DNR college (A); Bhimavaram
Department of Biochemistry
II B.Sc; Semester-III

UNIT-1

ENZYMOLOGY

1.Introduction to BIOCATALYSIS.

2.Difference between chemical and biological catalysis.

3.Nomenclature and classification of enzymes.

4.Defination of holo enzymes,

Apo enzyme, co enzyme, co factor, active site.

5.Enzyme and substrate specificity.

6.principles of energy of activation transition state.

7.Interaction between enzyme substrate- lock and key,induced fit models

8.Fundementals of enzyme assay,enzyme units.

9.Outlines of mechanism of enzyme action.

10.Factors affecting enzyme activity.

11. Comercial application of enzymes.

1.Definition of BIOCATALYSIS:-

Biocatalysis refers to the use of living (biological) systems or their parts to speed up (catalyze) chemical reactions. In biocatalytic processes, natural catalysts, such as enzymes, perform chemical transformations on organic compounds. Both enzymes that have been more or less isolated and enzymes still residing inside living cells are employed for this task.[1][2][3] Modern biotechnology, specifically directed evolution, has made the production of modified or non-natural enzymes possible. This has enabled the development of enzymes that can catalyze novel small molecule transformations that may be difficult or impossible using classical synthetic organic chemistry. Utilizing natural or modified enzymes to perform organic synthesis is termed chemoenzymatic synthesis; the reactions performed by the enzyme are classified as chemoenzymatic reactions.

Three dimensional structure of an enzyme. Biocatalysis utilizes these biological macromolecules to catalyze small molecule transformation.

2.Difference between chemical and biological catalysis:-

- Chemical catalysts are catalysts that can speed up chemical reactions. They may be artificial also.
- Biological catalysts are enzymes that speed up cellular process .

3.Nomenclature and classification of enzymes:-

An enzyme will interact with only one type of substance or group of substances, called the substrate, to catalyze a certain kind of reaction. Because of this specificity, enzymes often have been named by adding the suffix "-ase" to the substrate's name (as in urease, which catalyzes the breakdown of urea).

Enzymes Classification:- Earlier, enzymes were assigned names based on the one who discovered it. With further researches, classification became more comprehensive.According to the International Union of Biochemists (I U B), enzymes are divided into six functional classes and are classified based on the type of reaction in which they are used to catalyze. The six kinds of enzymes are hydrolases, oxidoreductases, lyases, transferases, ligases and isomerases

Oxidoreductases:-

These catalyze oxidation and reduction reactions, e.g. pyruvate dehydrogenase, catalysing the oxidation of pyruvate to acetyl coenzyme A.

Transferases:-

These catalyze transferring of the chemical group from one to another compound. An example is a transaminase, which transfers an amino group from one molecule to another.

Hydrolases:-

They catalyze the hydrolysis of a bond. For example, the enzyme pepsin hydrolyzes peptide bonds in proteins.

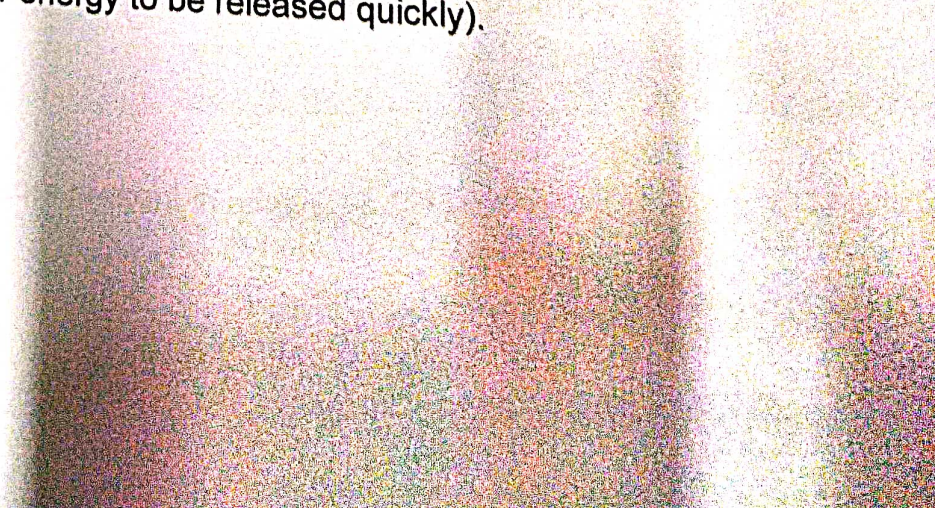
Lyases:-

These catalyze the breakage of bonds without catalysis, e.g. aldolase (an enzyme in glycolysis) catalyzes the splitting of fructose-1, 6-bisphosphate to glyceraldehyde-3-phosphate and dihydroxyacetone phosphate.

Isomerases:-

They catalyze the formation of an isomer of a compound. Example: phosphoglucomutase catalyzes the conversion of glucose-1-phosphate to glucose-6-phosphate (phosphate group is transferred from one to another position in the same compound) in glycogenolysis (glycogen is converted to glucose for energy to be released quickly).

Ligases



Ligases catalyze the association of two molecules. For example, DNA ligase catalyzes the joining of two fragments of DNA by forming a phosphodiester bond.

Holo enzyme:-

Holo enzyme is a complete, functional enzyme, which is catalytically active. Holoenzyme consists of an apoenzyme together with its cofactors. Holoenzyme contains all the subunits required for the functioning of an enzyme, e.g. DNA polymerase III, RNA polymerase.

Holoenzyme = Apoenzyme + Cofactor

Apo enzymes:-

Apoenzyme or apoprotein is an enzymatically inactive protein part of an enzyme, which requires a cofactor for its activity. Apart from catalytic RNA, most of the enzymes are proteins. Not all the enzymes require a cofactor. Enzymes that do not require any cofactor are known as simple enzymes, e.g. pepsin, trypsin, etc.A cofactor required by an apoenzyme can be a metal ion, e.g. Mg2+, Fe3+, etc. or an organic molecule called coenzyme such as NAD+, NADP+, FAD2+, etc.

Coenzymes:-A coenzyme binds to an enzyme only during catalysis. At all other times, it is detached from the enzyme. NAD+ is a common coenzyme.

Cofactor:-

Cofactors are non-proteinous substances that associate with enzymes. A cofactor is essential for the functioning of an enzyme. An enzyme without a cofactor is called an apoenzyme. An enzyme and its cofactor together constitute the holoenzyme.

There are three kinds of cofactors present in enzymes:

Prosthetic groups: These are cofactors tightly bound to an enzyme at all times. A fad is a prosthetic group present in many enzymes.

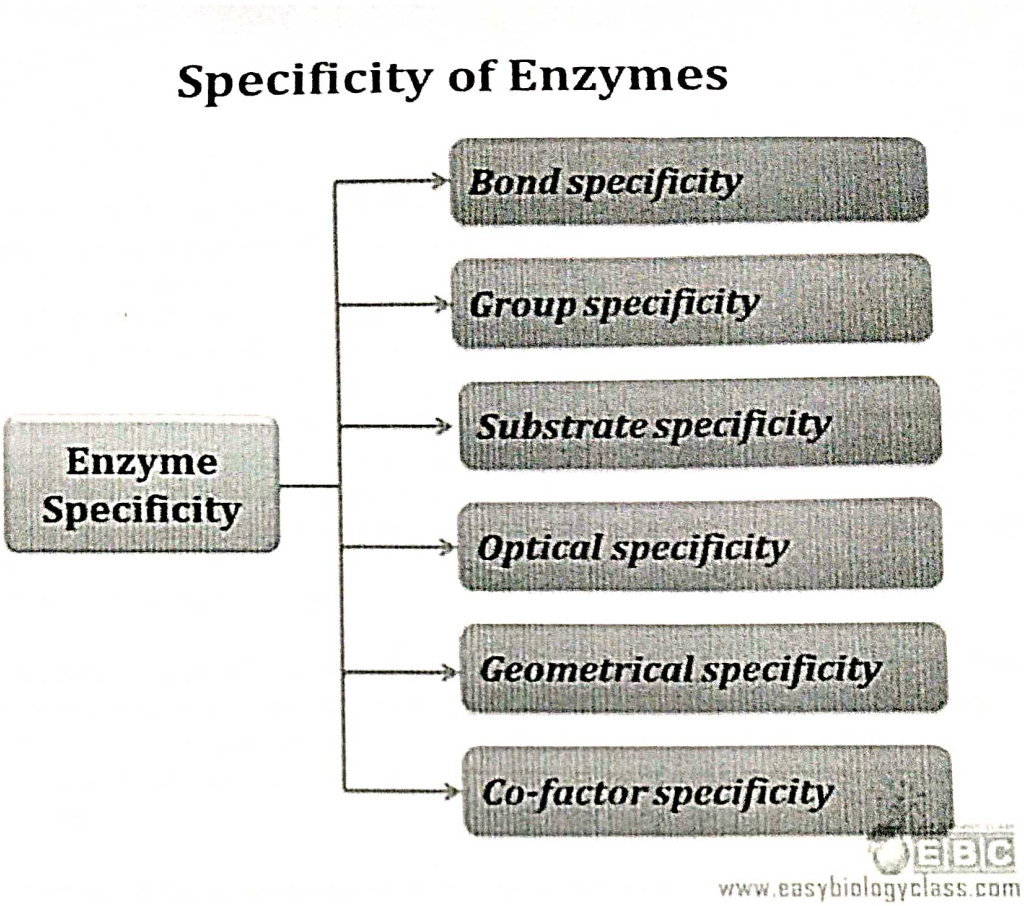
Coenzyme: A coenzyme binds to an enzyme only during catalysis. At all other times, it is detached from the enzyme. NAD+ is a common coenzyme.

