In the name of Allah, Most Gracious, Most Merciful.

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PROTEIN CHEMISTRY (Amino Acids)

By Dr. Kalsoom Tariq

Learning Objectives

- Define proteins
- Structure of amino acids
- Importance in pH maintenance
- Peptide bond
- Properties of amino acids
- Classification of amino acids
- Functions of amino acids
- Some important peptides

Definition

- Nitrogenous “macromolecules” made up of large no. of amino acids joined together by “peptide bond”
- contains nitrogen(16%) in addition to C,H,O(also present in carbohydrates and lipids)
- Others: Cu,Mn,Zn,Fe etc

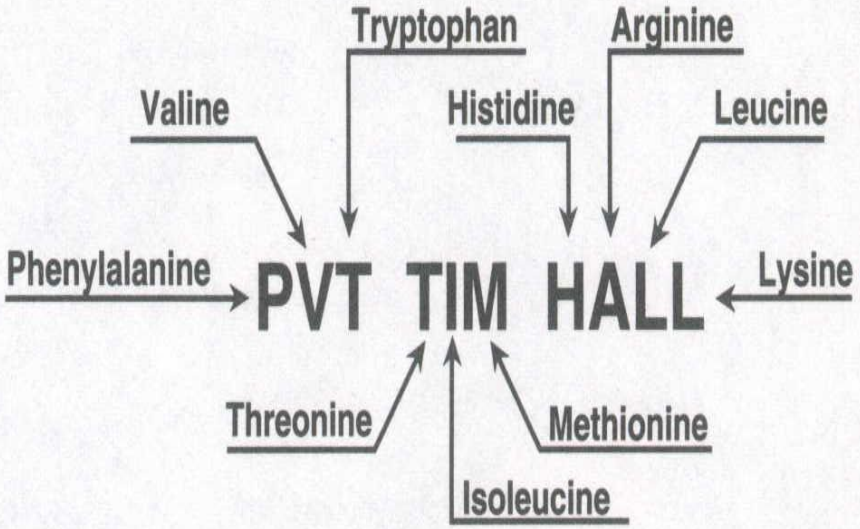
Amino acid composition of proteins

- All Proteins are polymers of 21 amino acids(standard or common amino acids)
- Many contain derived amino acids which are formed by post-translational enzymatic modification e.g; cystine, desmosine, iso desmosine(elastin); hydroxy proline and hydroxy lysine (collagen)

A

	Glucogenic	Glucogenic and Ketogenic	Ketogenic
Nonessential	Alanine Asparagine Aspartate Cysteine Glutamate Glutamine Glycine Proline Serine	Tyrosine	
Essential	Arginine Histidine Methionine Threonine Valine	Isoleucine Phenylalanine Tryptophan	Leucine Lysine

B



STRUCTURE OF AMINO ACID

Structure of Amino Acids:

- Although more than 300 amino acids have been described in nature, only 20 (standard amino acid) are isolated from different forms of life- animals, plants and microbial. Various proteins are made from these 20 a. a in different sequence and numbers.

