosine, an analog of the natural base cytosine, is a typical antibiotic used to treat bacterial infections. A novel strategy is to chemically disguise the medicine so that it may penetrate and kill the bacterial cell. In this manner, the patient's tissues won't be harmed by the medication. In the contemporary technique, a short peptide containing D-amino acids is linked to the amino group of the medication, for example, 5-fluorocytosine, so that typical human enzymes cannot cause its hydrolysis. Thus, the drug containing the peptide may enter the bacterial cell and be processed there to release the medication. Poly hydroxy aldehydes and ketones make up carbohydrates. Anomeric carbon is produced from an aldehyde group from an aldose or a keto group from a ketose when sugar cycles. If the oxygen on the anomeric is not connected to any other structure, this carbon might have either the or configuration. The monomers that make up the polymer DNA or RNA are called nucleotides. A nitrogenous base, a pentose sugar, and phosphoric acid make up nucleotides. Nitrogenous bases may be either pyrimidines with one ring or purines with two rings. The two strands of DNA are held together by interstrand hydrogen bonds between the adenine and thymine pair and the guanine and cytosine pair. Primary structure, secondary structure, tertiary structure, and quaternary structure are the four stages of protein structure. There are two common secondary structures: -helix and -sheets. The quaternary structure of a protein is formed by the joining of several polypeptides, while tertiary structure is the spatial arrangement of atoms in space.

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CHAPTER-15

ENZYME AND MECHANISM OF ENZYME ACTION

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Juice fermentation into alcoholic drinks is perhaps the earliest biochemical and bioorganic occurrence. Additionally, this was the first chemical change that was aided by enzymes found in live yeast cells. It was discovered in the 18th century that fermentation causes sugars to change into alcohol and carbon dioxide. The 19th century saw the discovery of fermentation as a physiological process carried out by yeast cells as well as the advancement of Pasteur's theory that fermentation and life are intertwined. Since enzyme extraction from living cells was already well known, this discovery, like most scientific ones, was made by accident. E. Buchner needed a certain amount of pure protein in 1897 for medical purposes. He crushed the yeast and sand, removed the broken cells, and preserved the filtrate by adding a significant quantity of sugar. Almost every metabolic process in a living system requires the use of enzymes, which are biochemical catalysts. In nature, enzymes are proteins that may be thought of as biocatalysts living cell-produced proteins. Greek-en: in and zyme: yeast are the two words that make up the term enzyme, which Kuhne employed. Greek for "to dissolve," Berzelius first used the word "catalysis" in 1836 and was able to catalyze the fermentation process.

Enzyme catalysis and the active site of an enzyme We are aware that enzymes provide their three-dimensional environment (composed of L-amino acids) to the substrates in order to demonstrate their amazing catalytic accomplishment. Only a very tiny percentage of the enzyme molecule is devoted to the active sites, or the functional portion, of an enzyme. Either of the representations may be used to display the active site of the enzyme in its entirety. A substrate moves toward the transition state when it binds to an enzyme, which alters the substrate's structure. The active site of an enzyme often resembles the transition state more so than the substrate. Analogs of the transition state are effective inhibitors for this area. The active sites (amino acid residues) of a protein enzyme are considerably closer together in the tertiary structure (enzyme folding) than they are in the primary structure. The letters A, B, and C indicate these amino acid residues. Every enzyme molecule has an active site where catalysis occurs. The amino acid residues (R-groups) bind the substrate in the proper position for the reaction at the binding site, which is a part of the active site.

This is comparable to the proper position of the reactive group in an intramolecular reaction. This binding is affected by a number of variables, including electrostatic interactions and hydrogen bonds. The transition state is stabilized by these advantageous interactions with the amino acid residues in the active site, which also lowers the process's active activation energy and speeds up the reaction. Additionally, there is a pocket (P) at the active site that, in the case of carboxypeptidase, may receive the side chain of the terminal amino acid when the latter is cleaved off a peptide chain by the enzyme. Many enzymes need cofactors, which are non-protein

molecules, in order for the reaction to happen. These cofactors might be either tiny organic molecules termed coenzymes (NAD+, NADP+) or metal ions. However, certain coenzymes are bound covalently and are referred to as prosthetic groups. The majority of coenzymes are attached by ionic bonds or other non-covalent bonding interactions. For carboxypeptidase A to function as an enzyme, zinc ion is required. The zinc ion is kept in place by two histidine side chains, a glutamate side chain, and a water molecule in a groove on the enzyme's surface. The R group of additional amino acids produces the catalytic activity after the substrate is correctly bound in the enzyme's active site [1].

Amazing Qualities of Enzymes as A Catalyst

Enzymes are powerful catalysts that increase the pace of a process by a factor of 105–101. Following that, the substrate is firmly bonded in the active site to create an ES complex. Like other catalysts, an enzyme lowers a process's activation energy and speeds up the reaction. The equilibrium of the process is unaffected by the enzyme. In general, weak interactions including hydrogen bonds, ionic contacts, and hydrophobic interactions provide the energy needed for enzymatic rate increase. These interactions are offered by the active sites, and they help to maintain the transition state. A lower energy approach is facilitated by general acid base catalysis, covalent catalysis, and metal ion catalysis. The binding energy may cause a conformational shift in the enzyme to provide induced fit and aid in reducing the entropy of the substrate. Additionally, binding energy explains why an enzyme acts as a catalyst.

Classification by The International Union of Biochemists (I.U.B.)

Based on the kind of reaction they catalyze, enzymes are divided into six functional classes, according to the International Union of Biochemists (IUB). Figure 1 illustrates the six kinds of enzymes: hydrolases, oxidoreductases, lyases, transferases, ligases, and isomerases.

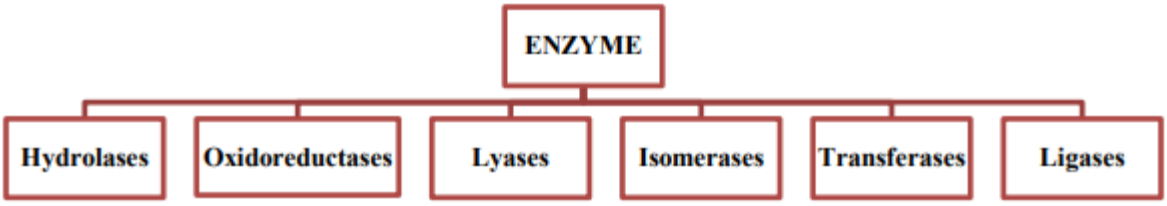

Figure 1: Classification of enzymes and their biochemical property.

Enzyme Extraction and Purification

Extraction

Material accessibility is important for the extraction and purification of enzymes. The concentration of a particular enzyme might vary across tissues. Selecting a tissue with a high enzyme concentration is essential. As a consequence, raw materials derived from yeast, bacteria, and fungus have certain benefits. The advantage is that these cells may be grown in a beneficial environment. However, there is one drawback: it is difficult to get significant amounts of microbial

cells other than yeast. A variety of procedures may be employed to extract and isolate the enzyme after choosing the starting material. Here are some concrete instances of several techniques:

Sedimentation: When liver tissue is homogenized utilizing the Potter-Elvenhjem equipment rather than customary blending methods, many mitochondrial & other particle cell bodies stay constant. They readily sediment out of solution and carry a large number of enzymes with them. Physical separation via sedimentation is only helpful early on in the separation process [2], [3].

Extraction: Previously, enzymes were categorized as either soluble (also known as lyoenzymes) or bound (also known as desmoenzymes). Desmonzymes are probably enzymes for which appropriate methods have not yet been established, hence this is a poor categorization. Acetone-powder, from which enzymes may be extracted using buffer, is often the simplest material from which to extract enzymes due to its lack of fat.

In any case, fine grinding is the first step. Some techniques for removing enzymes from microorganisms include autolysis, lysozyme digestion, grinding, freezing and thawing, sonic disintegration, shaking with solvents, shaking with fine-glass beads, and eventually, explosion by sudden release of pressure.

Salt Fractionation: Ammonium sulphate is the salt that is most useful in enzyme fractionation. High water solubility (760 g/lt) and a practically neutral reaction (pH 5 to 6) in concentrated solution are a few of its advantages. For making ammonium sulphate solutions, Dixon developed a monogram (chart), and Kunits created an equation for calculating how much ammonium sulphate to add to a solution to get the right final concentration. One drawback of utilizing ammonium sulphate in an alkaline solution is that, even at pH 9.3, half of the ammonium ions are converted to ammonia. To adjust the pH of the ammonium sulphate solution, a buffer should be utilized. However, glutamic dehydrogenase from cow liver has been routinely crystallized using sodium sulphate [4], [5].

Fractionation of a Solvent

Water-soluble solvents including acetone, ethanol, methanol, and dioxane facilitate the isolation of enzymes. Start at temperatures below 0 oC and increase them gradually while extracting acetone. At the maximum temperature, fractionation won't cause a considerable yield loss. Acetone must be completely removed by dialysis or distillation at a low pressure prior to spectral analysis since it absorbs considerably in the UV region. It is becoming usual to employ ethanol in enzyme isolation. Rat liver was employed to draw off crystalline lactic dehydrogenase.

Fractionation of Metal-Solvent Ions

An significant method for separating blood proteins is to combine metal ions with solvents, particularly Zn2+ and ethanol. Protein zinc salts separate out of solutions more rapidly and are often more soluble than sodium and potassium salts. Using citrate, ethylene diamine tetraacetate, or ion-exchange resin, metal ions may be removed from these. 6. Adsorption: A variety of substances have been used to create protein adsorbents, with hydrated aluminum oxide serving as one of the earliest. A calcium phosphate gel and bentonite have been shown to be useful in the isolation of lysozyme.

Adsorption Chromatography

Column chromatography using adsorbents is especially effective for the separation of proteins and subsequently enzymes. Anger came up with a gel made of calcium phosphate. The same adsorbent was explored by Swingle and Tiselius for general protein chromatography. On the subject of enzyme chromatography generally, Zechmeister has authored a review. Another technique separates enzymes based on their catalytic specialization rather than their overall properties as proteins by using a biochemically specialized adsorbent. For instance, in the separation of mushroom tyrosinase, several adsorbents containing p-azophenol and related groups were made from aromatic cellulose ethers [6].

Cleaning of Enzymes

Enzymes may be extracted from tissues using a variety of techniques. By combining the tissue (1 vol) with acetone (5–10 vol) at 0° C in one of the methods, acetone powders of tissues or cells are created. The fluid slurry is filtered and repeatedly washed with acetone to get rid of room moisture and lipids. After being cleaned with ether, it is dried. There is a powdery residue that could be an amalgam of enzymes left behind. The powdered material is divided into fractions, and the in vitro catalytic activity of each fraction is assessed. For fractional crystallization, the fraction with the appropriate activity is selected, resulting in the pure form of the desired enzyme. In the purifying process, fractionation techniques might be chemical or physical. The target enzyme will be kept mostly intact while being cleared of additional proteins, nucleic acids, and impurities. Heat-guiding the cell-free extract to 500C for 5 minutes will remove denatured protein. Ammonium sulfate may be precipitated to do this, and then techniques like gel filtration and ion exchange chromatography can be used.

Final enzyme purification is a time-consuming procedure that mostly relies on chromatographic technology, whether it be in a lab setting or a business one. Affinity and gel permeation chromatography show great potential for streamlining the purification of enzymes. The second technique comprises joining a crude enzyme preparation with a solid support that has a reversible inhibitor or other substances connected to it that will bind to the target enzyme selectively and reversibly. After the enzymes have been bound to immobilized inhibitors, the support inhibitor-enzyme complex is separated from the original crude feed, and the purified enzyme is eluted from the support inhibitor portion. Methods including gel filtration and affinity chromatography, as well as other chromatographic techniques, are useful due to the reduced cost of enzyme purification as well as the greater amount and diversity of enzymes. The task of scaling up these technologies still has to be completed. Purification may also be accomplished by anaphylactic or precipitation reactions. In this method, the antigen-antibody response is carried out in a gel, such as agar. The compounds may be seen as a precipitated zone in the gel.

Energy of an Enzyme

Fisher's lock-and-key theory

Because enzymes are very specialized, it makes sense to wonder how they work. Arrhenius asserts that enzymes catalyze reactions by creating unstable intermediates. Fischer's Lock & Key model

is the simplest explanation for enzyme activity. According to this concept, an enzyme is a hard, three-dimensional entity with active sites on its surface that include slots for accommodating certain substrates, much like how a key fits into a specific lock. Although the size of an enzyme molecule (100 to 200 amino acid residues) is fairly big, the active sites, which join with the substrate to form a fixed shape, are rather tiny. The amino acids that make up active sites are dispersed throughout the chain, but the amino acids that do not make up active sites are arranged in a certain order. This is because the region in question enables the whole enzyme molecule to fold precisely as needed.nWith enzymes like creatine kinase, phosphoglucomutase, and others, conformational changes during substrate binding and catalysis have been demonstrated. However, the precise sequence of events leading to a substrate-induced conformational change has not yet been established. There might be a number of options. It is difficult to determine precisely which residues an enzyme has, even when one is aware of its whole basic structure [7], [8].

Active (Enzyme Inhibition-Reversible and Irreversible): Concept And Identification

A particular cavity or location in an enzyme is where the substrate is anchored. The amino acids are gathered in the active core of the cleft where they may combine with the substrate. In the polypeptide chain, the reactive amino acids may be placed far apart. On the other hand, the chain folds in a manner that collects the reactive amino acids in the active site. It is believed that the Parts are kept together in a manner that causes chemical connections to be twisted, or weakened, when the substrate molecule links to the active site. The strain model of catalysis illustrates how the reaction products are freed because they are less firmly bound. This distortion increases the reactivity of the substrate or chemical bonds, which accelerates the reaction rate. Chemicals called inhibitors reduce the speed of an enzyme-catalyzed process.

Enzyme inhibitors are molecular substances that interfere with catalysis in order to either increase or decrease enzyme activity. These substances have the capacity to interact with certain enzymes, but they do not act as substrates; rather, they follow or even prevent enzymatic catalysis. By preventing enzyme activity, poisons affect living things. For instance, carbon monoxide poisoning prevents hemoglobin from serving as its normal function as a transporter of oxygen by mixing with it. Due to its interaction with natural molecules, notably the metallic center of cytochrome, cyanide poisoning results. The poisonous impact of arsenate is caused by its blockage of phosphate-replacement enzyme sites. Many naturally occurring and artificial substances have the capacity to bind reversibly or irreversibly to certain enzymes.

Permanent Inhibition

In order to permanently lose their catalytic characteristics, these chemicals are bound securely to the enzyme's active molecule. The functional groups of the enzyme molecules that are required for their catalytic activity are either bound to by these inhibitors or are destroyed by them. Diisopropyl fluorophosphate (DFP), for instance, is an irreversible inhibitor of the enzyme acetylcholinesterase, which is crucial for the transmission of nerve impulses. A catalytically inactive derivative is created when the highly reactive compound diisopropylfluorophosphate reacts with the hydroxyl group of a crucial serine residue in the enzyme's active site. Iodoacetamide, an enzyme inhibitor, may react with the imidazole group of an essential histidine

residue or with the sulfhydryl (-SH) group of an essential cysteine residue after this derivative has been produced.