Metal ions: For the catalysis of certain enzymes, a metal ion is required at the active site to form coordinate bonds. Zn2+ is a metal ion cofactor used by a number of enzymes

Active site:-

Enzymatic catalysis depends upon the activity of amino acid side chains assembled in the active centre. Enzymes bind the substrate into a region of the active site in an intermediate conformation.Often, the active site is a cleft or a pocket produced by the amino acids which take part in catalysis and substrate binding. Amino acids forming an enzyme's active site is not contiguous to the other along the sequence of primary amino acid. The active site amino acids are assembled to the cluster in the right conformation by the 3-dimensional folding of the primary amino acid sequence. The most frequent active site amino acid residues out of the 20 amino acids forming the protein are polar amino acids, aspartate, cysteine, glutamate, histidine, Serine, and lysine. Typically, only 2-3 essential amino acid Oo are involved directly in the bond causing the formation of the product. Glutamate, Aspartate, and histidine are the amino acid residues which also serve as a proton acceptor or donor.

Enzyme and substrate specificity:-



enzyme and substrate;-

1. Bond Specificity

Enzymes that show bond specificity are specific to substrates having similar bonds and structure .Therefore, they bind to substrates that contain specific bonds only, such as ester bonds, glycosidic bonds and peptide bonds. An example of such an enzyme is α-amylase. α-amylase can only hydrolyse α-1,4-glycosidic bonds in starch and glycogen, and not any other types of bonds.

2. Group Specificity

Enzymes that show bond specificity are specific to substrates having similar bonds and structure.Therefore, they bind to substrates that contain specific bonds only, such as ester bonds, glycosidic bonds and peptide bonds. An example of such an enzyme is α-amylase. α-amylase can only hydrolyse α-1,4-glycosidic bonds in starch and glycogen, and not any other types of bonds.

3. Substrate Specificity

Substrate specificity is also known as absolute specificity. Enzymes showing substrate specificity are only specific to one substrate and one reaction. This can be explained through the lock and key theory, which states that the enzyme has a

rigid active site which can only fit substrates with the complementary 3D configuration, explaining the high specificity of such enzymes.

4. Optical Specificity

Optical specificity of enzymes is also known as stereo-specificity. Enzymes showing optical specificity are not only specific to the substrate, but also to its optical configuration .For such enzymes, the spatial arrangement of the substrate is critical in determining if the enzyme will be able to catalyse the reaction. An example of such an enzyme showing optical specificity is the L-amino acid oxidase. L-amino acid oxidase can only bind specifically to L-amino acids. Conversely, D-amino acid oxidase can only catalyse reactions involving D-amino acids.

5. Geometrical Specificity

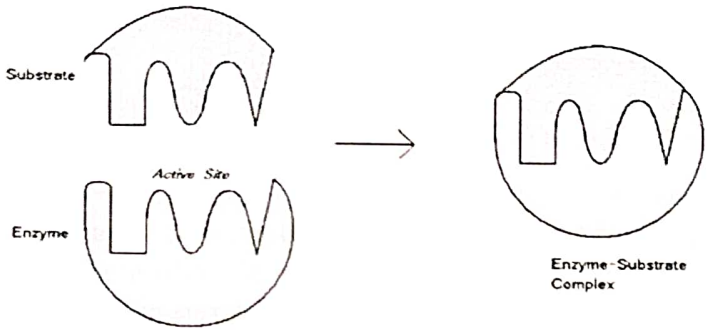
In geometrical specificity, an enzyme can bind to different substrate that have similar molecular geometry. Therefore, specificity is lower in this case. An example of such an enzyme is alcohol dehydrogenase, which is able to catalyse both methanol and ethanol since they have similar molecular geometry

Principles of energy of activation transition state:-

The activation energy of a chemical reaction is kind of like that "hump" you have to get over to get yourself out of bed. Even energy-releasing (exergonic) reactions require some amount of energy input to get going, before they can proceed with their energy-releasing steps. This initial energy input, which is later paid back as the reaction proceeds, is called the activation eenergy Activation energyreleasing with reaction a negative ΔG need energy to proceed? To understand this, we need to look at what actually happens to reactant molecules during a chemical reaction. In order for the reaction to take place, some or all of the chemical bonds in the reactants must be broken so that new bonds, those of the products, can form. To get the bonds into a state that allows them to break, the molecule must be contorted (deformed, or bent) into an unstable state called the transition state.

Lock and key :-

The Lock and Key model is a theory of enzyme action hypothesized by Emil Fischer in 1899. According to Fischer, enzymes exhibit a high degree of specificity to the substances they react with. He proposed that this is due to the shape of the enzyme fitting the shape of the substrate, similar to how a lock only fits a specific key. Using this analogy, the enzyme represents the lock and the substrate represents the key. The order in which the lock and key model works is as follows:



1.The substrate(s) bind to the enzyme at the active site, forming an enzyme-substrate complex.

2.The enzyme facilitates the chemical reaction. This reaction can be a synthesis reaction (building by forming bonds) or digestion (breaking bonds to form new substances).

3.The enzyme releases the product(s) of the reaction. Once an enzyme completes a reaction, it can be reused.

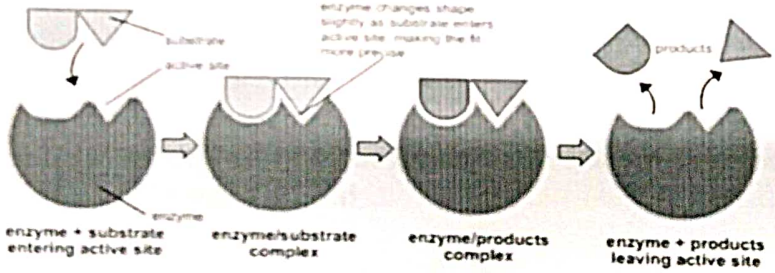
It was later discovered that enzymes do not always show complete specificity to only one type of substrate. In this regard, the Lock and Key model is flawed. Even though many enzymes may react with only one substance, there are also many enzymes that are able to facilitate the same chemical reaction with different, although similarly structured, substrates. For example, there are several protein-digesting enzymes in the

stomach that can break down multiple types of protein. These enzymes include pepsin and chymotrypsin. Synthetic substances that are similarly shaped like the natural substrate will also bind and react with enzymes.

Induced Fit Model Vs. Lock and Key

A more accurate description of enzyme structure is the **Induced Fit model of enzyme action**. The Induced Fit model was proposed by **Daniel Koshland** in 1958. According to Koshland's hypothesis, the active site is shaped similarly enough and has specific chemical properties that attract a substrate to bind. Once the substrate binds, the active site is induced, or prompted, to change shape. This results in a more precise fit. The Induced Fit model better explains the phenomenon of more than one type of substrate binding and reacting to an enzyme when similarly structured.

fundamentals of enzyme assay and enzyme units:- **Enzyme activity = moles of substrate converted per unit time = rate × reaction volume. Enzyme activity is a measure of the quantity of active enzyme present and is thus dependent on conditions, which should be specified. The SI**



unit is the katal, 1 katal = 1 mol s−1, but this is an excessively large unit. A more practical and commonly used value is enzyme unit (U) = 1 μmol min−1. 1 U corresponds to 16.67 nanokatals.Enzyme activity as given in katal generally refers to that of the assumed natural target substrate of the enzyme. Enzyme activity can also be given as that of certain standardized substrates, such as gelatin, then measured in gelatin digesting units (GDU), or milk proteins, then measured in milk clotting units (MCU). The units GDU and MCU are based on how fast one gram of the enzyme will digest gelatin or milk proteins, respectively. 1 GDU equals approximately 1.5 MCU.An increased amount of substrate will

increase the rate of reaction with enzymes, however once past a certain point, the rate of reaction will level out because the amount of active sites available has stayed constant.Specific activity.The specific activity of an enzyme is another common unit. This is the activity of an enzyme per milligram of total protein (expressed in μmol min−1 mg−1). Specific activity gives a measurement of enzyme purity in the mixture. It is the micro moles of product formed by an enzyme in a given amount of time (minutes) under given conditions per milligram of total proteins. Specific activity is equal to the rate of reaction multiplied by the volume of reaction divided by the mass of total protein. The SI unit is katal/kg, but a more practical unit is μmol/mgmin.Specific activity is a measure of enzyme processivity (the capability of enzyme to be processed), at a specific (usually saturating) substrate concentration, and is usually constant for a pure enzyme.An active site titration process can be done for the elimination of errors arising from differences in cultivation batches and/or misfolded enzyme and similar issues. This is a measure of the amount of active enzyme, calculated by e.g. titrating the amount of active sites present by employing an irreversible inhibitor. The specific activity should then be expressed as μmol min−1 mg−1 active enzyme. If the molecular weight of the enzyme is known, the turnover number, or μmol product per second per μmol of active enzyme, can be calculated from the specific activity. The turnover number can be visualized as the number of times each enzyme molecule carries out its catalytic cycle per second.

