Amino Acids

I. Introduction

Protein is a polymer of amino acids and serves as a component of body tissues, enzymes, hormones, etc., and is also an essential substance as a nutrient and as a source of energy. The nutritional value of protein is mainly determined by the types and amount of constituent amino acids.

Although more than 300 different amino acids have been described in nature, only 20 are commonly found as constituents of mammalian proteins (Table 1). [Note: These are the only amino acids that are coded for by DNA]. Of these, nine are dietarily essential for adults, as they cannot be made by the body in sufficient quantity. Children require arginine. The foods we consume must supply ample amino acids for optimal health. When we consume meat, milk, eggs, or other protein foods, the proteins are digested, or broken down, into amino acids. These amino acids are then absorbed through the intestinal lining, taken directly into the bloodstream, and transported to sites where they will be utilized. The body rapidly absorbs "free-form" (individual) amino acids.

Table 1: The 20 Common Amino Acids

Amino Acids	Three-letter abbreviations	One-letter symbol
1. Glycine	Gly	G
2. Alanine	Ala	A
3. Proline	Pro	P
4. Valine	Val	V
5. Leucine	Leu	L
6. Isoleucine	Ile	I
7. Methionine	Met	M
8. Phenylalanine	Phe	F
9. Tyrosine	Tyr	Y
10. Tryptophan	Trp	W
11. Serine	Ser	S
12. Threonine	Thr	T
13. Cysteine	Cys	C
14. Asparagine	Asn	N
15. Glutamine	Gln	Q
16. Lysine	Lys	K
17. Arginine	Arg	R
18. Histidine	His	H
19. Aspartate	Asp	D
20. Glutamate	Glu	E

II. Function of amino acids

A. Building blocks of proteins. Amino acids or their derivatives are also form components of lipids-e. g., serine in phospholipids and glycine in bile salts (Table 2).

B. Amino acids may be functional (neurotransmitters):

1. Glutamate and aspartate (excitatory).
2. Glycine (inhibitory).

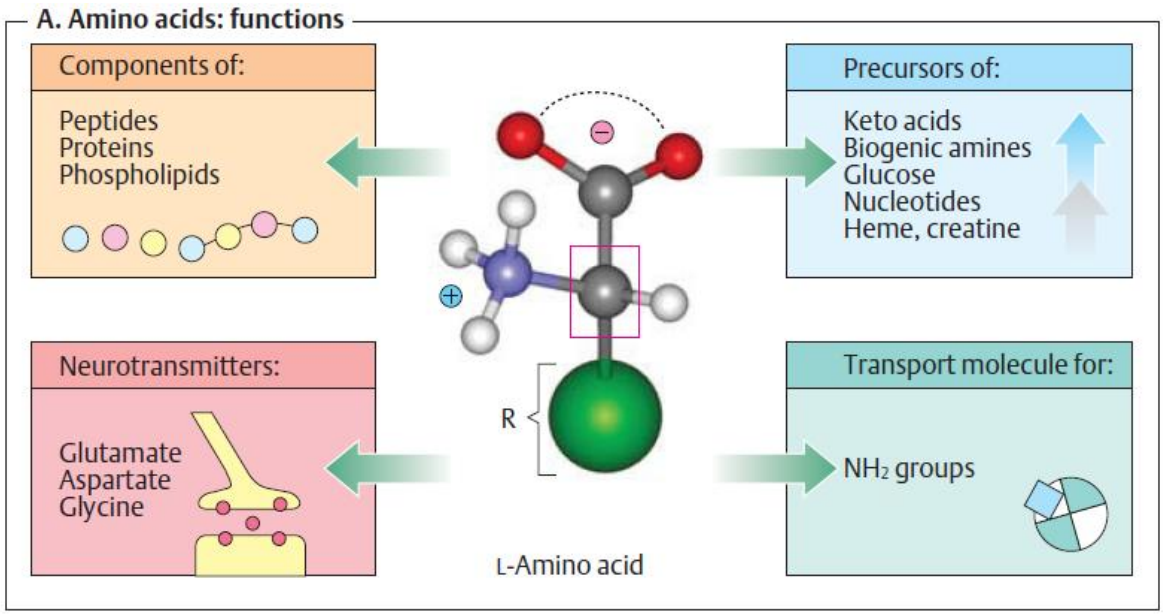
C. Precursors to other molecules:

1. Keto acids.
2. Biogenic amines- e.g, thyroxine (thyroid hormone) and histamine (mediator of immune response).
3. Glucose in gluconeogenesis.
4. Nucleotide synthesis.