» Each amino acid (except proline)has

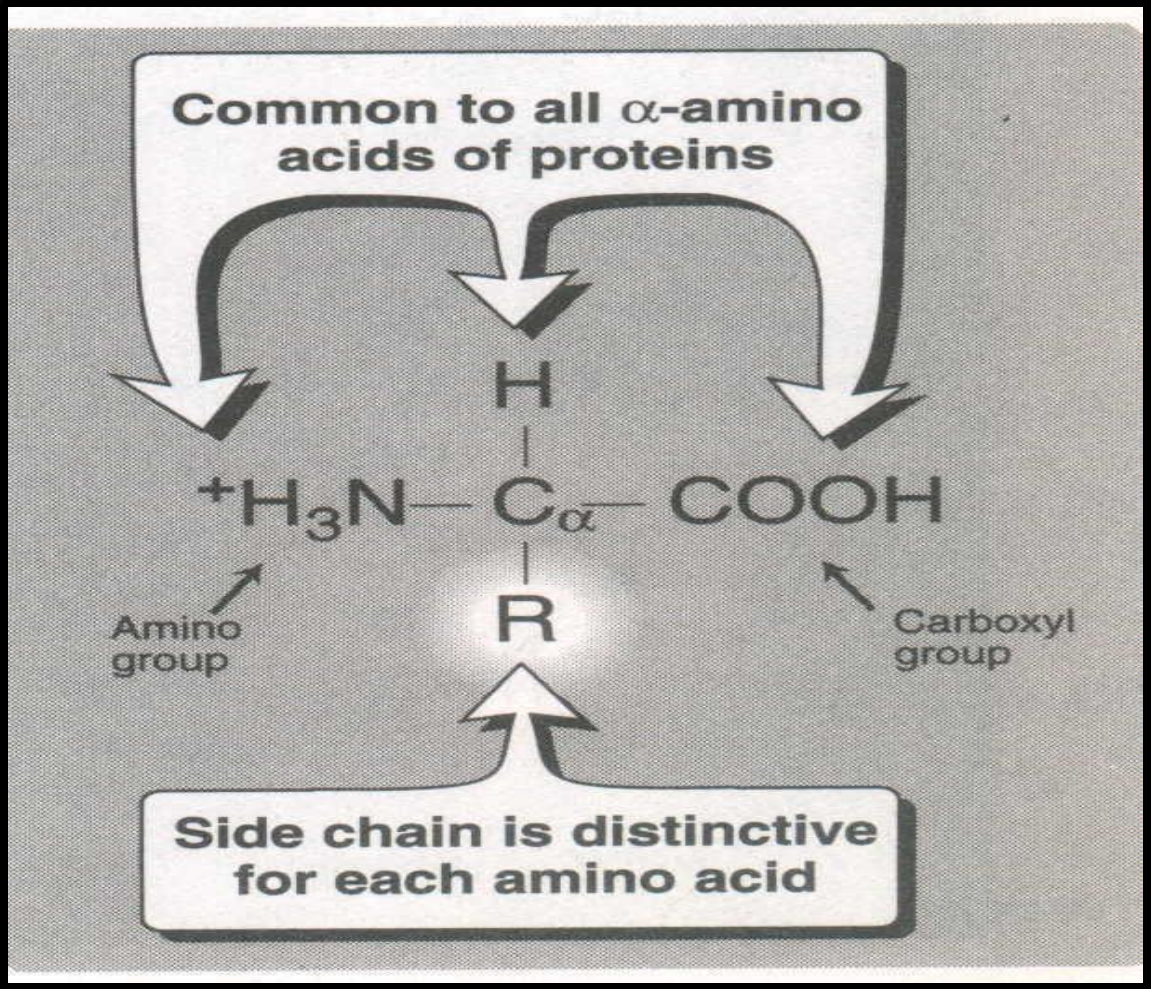
➥ a Carboxyl gp.,

➥ an Amino gp., &

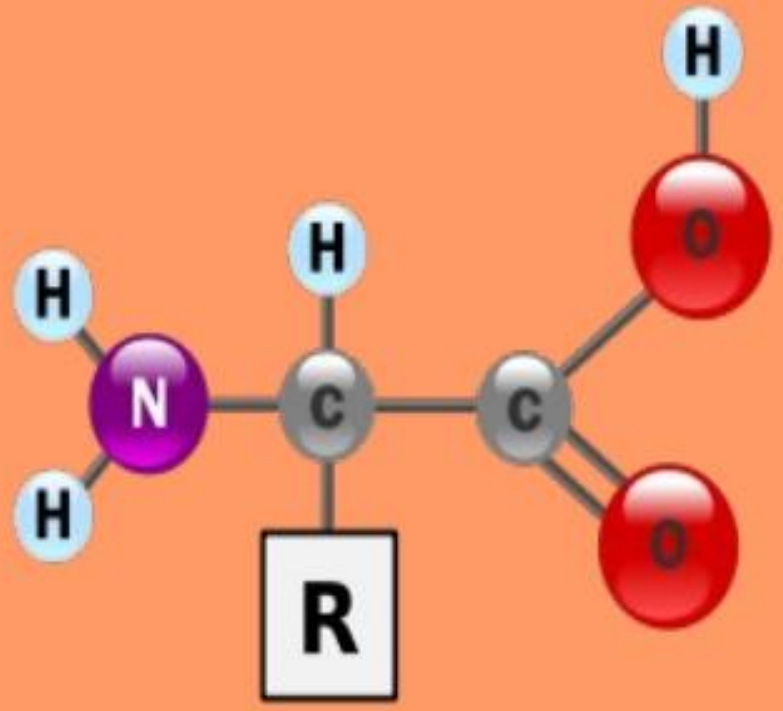
➥ a distinctive side chain(R – Group) bonded to **α– Carbon.**

Structural unit of protein

» Amino acid



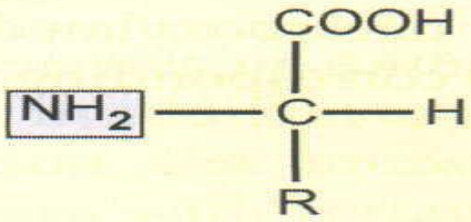
General Structure of Amino Acids



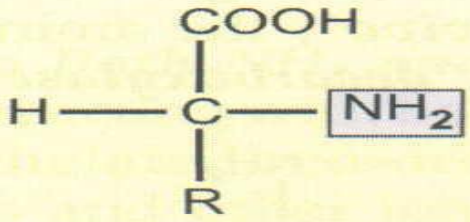
- The amino group is attached to the α- carbon which is next to the carboxyl group; hence the name α-amino acid