Factors affecting enzyme activity:-

The six factors are:. (1) Concentration of Enzyme . (2) Concentration of Substrate3. Effect of temperature(4) Effect of pH (5) Effect of Product Concentration and. (6) Effect of Activators.

1. Concentration of Enzyme:

As the concentration of the enzyme is increased, the velocity of the reaction proportionately increases .In fact, this property of enzyme is

made use in determining the activities of serum enzymes for diagnosis of diseases.

2. Concentration of

Increase in the substrate concentration gradually increases the velocity of enzyme reaction within the limited range of substrate levels. A rectangular hyperbola is obtained when velocity is plotted against the substrate concentration

Enzyme kinetics and Km value:

The enzyme € and substrate (S) combine with each other to form an unstable enzyme-substrate complex (ES) for the formation of product (P).

Here k1, k2 and k3 represent the velocity constants for the respective reactions, as indicated by arrows.

Km, the Michaelis-Menten constant (or Brig's and Haldane's constant), is given by the formula

The following equation is obtained after suitable algebraic manipulation.

For the determination of K_m value, the substrate saturation curve (Fig. 66.2) is not very accurate since V_{max} is approached asymptotically. By taking the reciprocals of the equation (1), a straight line graphic representation is obtained.

The Line weaver-Burk plot is shown in Fig. 66.3. It is much easier to calculate the K_m from the intercept on x-axis which is $-(1/K_m)$. Further, the double reciprocal plot is useful in understanding the effect of various inhibitions.

3. Effect of Temperature:

Velocity of an enzyme reaction increases with increase in temperature up to a maximum and then declines. A bell-shaped curve is usually observe The optimum temperature for most of the enzymes is between 40°C-45°C. However, a few enzymes (e.g. venom phosphokinases, muscle adenylate kinase) are active even at 100°C. In general, when the enzymes are exposed to a temperature above 50°C, denaturation leading to derangement in the native (tertiary) structure of the protein and active site are seen. Majority of the enzymes become inactive at higher temperature (above 70

4. Effect of pH:

Increase in the hydrogen ion concentration (pH) considerably influences the enzyme activity and a bell-shaped curve is normally obtained (Fig. 66.5). Each enzyme has an optimum pH at which the velocity is maximum.

Most of the enzymes of higher organisms show optimum activity around neutral pH (6-8). There are, however, many exceptions like pepsin (1-2), acid phosphatase (4-5) and alkaline phosphatase (10-11) for optimu

5. Effect of Product Concentration:

The accumulation of reaction products generally decreases the enzyme velocity. For certain enzymes, the products combine with the active site of enzyme and form a loose complex and, thus, inhibit the enzyme activity. In the living system, this type of inhibition is generally prevented by a quick removal of products formed

6. Effect of Activators:

Some of the enzymes require certain inorganic metallic cations like Mg^{2+}, Mn^{2+}, Zn^{2+}, Ca^{2+}, Co^{2+}, Cu^{2+}, Na^{+}, K^{+} etc. for their optimum activity. Rarely, anions are also needed for enzyme activity e.g. chloride ion (Cl^{-}) for amylase.

Unit-II

BIOENERGITICS AND BIOLOGICAL OXIDATION BIO ENERGITICS

THERMODYNAMIC CONCEPTS

chemical equilibrium, condition in the course of a reversible chemical reaction in which no net change in the amounts of reactants and products occurs. A reversible chemical reaction is one in which the products, as soon as they are formed, react to produce the original reactants. At equilibrium, the two opposing reactions go on at equal rates, or velocities, and hence there is no net change in the amounts of substances involved. At this point the reaction may be considered to be completed; i.e., for some specified reaction condition, the maximum conversion of reactants to products has been attained.

The conditions that pertain to equilibrium may be given quantitative formulation. For example, for the reversible reaction $A \leftrightharpoons B + C$, the velocity of the reaction to the right, r_1, is given by the mathematical expression (based on the law of mass action) $r_1 = k_1(A)$, where k_1 is the reaction-rate constant and the symbol in parentheses represents the concentration of A. The velocity of the reaction to the left, r_2, is $r_2 = k_2(B)(C)$. At equilibrium, $r_1 = r_2$

$$k_1(A)_e = k_2(B)_e(C)_e \quad \text{or}$$
$$k_1/k_2 = (B)_e(C)_e/(A)_e = K.$$

The subscript e represents conditions at equilibrium. For a given reaction, at some specified condition of temperature and pressure, the ratio of the amounts of products and reactants present at equilibrium, each raised to their respective powers, is a constant, designated the equilibrium constant of the reaction and represented by the symbol K. The value of the equilibrium constant varies with the temperature and pressure according to the principle of Le Chatelier.

By methods of statistical mechanics and chemical thermodynamics, it can be shown that the equilibrium constant is related to the change in the thermodynamic quantity called the standard Gibbs free energy accompanying the reaction. The standard Gibbs free energy of the reaction, ΔG°, which is the difference between the sum of the standard free energies of the products and that of the reactants, is equal to the negative natural logarithm of the equilibrium constant multiplied by the so-called gas constant R and the absolute temperature T:

$$\Delta G^\circ = -RT \ln K.$$

The equation allows the calculation of the equilibrium constant, or the relative amounts of products and reactants present at equilibrium, from measured or derived values of standard free energies of substances.

The **thermodynamic free energy** is a concept useful in the thermodynamics of chemical or thermal processes in engineering and science. The change in the free energy is the maximum amount of work that a thermodynamic system can perform in a process at constant temperature, and its sign indicates whether a process is thermodynamically favorable or forbidden. Since free energy usually contains potential energy, it is not absolute but depends on the choice of a zero point. Therefore, only relative free energy values, or changes in free energy, are physically meaningful.

The free energy is a thermodynamic state function, like the internal energy, enthalpy, and entropy.

Free energy is that portion of any first-law energy that is **available** to perform thermodynamic work at constant temperature, *i.e.*, work mediated by thermal energy. Free energy is subject to irreversible loss in the course of such work.[1] Since first-law energy is always conserved, it is evident that free energy is an expendable, second-law kind of energy. Several free energy functions may be formulated based on system criteria. Free energy functions are Legendre transforms of the internal energy.

The Gibbs free energy is given by $G = H - TS$, where H is the enthalpy, T is the absolute temperature, and S is the entropy. $H = U + pV$, where U is the internal energy, p is the pressure, and V is the volume. G is the most useful for processes involving a system at constant pressure p and temperature T, because, in addition to subsuming any entropy change due merely to heat, a change in G also excludes the $p\,dV$ work needed to "make space for additional molecules" produced by various processes. Gibbs free energy change therefore equals work not associated with system expansion or compression, at constant temperature and pressure. (Hence its utility to solution-phase chemists, including biochemists.)

The historically earlier Helmholtz free energy is defined as $A = U - TS$. Its change is equal to the amount of reversible work done on, or obtainable from, a system at constant T. Thus its appellation "work content", and the designation A from *Arbeit*, the German word for work. Since it makes no reference to any quantities involved in work (such as p and V), the Helmholtz function is completely general: its decrease is the maximum amount of work which can be done *by* a system at constant temperature, and it can increase at most by the amount of work done *on* a system isothermally. The Helmholtz free energy has a special theoretical importance since it is proportional to the logarithm of the partition function for the canonical ensemble in statistical mechanics. (Hence its utility to physicists; and to gas-phase chemists and engineers, who do not want to ignore $p\,dV$ work.)

Historically, the term 'free energy' has been used for either quantity. In physics, *free energy* most often refers to the Helmholtz free energy, denoted by A (or F), while in chemistry, *free energy* most often refers to the Gibbs free energy. The values of the two free energies are usually quite similar and the intended free energy function is often implicit in manuscripts and presentations.

Enthalpy a property of a thermodynamic system, is the sum of the system's internal energy and the product of its pressure and volume.[1] It is a state function used in many measurements in chemical, biological, and physical systems at a constant pressure, which is conveniently provided by the large ambient atmosphere. The pressure–volume term expresses the work required to establish the system's physical dimensions, i.e. to make room for it by displacing its surroundings.[2][3] The pressure-volume term is very small for solids and liquids at common conditions, and fairly small for gases. Therefore, enthalpy is a stand-in for energy in chemical systems; bond, lattice, solvation and other "energies" in chemistry are actually enthalpy differences. As a state function, enthalpy depends only on the final configuration of internal energy, pressure, and volume, not on the path taken to achieve it.

