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PROTEINS CHEMISTRY

BIOCHEMISTRY

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BIOMEDICAL IMPORTANCE

- 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 as diverse as nerve transmission and the biosynthesis of porphyrins, purines, pyrimidines, and urea.

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- Short polymers of amino acids called peptides perform prominent roles in the neuroendocrine system as hormones, hormone-releasing factors, neuromodulators, or neurotransmitters.

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- Certain other microbial peptides are toxic. The cyanobacterial peptides microcystin and nodularin are lethal in large doses, while small quantities promote the formation of hepatic tumors.

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- While proteins contain only L-α-amino acids, microorganisms elaborate peptides that contain both D- and L-α-amino acids. Several of these peptides are of therapeutic value, including the antibiotics bacitracin and gramicidin A and the antitumor agent bleomycin.

- D-Amino acids that occur naturally include free D-serine and D-aspartate in brain tissue,
- D-alanine and D-glutamate in the cell walls of grampositive bacteria,
- and D-amino acids in some non mammalian peptides and certain antibiotics.

INTRODUCTION

- There are approximately 20 different amino acids found in proteins.

- Neither humans nor any other higher animals can synthesize 10 of the 20 common L-α-amino acids in amounts adequate to support infant growth or to maintain health in adults.

- The amino acids are distinguished from each other by the R group often referred to as the side-chain in proteins.

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- Most of the 20 common amino acids (a.a.) have the following general structure.

- The amino acids have an amino and a carboxylic acid group that are joined to the same carbon atom. This carbon atom is referred to as the α carbon.

- In proteins, amino acids are covalently linked to one another by peptide (amide) bonds involving the carboxyl group of one a.a. and the amino group of another a.a. to form linear polymers.

Standard amino acids

- There are about three hundred amino acids known
- Only 20 take part in the formation of proteins
- They have genetic codons

Structure and Properties of the amino acids.

- The a.a. are usually grouped according to the polarity and charge of the R group which relates to their role in proteins.

- in particular, their **polarity**, or tendency to interact with water at biological pH (near pH 7.0). The polarity of the R groups varies widely, from nonpolar and hydrophobic (water-insoluble) to highly polar and hydrophilic (water-soluble).

Classification

- a.a. with non polar aliphatic side chains
- a.a with aromatic side chains
- a.a with side chains containing hydroxyl group
- a.a with side chains containing sulfur atom
- a.a with acidic side chains
- a.a with basic side chains

Amino acids are classified as follows:

- a.a. with nonpolar side chains,
- a.a. with uncharged polar side chains and
- a.a. with charged polar side chains.

Nonpolar Aliphatic

- Glycine
- Alanine
- Proline
- Valine
- Leucine
- Isoleucine
- Methionine

Aromatic

- Phenylalanine
- Tyrosine
- Tryptophan

Polar, uncharged

- Serine
- Threonine
- Cysteine
- Asparagine
- Glutamine

Positively (Basic) charged

- Lysine
- Histidine
- Arginine

Negatively (Acidic) charged

- Aspartate
- Glutamate

Hydroxyl containing

- Serine
- Threonine

Sulfur containing

- Methionine
- Cysteine
- Cystine

Nonpolar, Aliphatic R Groups

- The R groups in this class of amino acids are nonpolar and hydrophobic. The side chains of **alanine, valine, leucine, and isoleucine** tend to cluster together within proteins, stabilizing protein structure by means of hydrophobic interactions.

- **Glycine has the simplest structure.**

Aromatic R Groups

- are relatively nonpolar (hydrophobic). All can participate in hydrophobic interactions. The hydroxyl group of tyrosine can form hydrogen bonds, and it is an important functional group in some enzymes.

Polar, Uncharged R Groups

- The R groups of these amino acids are more soluble in water, or more hydrophilic, than those of the nonpolar amino acids, because they contain functional groups that form hydrogen bonds with water.

- This class of amino acids includes **serine, threonine, cysteine, asparagine, and glutamine.** The polarity of serine and threonine is contributed by their hydroxyl groups; that of cysteine by its sulfhydryl group; and that of asparagine and glutamine by their amide groups.