1:**Optical Properties *or* Isomerism in A.A:**

- The α – Carbon of each a. a is attached to four different chemical groups & it is therefore chiral carbon Or optically active or asymmetric carbon atom (except Glycine …… Two H – substituents)
- A.A that have an asymmetric centre at α – Carbon can exist in Two Forms, designated as "D & L" that are the **"Mirror Images"** of each other



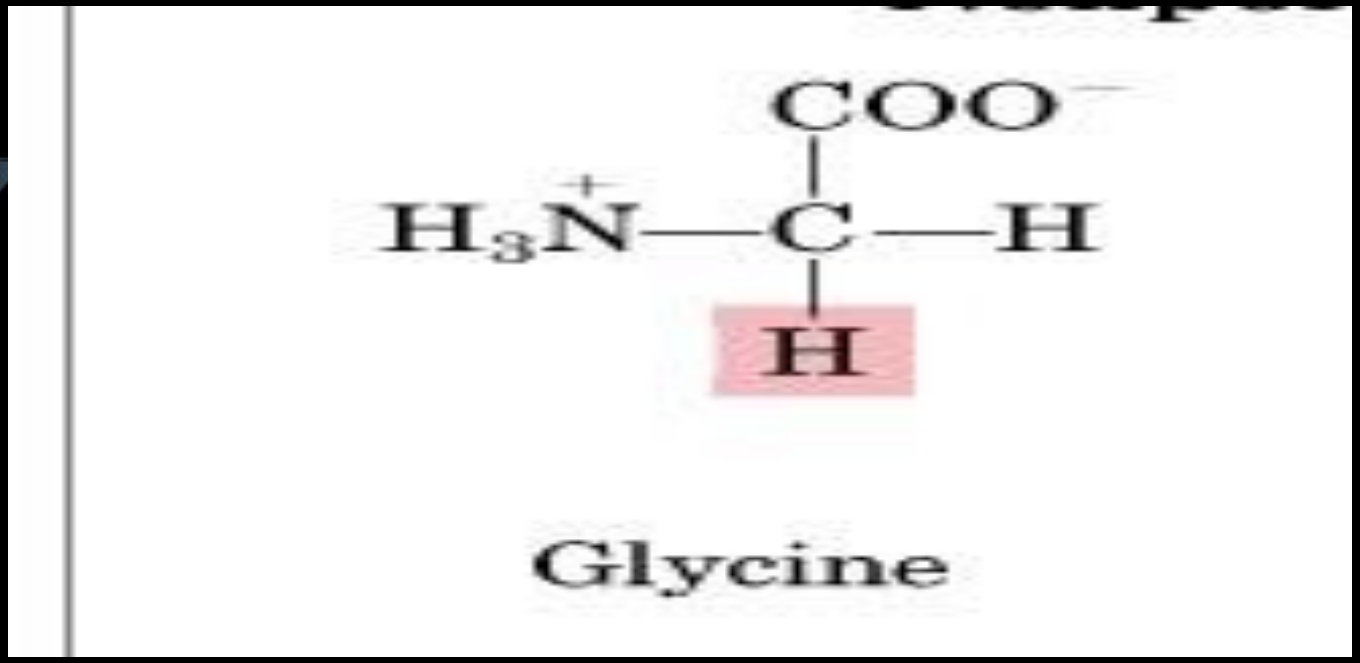
L-Amino acid



D-Amino acid

FIG. 6.1: L AND D-FORMS OF AMINO ACID

- » Symmetric carbon atom
- » Optically inactive
- » Simplest amino acid



Properties of Amino Acids

2- Amphoteric Nature & isoelectric pH:

- which mean they can act as acids and bases.
- Due to presence of carboxyl group COOH that able to donate proton(H^+), and convert to COO^-.
  - -COOH → - COO^-.
- Also presence of amino group NH2 which is enable to accept this proton(H^+) and convert into $NH3^+$
  - -NH2 → - $NH3^+$

Properties of Amino Acids

Amphoteric nature & Iso electric point (PI) :

- -It is the pH value at which concentration of anionic and cationic groups are equal (i.e. the net charge of this molecule equals zero).
- -Each amino acid have a different PI.