In the International System of Units (SI), the unit of measurement for enthalpy is the joule. Other historical conventional units still in use include the calorie and the British thermal unit (BTU).

The total enthalpy of a system cannot be measured directly because the internal energy contains components that are unknown, not easily accessible, or are not of interest in thermodynamics. In practice, a change in enthalpy is the preferred expression for measurements at constant pressure because it simplifies the description of energy transfer. When transfer of matter into or out of the system is also prevented and no electrical or shaft work is done, at constant pressure the enthalpy change equals the energy exchanged with the environment by heat.

In chemistry, the standard enthalpy of reaction is the enthalpy change when reactants in their standard states (p = 1 bar; usually T = 298 K) change to products in their standard states.[4] This quantity is the standard heat of reaction at constant pressure and temperature, but it can be measured by calorimetric methods even if the temperature does vary during the measurement, provided that the initial and final pressure and temperature correspond to the standard state. The value does not depend on the path from initial to final state because enthalpy is a state function.

Enthalpies of chemical substances are usually listed for 1 bar (100 kPa) pressure as a standard state. Enthalpies and enthalpy changes for reactions vary as a function of temperature,[5] but tables generally list the standard heats of formation of substances at 25 °C (298 K). For endothermic (heat-absorbing) processes, the change ΔH is a positive value; for exothermic (heat-releasing) processes it is negative.

The enthalpy of an ideal gas is independent of its pressure or volume, and depends only on its temperature, which correlates to its thermal energy. Real gases at common temperatures and pressures often closely approximate this behavior, which simplifies practical thermodynamic design and analysis.

entropy, the measure of a system's thermal energy per unit temperature that is unavailable for doing useful work. Because work is obtained from ordered molecular motion, the amount of entropy is also a measure of the molecular disorder, or randomness, of a system. The concept of entropy provides deep insight into the direction of spontaneous change for many everyday phenomena. Its introduction by the German physicist Rudolf Clausius in 1850 is a highlight of 19th-century physics.

The idea of entropy provides a mathematical way to encode the intuitive notion of which processes are impossible, even though they would not violate the fundamental law of conservation of energy. For example, a block of ice placed on a hot stove surely melts, while the stove grows cooler. Such a process is called irreversible because no slight change will cause the melted water to turn back into ice while the stove grows hotter. In contrast, a block of ice placed in an ice-water bath will either thaw a little more or freeze a little more, depending on whether a small amount of heat is added to or subtracted from the system. Such a process is reversible because only an infinitesimal amount of heat is needed to change its direction from progressive freezing to progressive thawing. Similarly, compressed gas confined in a cylinder could either expand freely into the atmosphere if a valve were opened (an irreversible process), or it could do useful work by pushing a moveable piston against the force needed to confine the gas. The latter process is reversible because only a slight increase in the restraining force could reverse the direction of the process from expansion to compression. For reversible processes the system is in equilibrium with its environment, while for irreversible processes it is not.To provide a quantitative measure for the direction of spontaneous

Tochange, Clausius introduced the concept of entropy as a precise way of expressing the second law of thermodynamics. The Clausius form of the second law states that spontaneous change for an irreversible process in an isolated system (that is, one that does not exchange heat or work with its surroundings) always proceeds in the direction of increasing entropy. For example, the block of ice and the stove constitute two parts of an isolated system for which total entropy increases as the ice melts.

CHANGE IN BIOLOGICAL TRANSFORMATION IN LIVING SYSTEM

For chemical reactions occurring in solution, we can define a **system** as all of the reactants and products present, the solvent, and the immediate atmosphere, in short, everything within a defined region of space.
The system and its surroundings together constitute the **Universe**. The system has been classified into three levels based on energy transformation. Let us see the energy transformation in nature.

1. **Closed System**
2. **Isolated System**
3. **Open System**

1. Closed System

If the system exchanges neither matter nor energy with its surroundings, it is said to be a "Closed system". **E.g:** Boiling water in a cold beaker, Chlorophyll system. In the system, no change in matter, but can exchange heat through the beaker edges.

$$\Delta m = 0$$
$$\Delta Q \neq 0$$

Δm = Change in MASS
ΔQ = Change in HEAT

2. Isolated System

If the system exchanges energy but not matter with its surrounding. it is an "Isolated system". **Eg:** Earth System.

3. Open System

If it exchanges both energy and material with its surroundings, it is an "Open system". **Eg:** Boiling water in open beaker in the laboratory, Cell system. In the system, both energy and material can exchange with its surroundings.

$$\Delta m \neq 0$$
$$\Delta Q \neq 0$$

Living organisms is an open system. it exchanges both matter and energy with its surrounding. Living organisms use either of two strategies to derive energy from their surroundings.

1. They take up chemical fuels from the environment and extract energy by oxidizing them.
2. They absorb energy from sunlight.

Focus points on Energy transformation

- Living cells are "**chemical engines**" that function at constant temperatures.
- Living cells at any given moment exist in a steady state in which the rate of input of matter equals the rate of output of matter.
- Organisms transfer energy and matter from their surroundings.
- Organisms are never at equilibrium with their surroundings.
- Organisms are islands of low entropy in an increasingly random universe.

Understanding Terms: Before studying thermodynamics, we want to understand some terms.

1. **System:** The Collection of matter under study and refer to the rest of the universe.
2. **Surrounding:** Everything outside of the system.
3. **Energy:** Energy is the capacity to do work
4. **Entropy:** The randomness of the components of a chemical system is expressed as "Entropy", denoted simply as "S".
5. **Enthalpy:** The heat content of a system, denoted simply as "H".

Energy is defined as **the capacity to do work,** which is the product of a given force acting through a given distance.

Work = Force X Distance

In living organisms, the following are some of the sources of energy and forms of biological work. Here are the basic examples of energy transformation.

1. **Muscle Contraction**
2. **Synthesis of Biomolecules**
3. **Membrane function**
4. **Generation and conduction of nerve impulse**

High energy compounds

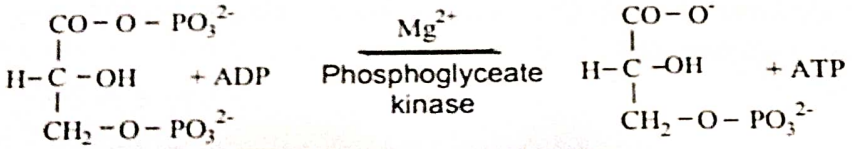
The high energy compound is the ATP. The other high energy compoundsinclude ADP,1,3-diphospho glycerate, phosphoenol pyruvate and also creatine phosphate.

The phosphate group of the high energy phosphate may transfer directly to another organic compound. For this reason the term group transfer potential is preferred by some high energy bond. However, the phosphorylated compound may or may not have high energy phosphate bond, though the total energy content of the molecule is higher than a non phosphorylated compound.

Storage form of high energy compounds

They are called as **phosphogens** and help to store the high energy. The example for this the creatine phosphate present in the vertebrate muscles, the reaction works in both directions it is a reversible reaction form ATP when ATP is required. When ATP is more, creatine reacts with ATP and forms the phosphocreatine.

1. 1, 3-diphosphoglycerate



1,3-diphosphoglycerate 3-phosphoglycerate

One of the phosphate groups undergoes hydrolysis to form the acid and a phosphate ion, giving off energy. This first energy producing reaction is coupled with the next endothermic reaction making ATP. The phosphate is transferred directly to an ADP to make ATP and this is catalysed by phosphoglycerate Kinase enzyme. Since one molecule of glucose yield 2 molecule of Glyceraldehyde 3-phosphate, 2 high energy ATP are produced for one molecule of glucose.

Role of Phosphoenol pyruvate

Unit 3

Carbohydrates

Anabolism and Catabolism Definition and Examples

Anabolism and catabolism are the two broad types of biochemical reactions that make up metabolism. Anabolism builds complex molecules from simpler ones, while catabolism breaks large molecules into smaller ones.