5. Heme and creatine.

D. Transport molecule

Table 2: Function of amino acids.



III. Structure of the amino acids

The term amino acid might mean any molecule containing both an amino group and any type of acid group; however, the term is almost always used to refer to a carboxylic acid. Each amino acid (except for proline, which has a secondary amino group) has a carboxyl group, a primary amino group, and a distinctive side chain ("R-group") bonded to the α-carbon atom (Figure 1).

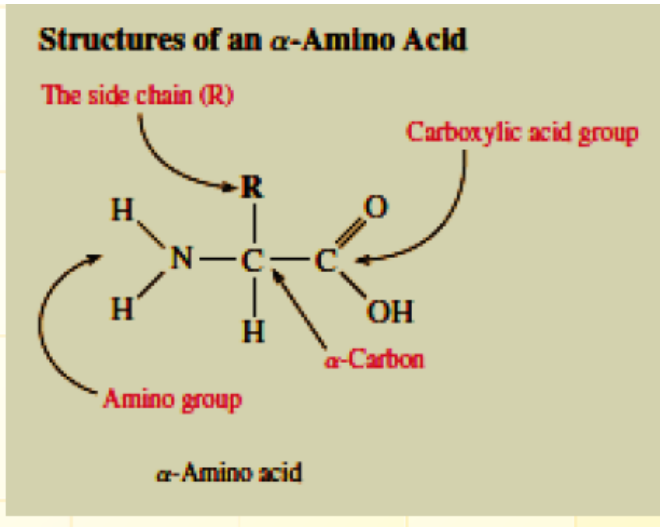


Figure 1: Amino acid structure.

At physiologic pH (approximately pH 7.4), the carboxyl group is dissociated, forming the negatively charged carboxylate ion ($–COO^-$), and the amino group is protonated ($–NH3^+$). In proteins, almost all of these carboxyl and amino groups are combined through peptide linkage and, in general, are not available for chemical reaction except for hydrogen bond formation (Figure 2).

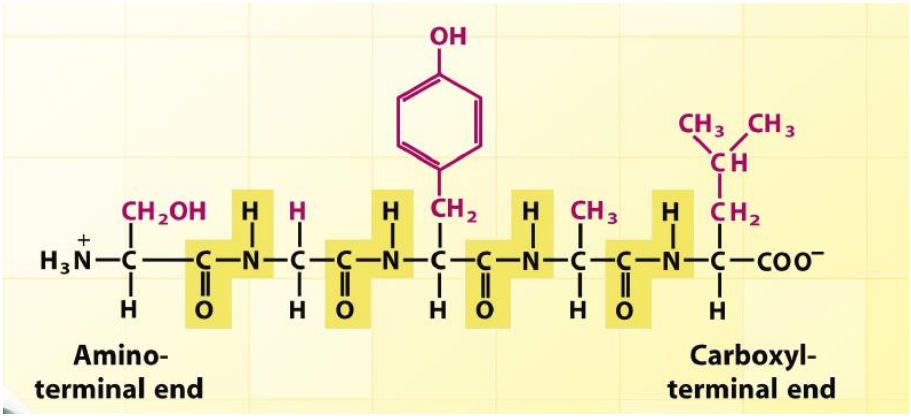


Figure 2: protein structure.

IV. Classification of amino acids

It is useful to classify the amino acids according to the properties of their side chains:

1. Amino acids with nonpolar side chains

Each of these amino acids has a nonpolar side chain that does not gain or lose protons or participate in hydrogen or ionic bonds (Figure 3). The side chains of these amino acids can be thought of as "oily" or lipid-like, a property that promotes hydrophobic interactions.

- **Location of nonpolar amino acids in proteins:** In proteins found in aqueous solutions (a polar environment) the side chains of the nonpolar amino acids tend to cluster together in the interior of the protein. This phenomenon, known as the hydrophobic effect, is the result of the hydrophobicity of the nonpolar R-groups, which act much like droplets of oil that coalesce in an aqueous environment. The nonpolar R-groups thus fill up the interior of the folded protein and help give it its three-dimensional shape. However, for proteins that are located in a hydrophobic environment, such as a membrane, the nonpolar R-groups are found on the outside surface of the protein, interacting with the lipid environment.