Competitive Restraint

These kinds of inhibitors compete with the substrate for attachment to the enzyme's active site, but once bound, the enzyme is unable to catalyze their transformation. Simply raising the substrate concentration may reverse or alleviate their effects. The three-dimensional structure of these inhibitors often resembles that of the typical substrate. As a consequence, the substrate's capacity to bind to the enzyme is diminished. The competitive inhibitor deceives the enzyme into attaching to the active site due to similarity. The enzyme molecules, however, are unable to assault the inhibitor molecules since their active site is already filled. However, if the enzyme's substrate concentration rises, the inhibitor molecules are driven away and the enzyme starts to work. In order to obtain the same rate of reaction, a larger concentration is thus required than usual. These kinds of inhibitors compete with the substrate for attachment to the enzyme's active site, but once bound, the enzyme is unable to catalyze their transformation. Simply raising the substrate concentration may reverse or alleviate their effects.

The inhibition of ribulose biphosphate carboxylase by an oxygen molecule is another typical example of this kind of inhibition. The typical substrate for ribulose 'biphosphate carboxylase, a crucial enzyme during photosynthesis, is carbon dioxide (CO2). O2 competitively inhibits this enzyme, and even very low levels of O2 slow down the rate of CO2 incorporation into carbohydrates. Structure analogues of substrates are not usually found in competitive inhibitors. Because there is no change in the number of active sites, competitive inhibitors only affect Km and not Vmax of enzyme-catalyzed reactions. The maximal usage of active sites, however, necessitates a higher substrate concentration, which is why Km is raised. Uncompetitive inhibition: These kinds of enzyme inhibitors attach to an area of the enzyme other than the active site and are not highly selective. This interaction causes reversible inactivation of the active site by changing the shape of the enzyme molecule. To create the inactive complexes, these inhibitors reversibly bind to both the free enzyme and the enzyme substrate complex.

Site-Directed Mutagenesis for Enzyme Modification

Mutagenesis may provide a crucial link between a structure's structure and function. This technique substitutes one amino acid for another in a protein. Although chymotrypsin's capacity to bind the substrate is unaffected by the substitution of Asp 102, its ability to catalyze the reaction declines to less than 0.05% of what it was when the natural enzyme was present. This demonstrates how Asp 102 participates in the catalytic process by stabilizing the positive charge of histidine with its negative charge.

Isoenzymes

Oligomeric enzymes called isoenzymes, commonly referred to as isozymes, catalyze the same process but have different component compositions. These variations alter how quickly molecular species change the substrate. A secondary or main isozyme may exist. Primary isozymes may be created by a single gene locus or by many alleles at several gene loci that each code for a different

protein molecule. These also go by the name alloenzymes. Glycosylation is one of the post-translational changes that results in secondary isozymes. Primary isozymes may be distinguished from one other based on their varied electrophoretic mobilities due to their diverse amino acid compositions. Enzyme differences within a species of game are referred to be intra-specific variants. However, interspecific or phylogenetic variance refers to enzyme variation from distinct species. Lactate dehydrogenase is an oligomeric enzyme with identical functions carried out by each of its subunits.

An enzyme test that measures catalytic activity is unable to discriminate between isoenzymes. The total contribution of the active forms of the enzymes being analyzed will be used to calculate activity. Even when a single coenzyme is present, its molar activity, for instance, differs from that of the pure form in a homogenate. All five LDH isoenzymes may be separated from plasma using electrophoresis (for example, using cellulose acetate strips) at a pil of 8.6. If LDH is present to catalyze a particular stage of the process, a combination of lactate, NAD+, and a chromogen will produce colored product, making it possible to find all of these isoenzymes. An aberrant pattern aids in diagnosis. On-exchange chromatography, such as on QAE-Sephadex, may also be used to separate substances. With their separation and consideration of their individual characteristics, one may determine the relative amounts of isoenzyme in plasma. whether total LDH activity is greater than normal, it may be identified whether the cause is an excess of M4 (as in cases of skeletal muscle or liver illness) or an excess of (as in cases of cardiac disease, haematological issue, or renal disease).

Theory of Transition-States

All reaction groups are brought together at the active site during an enzyme reaction at the ideal position for the reaction. Some of the amino acid residues operate as catalytic groups because their side chains are in the ideal location with respect to the substrate. Similar rate improvements have been seen for intermolecular catalysis. After attaching to a substrate, an enzyme changes its conformation, which may put pressure on the substrate and increase its reactivity. By van der Waals, electrostatic, and hydrogen bonding interactions, groups on the enzyme may stabilize an intermediate and, therefore, the transition state leading to the intermediate. The transition state's stability has a direct impact on lowering the reaction's activation energy.

Lysozyme

An enzyme called lysozyme hydrolyzes polysaccharide chains. By cleaving the polysaccharide chains that make up the cell wall of certain bacteria, it destroys those cells. The lysozyme from hen egg whites has undergone the most extensive research. The Russian scientist P. initially identified the bacteriolytic characteristics of hen egg white lysozyme in 1909. Laschtchenko. Because it was an enzyme that produced bacterial lysis, Alexander Fleming named the substance in mucus and tears that killed certain bacteria the name lysozyme in 1922. An enzyme is a biological catalyst that lowers the activation energy of biological reactions while increasing their pace. Enzymes are categorized in several ways. The function of an inhibitor at several substrate sites. In the presence of an enzyme, it affects the rate of the reaction. Acquired knowledge of the mechanism of the chymotrypsin, lysozyme, and carboxypeptidase A enzymes in various processes.

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CHAPTER-16

REACTIONS THAT ENZYMES CAN CATALYZE

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The majority of biochemical activities in a living system need enzymes, which are biological catalysts, or "biocatalysts." Since they are produced by living cells, natural enzymes are proteins that may be thought of as biocatalysts. However, it has also recently been shown that a tiny subset of RNA molecules contains some catalytic activity. It takes a protein a few days to be degraded by a strong acid at pH 100 in a laboratory environment. But the same protein is broken down by the digestive enzyme over a period of time at a much lower temperature (37 C, body temperature). More solvents, higher reagent concentrations, and higher temperatures are required for many laboratory processes. These conditions prevent a living cell from accessing anything, but they also won't kill it. With just moderate reagent concentrations in water, the cell's solvent, and body temperature, enzymes enable the body's processes to take place fast and successfully. Before Berzelius used the term "catalyst" (Greek: to dissolve) in 1836, Kuhne used the word enzyme (Greek: in yeast) to describe the catalysis that occurs in biological systems. The term "substance" was first used by Duclaux in 1883. The enzyme could catalyze the fermentation processes and was identified in yeast (Greek: en =, and zyme = yeast). From a yeast extract devoid of yeast cells, Buchner was able to isolate an enzyme system in 1883. The substance that could convert sugar into alcohol was known as zymase.

Displacement of Nucleophilics on the Phosphorus Atom

The chemical ATP is significant to living organisms. Phosphoric esters account for more than 3% of the organic components in the majority of biological tissues. They take part in almost every aspect of cellular function. One of their most important processes is phosphorylation, which is the transfer of a phosphoryl group from one group to another. Similar structural alterations are produced by the reaction, which includes a nucleophilic substitution on phosphorus in Figure 1, as in acyl transfer reactions involving carboxylic acid derivatives.

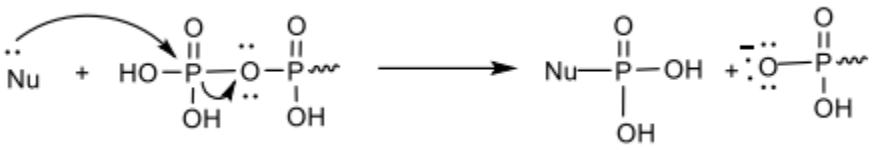

Figure 1: Nucleophilic substitution on phosphorus.

Glucose Hosphorylation

The equilibrium of unfavorable biological processes is shifted in the desired direction using the favorable free energy shift caused by ATP hydrolysis. Consider how the biological process of glycolysis, which is derived from the Greek words for "sweet" and "splitting," allows glucose to

be converted into energy. The breakdown of glucose requires a series of enzyme-catalyzed reactions to create two molecules of pyruvate, in contrast to glycolysis, which starts with the phosphorylation of glucose with ATP to form glucose-6-phosphate. In the case of the D-glocose and hydrogen phosphate reaction, a phosphate ester is created [1], [2].

ATP Cleavage and Energetic Processes in Couple

High energy compound exergonic reactions may be coupled to endergonic processes to push them to completion as long as the entire route is exergonic. Free energy is provided for a variety of biological processes by the exergonic hydrolysis of ATP to create ADP and Pi. Exergonic and endergonic, as opposed to the traditional chemical words "exothermic" and "endothermic," are used to describe processes that include the loss or gain of free energy in all forms, not only heat.The only way an endergonic reaction can exist independently is in a coupled exergonic-endergonic reaction system with an overall net change that is exergonic. The breakdown of fuel molecules is referred to as catabolism in exergonic processes. Anabolism involves the synthetic assembly of molecules. During metabolism, both catabolic and anabolic processes take place. A variety of organophosphates, including as ATP, ADP, and phosphoenolpyruvate, are crucial for energy storage and transmission.

This ATP cleavage is commonly linked to an upwards thermodynamically pushed endergonic metabolic activity. Two separate kinds of reactions must be sequentially displaced in order for these reactions to occur. Two processes are connected by the sequential displacement of phosphorus followed by carbon atoms, or vice versa. The displacement of one of the three phosphorus atoms, on which the phospho, pyrophospho, and adenyly groups from the ATP molecule are transferred to a nucleophile, is the first step in the coupling process. The transferred group is then displaced in the subsequent phase by a second nucleophile attacking a carbon atom.A common example of a multiple displacement reaction is the synthesis of acetyl CoA. An S-acetyl transferase and an acetate kinase are both involved in the two distinct mechanisms in which bacteria manufacture acetyl-CoA from acetate. In the first step, the oxygen atom in the carboxylate group functions as a nucleophile to displace the phosphorus in ATP to produce acetyl phosphate. The S atom of the coenzyme an SH group replaces Pi in the second reaction, functioning as a second nucleophile and attacking the carbon atom of acetyl phosphate.

Shifting of Sulphate

Sulfation of natural products is a frequent phenomenon. Inorganic sulphate is brought to cells and activated there by the enzyme ATP sulphurylase, which has been studied using kinetic and stereochemical methods. The direct "in line" displacement of inorganic pyrophosphate by inorganic sulphate from P of ATP by the enzyme has been shown to occur. In order to create 3'-phosphoadenosine 5'-phosphosulphate, the most common sulphating species in biology, APS kinase first phosphorylates the resultant adenosine 5'-phosphosulphate at the 3' site. This reaction is seen in Figure 2.

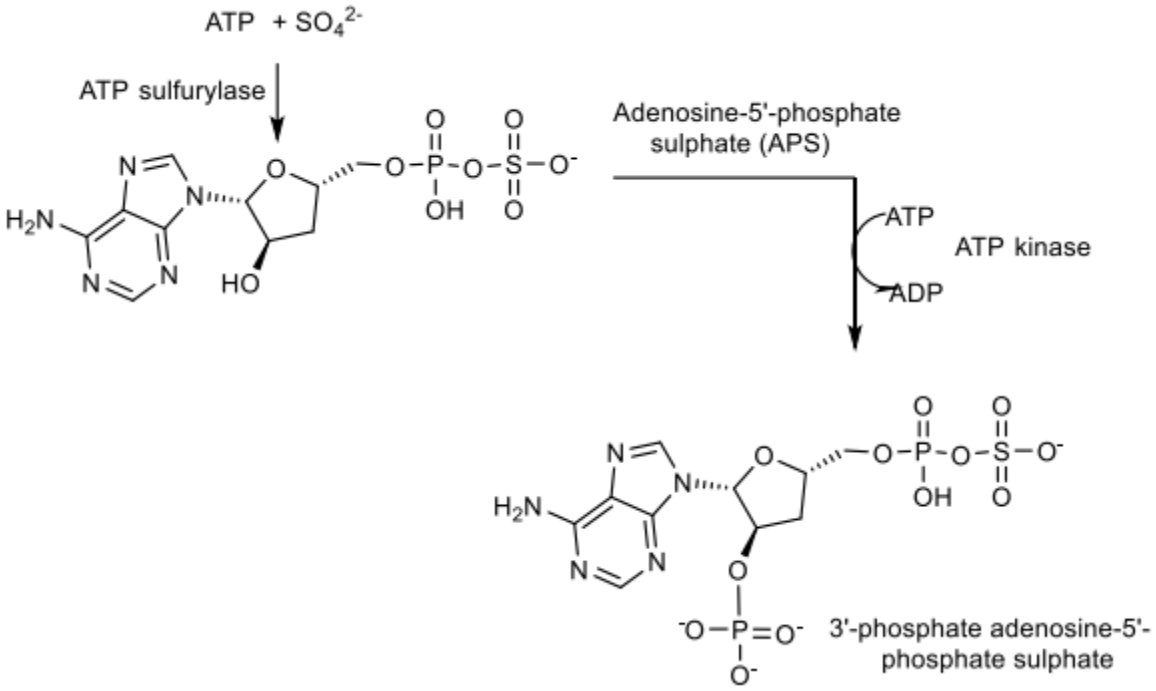

Figure 2: Illustrate the Activation of sulphate.

A technique has been developed for the stereochemical analysis of chiral [16O 17O 18O]-sulphate esters using Fourier Transform Infrared Spectroscopy. Additionally, a general approach to their synthesis has been suggested. It has been shown that the stereochemical course of an Aspergillus oryzae aryl sulphotransferase proceeds with the retention of configuration at sulfur, supporting a ping-pong-type mechanism with a sulpho-enzyme intermediate on the reaction pathway. Nucleophilic displacements of the sulphur atom also occur during enzymatic reactions mediated by sulfotransferases. These enzymes help an acceptor molecule's oxygen and nitrogen atoms get the sulphate group from 3′-phospho-adenosine-5′-phospho sulphate (PAPS). PAPS is produced when the enzymes ATP sulfurylase and APS kinase combine to produce sulphate, sometimes referred to as activated sulphate. Sulfatides are created, for instance, by transferring the sulphate group from PAPS to the C3-OH group of galactose in cerebroside, which is one of the brain lipids. Sulfatides account for 15% of the white matter lipids in the brain [3].

Reactions to Additions

A polarized double bond, such as C=O or C=N, is added to by a nucleophile and a proton in an addition process. The nucleophile may also attack a C=C bond that has been polarized by conjugation with C=O or C=N. The most often used nucleophiles are alcohols, amines, and thiols because of how fast they attack the electrophilic carbon atom of the carbonyl group. As a nucleophile, the water molecule may add to the carbonyl group. An example of an addition process is the conversion of CO2 into bicarbonate ion, which is facilitated by the enzyme carbonic anhydrase.