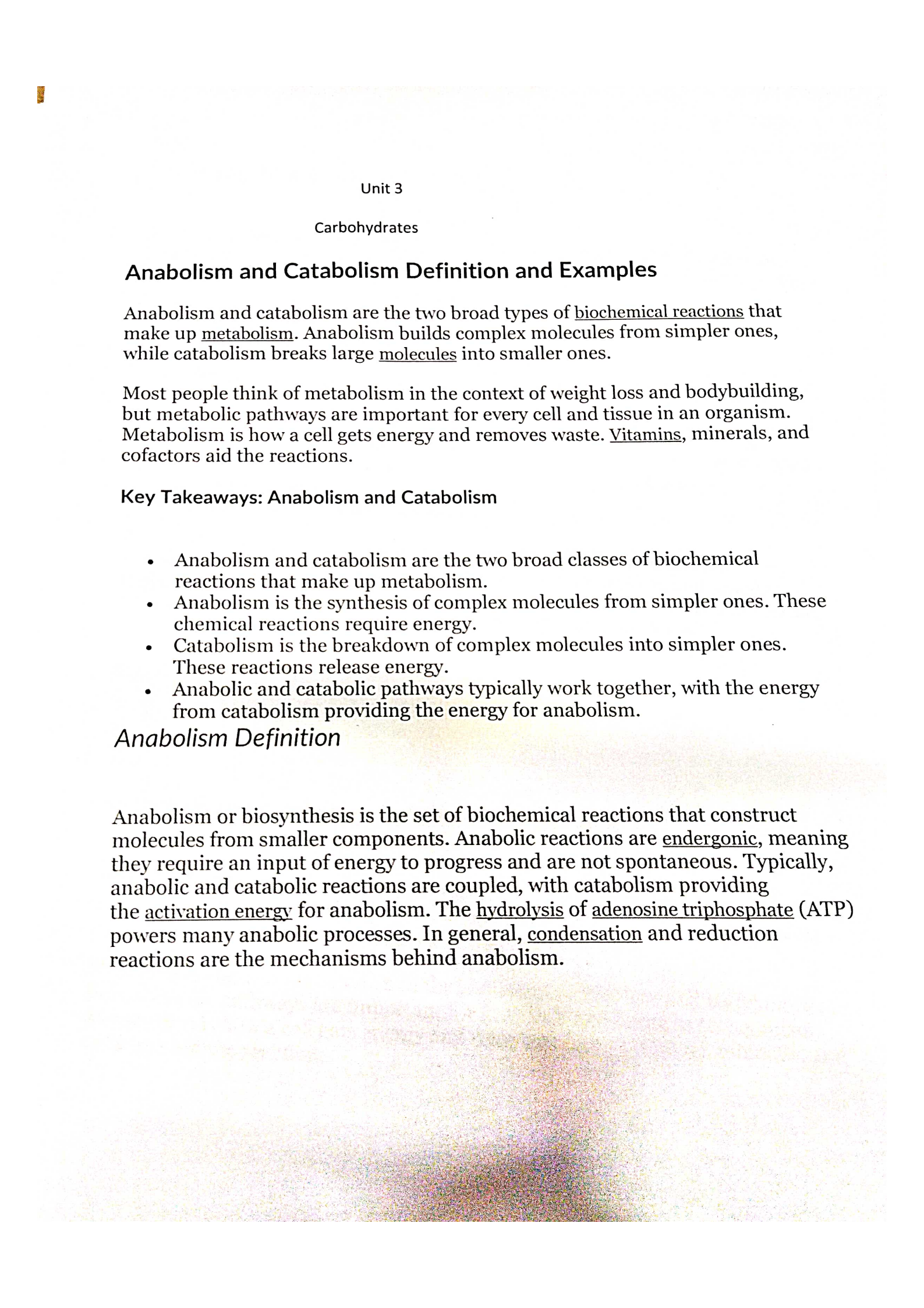
Most people think of metabolism in the context of weight loss and bodybuilding, but metabolic pathways are important for every cell and tissue in an organism. Metabolism is how a cell gets energy and removes waste. Vitamins, minerals, and cofactors aid the reactions.

Key Takeaways: Anabolism and Catabolism

- Anabolism and catabolism are the two broad classes of biochemical reactions that make up metabolism.
- Anabolism is the synthesis of complex molecules from simpler ones. These chemical reactions require energy.
- Catabolism is the breakdown of complex molecules into simpler ones. These reactions release energy.
- Anabolic and catabolic pathways typically work together, with the energy from catabolism providing the energy for anabolism.

Anabolism Definition

Anabolism or biosynthesis is the set of biochemical reactions that construct molecules from smaller components. Anabolic reactions are endergonic, meaning they require an input of energy to progress and are not spontaneous. Typically, anabolic and catabolic reactions are coupled, with catabolism providing the activation energy for anabolism. The hydrolysis of adenosine triphosphate (ATP) powers many anabolic processes. In general, condensation and reduction reactions are the mechanisms behind anabolism.



Anabolism Examples

Anabolic reactions are those that build complex molecules from simple ones. Cells use these processes to make polymers, grow tissue, and repair damage. For example:

- Glycerol reacts with fatty acids to make lipids:
  $CH_2OHCH(OH)CH_2OH +$
  $C_{17}H_{35}COOH \rightarrow CH_2OHCH(OH)CH_2OOCC_{17}H_{35}$
- Simple sugars combine to form disaccharides and water:
  $C_6H_{12}O_6 + C_6H_{12}O_6 \rightarrow C_{12}H_{22}O_{11} + H_2O$
- Amino acids join together to form dipeptides:
  $NH_2CHRCOOH + NH_2CHRCOOH \rightarrow NH_2CHRCONHCHRCOOH + H_2O$
- Carbon dioxide and water react to form glucose and oxygen in photosynthesis:
  $6CO_2 + 6H_2O \rightarrow C_6H_{12}O_6 + 6O_2$

Anabolic hormones stimulate anabolic processes. Examples of anabolic hormones include insulin, which promotes glucose absorption, and anabolic steroids, which stimulate muscle growth. Anabolic exercise is anaerobic exercise, such as weightlifting, which also builds muscle strength and mass.

Anabolism and Catabolism Definition and Examples

Anabolism and catabolism are the two broad types of biochemical reactions that make up metabolism. Anabolism builds complex molecules from simpler ones, while catabolism breaks large molecules into smaller ones.

Most people think of metabolism in the context of weight loss and bodybuilding, but metabolic pathways are important for every cell and tissue in an organism. Metabolism is how a cell gets energy and removes waste. Vitamins, minerals, and cofactors aid the reactions.

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Catabolism Definition

Catabolism is the set of biochemical reactions that break down complex molecules into simpler ones. Catabolic processes are thermodynamically favorable and spontaneous, so cells use them to generate energy or to fuel anabolism. Catabolism is exergonic, meaning it releases heat and works via hydrolysis and oxidation.

Cells can store useful raw materials in complex molecules, use catabolism to break them down, and recover the smaller molecules to build new products. For example, catabolism of proteins, lipids, nucleic acids, and polysaccharides generates amino acids, fatty acids, nucleotides, and monosaccharides, respectively. Sometimes waste products are generated, including carbon dioxide, urea, ammonia, acetic acid, and lactic acid.

Catabolism Examples

Catabolic processes are the reverse of anabolic processes. They are used to generate energy for anabolism, release small molecules for other purposes, detoxify chemicals, and regulate metabolic pathways. For example:

- During cellular respiration, glucose and oxygen react to yield carbon dioxide and water
  $C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$
- In cells, hydroxide peroxide decomposes into water and oxygen:
  $2H_2O_2 \rightarrow 2H_2O + O_2$

Many hormones act as signals to control catabolism. The catabolic hormones include adrenaline, glucagon, cortisol, melatonin, hypocretin, and cytokines. Catabolic exercise is aerobic exercise such as a cardio workout, which burns calories as fat (or muscle) is broken down.

Amphibolic Pathways

A metabolic pathway that can be either catabolic or anabolic depending on energy availability is called an amphibolic pathway. The glyoxylate cycle and the citric acid cycle are examples of amphibolic pathways. These cycles can either produce energy or use it, depending on cellular needs.

- **The citric acid cycle**
- Overview and steps of the citric acid cycle, also known as the Krebs cycle or tricarboxylic acid (TCA) cycle.

Introduction

How important is the citric acid cycle? So important that it has not one, not two, but three different names in common usage today!

The name we'll primarily use here, the citric acid cycle, refers to the first molecule that forms during the cycle's reactions—citrate, or, in its protonated form, citric acid. However, you may also hear this series of reactions called the tricarboxylic acid (TCA) cycle, for the three carboxyl groups on its first two intermediates, or the Krebs cycle, after its discoverer, Hans Krebs.

Whatever you prefer to call it, the citric cycle is a central driver of cellular respiration. It takes acetyl \text{CoA}CoAstart text, C, o, A, end text—produced by the oxidation of pyruvate and originally derived from glucose—

as its starting material and, in a series of redox reactions, harvests much of its bond energy in the form of \text{NADH}NADHstart text, N, A, D, H, end text, \text{FADH}_2FADH2start text, F, A, D, H, end text, start subscript, 2, end subscript, and \text{ATP}ATPstart text, A, T, P, end text molecules. The reduced electron carriers—\text{NADH}NADHstart text, N, A, D, H, end text and \text{FADH}_2FADH2start text, F, A, D, H, end text, start subscript, 2, end subscript—generated in the TCA cycle will pass their electrons into the electron transport chain and, through oxidative phosphorylation, will generate most of the ATP produced in cellular respiration.

Below, we'll look in more detail at how this remarkable cycle works.

Overview of the citric acid cycle

In eukaryotes, the citric acid cycle takes place in the matrix of the mitochondria, just like the conversion of pyruvate to acetyl \text{CoA}CoAstart text, C, o, A, end text. In prokaryotes, these steps both take place in the cytoplasm. The citric acid cycle is a closed loop; the last part of the pathway reforms the molecule used in the first step. The cycle includes eight major steps.

