PROTEIN STRUCTURE & FUNCTION OF AMINO ACIDS

Proteins are the most abundant and functionally diverse molecules in living systems. Virtually every life process depends on this class of molecules.
For example:

- **Enzymes and polypeptide hormones.**
- **Myosin, a contractile protein of muscle.**
- **Bone, consisted from the protein collagen.**
- **Blood proteins, such as hemoglobin and plasma albumin and immunoglobulins.**

Proteins all share the common structural feature of being linear polymers of amino acids.

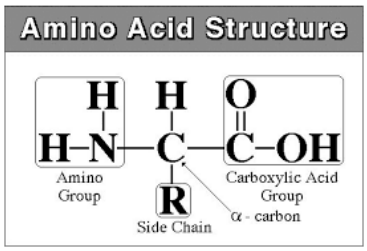
❖ AMINO ACIDS

Amino acids are a group of organic compounds containing two functional groups, amino group (-NH2) which is basic and carboxyl group (-COOH) which is acidic in nature.

❖ STRUCTURE OF THE AMINO ACIDS

Each amino acid (except for proline) consist of α-carbon atom that attached to

- **A carboxyl group**
- **A primary amino group**
- **A hydrogen atom**
- **A distinctive side chain ("R-group")**



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 ($-NH3^+$).

❖ CLASSIFICATION OF AMINO ACIDS

There are different ways of classifying the amino acids based on the structure and polarity, nutritional requirement, metabolic fate etc.

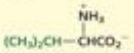
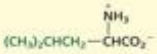
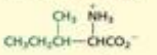
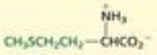
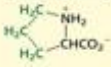
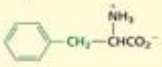
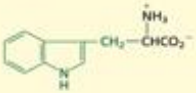
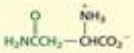
A. Amino acid classification based on the structure:

- **A comprehensive classification of amino acids is based on their structure and chemical nature.**
- **Each amino acid is assigned a 3 letter or 1 letter symbol. These symbols**

are commonly used to represent the amino acids in protein structure. (Table 27.1: presents the different groups of amino acids, their symbols and structures are given.)

- **The 20 amino acids are classified according to he nature of the side chains that ultimately dictates their role in a protein, therefore, its useful to classify the amino acids according to the properties of their side chains into:**
  1. **Amino acids with non-polar side chains**
  2. **Amino acids with uncharged polar side chains**
  3. **Amino acids with acidic side chains**
  4. **Amino acids with basic side chains**

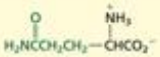
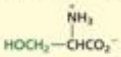
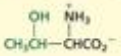
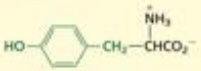
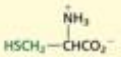
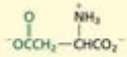
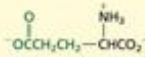
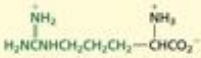
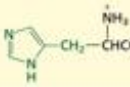
TABLE 27.1 α-Amino Acids Found in Proteins

Name	Abbreviation	Structural formula*
Amino acids with nonpolar side chains		
Glycine	Gly (G)	
Alanine	Ala (A)	
Valine†	Val (V)	
Leucine†	Leu (L)	
Isoleucine†	Ile (I)	
Methionine†	Met (M)	
Proline	Pro (P)	
Phenylalanine†	Phe (F)	
Tryptophan†	Trp (W)	
Amino acids with polar but nonionized side chains		
Asparagine	Asn (N)	

*All amino acids are shown in the form present in greatest concentration at pH 7.
†An essential amino acid, which must be present in the diet of animals to ensure normal growth.

(Continued)

TABLE 27.1 α-Amino Acids Found in Proteins *(Continued)*

Name	Abbreviation	Structural formula*
Amino acids with polar but nonionized side chains		
Glutamine	Gln (Q)	
Serine	Ser (S)	
Threonine†	Thr (T)	
Tyrosine	Tyr (Y)	
Cysteine	Cys (C)	
Amino acids with acidic side chains		
Aspartic acid	Asp (D)	
Glutamic acid	Glu (E)	
Amino acids with basic side chains		
Lysine†	Lys (K)	
Arginine†	Arg (R)	
Histidine†	His (H)	