» R-–CH–COOH gen formula

NH2

» R – CH– COO- zwitter ion formula

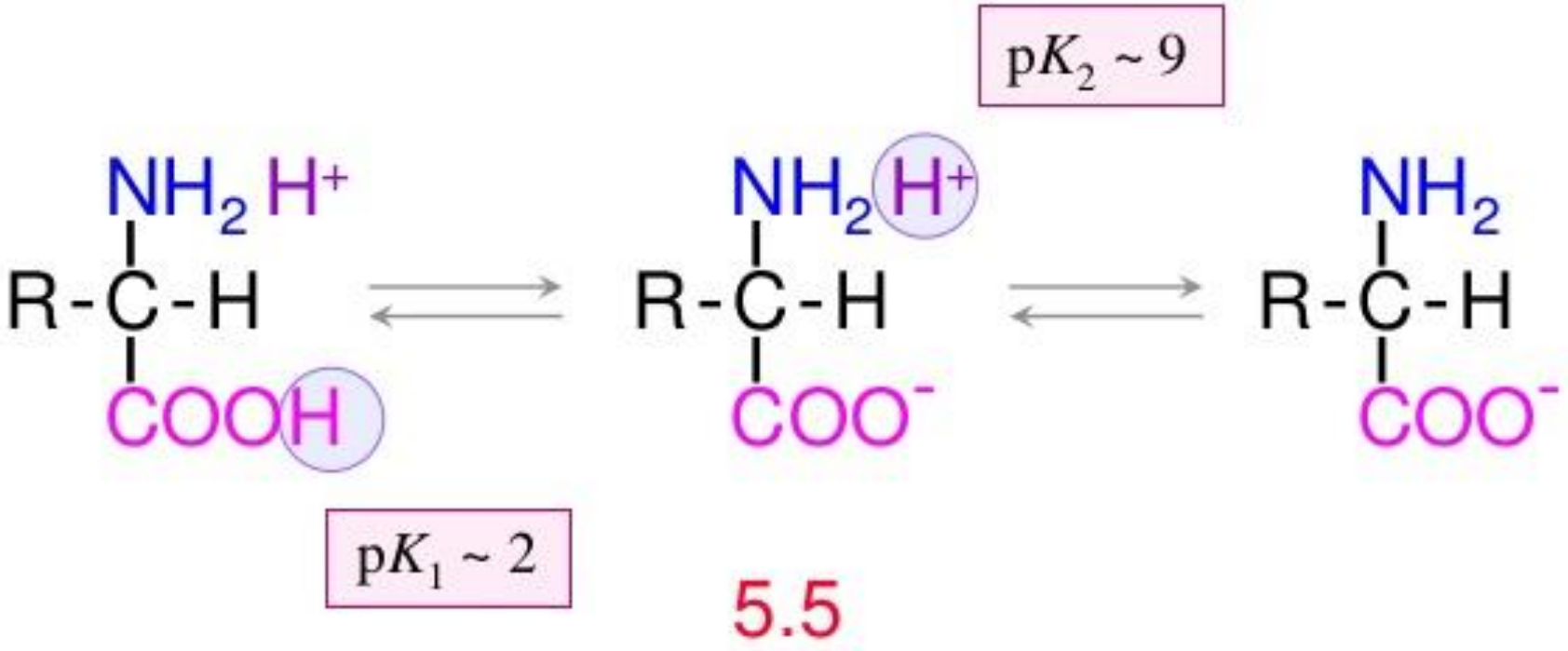
NH3+ or

dipolar ion

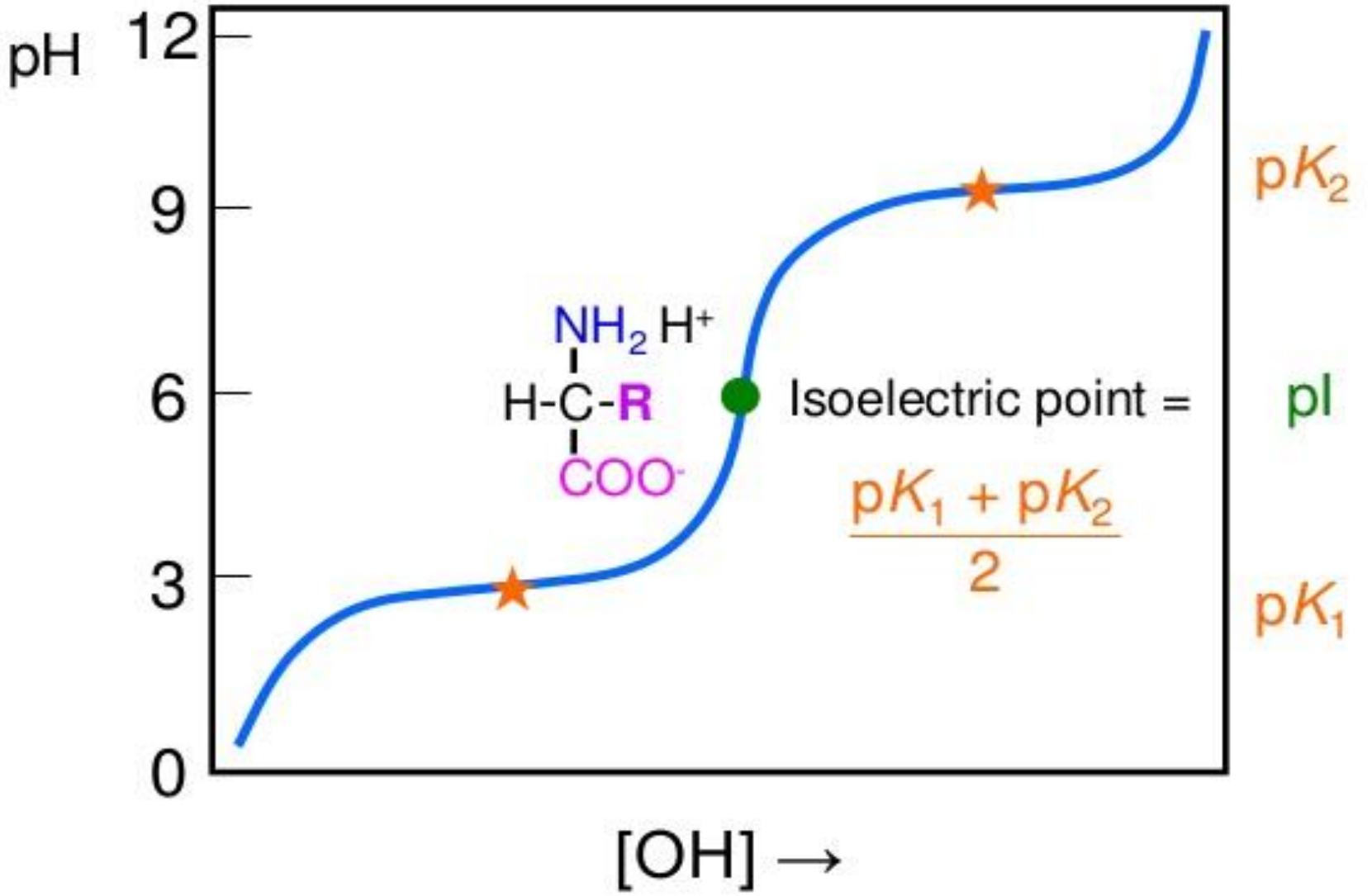
Zwitter ion or dipolar ion:

- Meaning of Zwitter ion is a hybrid molecule which carries both +ve and -ve charge.
- Depending on the pH of the medium amino acid either carry +ve charge or -ve.
- Each AA has a characteristic pH at which it carry both charges and exist as Zwitter ion.
- Example-leucine, pH-6.0

Acidic environment **Neutral environment** **Alkaline environment**



Amino Acids Have Buffering Effect



Zwitterions

- At acidic pH, the carboxyl group is protonated and the amino acid is in the cationic form
- At neutral pH, the carboxyl group is deprotonated but the amino group is protonated. The net charge is zero; such ions are called Zwitterions
- At alkaline pH, the amino group is neutral $-NH_2$ and the COOH acid is in the anionic form.