Unit- 4 :

NADPH is able to give antioxidants their constant flow of electrons to fight oxygen crime.

• Carbohydrate Metabolism Disorders

- Metabolism is the process your body uses to make energy from the food you eat. Food is made up of proteins, carbohydrates, and fats. Chemicals in your digestive system (enzymes) break the food parts down into sugars and acids, your body's fuel. Your body can use this fuel right away, or it can store the energy in your body tissues. If you have a metabolic disorder, something goes wrong with this process.
- Carbohydrate metabolism disorders are a group of metabolic disorders. Normally your enzymes break carbohydrates down into glucose (a type of sugar). If you have one of these disorders, you may not have enough enzymes to break down the carbohydrates. Or the enzymes may not work properly. This causes a harmful amount of sugar to build up in your body. That can lead to health problems, some of which can be serious. Some of the disorders are fatal.
- These disorders are inherited. Newborn babies get screened for many of them, using blood tests. If there is a family history of one of these disorders, parents can get genetic testing to see whether they carry the gene. Other genetic tests can tell whether the fetus has the disorder or carries the gene for the disorder.
- Treatments may include special diets, supplements, and medicines. Some babies may also need additional treatments, if there are complications. For some disorders, there is no cure, but treatments may help with symptoms.

• / 3

- **metabolic disease**
- Table of Contents
- **Disorders of carbohydrate metabolism**
- The metabolism of the carbohydrates galactose, fructose, and glucose is intricately linked through interactions between different enzymatic pathways, and disorders that affect these pathways may have symptoms ranging from mild to severe or even life-threatening. Clinical features include various combinations of hypoglycemia (low blood sugar), liver enlargement, and muscle pain. Most of

these disorders can be treated, or at least controlled, with specific dietary interventions.

- ***Galactose and fructose disorders***

Galactosemia usually is caused by a defective component of the second major step in the metabolism of the sugar galactose. When galactose is ingested, as in milk, galactose-1-phosphate accumulates. Therefore, the clinical manifestations ofgalactosemia begin when milk feeding is started. If the feeding is not stopped, infants with the disorder will develop lethargy, ***jaundice***, progressive liver dysfunction, kidney disease, and weight loss. They are also susceptible to severe bacterial infections, especially by ***Escherichia coli***. Cataracts develop if the diet remains galactose-rich. ***Intellectual*** disability occurs in most infants with galactosemia if the disorder is left untreated or if treatment is delayed. Therapy is by exclusion of galactose from the diet and results in the reversal of most symptoms. Most children have normal intelligence, although they may have learning difficulties and a degree of ***intellectual disability*** despite early therapy.

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- ***In essence, metabolism involves all the physical and chemical processes by which cells are produced and...***

- Hereditary fructose intolerance (HFI) is caused by a deficiency of the liver ***enzyme fructose-1-phosphate aldolase***. Symptoms of HFI appear after the ingestion of fructose and thus present later in life than do those of galactosemia. ***Fructose*** is present in ***fruits***, table sugar (***sucrose***), and infant formulas containing sucrose. ***Symptoms*** may include failure to gain weight satisfactorily, ***vomiting***, ***hypoglycemia***, liver dysfunction, and ***kidney*** defects. Older children with HFI tend to avoid sweet foods and may have teeth notable for the absence of caries. Children with the disorder do very well if they avoid dietary fructose and sucrose.

- Fructose 1,6-diphosphatase deficiency is associated with an impaired ability to form glucose from other substrates (a process called ***gluconeogenesis***). Symptoms include severe ***hypoglycemia***, intolerance to ***fasting***, and enlargement of the liver. Rapid treatment of hypoglycemic episodes with

intravenous fluids containing glucose and the avoidance of fasting are the mainstays of therapy. Some patients require continuous overnight drip feeds or a bedtime dose of cornstarch in order to control their tendency to develop hypoglycemia.

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- Glycogen storage disorders

- The brain, red blood cells, and inner portion of the ***adrenal gland*** (adrenal medulla) depend on a constant supply of ***glucose*** for their metabolic functions. This supply begins in the ***small intestine***, where transport ***proteins*** mediate the uptake of glucose into cells lining the gut. Glucose subsequently passes into the bloodstream and then the ***liver***, where it is stored as ***glycogen***. In times of starvation or fasting or when the body requires a sudden energy supply, glycogen is broken down into glucose, which is then released into the blood. ***Muscle*** tissue also has its own glycogen stores, which may be degraded

during ***exercise***. If enzymes responsible for glycogen ***degradation*** are blocked so that glycogen remains in the liver or muscle, a number of conditions known as ***glycogen storage disorders*** (GSD) can arise. Depending upon which enzyme is affected, these conditions may affect the ***liver***, muscles, or both. In GSD type I

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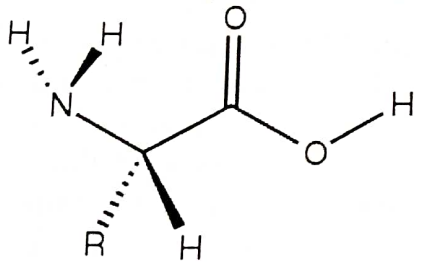
UNIT-5

1. GENERAL REACTIONS OF AMINO ACIDS METABOLISM .
2. TRANSAMINATION .
3. DECARBOXYLATION .
4. DEAMINATION .
5. UREA CYCLE .
6. REGULATION .
7. CATABOLISM OF CARBON SCELETON OF AMINO ACIDS .
8. GLUCOGENIC & KETOGENIC AMINO ACID .
9. METABOLISM OF GLYCINE , SERINE , ASPARTIC ACID , METHIONINE PHENYLALANINE & LEUCINE .
10. BIOSYNTHESIS OF CREATINE .
11. INBORN ERRORS OF AROMATIC & BRANCHED CHAIN AMINO ACID METABOLISM

General reactions of Amino acids metabolism

Amino acids are organic compounds that contain amino[a] (−NH+3) and carboxylate −CO−2 functional groups, along with a side chain (R group) specific to each amino acid.[1] The elements present in every amino acid are carbon (C), hydrogen (H), oxygen (O), and nitrogen (N); in addition sulfur (S) is present in the side chains of cysteine and methionine, and selenium (Se) in the less common amino acid selenocysteine. More than 500 naturally occurring amino acids are known to constitute monomer units of peptides, including proteins, as of 2020[2] (though only 20 appear in the genetic code, plus selenocysteine, which is encoded in a special way).[3]



Structure of a generic L-amino acid in the "neutral" form needed for defining a systematic name, without implying that this form actually exists in detectable amounts either in aqueous solution or in the solid state.

Amino acids are formally named by the IUPAC-IUBMB Joint Commission on Biochemical Nomenclature[4] in terms of the fictitious "neutral" structure shown in the illustration. For example, the systematic name of alanine is 2-aminopropanoic acid, based on the formula $CH_3{-}CH(NH_2){-}COOH$. The Commission justified this approach as follows:

The systematic names and formulas given refer to hypothetical forms in which amino groups are unprotonated and carboxyl groups are undissociated. This convention is useful to avoid various nomenclatural problems but should not be taken to imply that these structures represent an appreciable fraction of the amino-acid molecules.

They can be classified according to the locations of the core structural functional groups, as alpha- (α-), beta- (β-), gamma- (γ-) or delta- (δ-) amino acids; other categories relate to polarity, ionization, and side chain group type (aliphatic, acyclic, aromatic, containing hydroxyl or sulfur, etc.). In the form of proteins, amino acid residues form the second-largest component (water is the largest) of human muscles and other tissues.[5] Beyond their role as residues in

proteins, amino acids participate in a number of processes such as neurotransmitter transport and biosynthesis.

General structureEdit

In the structure shown at the top of the page R represents a side chain specific to each amino acid. The carbon atom next to the carboxyl group is called the α–carbon. Amino acids containing an amino group bonded directly to the α-carbon are referred to as *α-amino acids*.[19] These include proline and hydroxyproline,[c] which are secondary amines. In the past they were often called *imino acids*, a misnomer because they do not contain an imine grouping HN=C.[20] The obsolete term remains frequent.

IsomerismEdit

The common natural forms of amino acids have the structure −NH+3 (−NH+2− in the case of proline) and −CO−2 functional groups attached to the same C atom, and are thus α-amino acids. With the exception of achiral glycine, natural amino acids have the L configuration,[21] and are the only ones found in proteins during translation in the ribosome.

The L and D convention for amino acid configuration refers not to the optical activity of the amino acid itself but rather to the optical activity of the isomer of glyceraldehyde from which that amino acid can, in theory, be synthesized (D-glyceraldehyde is dextrorotatory; L-glyceraldehyde is levorotatory).