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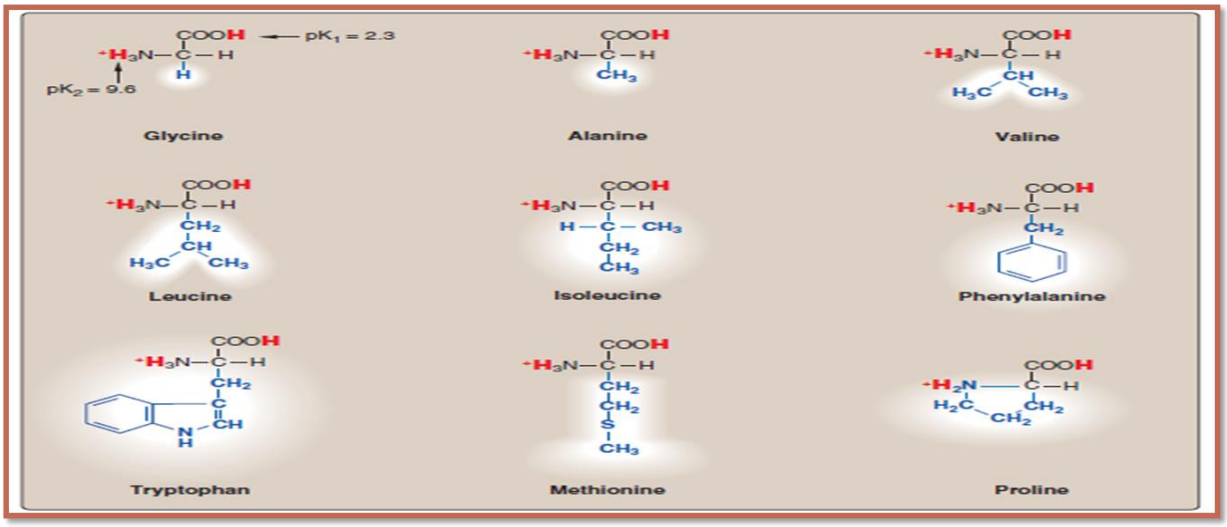
1. Amino acids with non-polar side chains:

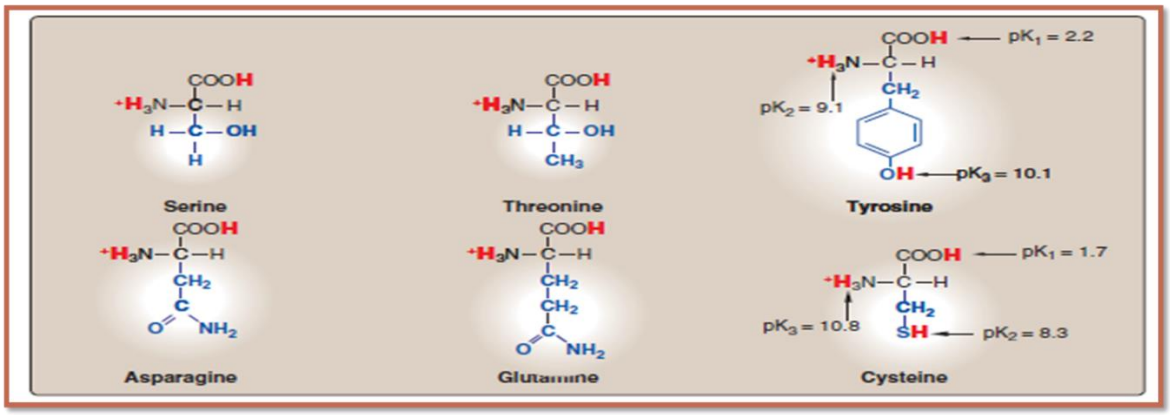
- **These amino acids are: Glycine, Alanine, Valine, Leucine, Isoleucine, Phenylalanine, Tryptophan, Methionine and Proline.**
- **The side chains cluster in the interior of the protein due to hydrophobicity.**

- **Proline (The imino acid) gives the fibrous structure of collagen, and interrupts the α-helices found in globular proteins. The side chain of proline and its α-amino group form a ring structure**



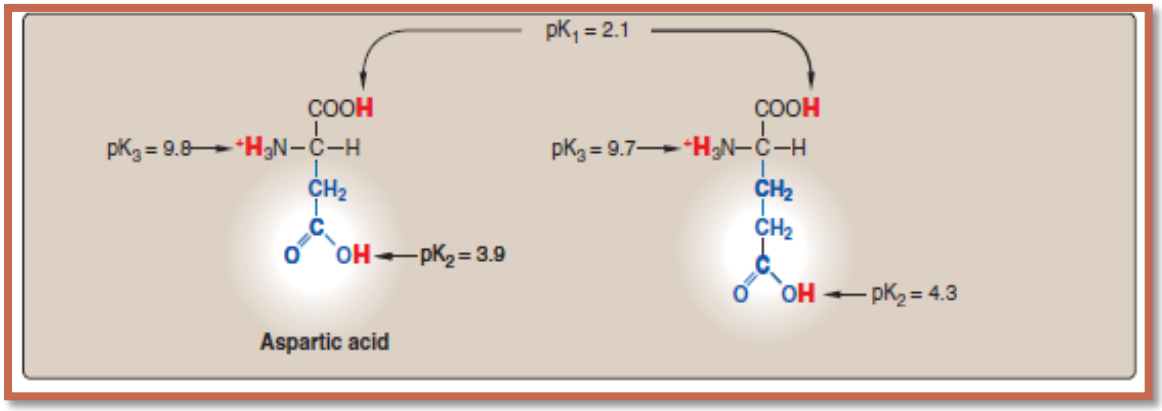
2. Amino acids with uncharged polar side chains