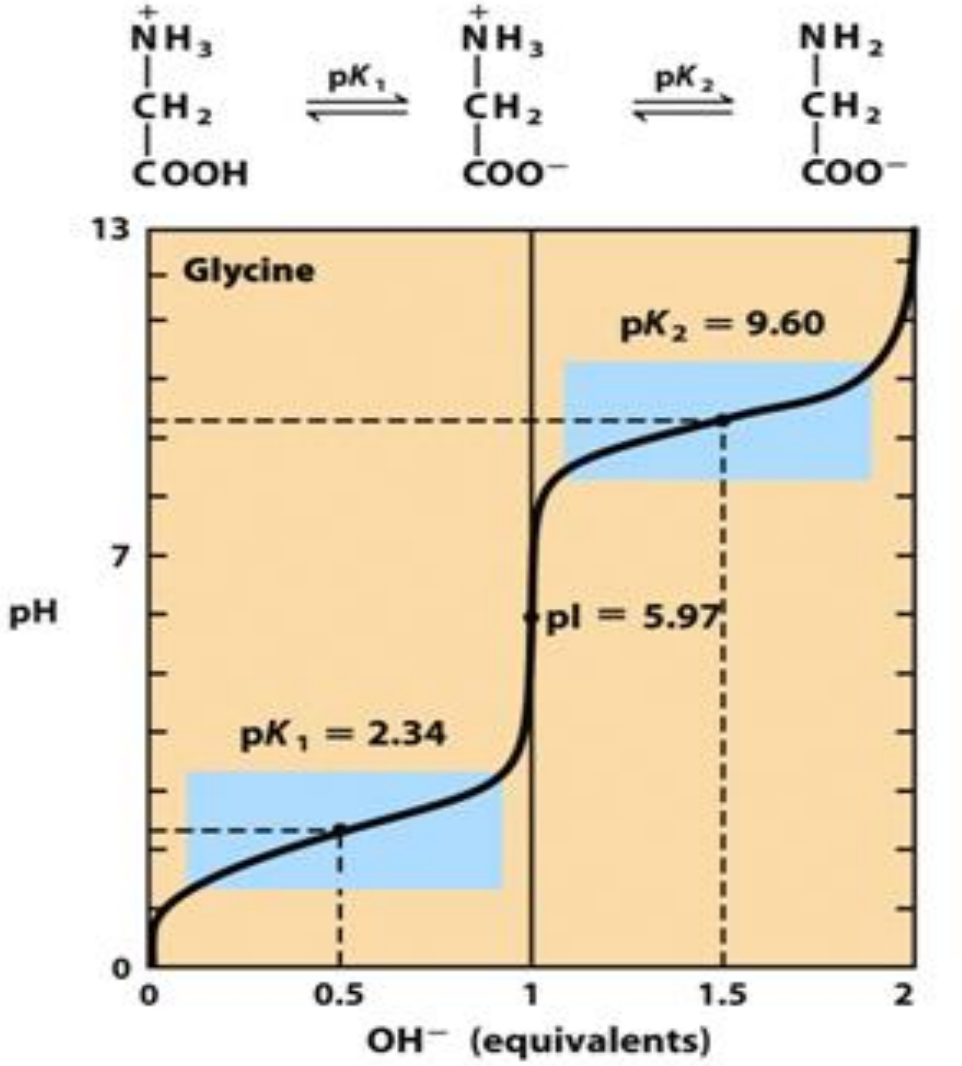


Figure 3-10
Lehninger Principles of Biochemistry, Fifth Edition

3:Peptide Linkage Or Bond:

In a peptide linkage a.a, are attached to their neighboring a.a, by – COOH group on one side and by – NH_2 group on other side

Peptide and Peptide Bonds

Peptide bond in a di-peptide

"Peptides" are small condensation products of amino acids

They are "small" compared to proteins (di, tri, tetra… oligo-)