Three histidine residues are tetrahedrally attached to the Zn2+ ion that is associated to the protein, while the fourth co-ordination site is occupied by a water molecule. His 64 acts as a base, luring a

proton from the water molecule and attaching it to Zn2+ to form an OH ion. However, His 64 is unable to directly steal a proton from the water-bound Zn2+ due to the distance between the two molecules. As a consequence, a hydrogen bonding network links the two molecules. As a proton shuttle, the hydrogen-bonded network does its job. In order to convert the CO2 substrate into HCO3, the Zn2+-bound OH attacks it by acting as a nucleophile. A frequent step in many enzymatic activities is the synthesis of imine intermediates. Schiff bases are the imine intermediates in question. The amine attacks the carbonyl group in a nucleophilic manner to produce amine intermediates, which is followed by the elimination of the OH ion. The binding of the substrate fructose 1,6-bisphosphate to the lysine residue in the active site of the aldolase enzyme results in the protonated Schiff base, an iminium cation. The breakage of the C—C link brought on by the release of glyceraldehyde-3-phosphate, the first reaction product, results in the production of the intermediate enamine. After protonating the enamine to an iminium cation and hydrolyzing it, dihydroxyacetone phosphate is the second product of the reaction with the regeneration of free enzyme. If the C=C bond is conjugated with the C=O bond and the polarization from the C=O is transferred to the C=C bond, there are additional metabolic processes in which the nucleophile is also added to the C=C bond [4].

Condensation and Cleavase

The catabolic and anabolic metabolic pathways both include steps that create or break carbon-carbon (C—C) bonds. Organic molecules are hard to build or break because of their closely bound carbon backbone. A C—C bond can only be created by joining an electrophilic carbon atom to a nucleophilic carbanion. The carbonyl atom is the most often occurring electrophilic carbon atom in these processes because of its capacity to take electrons from aldehydes, ketone esters, and CO2. A stabilized nucleophilic carbanion is required to add to an electrophilic center. The carbon atom of the carboxylate group on a neighboring carbon produces a resonance stabilized carbanion, also known as an enolate. In its role as a nucleophile, this enolate anion. The carbonyl group facilitates the breakage and formation of the C—C bond.

Aldol Cleavage

The process that fructose bisphosphate aldolase catalyzes during glycolysis is a classic illustration of aldol cleavage, which is a frequent reaction of C—C bond formation. Aldol cleavage is catalyzed by stabilizing its enolate intermediate, which serves as a nucleophile. Type I and type II aldolases are available. The type I aldolases, which are present in both plants and animals, stabilize the intermediate enolate ion. The carbonyl group is changed into a protonated Schiff base to accomplish this. The type-II aldolases, which are present in fungus, algae, and certain bacteria, stabilize the enolate ion. They do this by pairing a metal ion, often Zn 2+ or Fe 2+, with the enolate ion [5].

Decarboxylation and Carboxylation Catastlyzed by Enzymes

In biological activities, the most significant C—C bond forming and breaking events lead to the acquisition or loss of one carbon, in the form of CO2. Decarboxylation refers to the removal of carbon in the form of CO2, while carboxylation refers to the addition of a CO2 unit to a substrate molecule. RuBisCO and biotin-dependent carboxylases serve as the primary catalysts for the

majority of carboxylation processes that take place in metabolic pathways. The production of 3-phosphoglycerate from ribulose-1, 5-bisphosphate (RuBP) is catalyzed by the enzyme ribulose-1, 5-bisphosphate carboxylase oxygenase (RuBisCO). This enzyme comprises up to 50% of the proteins found in leaves, making it the most common protein on the earth. Eight large (L) subunits are encoded by chloroplast DNA, and eight small (S) subunits are encoded by a number of nuclear genes. Together, these subunits make up the 500–560 KD protein known as RuBisCO from higher plants. Eight tiny subunits form two caps (tetramers) at the top and bottom of the protein, while eight large subunits fill the space in between the two caps. The enzyme's catalytic site is located in the L-subunit. The carboxylation of RuBisCO is started by the removal of a proton from RuBP's C-3, which creates an enediolate. The intermediate enediolate subsequently engages in nucleophilic attack on CO2 to make a -keto acid. The subsequent reaction between this -keto acid and water results in an adduct, which separates to provide a molecule of 3-phosphoglycerate and an intermediary carbanion. The carbanion is protonated to provide a second molecule of 3-phosphoglycerate. The mechanism of this enzyme is supported by the discovery that the homolog of the -keto acid intermediate, 2-carboxyarabinitol-1-phosphate (CA1P), binds tightly to the active site of the enzyme from spinach.

The five kinds of metabolic processes that enzymes catalyze include substitution, addition, elimination, isomerization, and rearrangement events. A substitution reaction involves the replacement of one atom or group with another. A nucleophile is used in a nucleophilic substitution reaction, whereas an electrophile is used in an electrophilic substitution reaction to replace the atom or group. Nucleophilic substitution may take place on saturated C-atoms, carbonyl C-atoms, phosphorus atoms, and sulfur atoms. Numerous displacement mechanisms link the endergonic and ATP hydrolysis processes. When the attacking reagent adds to the substrate, the reactions referred to as addition reactions take place.

In elimination reactions, small molecules are eliminated during the process of product formation. The intramolecular movement of the H atom to alter the double bond's position takes place during the isomerization process. The initial stage in isomerization processes is the synthesis of the intermediate enediol. To produce the molecule's structural isomer, substituents are shifted around inside the molecule during rearrangement events. The processes that produce and dissolve a C—C bond between the carbon atoms of a carbonyl group are referred to as condensation and cleavage, respectively. In contrast to a carboxylation process, which adds CO2 to the substrate, a decarboxylation reaction removes CO2 [6].

Chemistry of the Coenzyme

The most effective catalyst found in nature is an enzyme. By reducing the reaction's activation energy and maintaining the reacting molecules in their activated complex states, they may increase the rate at which reactions occur. Enzymes can catalyze a broad range of chemical processes, although they are less appropriate for catalyzing many types of group transfer events and other biological reactions due to their amino acid side chains. Although, in conjunction with some other non-enzymatic material, enzyme catalyze these reactions. Co-factors are those substances. These co-factors significantly increase the enzyme's capacity for catalysis. Enzymes function as both a receptor and a biological catalyst by interacting with a substrate.

Co-Factors

Co-factors support the catalytic function of the enzymes. Haloenzyme is a name for an enzyme co-factor complex that is catalytically active. An apoenzyme is a protein that is enzymatically inactive as a consequence of the loss of a co-factor.

$$\text{Co-factor} + \text{apoenzyme} = \text{haloenzyme}$$

Metal ions, such as Zn+2, which is necessary for carboxypeptidase-A's catalytic activity, may function as co-factors. Metallocenzymes are such enzymes that are bound to metal ions. Cofactors are referred to as coenzymes if they are organic compounds. A particular enzyme has a brief association with a certain factor, such as NAD+. The term "prosthetic group" refers to other co-factors that are firmly linked to proteins by covalent bonds as well as significant hydrogen bonds and hydrophobic interactions, such as heme, which is the prosthetic group of hemoglobin.

Co-Enzyme

For example, an enzyme called alcohol dehydrogenase uses NAD+ as a coenzyme in the catalytic oxidation of primary or secondary alcohols. Coenzyme plays crucial roles in biochemical reactions, such as transferring atoms or groups from substrate to other molecules, participating in redox reactions, and participating in redox reactions. Coenzyme is an organic molecule derived from vitamins that is required by many enzymes for catalytic activity [7].

A Coenzyme

Adenosine triphosphate, a vitamin called pantothenic acid, cysteamine, and other compounds make up the intricate structure of coenzyme A. Coenzyme is engaged in acyl-group transfer. One of the most significant CoA derivatives, acetyl-CoA, is created when the cysteamine moiety of this coenzyme forms a thioester with the carboxyl (-COOH) group of an acyl molecule, such as acetic acid. Coenzyme A is an acyl activating enzyme generated from the vitamin pantothenic acid, and it may quickly transfer the acetyl-group to an acceptor due to the energy-rich thioester bond. Adenosine 3, 5 diphosphate and pantotheine, which is produced by combining pantothenic acid and mercaptoethylamine, are the two components of coenzyme A. Pantotheric acid is created when pentoic acid and alanine are coupled together in an amide linkage. Coenzyme A is referred to as CoA or CoASH and the SH group of the thioethanol amine moiety is an active group serving as a carrier. The remainder of the molecule acts as an enzyme binding site. Acetyl-coenzyme A is an example of an acylated derivative in which the acyl group is connected to the thiol group to generate an energy-rich thio ester.

Succinyl Co-A and acetyl Co-A are crucial intermediates found at the intersection of several metabolic pathways. Acyl Co-A is created as an intermediary during the oxidation and biosynthesis of fatty acids. Coenzyme A comes in two forms: acylated and unacylated. The acylated form of coenzyme A is referred to as or acyl Co-A, and the unacylated form as CoA-SH. The acyl group [such as acetyl or aceto acetyl group] is attached to the Co-A through a thio ester linkage to the -mercaptoethylamine moieties, and the acyl group is carried by the Co-A in a wide range of other metabolic reactions.

The pyruvate dehydrogenase complex is a group of three enzymes responsible for the conversionof pyruvate to acetyl-CoA, viz. pyruvate dehydrogenase, dihydrolipoyl transacetylase, and dihydrolipoyl dehydrogenase. The pyruvate dehydrogenase complex also requires TPP along with four other coenzymes (lipoate, coenzymeA, FAD and NAD+). The first enzyme pyruvate dehydrogenase, a TPP requiring enzyme, decarboxylates pyruvate, with the intermediate formation of hydroxyethyl thiamine pyrophosphate. This reaction is same as catalyzed by pyruvate decarboxylase, however, unlike pyruvate decarboxylase, pyruvate dehydrogenase does not convert the intermediate hydroxyethyl thiamine pyrophosphate into TPP and acetaldehyde but transfer the intermediate to the second enzyme dihydrolipoyl transterase.

Second enzyme requires lipoate, a coenzyme that is attached to its enzyme by an amide linkage to a lysine residue. The hydroxyethyl thiamine pyrophosphate carbanion attacks the disulphide linkage of lipoate followed by the eliminationof TPP carbanionfrom the intermediate adduct to form acetyldihydrolipoamide and regenerate active pyruvate dehydrogenase. Dihydrolipoyl transacetylasecatalyzesthe transfer of the acetyl group to CoA forming acetyl CoA and dihydrolipoamide-dihydrolipoyl transacetylase. The third enzyme dihydrolipoyl dehydrogenasealso calledlipoamidedehydrogenasereoxidizesdihydrolipoamide utilizing the coenzyme FAD. Oxidation of dihydrolipoate by FAD forms enzyme bound FADH2. NAD+ then oxidizes FADH2 back to FAD. NAD+ AND NADP+ Nicotinamide adenine dinucleotide (NAD+) and nicotinamide adenine dinucleotide phosphate (NADP+), two dinucleotide coenzymes that are derived from the vitamin niacin (nicotinic acid), are essential for biochemical reactions.

Flavin Mononucleotide and Flavin Adenine Dinucleotide

Riboflavin (vitamin B2) is the source of flavin nucleotides. Skin inflammation results from a vitamin B2 deficiency. Both flavin adenine mononucleotide (FMN) and flavin adenine dinucleotide (FAD) engage in the oxidation-reduction pathway, much as nicotinamide nucleotide. Riboflavin, a form of vitamin B12, is used to make flavin nucleotides, which are crucial in hydrogen transfer processes.When bonded to ribitol, riboflavin is 6, 7 dimethyl-iso-alloxan. The iso-alloxan ring is responsible for the bright yellow hue. FMN and FAD are the forms of active coenzymes [8].

Co-enzymes of proteins called flavoproteins include FAD and FMN.The flavin nucleotides, which are coenzymes, are generated from the vitamin riboflavin. As the names suggest, FAD is a dinucleotide in which flavin and adenine are both heterocyclic components. FMN is a mononucleotide since it does not include adenine but does contain flavin. Thus, flavin and ribitol combine to form riboflavin (vitamin B2). A variety of enzyme-catalyzed oxidation/reduction processes involve FAD and FMN.FAD or FMN cause a carbon-carbon single bond in the hydrocarbon chain to oxidize into a carbon-carbon double bond. The two-electron oxidation of the hydrocarbon chain and the two-electron reduction of FAD are related, as can be observed from balanced half-reactions.

Co-enzyme's involvement in Metabolism

Flavoproteins are proteins that contain riboflavin. Many oxido-reductase enzymes are flavoproteins with the prosthetic groups FMN and FAD. For instance, succinate dehydrogenase in

the citric acid cycle is FAD+ reliant, whereas L-amino oxidase is FMN dependent. Reversible oxidation-reduction processes include these enzymes. The riboflavin isoalloxan ring's N-atoms at positions 1 and 10 experience oxidative reduction. An illustration of an enzyme that needs FMN or FAD as a cofactor and the process in which they are active.

Alcohol Lipoic

Lipoic acid, commonly known as lipoic acid, is a substance that occurs naturally and is also produced by humans. Hydrogen is transferred during oxidative decarboxylation processes thanks to lipoic acid. In the lipoamide structure, the amino group of the lysine residue of the dehydrolipoamide acyl transferases is where lipoic acid is attached in the amide linkage. Lipoic acid is required for the complicated processes of the metabolism of carbohydrates that are performed by the pyruvate dehydrogenase system and -ketoglutarate dehydrogenase. In addition to serving as a carrier, it converts between reduced and oxidized forms. A disulfide (-s-s-) may form between the two thiol groups, much as there is one between two Cys residues in a protein. Lipoate may behave as both an acyl carrier and an electron hydrogen carrier due to its ability to conduct oxidation-reduction processes. Other names for lipoic acid include ALA, thioctic acid, and -Lipoic acid. At least five enzyme systems need lipoic acid as a cofactor, two of which are involved in the citric acid cycle, which is used by many organisms to convert nutrients into energy, such as sugar. Ketoglutarate dehydrogenase and the pyruvate dehydrogenase complex.

Supplement B12

When generated from vitamin B12, coenzyme B12 catalyzes several rearrangement processes. The cobalt metal is coordinated with a tetra pyrole ring system, known as a corrin ring and similar to the porphyrin ring of heme compounds, in the structure of vitamin B12. A covalent connection and three coordinate bonds connect the metal ion to the ring's four nitrogen atoms, however owing to resonance, the four bonds are almost identical. The fifth is the same as the fourth in that a nitrogen atom from an imidazole ring [dimethyl benzimidazole (DMB)] fills the ring by one orientation site on the cobalt. OH group or cyano group occupy the sixth co-ordination site. The cyano group is swapped out for a 5-deoxyadenosyl group in coenzyme B12. The metal ion in vitamin B12 has an oxidation state of +3, making it the only vitamin to have one. Pernicious anemia is caused by a vitamin B12 deficiency.