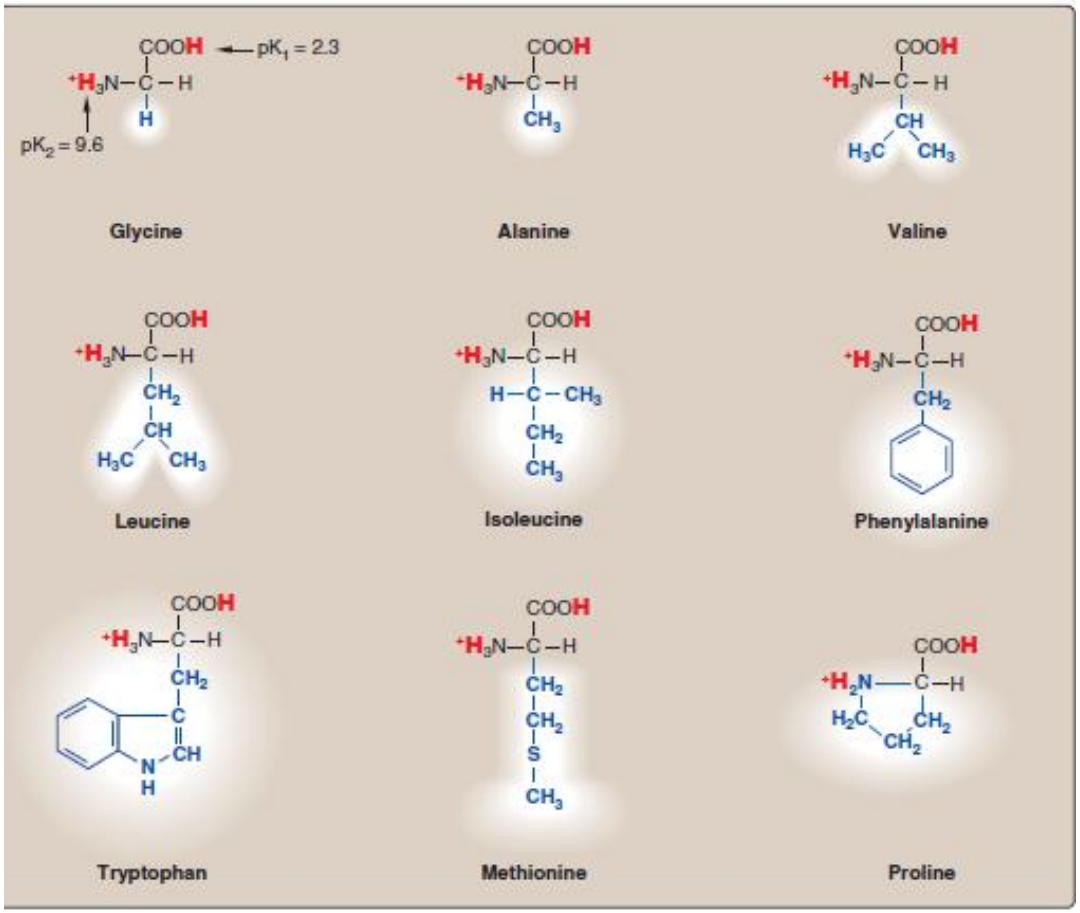


Figure 3: Nonpolar amino acids.

- **Sickle cell anemia**, a sickling disease of red blood cells, results from the substitution of polar glutamate by nonpolar valine at the sixth position in the β subunit of hemoglobin.

- **Proline:** Proline differs from other amino acids in that proline's side chain and α-amino N form a rigid, five-membered ring structure (Figure 4). Proline, then, has a secondary (rather than a primary) amino group. It is frequently referred to as an imino acid. The unique geometry of proline contributes to the formation of the fibrous structure of collagen, and often interrupts the β-helices found in globular proteins.

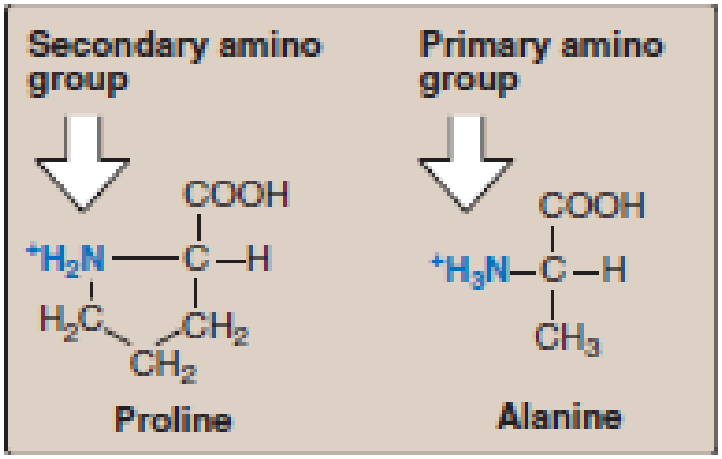


Figure 4: Proline.