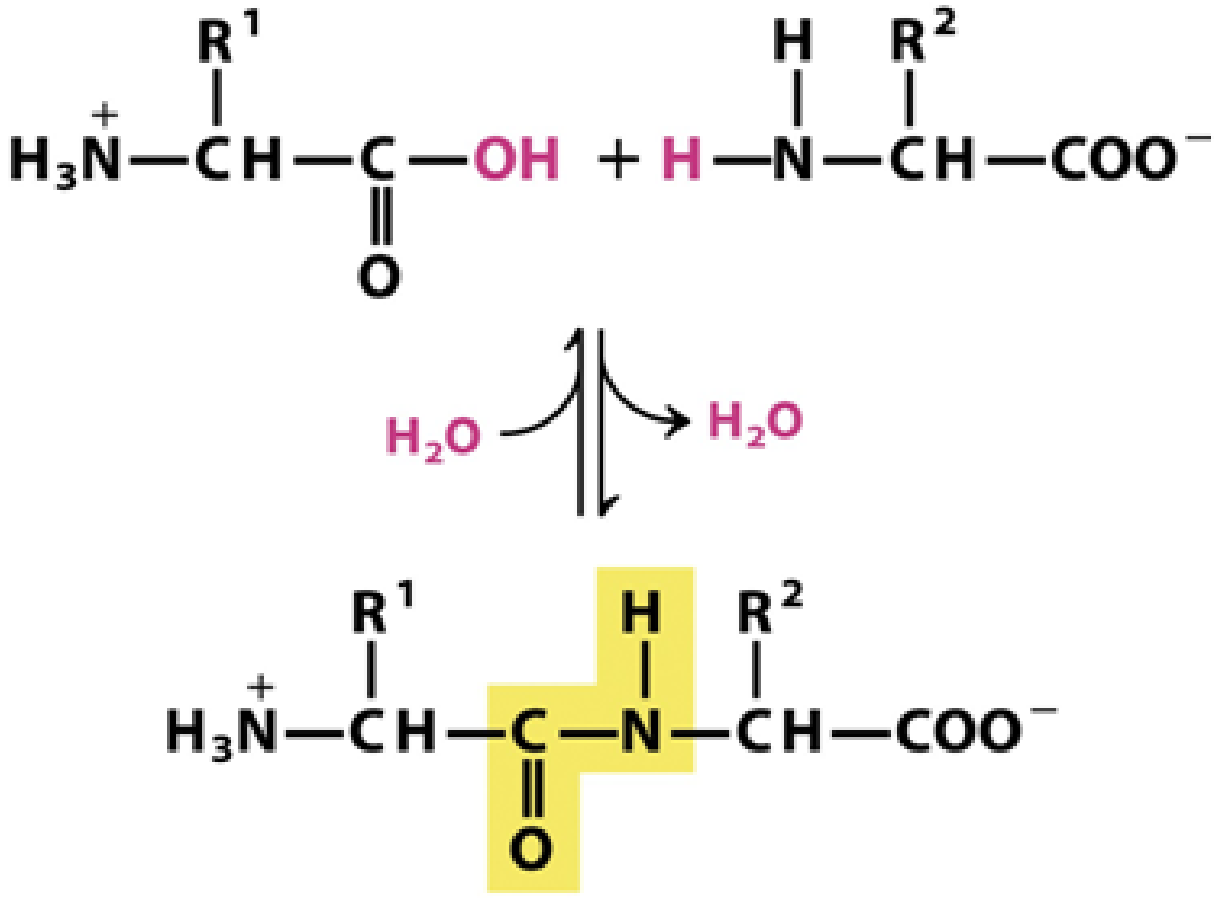


Figure 3-13
Lehninger Principles of Biochemistry, Fifth Edition

Features:

1. Partial double bond character
2. No freedom of rotation
3. Strong acid or base at high temperature hydrolyze it
4. Linkage of more than 10 a. as, form Polypeptide
5. Polypeptide of high molecular weight (7,10000); Proteins
6. A. as, present within a Peptide are called a.a residues.

Physical properties of Amino Acids:

A. Amphoteric Nature(zwitter ion)

B. Optical properties i.e., D & L amino acids(glycine is optically inactive)

C. Crystalline substances, more soluble in Polar Solvents (H_2O)

D. Have high M.P….Usually more than 200^oC

E. They don't absorb visible light, so mostly colorless

F. Tasteless ,sweet or bitter

G. Aromatic amino acids can absorb UV light e.g tyrosine, tryptophan

CHEMICAL PROPERTIES:

Chemical Properties are due to –COOH, NH_2 or – R groups, which gives different chemical reactions, that can be done in Lab.

For example

Ninhydrin, Xanthproteic, Millon's Cystine Tests