- **These are more hydrophilic because they form hydrogen bonds with water.**
- **These include: Serine, Threonine, Cysteine, Tyrosine, asparagine, and glutamine.**
- **These amino acids have zero net charge at neutral pH.**
- **Cysteine contains a sulfhydryl group (-SH), an important component of the active site of many enzymes.**
- **Two cysteines can become oxidized to form a dimmer cystine, which contains a covalent cross-link called a disulfide bond (-S-S-).**
- **Serine and threonine contain a polar hydroxyl group that serve as a site of attachment (in enzymes) for groups such as a phosphate.**
- **Amide group of asparagine, as well as the hydroxyl group of serine or threonine serve as a site of attachment for oligosaccharide chains in glycoproteins.**



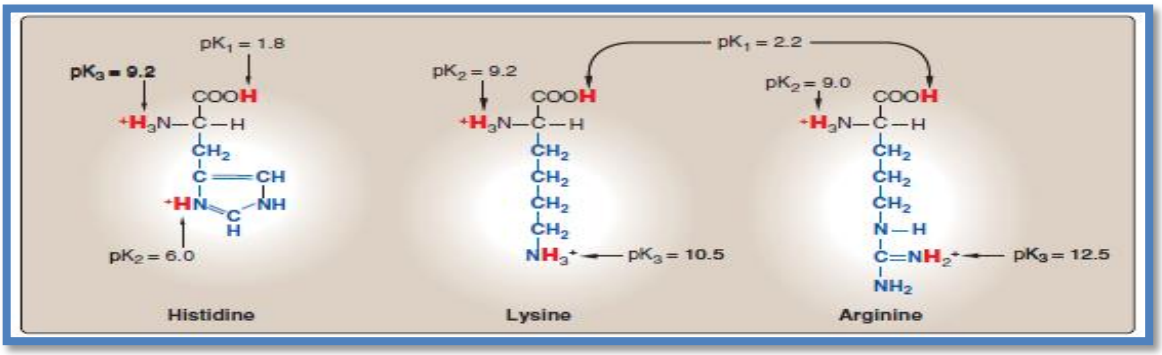
3. Amino acids with acidic side chains

- **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.**



4. Amino acids with basic side chains

- **These include: Lysine, Arginine & Histidine amino acids.**
- **The R groups have significant positive charge.**
- **Lysine has a second positive amino group at the ε position on its (R) chain.**
- **Arginine has a positively charged guanidino group.**
- **Histidine has a positive imidazole group facilitates the enzyme-catalyzed reaction by serving as a proton donor/acceptor**



B. Nutritional classification of amino acids

Amino acids can be classified into:

1- Essential amino acids:

These amino acids can't be formed in the body and so, it is essential to be taken in diet. Their deficiency affects growth, health and protein synthesis.

Essential amino acids include: valine, leucin, isoleucine, phenylalanine, tryptophan, methionine, lysine, histidine, threonine and arginine.

2- Semi essential amino acids:

These are formed in the body but not in sufficient amount for body requirements especially in children. The two amino acids namely arginine and histidine can be synthesized by adults but in growing children the rate of their biosynthesis cannot cope with rate of protein synthesis, so must be supplied in diet, hence these are considered as semi–essential amino acids

3- Non essential amino acids:

These are the rest of amino acids that are formed in the body in amount enough for adults and children.

These include: alanine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, proline, serine, and tyrosine.

Tyrosine is produced from phenylalanine, so if the diet is deficient in phenylalanine, tyrosine will be required as well.

C. Amino acid classification based on their metabolic fate:

The carbon skeleton of amino acids can serve as a precursor for the synthesis of glucose (glycogenic) or fat (ketogenic) or both. From metabolic view point, amino acids are divided into three groups.

1. Glycogenic amino acids: Those amino acids in which their carbon skeleton gets degraded to pyruvate, α-ketoglutarate, succinyl CoA, fumarate and oxaloacetate and then converted to glucose.