Positively Charged (Basic) R Groups

- The most hydrophilic R groups are those that are either positively or negatively charged. The amino acids in which the R groups have significant positive charge at pH 7.0 are **lysine**, **arginine**, **histidine**,

Negatively Charged (Acidic) R Groups

- The amino acids in which the R groups have significant negative charge at pH 7.0 are:

  Glutamate and Aspartate

Non-Standard amino acids

- **Hydroxyproline, a derivative of proline, and**
- **Hydroxylysine, derived from lysine.**
- **Methyllysine- Myosin**
- **Carboxyglutamate- Prothrombin**
- **Desmosine- Elastin**
- **Selenocysteine- active site**
- **Ornithine**
- **Citrulline**

- **Homocysteine**
- **GABA-(γ-amino-butyric acid)**
- **DOPA**
- **Iodinated amino acids**
- **Pantothenic acid**
- **Argininosuccinic acid**
- **β-alanine**

Classification Of Proteins

- This is based on physiochemical properties of proteins:
- Protein may belong to one of the three types:

1. Simple proteins
2. Compound proteins
3. Derived proteins

Simple proteins

- Albumins
- Globulins
- Globins
- Histones
- Prolamines
- Protamines
- Albuminoids (collagen, Elastin, keratin)

Compound proteins

- Nucleoproteins (histones+ DNA,RNA)
- Phosphoproteins (casein of milk, vitellin of egg)
- Lipoproteins
- Proteo/Glycoproteins
- Chromoproetins (hemoglobin, rhodopsin, cytochromes)
- Metalloproteins (ferritin-Fe, carbonic anhydrase-Zn, ceruloplasmin-Cu).

Derived Proteins

- Primary derived
- Secondary derived

Primary Derived Proteins

- **NATIVE PROTEINS** – if its amino acid composition and molecular conformation are unchanged from that found in the natural state.

- These properties control all the functions of a protein:

1. Solubility
2. Enzyme activity
3. Specialized role

- **DENATURATION-** takes place when some or all of the cross linkages which keep the protein intact are broken down.
- Denaturation is not reversible, except in certain cases.

- May be brought about by:

1. Heat
2. X-rays
3. Ultrasonic waves

- Shaking or stirring for a long time
- Extremes of pH
- Salts of heavy metals
- Urea
- Alcohol & acetone.

- Denatured proteins are easily precipitated out at their isoelectric pH.
- Denatured proteins are easily digested.

Secondary derived proteins

- These are formed as intermediates during the hydrolysis of proteins.
- They are of different sizes and
- Different amino acid composition
- Grouped into:

1. Proteoses
2. Peptones
3. Peptides (poly & oligo peptides)

Classification based on Function

- Catalytic proteins (enzymes)
- Transport proteins (Transferrin, ceruloplasmin)
- Structural proteins (collagen, elastin)
- Immune proteins (γ-globulins)
- Contractile proteins (actin, myosin)
- Genetic proteins (histones)
- Storage proteins (ovalabumin, casein,gluten)

Classification based on Molecular Length and Shape

Depend upon axial ratio(mol length ÷ mol width)

- Fibrous (axial ratio more then 10)
- Globular (axial ratio less then 10)

Amphoteric Properties of amino acids

- Many biomolecules are **amphoteric in aqueous solution** that is they can accept or donate protons.

- At physiologic pH all the amino acids have a positive group and a negative group. Thus they can act as an acid or a base.
- Such substances are called Ampholytes.

- Since protonation-deprotonation effects are responsible for the charges on biomacromolecules which maintain their solubility in water, their solubility is often **lowest at their isoelectric point pI, the pH value at which the molecule has no net charge**.

- pH term was introduced in 1909 by Sorensen.

- pH is defined as the negative log of the hydrogen ion concentration.

$$pH = -\log (H^+)$$

- pKa - the negative log of the dissociation constant, which is a measure of strength of an acid/base .
- when pKa = pH, there is equal concentration of acid and its conjugate base.

- The exact probability that a molecule will be protonated or deprotonated depends on the pK_a of the molecule and the pH of the solution.

- At pH values less(acidic) than pka, protonated acid form is more (it will give out its H^+ ions)
- At pH values(basic) greater than the pka, deprotonated base form is more in the solution (it will take H^+ ions to neutralize the pH and bring it down).

- For example in alanine two groups are present.
- α-amino and α-carboxyl group.
- At low pH both these groups are protonated (Form I). Net charge is positive(NH^{+}_{3}).
- When pH is slightly raised carboxyl group gives out its Proton and becomes COO^{-}(Form II).

In this form the net charge on protein is zero because COO^{-} and NH^{+}_{3} charge.

- This form is called Zwitterion and is the isoelectric form.

- When pH is further raised NH_3 will give out its proton and will become NH_2 (form III).

Net charge on this form is only negative.

- At physiologic pH all the amino acids have a positive group and a negative group. Thus they can act as an acid or a base.
- Such substances are called Ampholytes.

- Importance:
- Separation of plasma proteins by charge is done in this manner.
- pH is kept higher then the isoelectric pH (pI). The proteins will have negative charge and so the proteins will move towards the positive electrode. Variations in the mobility pattern are suggestive of diseases.

- Pka of amino acid side chains play an important role in defining the pH-dependent characteristics of a protein.
- E.g. The pH-dependent activity of enzymes and the pH-dependence of protein stability are determined by the pKa values of amino acid side chain .