CLASSIFICATION OF AMINO ACIDS

» Classified into various ways:

1. **Standard /non standard amino acid**
2. **Depending on nutritional value**
3. **According to metabolic fate**
4. **According to reaction in solution**
5. **Polarity of R-group**

1.a)Standard Amino Acids

- Standard /common a. acids are those for which at least one CODON exists in the genetic code(20 amino acids)

1.b)Non Standard Amino Acid

MODIFIED

- Modified after protein is synthesised
- Eg hydroxyproline in collagen

NON-PROTEIN

- Never found in protein
- Serves important functions eg thyroxine

D-AMINO ACIDS

- Part of bacterial cell wall
- Anti biotics eg actinomycin D

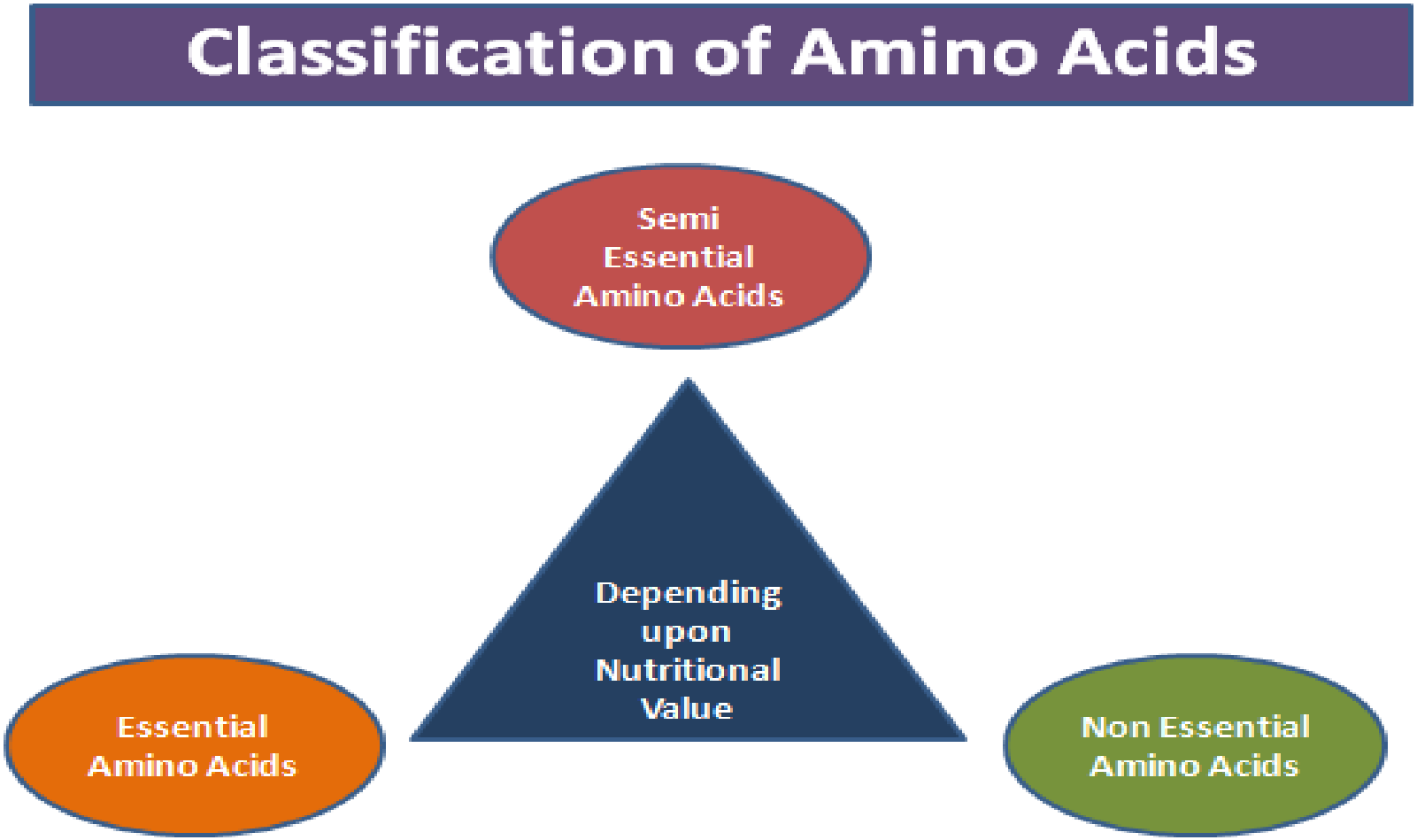
- Many proteins also contain “Derived a. acids” or“Modified a. acids” which are usually formed by Enzymatic modification of common a. acids after it has been incorporated into a Protein e.g hydroxproline and hydroxylysine (collagen) ,gamma carboxyglutamic acid(clotting factors),cysteine(cystine).