2. Amino acids with uncharged polar side chains

These amino acids have zero net charge at neutral pH, although the side chains of cysteine and tyrosine can lose a proton at an alkaline pH (see Figure 5). Serine, threonine, and tyrosine each contain a polar hydroxyl group that can participate in hydrogen bond formation. The side chains of asparagine and glutamine each contain a carbonyl group and an amide group, both of which can also participate in hydrogen bonds.

- **Disulfide bond:** The side chain of cysteine contains a sulf hydryl group (–SH), which is an important component of the active site of many enzymes. In proteins, the –SH groups of two cysteines can become oxidized to form a dimer, cystine, which contains a covalent cross-link called a disulfide bond (–S–S–). Many extracellular proteins are stabilized by disulfide bonds. Albumin, a blood protein that functions as a transporter for a variety of molecules, is an example.

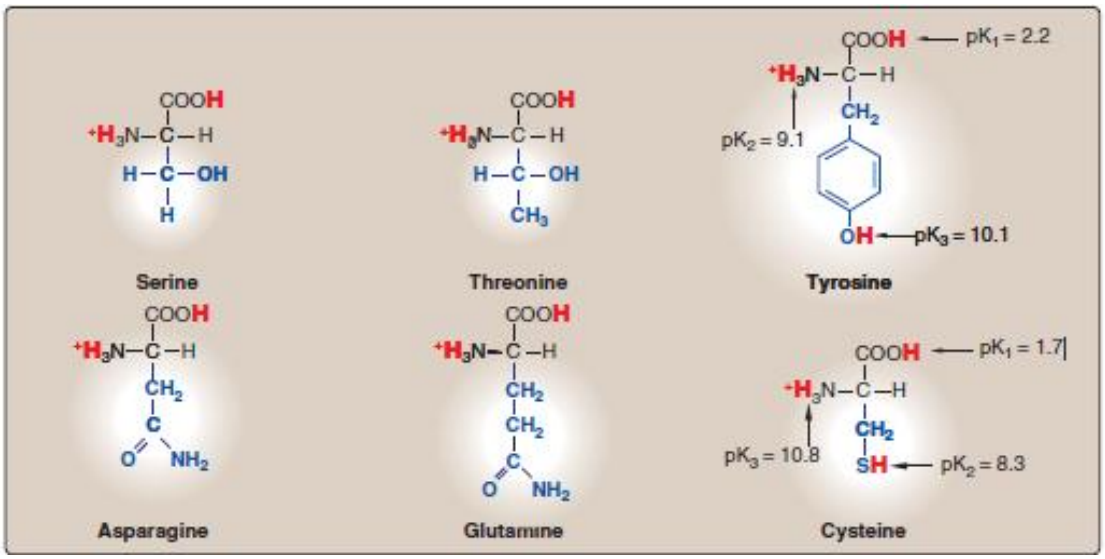


Figure 5: Amino acids with uncharged polar side chains.

- **Side chains as sites of attachment for other compounds:** The polar hydroxyl group of serine, threonine, and, rarely, tyrosine, can serve as a site of attachment for structures such as a phosphate group. In addition, the amide group of asparagine, as well as the hydroxyl group of serine or threonine, can serve as a site of attachment for oligosaccharide chains in glycoproteins.

3. Amino acids with acidic side chains

The amino acids aspartic and glutamic acid are proton donors. At physiologic pH, the side chains of these amino acids are fully ionized, containing a negatively charged carboxylate group ($-COO^-$). They are, therefore, called aspartate or glutamate to emphasize that these amino acids are negatively charged at physiologic pH (Figure 6).