Vitamin B12 is converted to its coenzyme form by the activation of NADH-linked reduction mechanisms. The adenosyltransferase-mediated reaction with ATP results in the production of the coenzyme 5'-deoxyadenosylcobalamin. The co-factor form of vitamin B12 is coenzyme B12. This vitamin stands out from the others since it contains the crucial trace element Cobalt as well as complex chemical molecules. Methyl malonyl Co-A mutase uses coenzyme B12 to convert methyl malonyl CoA to succinyl CoA. The 5-deoxyadenosyl radical and cobalamin in its +2 oxidation state are produced when the C-Cobond breaks. The deoxyadenosyl radical removes a proton from methyl malonyl CoA to produce method Co-Aradical. Arrangement of the succinyl CoA radical in its intermediate state. A succinyl Co-A radical is removed from 5-deoxyadenosine to produce succinyl Co-A, which then interacts with a 5-deoxyadenosyl radical to produce the coenzyme. B12 in coenzyme form there are two B12 active forms that are used in metabolism. Only two processes

employ vitamin B12 as a coenzyme: (a) methyl cobalamin and (b) 5'-deoxy adenosyl cobalamine, commonly known as cobamide coenzyme. Methyl cobalamine serves as the coenzyme in the conversion of homo cysteine to methionine. The coenzyme employed in the conversion of methyl malonyl CoA to succinyl CoA is 5'-deoxyadenosyl cobalamine. Isomerizations involving the interchange of a carbon-bound hydrogen atom with another carbon-bound functional group, such as methyl malonyl, are necessary for the 5'-deoxyadenosylcobalamin's activity. Such a process is catalyzed by Co-A mutase.

Vitamin B12, biotin, TPP, and coenzyme A are four enzymes that are involved in group transfer. The transfer of carboxylic groups involves biotin. Thiamin pyrophosphate, also known as thiamine TDP, is a coenzyme that is produced when vitamin B is phosphorylated and is used to transfer aldehydes and glyoxal groups. Pantothenic acid is a component of the vitamin coenzyme A. This is referred to as CoA. Another name for it is acetylation coenzyme. The cofactor form of vitamin B12, coenzyme B12, participates in methyl group transfer and isomerization reactions.

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CHAPTER-17

ENZYME APPLICATIONS IN BIOTECHNOLOGY

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High molecular weight proteins called enzymes function as biological catalysts. Enzymes often contribute to reactions and speed them up by decreasing the activation energy. Enzymes have a broad range of industrial uses because of these features, including the paper and food industries, the starch business, the textile industry, the baking and brewing industries, etc. Enzymes may be extracted from a variety of sources, including animals, plants, and microbes, for use in industrial applications. Enzymes are crucial in the production of several industrial food items as well. These are only a few examples: vinegar, cheese, beer, and wine. Enzymes are useful for regulating a number of processes, including process time, flavor enrichment, texture improvement, and shelf-life extension.

The commercial methods for producing enzymes, various immobilization techniques, its applications in various industries, such as the food and beverage industry, cheese making, etc., enzymes used as targets for drug design, enzyme therapy, and recombinant DNA technology for creating recombinant enzymes are all covered in this unit. A common approach to produce more stable, active, and reusable enzymes is enzyme immobilization. In this method, enzyme molecules are physically, chemically, or both contained onto or within a support or matrix to maintain full activity. Both the industrial and medical industries are powered by enzymes. There are now many different types of enzyme-related illnesses that may be treated with enzyme therapy or medications that target specific enzymes. Lysosomal storage disorders, cancer, Alzheimer's disease, irritable bowel syndrome, exocrine pancreatic insufficiency, hyperuricemia, and other conditions may fall under this category. In many diseases, including myocardial infarction, jaundice, pancreatitis, cancer, and neurodegenerative illnesses, enzymes may serve as indicators. Enzymes can thereby diagnose a condition, predict its prognosis, and evaluate how well a treatment is working.

Large-Scale Enzyme Production and Purification

Enzymes are particular, adaptable, and effective biocatalysts that take part in reactions and reduce activation energy. The smallest additional energy needed by a reactive molecule to transform into a product is known as activation energy. Pepsin, trypsin, pancratin, chimosin, papain, bromelain, ficin, and other industrial enzymes are derived from animals; amylase, proteases, isomerases, glucose oxidases, pectinases, lactase, cellulase, xylanase, lipase, phytase, invertase, catalase, etc. One of the crucial stages in the manufacturing of enzymes is industrial fermentation, which transforms substrates into products. Temperature, substrate, pH, aeration and agitation, inhibitors, etc. are some of the variables that may have an impact on this process. Upstream and downstream processes are two groups into which the crucial phases for industrial enzyme synthesis may be divided [1].

Prior Procedure

The term "upstream process" refers to all of the procedures necessary to acquire the raw materials needed to produce a certain intended industrial output, such as medium preparation, inoculum formation, cell culture, cell separation, and harvest. The cells are collected and transferred to the downstream stage of the bioprocess after they have attained the necessary density.

Sources

Plants, animals, and microbes are only three of the sources from which enzymes may be derived. Some commercial enzymes are derived from plants, including papain, bromelain, ficin, and malt diastase. While pancreatic enzymes, lipase, catalase, rennin, alpha-chymotrypsin, trypsin, pepsin, and trypsin are sourced from animal sources. Fungi, bacteria, and yeast are the main microorganisms utilized to produce industrial enzymes.

Screening of Bacteria

The process of isolating, identifying, and separating microorganisms of interest from a specific population is known as microbial screening. Figure 1 illustrates how a screening technique might assist identify prospective bacteria with better yields or synthesis of certain enzymes. Examples of potential microorganisms used in various industrial production include leather processing, the food industry, pharmaceuticals, etc. include fungi (Trichodermareesei, T. viride, Penicillium sp., Humicolagrisea, Aspergillus sp., Chrysosporiumlucknowense, Acremonium sp.), yeast (Saccharomycescerevisiae), and bacteria (Bacillussub) [2].

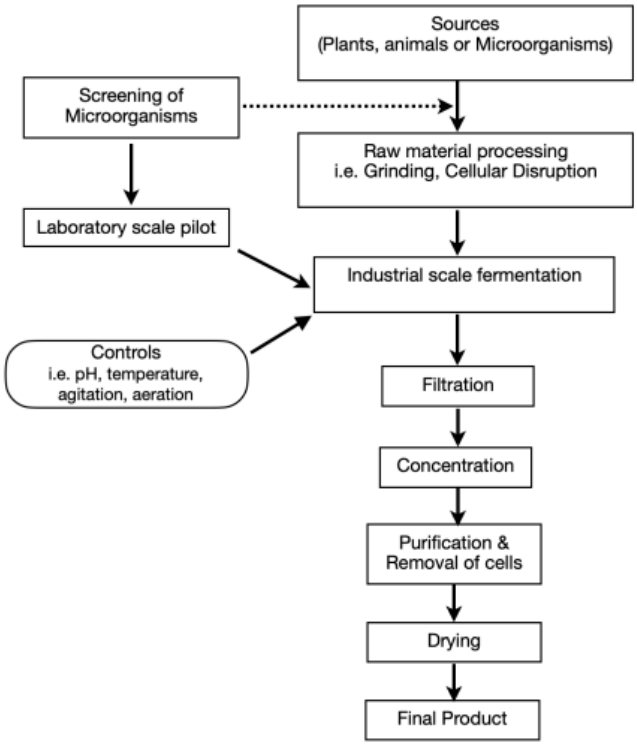

Figure 1: Steps of Industrial enzyme production.

Materials, creation of the medium, and processing the majority of enzymes come from microorganisms, however certain enzymes are also found in plants and mammals. Traditional enzyme synthesis used natural hosts as its primary raw source. Selecting wild or genetically altered microbes, however, may result in sufficiently greater yields of enzymes. The development of cultural media is a crucial stage. It should supply all nutrients supporting for enzyme formation in large quantity but not for optimal microbial development. A inexpensive supply of carbon, amino acids, nitrogen, growth stimulants, trace elements, and a negligible quantity of salts are necessary for this. The culture media's pH, temperature, and other factors should all be controlled. In order to prepare media, molasses, barley, maize, wheat, and starch hydrolysate are often used as sources of carbohydrates, whereas meals of soybean, cotton seed, peanut, and whey as well as corn steep liquor and yeast hydrolysate are typically used as sources of proteins.

Commercial Fermentation Procedure

An enormous fermenter is used to sterilize the medium in batches. For this aim, continuous sterilization procedure is commonly utilized. An appropriate quantity of inoculum is added to the medium after sterilization to initiate the fermentation process. In conventional approach, enzymes production are done by surface culture technique where inoculum stays on top surface of broth. Amylase (from Aspergillus sp.), protease (from Mucor sp. and Aspergillus sp.), and pectinase (from Penicillium sp. and Aspergillus sp.) may all be produced using this method. Currently, submerged culture technique is frequently employed owing to decreased potential for contamination and better production of enzymes. In the fermenter, the growth parameters, such as pH, temperature, and oxygen, are maintained at their ideal levels. Depending on the individual group of microorganisms, these parameters may change. To prevent foaming during the fermentation process, antifoaming chemicals may be added to the fermenter. Extracellular enzymes are created by the injected microorganism in culture media after 30-150 h of incubation. The majority of enzymes are created after the exponential period of development is through, however this is not always the case. In addition to extracellular enzymes, the fermented broth also produces additional metabolites (10–15%). After the enzyme is purified, these metabolites are eliminated. To prevent contamination, broth is held at 5°C once fermentation is finished [3].

Downstream Method

Restoration of enzymes the method of purifying enzymes is complicated. In compared to filamentous fungus, recovering enzymes from the fermented broth (fluid) of bacteria is relatively challenging. After pH correction, the fungus broth is either centrifuged or immediately filtered. As a result, calcium salts are added to the bacterial broth to precipitate calcium phosphate, which aids in the separation of bacterial cells from colloids. To eliminate cell debris, the liquid is then filtered and centrifuged. As a result, the crucial purification stages are listed below:

(i) Vacuum evaporation at low temperatures or ultrafiltration for the preparation of concentrated solutions

(ii) Polishing filtration for the clarification of concentrated enzymes to get rid of other microorganisms

(iii) Adding preservatives or stabilizers, such as sodium chloride (18–20%), sodium benzoate, calcium salts, proteins, starch, sugar, and alcohols. acetone, alcohols, or organic salts, such as ammonium sulfate or sodium sulfate, are used to precipitate enzymes.

(iv) Free drying, vacuum drying, spray drying, and packaging for commercial delivery of the precipitate.

Enzyme Immobilization Techniques and Methods

A common approach to produce more stable, active, and reusable enzymes is enzyme immobilization. In order to maintain their full function, enzyme molecules may be physically, chemically, or both immobilized onto or inside a support or matrix. Inertness, physical strength and stability, cost-effectiveness, regenerability, biocompatibility, ease of derivatization, mean particle diameter and swelling behavior, reduction in product inhibition, enhanced enzyme specificity, and composition of insoluble material, such as calcium alginate, are the qualities of an ideal support or matrix to be used. Amino acylase, which was isolated from Aspergillus oryzae for the synthesis of L-amino acids in Japan, was the first enzyme to be immobilized [4], [5].

Adsorption

The simplest, oldest, and most reversible approach is adsorption. Enzyme is adsorbed on the support's outside surface using this technique. The support may come in a variety of forms, including: (1) modified sepharose and ion exchange resins; (2) organic support (such as starch); (3) mineral support (such as aluminum oxide, clay), and so on. In this approach, there is no permanent link forming between the carrier and enzyme. Enzyme adsorption may occur through a variety of interactions, including hydrogen bonds, hydrophobic bonds, and van der Waals forces.

Covalent Ties

A traditional technique is covalent bonding. Through a covalent bond, the enzyme is directly attached to the support matrix. As they are created by interactions between functional groups in the support matrix and the enzyme surface, which is made up of amino acid residues, it offers a strong and stable attachments. Since unmodified proteins rely solely on naturally occurring functional groups, they may be employed. The use of a spacer arm may provide enzymes more mobility, resulting in enhanced enzyme activity. Polyacrylamide porous glass, cellulose, collagen, gelatin, DEAE cellulose, and porous silica are examples of common supports or carriers.

Entrapment

This technique involves physically trapping enzymes within a porous matrix. The best immobilization technique to prevent any detrimental effects on enzyme structure is this one. Occlusion in artificial or natural polymeric networks immobilizes enzymes. Microencapsulation and gel or fiber entrapment are methods for achieving entrapment. Highly porous silica materials called Sol-gels are often utilized for protein immobilization, notably in the construction of biosensors.

Copolymerization or Cross-Linking

An irreversible carrier-free enzyme immobilization is achieved using this approach. It serves as its own carrier, the enzyme.By using two- or multifunctional reagents, such as glutaraldehyde, the enzyme molecules may form intermolecular cross links. Electrospun nanodiametric supports are one example. In order to create cross-linked enzyme aggregates, the enzymes are first gathered in a precipitant such acetone, ammonium sulfate, ethanol, or 1,2-dimethoxyethane. Next, a cross-linker like glutaraldehyde is added [6].

Metal-Linked Imprisonment

With this technique, heating or neutralization is used to precipitate transition metal salts or hydroxides onto the support. Not all metal coordination sites may be occupied by the deposited matrix; some are available for enzyme binding. Salts of titanium and zirconium are employed as metals, whereas cellulose, chitin, algenic acid, and silica-based carriers are used as supports. The immobilized metal-ion affinity (IMA) absorbents and chelator ligands, such as EDTA, may be attached to solid supports via stable covalent connections before the metal irons are coordinated to them.

Clinical Applications of Enzymes

In many diseases, including myocardial infarction, jaundice, pancreatitis, cancer, and neurodegenerative illnesses, enzymes serve as indicators. By assessing the prognosis, response to treatment, and diagnosis, they may provide light on the illness process. The main functions and applications of these enzymes in the medical field are described below.

In Cleaning Medical Equipment

Many reusable medical gadgets are cleaned using enzyme-based detergents. It mostly utilizes the enzymes lipase and protease. Proteases break down soils that are high in protein, such as blood. While adipose tissues and other fatty soils are treated with lipases. Other examples are cellulases and amylases, which aid in the disintegration of starch and cellulose polymers.

In Health

Enzymes are often used as medications to replace enzyme deficits in patients, such as blood coagulation factors to treat bleeder's disease, cleansing and healing of wounds, enhancing metabolism, in illness detection, etc. Proteases, carbohydrases, and lipases are a few well-known enzymes that are often employed in the pharmaceutical and healthcare industries.

Treating Disorders

Enzymes are used to treat problems in three different situations:

1. To dissolve internal blood clots,
2. To dissolve the hardening of blood vessel walls, and
3. To dissolve wound swelling to speed up recovery.

There is a potential that blood clots may develop in certain conditions, such as low blood pressure or head or spinal traumas. To dissolve the clots is the only option, thus. Typically, these clots are eliminated by being broken down by enzymes. The walls of blood vessels stiffen and thicken when there is atherosclerosis. At this point, cutting down on fat consumption and dissolving any thickenings that have developed is the best course of action. Serratiopeptidase and other enzymes perform well here. When a wound is healing, the swelling that develops has a tendency to enlarge and produce pus. To reduce the edema, trypsin, chymotrypsin, and serratiopeptidase are utilized.

Used to Support Metabolism

Due to inadequate release of digestive enzymes, the digestive capacity is reduced in elderly people. Patients may suffer from malnutrition, constipation, bloating, etc. under such circumstances. Papain and other digestive enzymes are given orally after meals to help with such digestive conditions.

Facilitating Medication Delivery

Some medications may penetrate tissues more deeply than others. For this, some medicines are administered intramuscularly together with certain enzymes, such as hyaluronidase. One kind of naturally occurring enzyme, hyaluronidase, helps sperms enter female internal reproductive organs and fertilize eggs.