These amino acids include: alanine, cysteine, glycine, Arginine, glutamine,

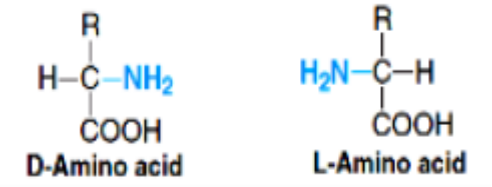
isoleucine, tyrosine etc. except those in the next two groups.

2. Ketogenic amino acids: Fat can be synthesized from these amino acids. Two amino acids leucine and lysine are exclusively ketogenic.

3. Glycogenic and ketogenic amino acids: The five amino acids isoleucine, phenylalanine, tryptophan, tyrosine and threonine are precursors for synthesis of glucose as well as fat

❖ OPTICAL PROPERTIES OF AMINO ACIDS

- **The α-carbon of amino acid is attached to four different chemical groups, thus it's a chiral or optically active carbon atom. Glycine is the exception.**
- **Amino acids exist in two forms, D and L, that are mirror images of each other.**
- **All amino acids found in proteins are of the L-configuration.**



❖ PROPERTIES OF AMINO ACIDS

The amino acids differ in their physico–chemical properties which ultimately determine the characteristics of proteins.

1. Solubility: Most of the amino acids are usually soluble in water and insoluble in organic solvents.

2. Melting points: Amino acids generally melt at higher temperatures, often above 200°C.

3. Optical properties: All the amino acids except glycine possess optical isomers due to the presence of asymmetric carbon atom. Some amino acids also have a second asymmetric carbon e.g., isoleucine, threonine.

4. Amino acids as ampholytes: Amino acids contain both acidic (-COOH) and basic (-NH2) groups. They can donate a proton or accept a proton; hence amino acids are regarded as ampholytes.

5. Zwitter ion or dipolar ion: The name zwitter is derived from the German word which means hybrid. Zwitter ion (or dipolar ion) is a hybrid molecule containing

positive and negative ionic groups.The amino acids rarely exist in a neutral form with free carboxylic (-COOH) and free amino (-NH2) groups. In strongly acidic pH (low pH), the amino acid is positively charged (cation) while in strongly alkaline pH (high pH), it is negatively charged (anion). Each amino acid has a characteristic pH (e.g., leucine, pH 6.0) at which it carries an equal amount of both positive and negative charges and exists as zwitterion.

❖ UNCOMMON AMINO ACIDS

In addition to the 20 common amino acids, proteins may contain residues created by modification of common residues already incorporated into a polypeptide. Among these uncommon amino acids are:

1. **4-hydroxyproline, a derivative of proline, and 5-hydroxylysine, derived from lysine.The former is found in plant cell wall proteins, and both are found in collagen, a fibrous protein of connective tissues.**
2. **Another important uncommon amino acid is γ-carboxyglutamate, found in the bloodclotting protein prothrombin and in certain other proteins that bind Ca2 as part of their biological function.**
3. **Desmosine, a derivative of four Lys residues, which is found in the fibrous protein elastin.**
4. **Selenocysteine is a special case. This rare amino acid residue is introduced during protein synthesis rather than created through a postsynthetic modification. It contains selenium rather than the sulfur of cysteine. Actually, derived from serine, selenocysteine is a constituent of just a few known proteins. In recent years, it considered the 21st amino acid**
5. **Some 300 additional amino acids have been found in cells. They have a variety of functions but are not constituents of proteins, e.g. Ornithine and citrulline**

❖ FUNCTION OF AMINO ACIDS:

In addition to providing the monomer units from which the long polypeptide chains of proteins are synthesized, the L-α -amino acids and their derivatives participate in cellular functions in that:

1. **Several amino acids function as neurotransmitters themselves, while others are precursors of neurotransmitters, mediators, or hormones**
2. **Specific amino acids form precursors for other metabolites e. g., for glucose in gluconeogenesis, also in the biosynthesis of porphyrins, purines, pyrimidines, and urea.**
3. **Short polymers of amino acids called peptides act as hormones, or**

neuromodulators

4. Some form components of lipids e. g., serine in phospholipids and glycine in bile salts.
5. Present in polypeptide antibiotics

❖ PEPTIDE CHAIN

- Peptide: are biologically occurring short chains of amino acid monomers linked by peptide (amide) bonds.
- The covalent chemical bonds are formed when the carboxyl group of one amino acid reacts with the amine group of another.
- The shortest peptides are dipeptides, consisting of 2 amino acids joined by a single peptide bond, followed by tripeptides, tetrapeptides, etc.
- A polypeptide is a long, continuous, and unbranched peptide chain.
- Each polypeptide chain starts on the left side by free amino group of the first amino acid enter in chain formation. It is termed (N- terminus).
- Each polypeptide chain ends on the right side by free COOH group of the last amino acid and termed (C-terminus).