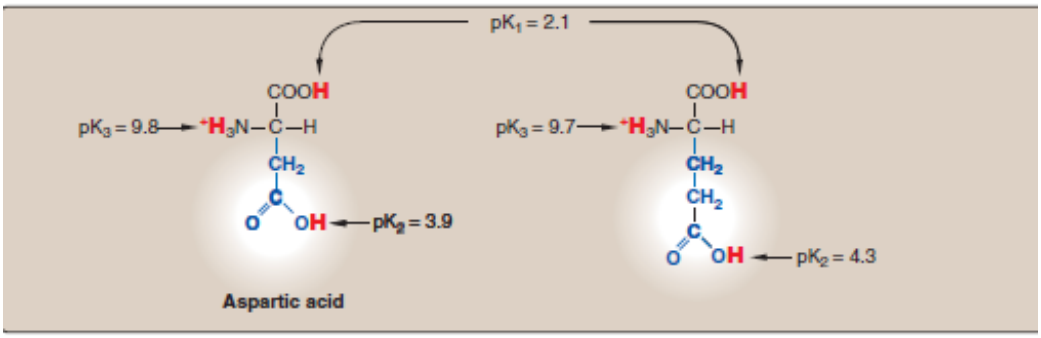


Figure 6: Amino acids with acidic side chains.

4. Amino acids with basic side chains

The side chains of the basic amino acids accept protons.

At physiologic pH the side chains of lysine and arginine are fully ionized and positively charged (Figure 7). In contrast, histidine is weakly basic, and the free amino acid is largely uncharged at physiologic pH. However, when histidine is incorporated into a protein, its side chain can be either positively charged or neutral, depending on the ionic environment provided by the polypeptide chains of the protein. This is an important property of histidine that contributes to the role it plays in the functioning of proteins such as hemoglobin.

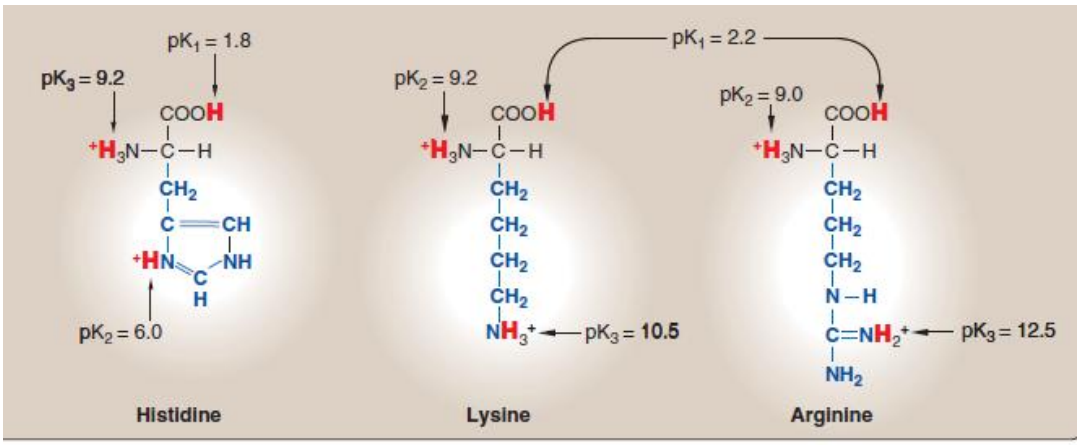


Figure 7: Amino acids with basic side chains.

V. Properties of amino acids

1. Optical properties of amino acids

The α-carbon of an amino acid is attached to four different chemical groups and is, therefore, a chiral or optically active carbon atom. **Glycine** is the exception because its α-carbon has two hydrogen substituents and, therefore, is optically inactive. Amino acids that have an asymmetric center at the α-carbon can exist in two forms, designated D and L that are mirror images of each other (Figure 8). The two forms in each pair are termed stereoisomers, optical isomers, or enantiomers. All amino acids found in proteins are of the L-configuration. However, D-amino acids are found in some antibiotics and in plant and bacterial cell walls.

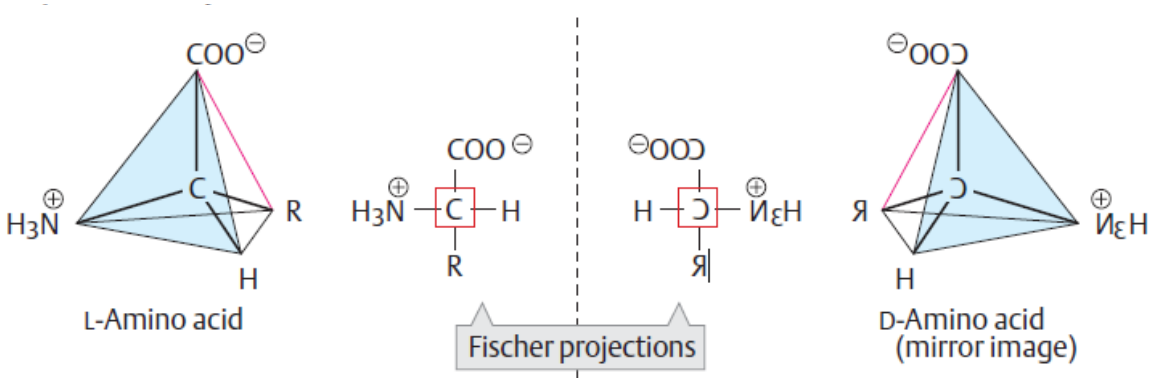


Figure 8: Optical properties of amino acids.