An alternative convention is to use the (*S*) and (*R*) designators to specify the *absolute configuration*.[22] Almost all of the amino acids in proteins are (*S*) at the α carbon, with cysteine being (*R*) and glycine non-chiral.[23] Cysteine has its side chain in the same geometric location as the other amino acids, but the *R/S* terminology is reversed because sulfur has higher atomic number compared to the carboxyl oxygen which gives the side chain a higher priority by the **Cahn-Ingold-Prelog sequence rules**, whereas the atoms in most other side chains give them lower priority compared to the carboxyl group.[22]

D-amino acid residues are found in some proteins, but they are rare.

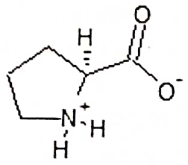
Side chainsEdit

Amino acids are designated as α- when the amino nitrogen atom is attached to the α-carbon, the carbon atom adjacent to the carboxylate group.

In all cases below in this section the values (if any) refer to the ionization of the groups as amino acid residues in proteins. They are not values for the free amino acids (which are of little biochemical importance).

Aliphatic side-chainsEdit

Several side-chains contain only H and C, and do not ionize. These are as follows (with three- and one-letter symbols in parenthesis):



Structure of proline

- Glycine (Gly, G): H−
- Alanine (Ala, A): CH_3−
- Valine (Val, V): $(CH_3)_2CH$−
- Leucine (Leu, L): $(CH_3)_2CHCH_2$−
- Isoleucine (Ile, I): $CH_3CH_2CH(CH_3)$
- Proline (Pro, P): $-CH_2CH_2CH_2-$ cyclized onto the amine

Polar neutral side-chainsEdit

Two aminoacids contains alcohol side-chains. These do not ionize in normal conditions, though one, serine, becomes deprotonated during the catalysis by serine proteases: this is an example of severe perturbation, and is not characteristic of serine residues in general.

- Serine (Ser, S, no when not severely perturbed): $HOCH_2$−
- Threonine (Thr, T, no): CH_3CHOH−

Threonine has two chiral centers, not only the L (2*S*) chiral center at the α-carbon shared by all amino acids apart from achiral glycine, but also (3*R*) at the β-carbon. The full stereochemical specification is L-threonine (2*S*,3*R*).

Amide side-chainsEdit

Two amino acids have amide side-chains, as follows:

- Asparagine (Asn, N): NH_2COCH_2−
- Glutamine (Gln, Q): $NH_2COCH_2CH_2$−

These side-chains do not ionize in the normal range of pH.

Sulfur-containing side-chainsEdit

Two side-chains contain sulfur atoms, of which one ionizes in the normal range (with indicated) and the other does not:

- Cysteine (Cys, C,): $HSCH_2-$
- Methionine (Met, M, no): $CH_3SCH_2CH_2-$

Aromatic side-chainsEdit

Side-chains of phenylalanine (left), tyrosine (middle) and tryptophan (right)

Three amino acids have aromatic ring structures as side-chains, as illustrated. Of these, tyrosine ionizes in the normal range; the other two do not).

- Phenylalanine (Phe, F, no): left in the illustration
- Tyrosine (Tyr, Y,): middle in the illustration
- Tryptophan (Trp, W, no): right in the illustration

Anionic side-chainsEdit

Two amino acids have side-chains that are anions at ordinary pH. Although the misnomer is so widespread as to be ineradicable, they should **not** be called *acidic amino acids*, because they act as Brønsted **bases** in all circumstances except for enzymes like pepsin that act in environments of very low pH like the mammalian stomach.

- Aspartate (**not** "aspartic acid", Asp, D,): $^-O_2CCH_2-$
- Glutamate (**not** "glutamic acid", Glu, E,): $^-O_2CCH_2CH_2-$

Cationic side-chainsEdit

Side-chains of histidine (left), lysine (middle) and arginine (right)

There are three amino acids with side-chains that are cations at neutral pH (though in one, histidine, cationic and neutral forms both exist). They are commonly called *basic amino acids*, but this term is misleading: histidine can act both as a Brønsted acid and as a Brønsted base at neutral pH, lysine acts as a Brønsted acid, and arginine has a fixed positive charge and does not ionize in neutral conditions. The names *histidinium, lysinium* and *argininium* would be more accurate names for the structures, but have essentially no currency.

- Histidine (His, H,): Protonated and deprotonated forms in equilibrium are shown at the left of the image
- Lysine (Lys, K,): Shown in the middle of the image
- Arginine (Arg, R,): Shown at the right of the image

β- and γ-amino acidsEdit

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β- and γ-amino acidsEdit

Amino acids with the structure NH+3–CXY–CO–3, such as β-alanine, a component of carnosine and a few other peptides, are β-amino acids. Ones with the structure NH+3–CXY–CXY–CO–3 are γ-amino acids, and so on, where X and Y are two substituents (one of which is normally H).[4]

ZwitterionsEdit

Main article: Zwitterion

Ionization and Brønsted character of N-terminal amino, C-terminal carboxylate, and side chains of amino acid residues

In aqueous solution amino acids at moderate pH exist as zwitterions, i.e. as dipolar ions with both NH+3 and CO–2 in charged states, so the overall structure is NH+3–CHR–CO–2. At physiological pH the so-called "neutral forms" $–NH_2–CHR–CO_2H$ are not present to any measurable degree.[24] Although the two charges in the real structure add up to zero it is misleading and wrong to call a species with a net charge of zero "uncharged".

At very low pH (below 3), the caboxylate group becomes protonated and the structure becomes an ammonio carboxylic acid, $NH+3–CHR–CO_2H$. This is relevant for enzymes like pepsin that are active in acidic environments such as the mammalian stomach and lysosomes, but does not significantly apply to intracellular enzymes. At very high pH (greater than 10, not normally seen in physiological conditions), the ammonio group is deprotonated to give $NH_2–CHR–CO–2$.

Although various definitions of acids and bases are used in chemistry, the only one that is useful for chemistry in aqueous solution is that of Brønsted:[25] an acid is a species that can donate a proton to another species, and a base is one that can accept a proton. This criterion is used to label the groups in the above illustration. Notice that aspartate and glutamate are the principal groups that act as Brønsted bases, and the common references to these as *acidic amino acids* (together with the C terminal) is completely wrong and misleading. Likewise the so-called *basic amino acids* include one (histidine) that acts as both a Brønsted acid and a base, one (lysine) that acts primarily as a Brønsted acid, and one (arginine) that is normally irrelevant to acid-base behavior as it has a fixed positive charge. In addition, tyrosine and cysteine, which act primarily as acids at neutral pH, are usually forgotten in the usual classification.

Isoelectric pointEdit

Composite of titration curves of twenty proteinogenic amino acids grouped by side chain category

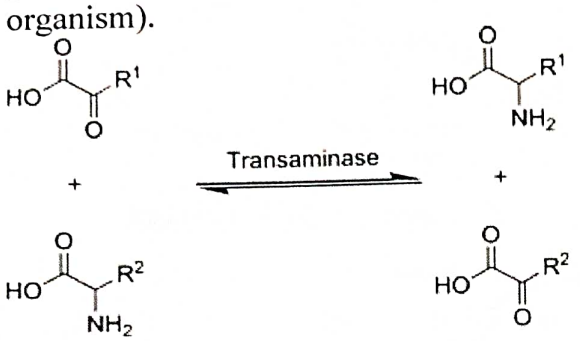
For amino acids with uncharged side-chains the zwitterion predominates at pH values between the two pK_a values, but coexists in equilibrium with small amounts of net negative and net positive ions. At the midpoint between the two pK_a values, the trace amount of net negative and trace of net positive ions balance, so that average net charge of all forms present is zero.[26] This pH is known as the isoelectric point pI, so $pI = 1/2(pK_{a1} + pK_{a2})$.
For amino acids with charged side chains, the pK_a of the side chain is involved. Thus for aspartate or glutamate with negative side chains, the terminal amino group is essentially entirely in the charged form NH+3, but this positive charge needs to be balanced by the state with just one C-terminal carboxylate group is negatively charged. This occurs halfway between the two carboxylate pK_a values: $pI = 1/2(pK_{a1} + pK_{a(R)})$, where $pK_{a(R)}$ is the side chain pK_a.

Similar considerations apply to other amino acids with ionizable side-chains, including not only glutamate (similar to aspartate), but also cysteine, histidine, lysine, tyrosine and arginine with positive side chains

Amino acids have zero mobility in electrophoresis at their isoelectric point, although this behaviour is more usually exploited for peptides and proteins than single amino acids. Zwitterions have minimum solubility at their isoelectric point, and some amino acids (in particular, with nonpolar side chains) can be isolated by precipitation from water by adjusting the pH to the required isoelectric point.

Transamination

Transamination, a chemical reaction that transfers an amino group to a ketoacid to form new amino acids. This pathway is responsible for the deamination of most amino acids. This is one of the major degradation pathways which convert essential amino acids to non-essential amino acids (amino acids that can be synthesized de novo by the organism).



Aminotransfer reaction between an amino acid and an alpha-keto acid

Transamination in biochemistry is accomplished by enzymes called transaminases or aminotransferases. α-ketoglutarate acts as the predominant amino-group acceptor and produces glutamate as the new amino acid.