To Identify Diseases

Associated diseases cause the leaking of enzymes from the liver, kidney, skeletal muscle, heart, etc. into the blood. The specific condition may be identified by measuring the quantity of the related protein in blood at high or low levels. For instance, creatine kinase is used to treat injured or weak muscles. Similar to this, polymerase chain reaction (PCR) aids in the prenatal diagnosis of genetic illnesses for conditions including beta-thalassemia, Huntington's disease, and sickle cell anemia, among others [7].

Making Toothpaste

The dentifrice contains papaya and pineapple enzymes. It has been discovered that they may whiten and brighten teeth by removing stains. 8.9 ENZYMES THERAPY Enzyme therapy is a treatment method for strengthening the body's defenses against illnesses or disorders connected to any of the enzymatic biological processes. The biological processes might include issues with the immune system, cancer, cardiovascular disease, or microbial system, among other things. Enzymes serve as a target for creating drugs to achieve the desired therapeutic effects, sometimes referred to as biological targets. Enzyme therapy is now being researched as a potential treatment for the CoVID-19 disease-causing viruses SARC-CoV2 and its associated additional viruses.

Systemic or non-systemic enzyme-based treatment options are available. There are many ways to administer them, including orally, topically, respiratoryly, or intravenously. Enzyme replacement therapy (ERT) is primarily used to treat diseases brought on by the lack or malfunctioning of enzymes. When contemplating ERT, the usage of enzymes for treatment differs with each medical state and is particularly illness-specific. Through intravenous enzyme delivery, these medical

diseases attempt to restore the lost or changed enzyme activity. Lysosomal storage abnormalities, cancer, Alzheimer's disease, irritable bowel syndrome, exocrine pancreatic insufficiency, and hyperuricemia are a few examples of such illnesses or conditions.

Advantages of Enzyme Treatment

Cancer, microbial infection, wound healing, gene treatments, lysosomal storage diseases, Alzheimer's disease, irritable bowel syndrome, exocrine pancreatic insufficiency, and hyperuricemia are only a few of the modern medicines that have been linked to enzymes.

Recombinant DNA Technology and Enzymes

Recombinant enzymes, such as those used in the recombinant DNA technology (RDT), are a collection of molecular tools for creating recombinant DNA (rDNA). DNA polymerases, exonucleases, DNA ligases, restriction enzymes, etc. These enzymes have a wide range of functions and may be effective tools in fields including genetic engineering, molecular biology, proteomics, and bioinformatics, among others. These enzymes perform a variety of tasks, including as methylation, host-controlled restriction, chain elongation, ligation, and protection against DNA cleavage for their own DNA [8].

Enzymes are particular, adaptable, and effective biocatalysts that take part in reactions and reduce activation energy. One of the crucial stages in the manufacturing of enzymes is industrial fermentation, which transforms substrates into products. Temperature, substrate, pH, aeration and agitation, inhibitors, etc. are some of the variables that may have an impact on this process. Upstream and downstream processes are two groups into which the crucial phases for industrial enzyme synthesis may be divided. Inoculum creation, medium setup, cell culture, cell separation, and harvest are all upstream processes. The recovery of enzymes from the fermented broth is part of the downstream process. A common approach to produce more stable, active, and reusable enzymes is enzyme immobilization. It is the physical, chemical, or combination of the two confinement of enzyme molecules onto/within a support or matrix to maintain complete activity.

Adsorption, covalent binding, entrapment, cross-linking or copolymerization, metal linked immobilization, and encapsulation are the six main categories of primary approaches for immobilizing enzymes. The benefits of enzyme immobilization include the ability to stop a reaction quickly by removing the enzyme from the reaction, development of multi-enzyme systems, protection from enzyme decomposition and deactivation, retention of enzymes, enzyme-free products, recycling or repetitive use of enzymes, enhanced stability and efficiency of enzymes, use as controlled release agents, and low reaction rate and high enzyme substrate ratio. Enzymes are often utilized in a variety of industrial applications, including baking, drinks, brewing, and dairy products. Enzymes are also used in the paper, leather, textile pulp, detergent, and paper industries. Alpha-amylase, beta-glucanase, lipase, papain, chymosin, pectinase, lactase, glucose oxidase, cellulase, and other enzymes are utilized in these processes. Rennet, proteases, catalases, lipases, and other enzymes are utilized in the production of cheese, accordingly. Enzymes are helpful while developing new drugs. They serve as biological targets for medications, which are intended to have the desired therapeutic impact.

In contrast to cell surface receptors, nuclear hormone receptors, ion channels, and transporters, enzymes provide novel potential for drug creation. Competitive inhibition, non-competitive inhibition, and uncompetitive inhibition are the three main forms of drug-induced enzyme inhibition. In many diseases, including myocardial infarction, jaundice, pancreatitis, cancer, and neurodegenerative illnesses, enzymes serve as indicators. By assessing the prognosis, response to treatment, and diagnosis, they may provide light on the illness process. Currently, recombinant DNA technology (RDT) offers a molecular tool to generate recombinant DNA (rDNA) by employing a collection of enzymes known as recombinant enzymes e.g. DNA polymerases, exonucleases, DNA ligases, restriction enzymes, etc. These enzymes have a wide range of functions and may be effective tools in fields including genetic engineering, molecular biology, proteomics, and bioinformatics, among others. These enzymes perform a variety of tasks, including as host-controlled restriction, chain elongation, ligation, protection against DNA cleavage of their own DNA, methylation, etc.

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CHAPTER-18

STUDY OF THE BIOLOGY CHEMISTRY

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Bioenergetics is the area of biochemistry that deals with the energy required to form and dissolve chemical bonds in living molecules. In biological organisms, energy exchanges, energy transformations, and energy transductions are all being studied. Energy may be obtained by all living creatures in the universe via a number of metabolic processes. Growth, development, anabolism, and catabolism are some of the most crucial processes in the study of living things since the role of energy is essential to such biological activities. Living creatures maintain their existence via the exchange of energy with their surroundings and living tissues and cells. For instance, photosynthesis may allow autotrophic organisms to get energy from sunlight without consuming or digesting food.

For instance, heterotrophs depend on food for nutrients to sustain their energy levels via metabolic processes like glycolysis and the citric acid cycle, which disintegrate chemical bonds in food. Autotrophic and heterotrophic organisms interact in a global metabolic network as a consequence of the first rule of thermodynamics.

Eaten by heterotrophs are autotrophs (plants), which provide them with energy. Chemical connections in a living thing are broken and new ones created when energy is transported and altered. When weak connections are destroyed and stronger ones are made, as during chemical synthesis and anabolic processes throughout development, energy becomes available for labor (such as mechanical activity) or other activities. We might release useable energy when our relationships are stronger. Making ATP from easily accessible starting materials (in the environment) and then converting them into ADP and inorganic phosphate for use in biological processes are the objectives of metabolic and catabolic processes. The "energy charge" of a cell is determined by the balance between ATP and ADP concentrations.

If there is more ATP than ADP available, the cell may do work using ATP; but, if there is more ADP than ATP, the cell must produce ATP by oxidative phosphorylation. Oxidative phosphorylation, which produces ATP primarily from oxygen or other oxidative energy sources, is a process that occurs in living things.

The terminal phosphate linkages deteriorate when ATP is hydrolyzed (broken down) into adenosine diphosphate and inorganic phosphate. The energy released here originates from the thermodynamically advantageous free energy of hydrolysis rather than from the phosphoanhydride bond between the terminal phosphate group and the rest of the ATP molecule. An organism uses its ATP reserve, which functions like a battery, to store energy in its cells. For their biological processes to function, all living things need the chemical energy produced by such molecular bond rearrangements [1].

Transformations of Biological Energy Follow The Thermodynamic Laws

Two fundamental thermodynamic concepts were developed in the nineteenth century as a result of many quantitative discoveries made by physicists and chemists on the interconversion of different kinds of energy. The first law of thermodynamics states that any physical or chemical change needs the conversion of energy. Energy may go from one place to another, but it cannot be created or destroyed; the total amount of energy in the universe is constant. The universe is constantly moving toward greater disorder, according to the second law of thermodynamics, which asserts that the entropy of the world is increasing in all natural processes. Despite the second law of thermodynamics, living organisms are composed of a group of molecules that are far more organized than the substance from which they were formed, and they maintain and create order. On the other hand, all living things strictly abide by the second rule. We must first identify the systems and the environment in which they operate in order to determine if the second rule of biological systems is applicable. The energy changes that occur during a chemical reaction are indicated by three thermodynamic variables [2]. Gibbs free energy, abbreviated G, is a term used to describe the amount of work carried out in a thermodynamic system under constant temperature and pressure. It is also known as the Gibbs function, Gibbs energy, or free enthalpy. Gibbs free energy is denoted by the letter "G." In many cases, the energy is measured in joules or kilojoules. The maximum amount of work that may be taken from a closed system is Gibbs free energy.In 1876, an American scientist by the name of Josiah Willard Gibbs made this discovery while performing research on how systems behave when they are linked or whether a process may take place simultaneously and spontaneously. Gibbs referred to his free energy as his "available energy". It is the total amount of energy that a thermodynamic system is capable of using. The system's enthalpy is subtracted from the temperature and entropy product to get the Gibbs free energy.

The Standard Stat and Chemical Equilibria

Free energy must change as well if entropy varies with concentration. As a result, a chemical process' free energy change is influenced by the concentrations of both reactants and products. This phenomenon is crucial because many biological processes may go either way depending on the relative concentrations of their reactants and products [3].

Biochemistry Standard State Conversions

In order to evaluate free energy changes for different processes, it is necessary to construct G values relative to some reference state that is arbitrarily given the height of zero, which we refer to as the heights of geographic regions. Physical chemistry rules indicate that a solute is in its standard state when the following conditions are met: temperature of 25 °C, pressure of 1 atm, and activity of 1 (a substance's activity is its concentration corrected for non-ideal behavior at larger concentrations than infinite dilution). The concentrations of reactants and products in the majority of biological processes are so low (millimolar or less) that their activity may be approximately predicted by their molar concentrations. Because biological activities take place around neutral pH, biochemists have devised a slightly modified standard state convention. (i) The activity of pure water is assigned a value of 1, even if its concentration is 55.5 M. The free energy formulae

for reactions in diluted solutions using water as a reactant are simplified since the [H2O] component may be ignored [4], [5].

Cells Need Free Energy Resources

Cells are examples of isothermal systems, which function under constant pressure and at a temperature that is typically constant. Heat flow is not a source of energy for cells since heat can only produce work when it flows to an area or item with a lower temperature. The direction of a chemical reaction, the precise equilibrium position, and the theoretical work output at constant temperature and pressure may all be predicted using the Gibbs free energy function, a mathematical function that estimates the amount of energy that cells may and must use. While photosynthetic cells acquire their free energy from sun rays absorbed, heterotrophic cells get it from food molecules. Both kinds of cells use this free energy to create ATP and other molecules rich in energy that can power biological processes at constant temperatures.

As a result, a reaction associated to it that is thermodynamically favorable might result in a reaction that is thermodynamically unfavorable. The reactions in this illustration are connected by a typical chemical intermediate called B. There are two main techniques to connect an uphill and a downhill response. An inefficient process may be accelerated by storing free energy in an active protein structure. Proteins have been used as energy conversion mechanisms in a variety of ways. Molecular motors like myosin, kinesin, and dynein transform the phosphoryl potential of ATP into mechanical energy. The sodium-potassium pump is phosphorylated by ATP and then dephosphorylated, resulting in active Na+ and K+ transport across membranes.

This reaction cycle alters the orientation of the pump's ion-binding sites in relation to the inside and outside of the cell, as well as its affinity for the transported ions. The versatility and power of proteins in energy transduction are highlighted by bacteriorhodopsin's ability to absorb photons and use them to pump protons across the cell membrane. Ionic gradients may also be used to connect activities that take place uphill and downstream. For instance, the electrochemical potential of Na+ may be used to pump Ca2+ out of cells or to transfer nutrients like carbohydrates and amino acids into them. Most of the ATP produced by cells is powered by proton gradients created by the oxidation of fuel molecules or photosynthesis.All of these energy conversion pathways are regulated by membrane-bound proteinos that cycle through conformational changes [6].

Hydrolysis of ATP: ATP'S Role in Biological Systems

Being such a complicated system, the human body requires a lot of energy to maintain good functioning. Adenosine triphosphate (ATP) is the energy source for cellular use and storage. Adenosine triphosphate (ATP) is a nucleoside triphosphate made composed of an adenine nitrogenous base, three serially linked phosphate groups, and ribose sugar. Because it generates quickly usable energy, the link between the second and third phosphate groups in ATP is known as the "energy currency" of the cell. In addition to producing energy, ATP hydrolysis carries out a number of functions in the cell, including DNA/RNA synthesis and signaling. Energy for ATP synthesis is provided by catabolic mechanisms such cellular respiration, beta-oxidation, and

ketosis. During cellular respiration, the majority of the ATP is produced by the mitochondrial matrix, with each glucose molecule oxidized producing around 32 ATP molecules.

Among the many functions carried out by ATP are ion transport, muscle contraction, transmission of nerve impulses, substrate phosphorylation, and chemical synthesis. For these processes as well as others, a significant quantity of ATP is needed. Therefore, for cells to function normally, 100 to 150 moles of ATP must be hydrolyzed each day in the human body. In the parts that follow, it will be highlighted how important ATP is as a chemical involved in cell function. ATP is a useful energy storage molecule that may be utilized as "money" due to the phosphate groups that interact via phosphodiester linkages. High-energy bonds are produced as a consequence of electronegative charges resisting the phosphate groups. There is still a substantial amount of energy present in the phosphate-phosphate bonds.

As a consequence, ADP, AMP, and free inorganic phosphate groups are hydrolyzed by metabolic processes. The Gibbs-free energy of ATP hydrolysis into ADP is -7.3 cal/mol. To keep the cell functioning, ATP has to be regularly replaced. Normally, the intracellular concentration of ATP varies from 1 to 10 uM. Numerous feedback mechanisms maintain the ATP level in the cell at a steady level. The ATP synthase enzyme may be stimulated or inhibited as a common regulatory strategy. Phosphofructokinase-1 (PFK1) and Pyruvate Kinase, two crucial glycolysis enzymes, are inhibited when cellular ATP levels are high enough, acting as a negative feedback loop to limit glucose breakdown. Only a few of the purinergic reactions that ATP may trigger include vascular tone regulation, pain management, and interactions between brain glia [7].

ATP Synthesis

It is now possible to create ATP using the proton-motive force. Studies on oxidative phosphorylation have benefitted from the use of submitochondrial particles, which are created when an ion breaks the inner mitochondrial membrane.In electron micrographs, ATP synthase is seen as spherical projections from the exterior of these inside-oul vesicles. These 85-diameter projections may be seen on the matrix side of the inner mitochondrial membrane in healthy mitochondria. Efrain Racker discovered that mechanical agitation might be used to take these knobs off in 1960. Although they are no longer able to synthesize ATP, the stripped submitochondrial particles may still move electrons along their electron transport chain. On the other side, ATP hydrolysis is catalyzed by the separated 85 spheres. According to Racker, the stripped submitochondrial particles' ability to make ATP was restored once the ATPase spheres were inserted into them. These objects are known as F1. The F1 unit's primary job is to catalyze the production of ATP [8].