2. Acidic and basic properties of amino acids

Although we commonly write amino acids with an intact carboxyl group (-COOH) and amino group (-NH_2), their actual structure is ionic and depends on the pH. The carboxyl group loses a proton, giving a carboxylate ion, and the amino group is protonated to an ammonium ion at neutral pH. This structure is called a **dipolar ion or zwitterions** (Figure 9).

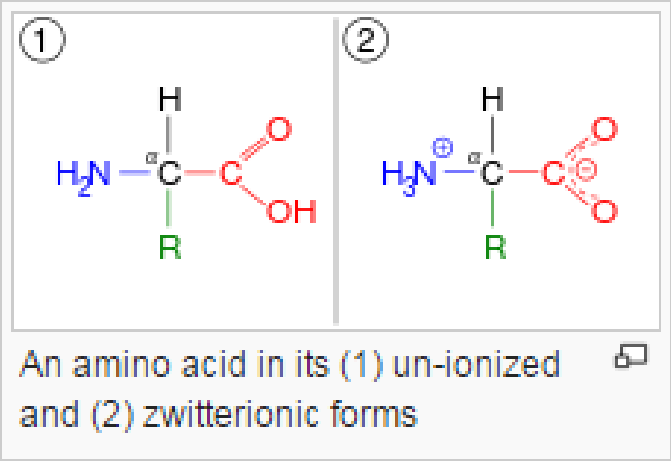


Figure 9: Zwitterionic form of amino acid.

The dipolar nature of amino acids gives them some unusual properties:

1. Amino acids have **high melting points**, generally over 200 °C.

2. Amino acids are more **soluble in water** than they are in ether, dichloromethane, and other common organic solvents.

3. Amino acids are less acidic than most carboxylic acids and less basic than most amines.

Because amino acids contain both weakly acidic α-carboxyl groups and weakly basic α-amino groups, so they have amphoteric properties:

- In acidic medium; the amino acid is **positively charged**, so it behaves as **a base** (proton acceptor).
- In alkaline medium; the amino acid is **negatively charged**, so it behaves as **an acid** (proton donor).

Amphoteric properties of amino acids; amino acids due to the presence of their ionizable α-amino and α-carboxylic group can act sometimes as acids and sometimes as bases depending on the pH of their media (Figure 9).

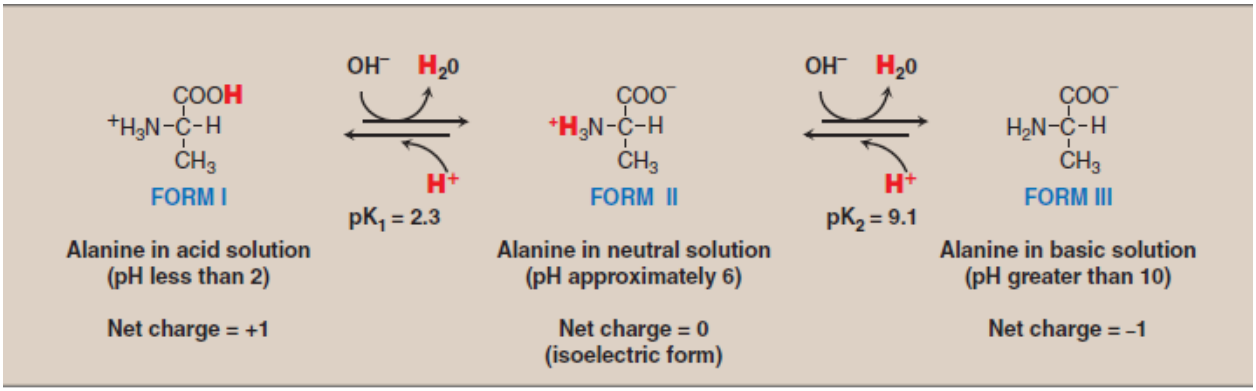


Figure 9: Amphoteric properties of amino acids.