Aminoacid + α-ketoglutarate ↔ α-keto acid + Glutamate

Glutamate's amino group, in turn, is transferred to oxaloacetate in a second transamination reaction yielding aspartate.

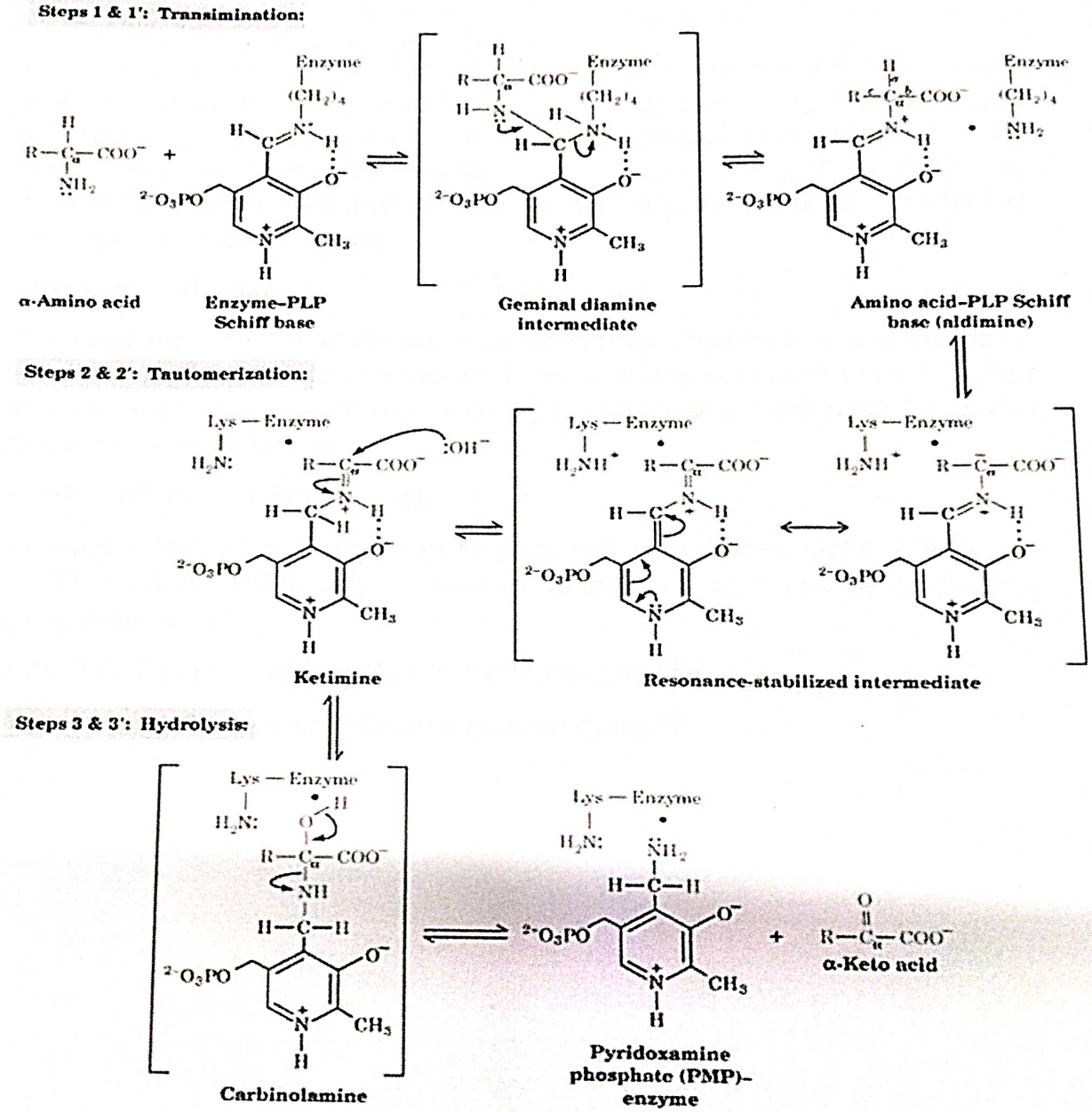
Glutamate + oxaloacetate ↔ α-ketoglutarate + aspartate

Transamination, a

Mechanism of ActionEdit

Transamination catalyzed by aminotransferase occurs in two stages. In the first step, the α amino group of an amino acid is transferred to the enzyme, producing the corresponding α-keto acid and the aminated enzyme. During the second stage, the amino group is transferred to the keto acid acceptor, forming the amino acid product while regenerating the enzyme. The chirality of an amino acid is determined during transamination. For the reaction to complete, aminotransferases require participation of aldehyde containing coenzyme, **pyridoxal-5'-phosphate (PLP)**, a derivative of Pyridoxine (Vitamin B_6). The amino group is accommodated by conversion of this coenzyme to **pyridoxamine-5'-phosphate (PMP). PLP** is covalently attached to the enzyme via a Schiff Base linkage formed by the condensation of its aldehyde group

with the ε-amino group of an enzymatic Lys residue. The Schiff base, which is conjugated to the enzyme's pyridinium ring, is the focus of the coenzyme activity.



Ping Pong Bi Bi mechanism of PLP dependent enzyme catalyzed transamination. Aminotransferase reaction occurs in two stages consisting of three steps: Transimination, Tautomerisation and Hydolysis. In the first stage, alpha amino group of the aminoacid is transferred to PLP yielding an alpha

ketoacid and PMP. In the second stage of the reaction, in which the amino group of PMP is transferred to a different alpha Ketoacid to yield a new alpha amino acid and PLP.

The product of transamination reactions depend on the availability of α-keto acids. The products usually are either alanine, aspartate or glutamate, since their corresponding alpha-keto acids are produced through metabolism of fuels. Being a major degradative aminoacid pathway, lysine, proline and threonine are the only three amino acids that do not always undergo transamination and rather use respective dehydrogenase.

Alternative Mechanism

A second type of transamination reaction can be described as a nucleophilic substitution of one amine or amide anion on an amine or ammonium salt.[1] For example, the attack of a primary amine by a primary amide anion can be used to prepare secondary amines:

$$RNH_2 + R'NH^- \rightarrow RR'NH + NH_2^-$$

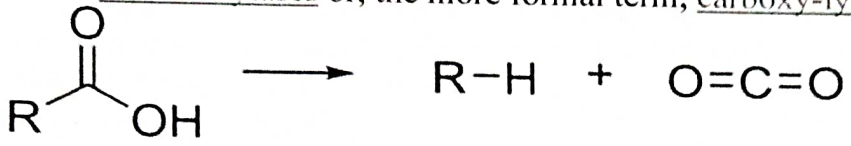
Symmetric secondary amines can be prepared using Raney nickel ($2RNH_2 \rightarrow R_2NH + NH_3$). And finally, quaternary ammonium salts can be dealkylated using ethanolamine:

$$R_4N^+ + NH_2CH_2CH_2OH \rightarrow R_3N + RN^+H_2CH_2CH_2OH$$

Aminonaphthalenes also undergo transaminations.[2]

Decarboxylation

Decarboxylation is a chemical reaction that removes a carboxyl group and releases carbon dioxide (CO_2). Usually, decarboxylation refers to a reaction of carboxylic acids, removing a carbon atom from a carbon chain. The reverse process, which is the first chemical step in photosynthesis, is called carboxylation, the addition of CO_2 to a compound. Enzymes that catalyze decarboxylations are called decarboxylases or, the more formal term, carboxy-lyases (EC number 4.1.1).



Decarboxylation

In organic chemistry Edit

The term "decarboxylation" usually means replacement of a carboxyl group (-COOH) with a hydrogen atom:

$$RCO_2H \rightarrow RH + CO_2$$

Decarboxylation is one of the oldest known organic reactions. It is one of the processes assumed to accompany pyrolysis and destructive distillation. Metal salts, especially copper compounds,[1] facilitate the reaction via the intermediacy of metal carboxylate complexes. Decarboxylation of aryl carboxylates can generate the equivalent of the corresponding aryl anion, which in turn can undergo cross coupling reactions.[2]

Decarboxylation of alkanoic acids is often slow. Thus, typical fatty acids do not decarboxylate readily. Overall, the facility of decarboxylation depends upon stability of the carbanion intermediate R^- .[3][4] Important exceptions are the decarboxylation of beta-keto acids, β,γ-unsaturated acids, and α-phenyl, α-nitro, and α-cyanoacids. Such reactions are accelerated due to the formation of a zwitterionic tautomer in which the carbonyl is protonated and the carboxyl group is deprotonated.[5]

Named decarboxylation reactions Edit

Decarboxylations are the bases of many named reactions. These include Barton decarboxylation, Kolbe electrolysis, Kochi reaction, and Hunsdiecker reaction. All are radical reactions. The Krapcho decarboxylation is a related decarboxylation of an ester. The Tsuji–Trost reaction involves the intermediacy of an allyl complex.

In ketonic decarboxylation a carboxylic acid is converted to a ketone.