Even in the absence of a proton gradient, the rate of incorporation of 18O into Pi suggests that nearly equal amounts of bound ATP and ADP are in equilibrium at the catalytic site. Adenosine triphosphate, on the other hand, does not leave the catalytic site until protons have passed. According to Paul Boyer, the proton gradient causes the synthase to release ATP as opposed to creating it. He also found that the nucleotide-binding sites of this enzyme interact. ATP is released from one site as a result of the movement of ADP and Pi between them. To put it another way, ATP synthase works with other enzymes to catalyze reactions. Living things are sustained through

the flow of energy between their tissues and cells and the environment. Every living thing in the universe is capable of obtaining energy via a variety of metabolic processes. The fundamental law of thermodynamics states that any physical or chemical change needs the conversion of energy. The second law of thermodynamics states that the universe is heading toward more chaos. However, living things consistently adhere to the second rule. The amount of work that may be accomplished in a thermodynamic system while the temperature and pressure are held constant is known as the Gibbs free energy. The difference between the change in enthalpy and the sum of the system's temperature and entropy changes is known as the Gibbs free energy. Living creatures keep their internal systems in order by taking in free energy from their environment in the form of nutrients or sunlight and giving it back in equal measure. A thermodynamic idea known as the Gibbs free energy function specifies how much energy cells can and must utilize. It makes it possible to forecast the course of chemical reactions, their precise equilibrium positions, and how much work they can produce at a given temperature and pressure. The daily operations of the cell depend on the molecule ATP. ADP or AMP are created during the hydrolysis of ATP, together with free inorganic phosphate groups. Normally, the intracellular concentration of ATP fluctuates between 1 and 10 uM.

Adenine and the carbohydrate pentose ribose combine to form the nucleotide adenosine triphosphate (ATP). Between two phosphate units, there are two oxygen-to-phospnorous connections. The most common combination of ATP with Mg2+ or Mn2+ is the active form of ATP. Uphill and downhill reflexes may be linked using two major strategies. It is possible to accelerate a process that is thermodynamically unfavorable by storing free energy in an active protein structure. The versatility and strength of proteins in energy transduction is shown by the capacity of bacteriorhodopsin to capture photons and utilize them to pump protons across the cell membrane.

Thermodynamics of Biopolymer Solutions and Biopolymer Interactions

Van der Walls forces and hydrogen bonds found in macromolecules act as intermolecular forces that affect the properties of biopolymers. Although these intermolecular interactions exist in simple molecules as well, they have a far less impact on them than they do on macromolecules. This is brought on by the cumulative influence of these pressures along the extensive polymer chains. The influence of intermolecular forces seems to increase with chain length. The four layers of protein structure are maintained through a variety of different kinds of links. There are two primary forms of covalent bonds in proteins. The first is the peptide bond that connects monomers of the initial amino acid sequence. The second is the disulfide bond (S-S bridge), which, as we've just seen, forms when two cysteine residues' -SH groups come together. This bond is in charge of some of the secondary and tertiary structure's characteristics. A polymer's solution depends on its molecular structure, content, and weight. Non-polar polymers are more soluble in non-polar solvents, such as polystyrene in toluene, while polar polymers are typically more soluble in polar solvents, such as polyvinyl alcohol, in water. The solvent in crystalline polymers has to overcome the intermolecular crystalline forces. In a suitable solvent, cross-linked polymers swell as opposed to dissolving. With increased molecular weight and lengthening side chains, the rate of solution declines.

Active Forces with Biopolymers

Numerous weak interactions are required for the development of secondary and tertiary structure. These weak bonds are all non-covalent, with the following types being the most common: Ionic or electrostatic connections are formed when ionized groups with opposing charges are drawn to one another. Hydrogen bonds are created when two neighboring electronegative atoms share a proton (H+). The H+ may be shared by oxygen or nitrogen atoms that are near to one another. Hydrogen bonds have several essential biological applications. They are essential for the exact matching of nucleic acid bases that serves as the main adhesive force keeping the two DNA strands together and for the correct conversion of DNA into RNA. DNA and proteins both heavily rely on hydrogen bonding. As a result, the pressures listed below help stabilize biopolymer structures:

1. **Hydrogen bonds:** Weak forces of attraction between two molecules' hydrogen atoms, which may be oxygen, fluorine, or nitrogen and are both partially positive and negatively charged.
2. **Ionic bonding:** When cationic and anionic side chains come into contact, side chain cross-linking may occur.
3. **Covalent bonding:** The most prevalent kind of inter-chain bonding is the disulfide bond formed between two cysteine residues. The two polypeptide chains that make up insulin are linked together by these sorts of bridges.
4. **Hydrophobic bonding:** Some amino acid residues have hydrophobic, or water-hating, side chains. Proteins fold under wet conditions such that the bulk of the hydrophobic chains collect within the folds. The hydrophilic (loving water) polar side chains are located on the outside or surface of the protein.

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CHAPTER-19

EXPANSION OF THE MOLECULE AND ELECTROSTATIC CHARGES

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Hydrophobic interactions include the clustering of molecular groups that interact with one another in a way that keeps them from coming into contact with water. The side chains of the most hydrophobic amino acid tend to concentrate within the molecule whereas the hydrophilic groups in globular proteins protrude from the surface of the structure. The hydrophobic residues' inclination to oppose the water molecules that surround the protein results in a more compact globular form. Van der Waals interactions are only able to occur when two atoms are very close to one another. At very near distances, the presence of two molecules may cause charge oscillations that can lead to reciprocal attraction. The essential difference is the amount of energy needed to break a covalent bond as compared to a noncovalent bond. For instance, a hydrogen bond may be broken with just 4.5 kcal mole-1 as opposed to the 110 kcal mole-1 required to break the covalent O-H bond in water. An illustration of how stable structures may be built even when each individual connection is weak is the double-stranded DNA structure. Covalent bonds are often broken by the activity of enzymes, but non-covalent bonds are easily broken by physicochemical causes.

Motivatory Pressure

Colligative properties (Colligates-collected together) describe a solution's qualities that depend only on the number of particles it contains. As a result, the bulk of thermodynamic properties, including reduced vapour pressure, raised bonding point, lowered freezing point, reduced osmotic pressure, etc., come under the heading of cooperative properties. Several collative properties, most notably osmotic pressure, are used to estimate the molecular weight of substances in solution. Osmotic refers to the net movement of water molecules over a semipermeable membrane from a pure water or diluted solution (solvent) to a concentrated solution. Only water may diffuse over this barrier; the solute cannot. As a result, a semipermeable barrier prevents water from entering. However, a net diffusion or osmosis of water from the diluted to the concentrated solution is generated by a higher number of water molecules diffusing in one direction than in the other. Water molecules diffuse across the semipermeable barrier in both directions.

Water continues to flow into the more concentrated solution across the membrane in this way until the hydrostatic pressure on the concentrated side of the membrane rises to a level where it causes a transmembrane diffusion of water in the opposite direction at the same rate as the osmotic input. The hydrostatic pressure that correctly balances the osmotic influx of water from pure water to concentrated solution is known as the osmotic pressure of a solution. The pressure that must be applied to a concentrated solution that is separated from pure water by a semipermeable barrier is hence another way to define osmotic pressure (g). to prevent and counteract the osmotic influx into the solution. It corresponds to the difference between the hydrostatic pressures on the two sides of the membrane. The overall characteristic of a solution is osmotic pressure. As the

concentration of solute particles in the solution rises, an increasing number of solvent particles are bound by solute particles in complexes. These complexes are referred to as solvates. Osmotic pressure may be attributed to the greater solvent concentration and increased partial pressure of solvent molecules on that side of the semipermeable membrane [1], [2].

The colloid osmotic pressure of plasma proteins, which also aids in maintaining water in the plasma, somewhat offsets the filtering effect of blood pressure. Hepatic issues and nephrosia in Kwashorkor diminish blood colloid osmotic pressure, decrease the quantity of water in circulation, and decrease albumin plasma concentration, all of which lead to oedema. Techniques for Measuring Osmotic Pressure The static approach, the dynamic method, or the half sum method may all be used to quantify osmotic pressure.

In the static technique, the solvent is let to pass through the membrane up until there is no longer any exchange in the internal head h. The osmometer measures the level equilibrium difference. Surface tension's effects must be taken into account, as must the equilibrium concentration of the solution brought about by solvent flowing through the membrane. Due to solvent adsorption occurring during equilibrium formation, which normally takes a long period, the concentration of the solution close to the membrane may sometimes increase. By creating the membrane correctly and keeping it in the solvent, this may be avoided. Despite being a simple strategy, equilibrium is reached after an unusually long period of time.

The dynamic method allows the solvent to traverse the membrane. We can determine the rate of penetration by applying an external gas pressure to the solution. The interpolated pressure with a zero rate will be osmotic pressure. By creating an equilibrium pressure that remains constant for a considerable period of time, more reliable results are achieved. It needs a complex leak-tight cell to complete this quick process. The internal head was initially adjusted to be considerably above or close to the projected equilibrium. The volume loss over time is routinely measured. Once enough time has elapsed, the h-time connection is plotted as shown by x. When the head is slightly out of equilibrium, the experiment is repeated, and the volume expansion over time is recorded until the asymptotic g curve, which is shown by Y. By calculating the ordinates of x and y at half their total for different values, a new curve A is produced that converges to a constant value. Since there is little volume change in either situation, the equilibrium concentration is taken to be equal to the critical concentration [3].

Mechanical Equalization

The first person to apply cupric ferrocyanide to the earthenware pot's pores and utilize it as a semipermeable membrane was Pfeiffer. Since then, a wide variety of materials, including cellulose and animal bladder, have been employed as semipermeable membranes. In osmometry, the semipermeable membrane is crucial. The right selection of membranes has a significant impact on the accuracy of osmotic measurements. High permeability to the solvent and virtual impermeability to the smallest solute molecules in the solution must be balanced when choosing a membrane. The membrane shouldn't swell much when exposed to the solvent, and it should contain enough tiny holes for the solvent molecules to readily flow through. The most practical material is cellulose, either in the form of carefully treated films of denitrated cellulose nitrate or

non-waterproof cellophane sheets. Since cellophane's pore size is only slightly increased when treated with ammonia solution or other chemicals, cellophane membrane is often employed. In accordance with the swelling and solvent transfer process, membranes of different porosity may be prepared. While nitrocellulose membranes may be employed up to molecular weights of 2000, Hookway has described some rapid membranes that are permeable to solutes of 50000. It is necessary to first wash the membrane with 25, 50, 75, and 100% acetone or alcohol solutions before replacing the alcohol or acetone with equivalent washings using the chosen organic solvent in order to condition the membrane in water for usage with organic solvents. It is important to take precautions to prevent the membranes from drying out. Always keep it in the solvent while storing. Semipermeable Membrane Theories Sieve theory, solution theory, and adsorption theory are the three semipermeable membrane theories [4], [5].

Sieve theory, first Traube saw the semipermeable membranes as bundles of capillaries, atomic or molecular sieves, or barriers to the diffusion of bigger molecules. He asserts that the size of the holes is the sole distinction between different membranes (copper ferrocyanide, parchment, etc.). This explanation falls short of explaining why a rubber membrane is permeable to big molecules like benzene and pyridine yet impenetrable to water.

Solution theory (II) According to Liebig and Hermite's theory, a membrane will be permeable to substances that dissolve in it and impermeable to those that do not, which explains why rubber is permeable to substances like benzene, toluene, pyridine, etc. that diffuse through it but not water because water is insoluble in rubber. The aforementioned information indicates that chemicals first dissolve in the membrane before diffusing across it. This proved to be a crucial need, but it wasn't the only one. Where neither a chemical reaction nor a solution could occur, Bigelow and Bartell found osmotic effects with inert substances: Porous cups that had very small holes or pores that were blocked with debris served as semipermeable membranes. When squeezed into disks with very small holes, silica, carbon, metallic copper, silver, and gold also served as semi-permeable membranes. According to Bartell's findings, the copper limit for pores should be 9.0 x 10-3 cm.

According to the adsorption principle, Wieser and other researchers have shown that inert membranes sometimes absorb significantly more solvent than solute. The process of the solution becoming more concentrated is known as negative adsorption. Similar phenomena were seen by Mathieu in a variety of solutions that used porous plates as membranes. He came to the conclusion that only water would be absorbed by suitably tiny capillaries. Similar to this, the copper ferrocyanide membrane negatively adsorbed sugar. Nitrogen cannot pass through thin palladium foil, although it may pass through hydrogen. Consequently, a semipermeable membrane functions more like a solvent than a filter. The chemical potential of the diffusing component on both sides of the membrane is the same, regardless of the method by which the semipermeable membrane functions.

Biopolymers' Molecular Weight Determination The idea of a mole was invented by Avogadro. A mole, in his estimation, is defined as a quantity of stuff with the same number of atoms as there are in 12 g of C-12. The value of this is 6.02291023. A mole's weight in kilos and a molecule's weight in atomic mass units (amu) are equivalent mathematically. Gram-atomic weight is the weight of one gram of an element's atom, while gram-molecular weight is the weight of one mole

of molecules. Atomic and molecular weights are a condensed form of them. The weight of one amu is 1.66 10-24 grams. The total number of atoms in the molecule, or its molecular weight [6], [7].

Physical Techniques

Numerous physical techniques rely on the assessment of kinetic behavior, thermodynamic characteristics, or a combination of the two in diluted solutions. Large deviations from the limiting infinite dilution behavior are seen in polymer solutions. As a result, every experiment is conducted at low concentrations and is always extrapolated to infinite dilution. In the case of chain molecules, a polymer molecule is considered to have a symmetrical statistical distribution of chain elements around a centre of gravity and the volume filled by this distribution is many times the actual molecular volume. Thus the volume across which a particular polymer molecule exerts its impact depends on the chain length and on the interaction between the polymer and the solvent. Hence the solution chosen for physical measurements should be so dilute that each of the molecule couples distinct section of the volume. In addition to exceedingly sensitive equipment to detect minute physical changes, the polymer must also be very carefully fractionated to avoid huge variations in molecular weight acquired by various techniques.

Numerous physical techniques rely on the assessment of kinetic behavior, thermodynamic characteristics, or a combination of the two in diluted solutions. Large deviations from the limiting infinite dilution behavior are seen in polymer solutions. As a result, every experiment is conducted at low concentrations and is always extrapolated to infinite dilution. In the case of chain molecules, a polymer molecule is considered to have a symmetrical statistical distribution of chain elements around a centre of gravity and the volume filled by this distribution is many times the actual molecular volume. Thus, the volume across which a particular polymer molecule exerts its impact depends on the chain length and on the interaction between the polymer and the solvent. Hence the solution chosen for physical measurements should be so dilute that each of the molecule couples distinct section of the volume. In addition to exceedingly sensitive equipment to detect minute physical changes, the polymer must also be very carefully fractionated to avoid huge variations in molecular weight acquired by various techniques [8], [9].