VI. General reactions of amino acids

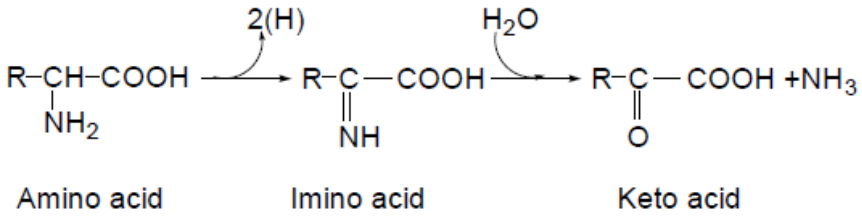
The general reactions of amino acids include deamination, transamination and decarboxylation. The reactions of deamination and transamination bring about the formation of keto acids which can undergo a further series of changes. Inter-conversion between keto acids and amino acids results in the synthesis of many nutritionally non essential amino acids. These provide for the synthesis of protein and important non-protein nitrogenous materials. During protein synthesis the amino acids are absorbed from the blood, as the liver does not store them.

1. Deamination

Deamination means removal of the amino groups from amino acids. This is the mechanism where in the amino acids lose two hydrogen atoms (dehydrogenation) to form keto acids and ammonia. Deamination is accompanied by oxidation and is catalysed by specific amino acid oxidases or more appropriately, dehydrogenases present in liver and kidneys. The process of oxidative deamination takes place in two steps:

a- The first step: is oxidation (dehydrogenation) of amino acid resulting in the formation of imino acid. The imino acid then undergoes the second step

b- The second step: namely hydrolysis which results in a keto acid and ammonia.



The first reaction is catalyzed by amino acid oxidase (also called dehydrogenase) and the coenzyme FAD or FMN takes up the hydrogen. There are two types of amino acid oxidases depending upon the substrate, on which they act, namely,

1. L-amino acid oxidases which act on L-amino acids (FMN acts as coenzyme).
2. D-amino acid oxidases which act on D-amino acids (FAD acts as coenzyme).

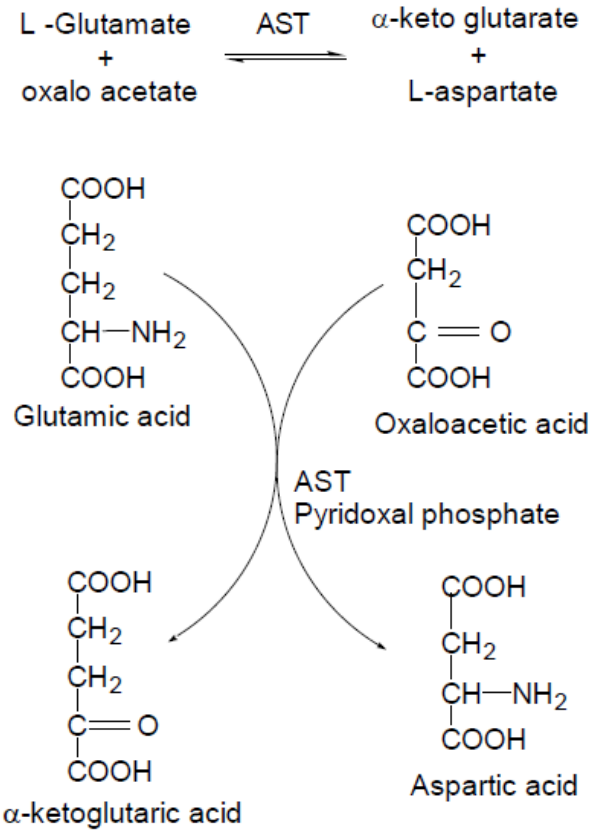
FMN occurs only in the liver and kidney and FAD occurs in all animal tissues. The major site of oxidative deamination is liver but kidney and other tissues also have a role.