When the electrophoresis detergent sodium dodecyl sulfate (SDS) is employed, the proteins are mostly segregated based on their molecular weight. This is because SDS attaches to the proteins, giving them vast quantities of negative charges owing to the sulfate. The majority of a protein's charges will thus originate from the SDS, limiting the impact of charge variations inside a protein (variations that would normally alter electrophoretic mobility), and all proteins move in accordance with their size. The molecular pathway inside the polyacrylamide gel used for electrophoresis presents bigger proteins with greater resistance, which causes them to move more slowly than smaller proteins. Protein molecular weights are often determined using SDS electrophoresis. In conclusion, vapours that obey the perfect gas equation may be calculated using the vapous pressure techniques. Victor Meyer's method is also more precise in this situation. Only oligomers with established critical temperature and critical pressure may use these.

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CHAPTER-20

A BREIF DISCUSSION ABOUT THE BIO-ORGANIC CHEMISTRY

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The field of chemistry known as "bioorganic chemistry" is, broadly speaking, a branch of science that applies the concepts, methods, and tools of organic chemistry to the study of biochemical and biophysical processes. As an obvious but entirely organic predecessor, consider the classical chemistry of natural products with its distinctive trio of isolation, structural evidence, and comprehensive synthesis. Analyzing the biosynthetic processes for the same natural products is straightforward biochemistry. However, one is definitely dealing with bioorganic chemistry when the complete synthesis of a neutral product explicitly relies on the recognized biosynthetic pathway or if the biosynthetic process has been translated into a structural and mechanistic organic chemical language.

As we just established, the discovery of methodologies to manufacture organic compounds with biological significance or analogs is connected to organic chemistry. Not all analogs, meanwhile, are strong enough to react with or with biological substances. Therefore, it is required to modify the synthesis, which can only be done by careful examination of biological processes, which are a subset of biochemistry. However, understanding biology provides insight into what would be necessary to synthesise for a successful response, which can only be accomplished via organic chemistry. Therefore, the requirement for the interdisciplinary approach became evident and there must have to have two laboratories-i) one for the synthesis and ii) another for the biological investigation. Thus, understanding of organic chemistry give birth to the notion of development of organic models chemically manufactured in the laboratory to investigate the complicated biological processes. Because biochemistry and organic chemistry overlap, a new and rapidly developing field of study known as bioorganic chemistry was born.

Bio-organic Chemistry A Borderline Science-Its Multiple Origin

Enzyme Chemistry: For a select few hydrolytic enzymes, the catalyzed reaction has already been converted into a sequence of typical organic reaction steps. At the same time organic chemists are imitating the features of enzyme catalysis in model organic reactions dealing with both the pace of reaction and selectivity. Investigations, involving metalloenzymes and cofactors, the contiguous areas of bioorganic and bioinorganic chemistry also merge [1].

Nutritional Research: Understanding biochemistry allows us to identify the components of the human diet that are necessary, and the structures and syntheses of these components with the aid of organic chemistry allowed us to identify the mechanisms of action of the so-called vitamins and associated cofactors, or coenzymes. Research on hormones: With the aid of organic chemists, hormones secreted substances that have a stimulatory influence on cellular activity—could be

better understood at the molecular level after their structures were established and synthesized, making them accessible in practical quantities.

Chemistry of Natural Products: The evolution of bioorganic chemistry was significantly influenced by ideas about the biogenesis of natural products, and this influence is still strong today. It is clear that the classical chemistry of natural products, with its distinctive trio of structural evidence, isolation, and comprehensive synthesis, has an organic origin. Analyzing the biosynthetic processes for the same natural products is straightforward biochemistry. However, one is definitely dealing with bioorganic chemistry when the whole synthesis of a natural product explicitly relies on the recognized pathway of biosynthesis or if the biosynthesis has been translated into structural and mechanistic organic chemical language.

The term "molecular recognition" refers to a particular interaction between two or more molecules that involves non-covalent bonding, such as hydrogen bonds, metal coordination, hydrophobic forces, van der Waals forces, pi-pi interactions, electrostatic and/or electromagnetic effects, and has its origins solely in physical organic chemistry. In molecular recognition, the host and visitor display molecular complementarities. In biological systems, molecular recognition is crucial and is shown between receptor-ligand, antigen-antibody, DNA-protein, sugar-lectin, RNA-ribosome, etc. The antibiotic vancomycin, which binds specifically to peptides in bacterial cells containing terminal D-alanyl-D-alanine via five hydrogen bonds, is a prime example of molecular recognition. Since these specific peptides cannot be utilized by the bacteria to build their cell walls when the vancomycin binds to them, it is fatal to the bacteria. As a result, a comprehensive descriptor for molecular recognition has been employed, which is the composite phrase "biophysical organic chemistry."

Protein Chemistry (sequencing) vs. Reagent Application: A simple chemical used in accordance with a well-known principle may result in significant progress in biological chemistry. Thus, Bernhard Witkop transformed neighboring group involvement into selective, restricted, non-enzymatic cleavage at methionine in a peptide chain by the reaction of cyanogens bromide.

Reagents vs. Modern Biotechnology: The automated synthesis of polypeptide and polynucleotide chains as well as the sequencing of DNA and RNA provide the foundation of modern biotechnology. Application of the reagent has helped not only the correct sequencing of peptide segments of many proteins but also the production of human insulin through genetic engineering by using a methionyl-containing precursor version at each step [2], [3].

Background from Biology:

An analysis of the RNA's cleavage by enzyme models revealed that the natural RNA's 3',5'-linked and 2',5'-linked isomers were both simultaneously isomerized. It is also known that ribonucleosides are transformed to deoxyribonucleosides by a biochemical process that eliminates the 2'-hydroxyl group, although a different enzymatic preference could have eliminated the 3'-hydroxyl group instead. These findings prompted the issue of whether DNA's natural structure, with its phosphate linkages connecting the 3' and 5' locations of neighboring bases, has any inherent chemical preference. Is the present preference only a byproduct of evolution, or does using a 3'-deoxy 2',5'-linked imitation of natural DNA have any inherent drawbacks?

Application of Chemical Synthesis: Professor Breslow and his team created iso-DNA, or DNA isomers, in the 1990s by using 3'-deoxynucleosides and artificial 2',5'-links. However, they noticed that iso-DNA creates a considerably weaker double helix with its conjugate, or with the conjugate based on regular DNA, since the helix has more hydrophobic surface exposed to solvent. As a result, it cannot serve as a replacement for natural DNA in an organism, and those that have attempted it would be uncompetitive. The conformation of the ribose ring in relation to that in deoxyribose is reflected in the fact that iso-DNA does form a strong heteroduplex with normal RNA [4].

Remote Oxidation Development in Chemistry

Because of the geometry imposed by the attached reagent or template, remote oxidation processes were developed by chemists as a result of the oxidation by cytochrome P-450. In these processes, reagents and templates are attached to substrates that can extend far from their attachment point (from ring A of the steroid all the way to ring D at the other end) and perform selective reactions on specific spots. Breslow and his team created a metalloporphyrin with cyclodextrin groups that could reversibly bind substrates like steroids in the enzyme mimic. These mimics of cytochrome P-450 executed selective oxidations that are of practical importance, with thousands of rotations. The outcome was a selective oxidation of certain C-H bonds, which could only be accomplished by natural biological enzymes.

The pyridoxamine cofactor was covalently bonded to PEI or PAMAM in our polymeric and dendrimer mimics. However, the pyridoxamine cofactor interacts noncovalently with the protein matrix of the enzyme in the actual transaminases. Thus, in order to create better transaminase mimics, we have recently created certain noncovalent polymer-pyridoxamine systems in which the coenzyme attaches to the polymer in a reversible manner. Given that they attach to the hydrophobic area of the polymer, we discover that they are even more effective than the covalently connected equivalents. Additionally, we have now created a brand-new catalytic cycle that recycles the pyridoxal cofactor to the pyridoxamine, achieving large turnovers in transamination in such enzyme mimics for the first time. Two novel semi-synthetic RNase-S proteins that have a pyridoxamine moiety at the active site have had their transaminase activity tested. In the form of an artificial coenzyme-amino acid chimera, "Pam," a chemically capable derivative of pyridoxamine phosphate was introduced into the C-peptide fragments of these non-covalent protein complexes.

The chimeric Pam residue was substituted for Phe8 in the Cpeptide sequence using conventional solid phase techniques. It incorporates the heterocyclic functionality of pyridoxamine phosphate into the side chain of an alpha-amino acid. The two semi-synthetic Pam-RNase constructs were created to see whether the natural ribonuclease catalytic machinery could be used to control a transamination process that is pyridoxamine-dependent. Both RNase complexes, H1SP and S1SP, displayed moderate rate improvements in the Cu(II)-assisted transamination of pyruvate to alanine under single turnover conditions, compared to 5'-deoxypyridoxamine and the uncomplexed C-peptide fragments. Due to the recycling of the pyridoxamine moiety, several revolutions of substrates were also accomplished in the presence of additional L-phenylalanine. The modest chiral inductions observed in the catalytic production of alanine and the differences in reactivity

between the two proteins could be rationalized by the participation of a general base (His12) in complex H1SP, and by the increased tolerance for large amino acid substrates by complex S1SP, which contains serine at this position [5], [6].

Chemical Source

To differentiate them from covalent and ionic bonding, types of intramolecular interactions, molecules' pull on one another is referred to as intermolecular interactions. The importance of intermolecular interactions is greatest in liquid and solid phases due to the near proximity of molecules. Intermolecular interactions are really only potent for molecules that are close to one another, even in liquids and solids. It is simple to see the substantial effects of molecular interactions in the liquid and solid phases. Boiling points, miscibility, and solubility are just a few of the traits that are influenced by how strong intermolecular interactions are. All molecules communicate with one another via London dispersion forces, also known as van der Waals interactions. The attractive forces between two transitory dipoles are known as London dispersion forces. For instance, if one argon atom in liquid argon had a momentary dipole, the argon atoms close to it would also experience the effects of the dipole. As a result, the transient dipoles spread across a liquid or solid. The likelihood of creating significant transient dipole interactions increases with increasing atom size and electron count. Non-polar molecules and non-polar functional groups of molecules only interact with other molecules or functional groups through London dispersion or van der Waals forces.

Polar-polar interaction: Due to the non-symmetric geometric arrangement of atoms with various electronegativity, certain molecules and functional groups exhibit persistent dipoles. A molecule's section with a permanent dipole will be drawn to an adjacent molecule's portion with a similar permanent dipole. A van der Waals interaction is weaker than a polar-polar interaction [7]. The weak non-covalent interactions are significant in a variety of chemical processes. These forces are very important in chemistry because they regulate reactivity, selectivity, and form. In actuality, weak forces which include Hbonding, electrostatic, stereo-electronic, stacking, hydrophobic, and steric interactions dominate the phenomena of "Molecular Recognition".

H-bonds: A hydrogen bond, which should not be confused with a covalent bond to hydrogen, is an attractive contact between a hydrogen atom and an electronegative atom, such as nitrogen, oxygen, or fluorine. To form the bond, the hydrogen must be covalently connected to an electronegative atom. These bonds may form intramolecularly inside a single molecule or between molecules (intermolecularly). The hydrogen bond (5 to 30 kJ/mole) is weaker than covalent or ionic bonds but stronger than a van der Waals contact. Both inorganic molecules like water and organic molecules include this kind of connection. Charge transfer complexes: An electron-donor-acceptor complex, also known as a charge-transfer complex (CT complex), is a chemical association of two or more molecules, or of different parts of one very large molecule, where the attraction between the molecules (or parts) is produced by an electronic transition into an excited electronic state, resulting in the transfer of a portion of the electronic charge between the molecular entities. The molecule combination is stabilized by the ensuing electrostatic attraction. The receiving molecule is known as the electron acceptor, while the source molecule from which the charge is transferred is known as the electron donor.

Hydrophobic interactions:

the propensity for hydrocarbons to form intermolecular aggregates in aqueous media and similar intramolecular interactions in solutes that include lipophilic hydrocarbon-like groups. 6. Interaction between stacking: Interatomic interactions lead to the adoption of a stacked configuration of often aromatic molecules, which is referred to as stacking. Although effects caused by the existence of an orbital are just one source of stacking and don't always seem to be the main contributors, the term "- interaction" is often used to refer to stacking. Even though the intermolecular forces have a purely chemical origin, they all have a significant impact on the biological world. One of the keys to understanding the effects of pressure on biomaterials in biochemistry is the concept of weak interactions. The fundamental reason is that weak interactions are heavily engaged in the structure of biomolecules and in the functioning of numerous bioprocesses. In the areas of chemical and biological molecular recognition, catalysis in chemical synthesis, prebiotics, (d) in vivo (how is the cell controlled?), and chemical models, noncovalent forces are actively involved. A careful balance between stabilizing and destabilizing interactions (strong or weak) within the polypeptide chains of proteins and with the solvent leads to the native structure of biological substances, i.e. the conformation that exhibits biological activity. Depending on the nature of the biomaterials themselves as well as the ambient factors (such as other proteins, nucleic acids, membranes, lipids, solutes, solvents, salts, pH, and temperature), native biocompounds are stable in a small physical-chemical zone [8].

Solvation plays a significant part in the interactions between the biocompounds under study and their surroundings, which are governed by weak interactions, in addition to the many other forces at play. For instance, the majority of amino acids found in natural globular proteins are buried inside the structure and have limited access to solvents. Other amino acids, on the other hand, could be present on the protein's surface. The latter are solvated and they play a key part in the intermolecular interactions. Proteins fit together firmly. They are tightly packed and feature plenty of intra-globular voids. Small cavities known as "voids" that are prone to dynamic variations may control protein structural dynamics. Protein fluctuations, such as side chain rotation and the formation of subcon formations, are both made possible by voids and weak interactions. A protein in solution is in an equilibrium of different conformers that is dynamic and thermodynamic. The various conformations also depend on the type of the associated interactions. One method includes perturbing these molecular oscillations in order to comprehend them. To distinguish between thermal and volume effects, it is crucial to conduct pressure and temperature tests on these systems. However, only biological stems often exhibit weak interactions. The knowledge of the effects of pressure on a variety of inorganic or bioinorganic processes, including synthesis, solvent exchange, legend substitution, addition, elimination, electron transfer, and radiation-induced reactions, is another area in which they are active [9].

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CHAPTER-21

EFFECT OF PROXIMITY IN ORGANIC CHEMISTRY

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Molecular Identification

Molecular recognition is the particular contact between two or more molecules via no covalent bonds such as hydrogen bonding, metal coordination, hydrophobic forces, van der Waals forces, pi-pi interactions, electrostatic and/or electromagnetic effects. In molecular recognition, the host and visitor display molecular complementarities. The term "molecular recognition" refers to a group of phenomena that are governed by certain noncovalent interactions. Such events have a significant role in both contemporary chemical research and biological systems. Though these are only intermolecular processes, "molecular recognition," which can refer to both intra- and intermolecular phenomena, also includes "host-guest chemistry," "supramolecular chemistry," and "self-assembly."

One well-known instance of intramolecular recognition is protein folding. It is the Host-Guest Interactions and the Lock-Key Interaction in Enzymology. Static vs. dynamic molecular recognition methods Static and dynamic molecular recognition are two subcategories of molecular recognition. Static molecular recognition is akin to the interaction between a key and a keyhole; it is a 1:1 type complexation process between a host molecule and a guest molecule to generate a host-guest complex. To accomplish enhanced static molecular recognition, it is required to develop recognition sites that are particular for guest molecules. Bond polarization is made possible by the proximity of reactive functional groups during a chemical reaction, which often accelerates the pace of the reaction.

In the case of dynamic molecular recognition, the association constant of a second guest with a third binding site is influenced by the binding of the first guest to the first binding site of a host. The binding of the first guest raises the second guest's association constant in the case of positive allosteric systems. The association constant with the second lowers when the first guest is bound in negative allosteric systems, however. This sort of molecular recognition is dynamic, which is crucial since it offers a way to control binding in biological systems. Additionally being researched is the use of dynamic molecular recognition in molecular devices and highly functioning chemical sensors [1], [2].

Beginning of the Encapsulation Era

Over the last two decades, molecular recognition research has advanced well beyond the ion sequestration by macrocyclic polyether's like crown ethers. As a result, several hosts in a wide range of forms have been conceived and created in order to bond charged or neutral guests. These hosts all have concave surfaces to accommodate convex guests, which unites them all. The hosts

of the future were created to interact with every potential visitor surface with exceptional selectivity. Recently, reversible encapsulation, a superstructure produced by numerous copies of tiny molecules by self-recognition through weak intermolecular interactions enclosing a target, was also discovered [3].

Encapsulation Complexes: Uses

In the presence of benzene and p-ethyl toluene, the capsule created by molecule X in figure Y exists as two complexes. The two molecules are too big to squeeze between them, and the length of the p-ethyl toluene prevents it from moving about freely within the capsule. As visitors gathered in the capsule, two benzene molecules took up 41% of the available area. One molecule of p-ethyl toluene only takes up 33% of the available area, and two molecules would be too lengthy to fit within the cavity. However, the author notes that benzene/p-ethyl toluene exhibits greatest space filling (53% of the space), which he refers to as "optimal filling of the capsule's space." This alignment of host space and guest size promotes significant encapsulation and is particularly useful for organizing internal bimolecular processes [4], [5].

Chemical Composition of Living Cells

Cells: The Foundation of Life

A cell is a tiny, structurally and functionally autonomous unit of all living things. A group of functional cells constitute a tissue, and tissues join together to create organs. Organs cooperate in more advanced living things in order to survive as a whole. However, the cell serves as a functional unit in all living things, and the activity of the cell is the center of biology. The term cell‘ was originally created by Robert Hooke in 1665 to identify the empty honey-comb like structures visible in a thin slice of bottle cork, which he inspected. In 1838, the German botanist Matthias Schleiden proposed that all the plants are made up of plant cells. Theodore Schwann, a colleague and anatomist, conducted research and came to the conclusion that all animals also include animal cells in 1839. The true nature of a cell remained unclear, however. Rudolf Virchow revised cell theory once again in 1858. According to his idea, cells make up all living things and all cells develop from pre-existing cells. The discovery that cells contain protoplasm rather than being empty as Hooke had seen came from the German scientist Schulze in 1861. During the 1950s scientists created the notion that all creatures may be classed as prokaryotes or eukaryotes. For instance, although eukaryotic cells contain a nucleus, prokaryotic cells have not. Prokaryotic organisms, which include bacteria and blue-green algae, and eukaryotic organisms, which include protozoa, fungi, mammals, and plants, vary significantly in that prokaryotic cells lack intracellular components [6]–[8].

The Chemistry of Living Things

We were thus aware that all living things are made up of cells and their byproducts. Organo-inorganic and inorganic chemical substances combine to form the cell's structural components. Inorganic compounds do not contain carbon and hydrogen together, whereas organic compounds always do (along with possibly some other elements). Simply put, the term "organic" denotes life, whereas the term "inorganic" denotes non-living substances. The waste products and leftovers of

living creatures include organic substances. Carbohydrates (sugars, starches), lipids (fats & waxes), proteins, enzymes, and nucleic acids (DNA & RNA) are a few examples of organic substances that are essential to life. Examples of inorganic substances are carbon dioxide and water. Covalent bonds, which are created when two atoms share two electrons, hold the elements (atoms) of organic molecules together [9].

As was previously said, networks of various interacting biopolymers, ions, and metabolites make up living systems. When the biomolecules are studied in their isolated, pure forms, many of the intricate cellular activities that these cellular components power cannot be seen. Instead of testing in test tubes in the lab, researchers have started to analyze biological processes in live cells and in complete organisms. Tracking the molecules within the cell's natural surroundings is required to do this. In a complex biomolecular environment, direct detection of a small number of biomolecules is feasible, but in all other situations, indirect detection methods must be used. As a result, a number of techniques have been created to label cellular components with reporter tags so they can be seen and isolated from biological samples. The most widely used technique for cellular imaging is attaching a green fluorescent protein (GFP) tag or one of its related variations to a target biomolecule.

These fluorescent probes may be attached to a target protein to allow for fluorescence microscopy viewing. GFP tags may also be used to concentrate on the proteins in entire organisms for analysis. Using tags similar to GFP, almost every biological activity involving proteins has been investigated. However, there are a number of drawbacks to GFP tagging, including: (a) it only works with protein-containing materials and cannot be used to visualize non-proteinaceous components of cells, such as glycans, lipids, nucleic acids, or the thousands of small organelles, which make up a significant portion of cellular biomass. (b) Visualization is only possible using optical methods. We would thus be able to comprehend the proteome of the whole organism if there were a way to perceive both proteins and their modifications as well as other non-proteinaceous components.

Antibody conjugates have been used extensively to monitor biomolecules in live cells and whole organisms. However, access of these reagents to antigens inside cells and outside of the vasculature in live animals is a challenge due to their huge size and physical characteristics. Thus, it is clear that a big molecular tag is not appropriate for addressing every research goal without impairing cellular function. Due to the availability of a reactive center or functionality inside a biomolecule, a small molecular fluorescent tagging strategy has been created and used (similar to the tagging of biotin, fluorophores, and countless other small-molecule reporters). The site-specific chemical alteration of biomolecules, however, is still a highly challenging undertaking [10].

Comparison between Organic and Biochemical Reactions

The synthesis of complex biological molecules, such as proteins and DNA, in nature with the aid of several enzymes and coenzymes may be compared to the synthesis of organic compounds in a laboratory. Nature's enzymatic synthesis differs from straightforward organic chemistry, nevertheless, in part because of its complexity and increased stereoregularity and stereospecificity. This explains why certain biological processes are difficult to perform in test tubes in a chemical

lab. Unconventional organic chemistry often results from coenzyme biochemistry. Coenzymes are nature's unique reagents in this regard. They are the perfect molecules to employ for establishing the notion of structure-function connections using bioorganic chemistry techniques, as is covered previously under the biomimetic chemistry section, due to their clearly defined chemical structures.

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CHAPTER-22

THE VARIETY OF METHODS USED IN BIOPHYSICAL CHEMISTRY

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Biophysical chemistry is an interdisciplinary branch of research that describes the quantitative, qualitative, energetics, structure, functions, and interactions phenomena of biological systems by using principles from chemistry and physics. The study of biophysical chemistry has used a broad variety of traditional and advanced approaches due to the complexity of biological systems; as a result, mathematical, physical, and chemical techniques are all used to characterize biological systems. Biophysical chemistry is a fascinating area of study that is now expanding quickly and seeing significant advances worldwide. In reality, three biophysical chemists shared the 2009 Nobel Prize in Chemistry for their work on ribosome X-ray diffraction. Molecular structure, molecular function, molecular dynamics, and the kinetics, interactions, and thermodynamics of macromolecules found in the cell membrane or other cytoplasmic components are the main topics that biophysical chemists are interested in. Generally speaking, biophysical chemistry is interested in providing answers to the following questions: how do biological processes occur, what kinds of molecules or particles are involved in this process and what are their structures, how long does it take for a biological process to occur and what are the energetics that accompany that change, what are the functions of biological molecules, and what are the effects on the cell if some biological molecules function improperly.

In this introduction chapter, we will discuss the significance of biophysical chemistry as a developing scientific discipline and the wide range of methodologies that have been used to explain the linked phenomena. These methods include spectroscopic, electrochemical, thermal, and physiological roots, therefore it would be impossible to discuss them all in a single introductory chapter. Instead, we'll go through some specific methods for examining the composition and operation of biological components. Some of these methods mimic environmental and semi-environmental circumstances seen in the natural habitat of biological molecules. We shall concentrate on four categories of currently used methodologies in the area of biophysical chemistry. Each approach has a brief explanation and is referenced with the necessary reference for more information [1], [2].

Thermal Methods

Differential scanning calorimetry (DSC) and isothermal titration calorimetry (ITC) are the most appropriate and proper techniques used in this category. These techniques provide unique complementary information for nucleic acids, modified nucleic acids, nucleic acid-ligand interactions, and protein-ligand interactions. They are also very helpful methods for finding thermodynamic parameters using the same straightforward Gibbs equation. DSC is a straightforward, model-independent measuring instrument that may be used in conjunction with a number of physicochemical techniques to get structural and bonding data. Originally, DSC was

used to investigate how biological responses or interactions changed depending on temperature and time when heat was gained endothermic, or heat absorption, or lost exothermic, or heat production. Based on a temperature differential between the sample and the reference material, the DSC method monitors a controlled heat change during a temperature difference that is emitted or absorbed by the sample [3], [4].

When conducting a DSC experiment, the reference cell, which only contains the same amount of solvent as the sample cell, and the sample cell, which contains the molecules of interest dissolved in the appropriate solvent, are heated simultaneously. As a result, the temperatures of both cells rise uniformly over time. Temperature is measured based on whether an energy activity is endothermic or exothermic. In order to achieve the difference, the temperatures of the two cells are increased concurrently. The idea of heat excess enters the picture because if the process is heat gaining, then more heat is necessary to equilibrate the two cells, which means more energy is needed to get the sample to the same temperature as the reference.

When it comes to the quality of the results, slower scan rates provide higher resolution, while high feedback strength will give the best interaction or reaction sensitivity. New instruments allow setting a variety of experimental parameters, such as the number of scans, post scan temperature, scan range and rate, as well as feedback strength. The instrument is now used in many applications because of its simplicity in measuring enthalpy changes, temperature differences, and phase transitions. Examples include studying protein interactions with ligands and drugs, protein mutations, protein folding, lipid interactions with drugs, protein interactions with lipids, DNA duplex stability, DNA helix-coil transition, thermodynamics of DNA melting, as well as DNA-DNA interactions. Isothermal titration calorimetry is another method. This method measures energy generated by interactions between a target molecule and a biological molecule extremely precisely. This method is primarily used for the qualitative and quantitative analysis of these interactions. The interaction system may be readily comprehended with the help of the Gibbs free energy equation and the equation of equilibrium free energy. The equilibrium constant for the binding process (K) and the binding stoichiometry (n) can both be obtained directly from the ICT instrument [5], [6].

Using Electrical Methods

The most cutting-edge and adaptable methods that have been applied to biological systems are shown in this area. Since experiments are used to examine biological systems in vivo and in vitro, it is clear that electrochemical approaches are successful. Both needs, for instance, very small electrodes that can penetrate a single biological cell without endangering it. As a result, much effort has been made to construct such an electrode. Recent advancement demonstrates that a new generation of ultramicroelectrodes are in use. Studying single cells are made by producing working electrodes normally from 5- to 10-μm diameter of carbon fibers. The electrode size should be close to the size of the detecting region of interest in order to improve signal-to-noise ratio in this context. Larger electrode sizes, on the other hand, can pick up more electrochemical events.

A single biological molecule may be studied utilizing the patch-clamp method to focus this application even further. A single ion channel's potential ionic current may be directly recorded

using this method. Additionally, variations in conductance and conformation between nonconducting and conducting conformations may be seen. This method might interfere with ion concentration since it could measure the conductance of a single channel, and conductance is the flow of an ion across a defined region. Therefore, extra care should be made to prevent this interference [7], [8].

The conductance of a single channel and the time needed for opening and closing the channel, or what we refer to as gating kinetics, can both be deduced from the current recording from the instrument that is produced from a single or few channel. This may first be accomplished by adding model holes made of gramicidin A to planar lipid bilayer membranes. The goal of this step is to insert a sufficient number of ion channels into the bilayer so that we can record expressed channels using both patch-clamp and voltage-clamp techniques while significantly reducing background noise by applying gigaseal resistance, which can be created by creating a very high resistance between the recording electrode and the membrane patch. Patch-clamp approach is explored thoroughly in the following sources.

Modern single-channel conductance recording methods include the inside-out patch, outside-out patch, and whole-cell patch. You may read more information in. The right electrode is essential when it comes to electrochemical methods used in biological systems. Bioelectrodes are now the term used to describe the electrode that is actively used in biological analysis. Since all biological processes occur inside the diameter of live cells, the term "microelectrodes" or "less" should refer to electrodes with a tip diameter of less than 10 nm or ultramicroelectrodes with a tip diameter of less than 1 nm. Such electrodes have a wide range of uses in biological systems. Neurochemical analysis, the detection of mutagenicity and toxicity, blood ion and gas analysis, blood flow analysis, and the analysis of small molecules, nucleic acids, and proteins are a few of them.

Patch-clamp recording may be used with other secondary methods to explore certain proteins. For instance, one may look at the pre-steady-state kinetics of membrane transporters using fast perturbation approaches. In this way, a transporter's current across the membrane may be measured, allowing the mechanism at work to be understood. This has a number of issues, including the fact that ion fluxes and consequently current generated by transporters are far smaller than those produced by channels. The inside-out or whole-cell patch approach is utilized as a result.

Voltage jump fluorometry mixed with site-directed fluorescent labeling is another intriguing method that is currently in use. The primary use of this method is the real-time, native environment detection of local protein mobility. This may be accomplished by inserting cysteine, an amino acid, at a precise place inside a protein structure. Site-directed mutagenesis is the most beneficial method for doing it. This allows for the cutting of certain amino acids and the substitution of others with the appropriate amino acids, which ultimately places cysteine where it is wanted to be.

In Xenopus oocytes, a new protein structure may be generated that enables fluorescently active dyes to bind cysteine, such as tetramethyl rhodamine-6-maleimide. For instance, a voltage pulse can stimulate expressed protein, which in turn causes current responses and fluorescence signals to be recorded in an electrophysiological experiment. This enables structural changes to be

correlated with particular ion transport steps, and thus a detailed mechanism to be illustrated. The references below include more information [9], [10].

Molecular simulations on a large timeframe. The computing capability at the time placed a limit on the size and duration of macromolecule molecular simulations. Due to this, it has been challenging to model for long enough to represent biological processes requiring more than tens of nanoseconds while still taking into account the complete complexity of the natural environment of proteins. However, more recently, lengthier simulations have been possible because to the constant rise in computer power, with some cutting-edge research reporting millisecond-long simulations.

Thus, it is now feasible to measure the energetics of physiological processes as well as directly explore the global conformational changes of proteins that are important for protein function. Analytical method based on radioactivity.

This method uses radioisotopes to detect the flow (influx and efflux) of ions and compounds through biological membranes. If the transporters are working electroneutrally (in which case the patch-clamp approach cannot be used) or if sensitive fluorescent dyes are not readily accessible, radioactive-based study of membrane transport is the preferred method. Particularly in the case of Na+ and K+ transfer, the latter.

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