2. Transamination

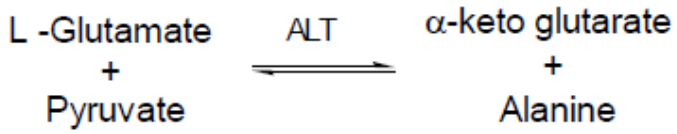
The process of transfer of an amino group from an amino acid to a keto acid, resulting in the formation of a new amino acid and keto acid is

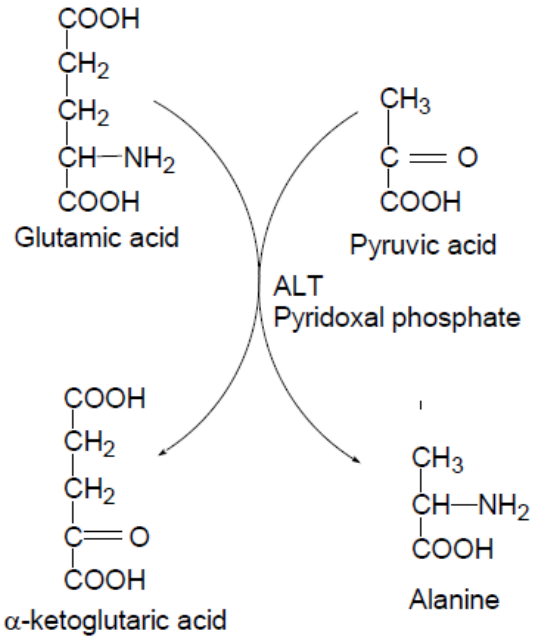
known as transamination. In other words, it is deamination of an amino acid, coupled with amination of a keto acid. Transamination is catalyzed by transaminases or aminotransferases with pyridoxal phosphate functioning as coenzyme. There are two active transaminases in tissues, catalyzing interconversions. They are

1. Aspartate aminotransferase (AST) is also known as Glutamate - oxalo acetate transaminase (GOT).



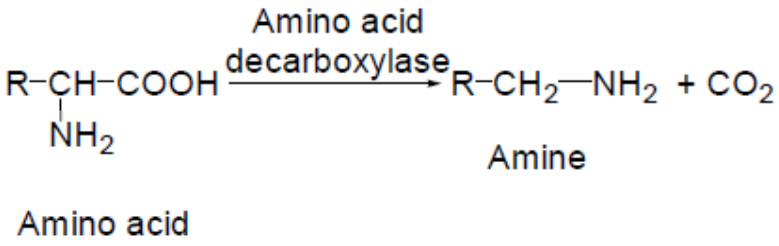
2. Alanine aminotransferase (ALT) is also known as Glutamate - pyruvate transaminase (GPT). It catalyses the transfer of NH_2 group from glutamate to pyruvate, resulting in the formation of a ketoglutaric acid and alanine.



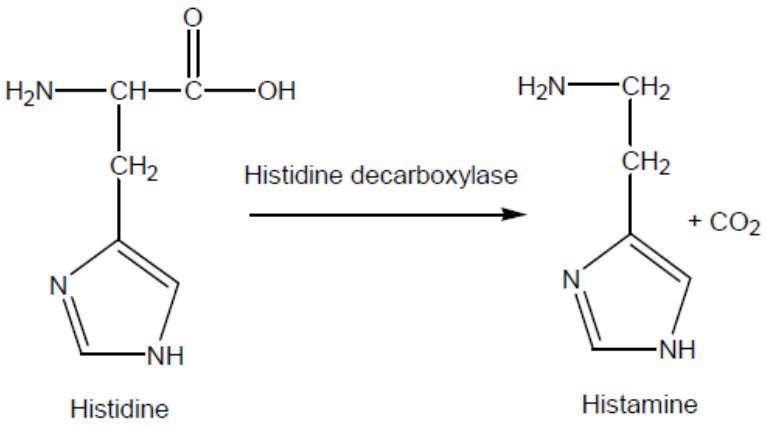


3. Decarboxylation

This refers to the removal of CO_2 from the carboxyl group of amino acids. The removal of CO_2 needs the catalytic action of enzymes decarboxylases and the pyridoxal phosphate coenzyme. The enzymes act on amino acids resulting in the formation of the corresponding amines with the liberation of CO_2.



There are several amino acid decarboxylases found in various tissues such as liver, kidney, intestine, spleen, lung and brain. They convert the amino acids into the respective amines and liberate CO_2. For example, histidine is converted to histamine by the action of histidine decarboxylase.



Histidine Histamine

The amino acid tryptophan is converted to tryptamine, tyrosine to tyramine, etc. Such amines are called biogenic amines which are physiologically important.

Study Questions

1) Explain the following:

- Proline differs from other amino acids.
- All the amino acids are optically active except the glycine.

2) Define the following:

- Transamination
- Decarboxylation
- Deamination

3) State the properties of amino acids and explain any two.

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