- **“Amino acid found in Special Sources”**[i.e., Non – Protein Amino Acid]:
  - These amino acids do not take part in protein synthesis but are found in various molecules & serves very imp. Physiologic functions

TABLE 4.2 A selected list of important non-protein amino acids along with their functions

Amino acids	Function(s)
I. α-Amino acids	
Ornithine, Citrulline, Arginosuccinic acid	Intermediates in the biosynthesis of urea.
Thyroxine, Triiodothyronine	Thyroid hormones derived from tyrosine.
S-Adenosylmethionine	Methyl donor in biological system.
Homocysteine	Intermediate in methionine metabolism. A risk factor for coronary heart diseases
Homoserine	Intermediate in threonine, aspartate and methionine metabolisms.
3, 4-Dihydroxy phenylalanine (DOPA)	A neurotransmitter, serves as a precursor for melanin pigment.
Creatinine	Derived from muscle and excreted in urine
Ovothiol	Sulfur containing amino acid found in fertilized eggs, and acts as an antioxidant
Azaserine	Anticancer drug
Cycloserine	Antituberculosis drug
II. Non-α-amino acids	
β-Alanine	Component of vitamin pantothenic acid and coenzyme A
β-Aminoisobutyric acid	End product of pyrimidine metabolism.
γ-Aminobutyric acid (GABA)	A neurotransmitter produced from glutamic acid
δ-Aminolevulinic acid (ALA)	Intermediate in the synthesis of porphyrin (finally heme)
Taurine	Found in association with bile acids.

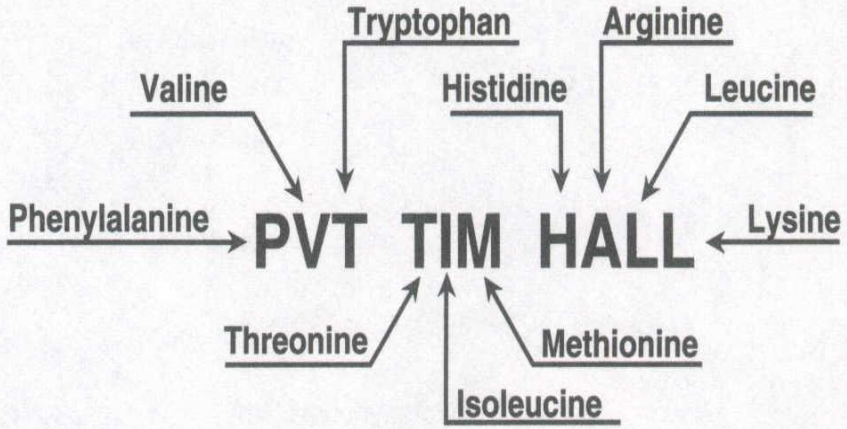
2.Classification based on nutritional value:



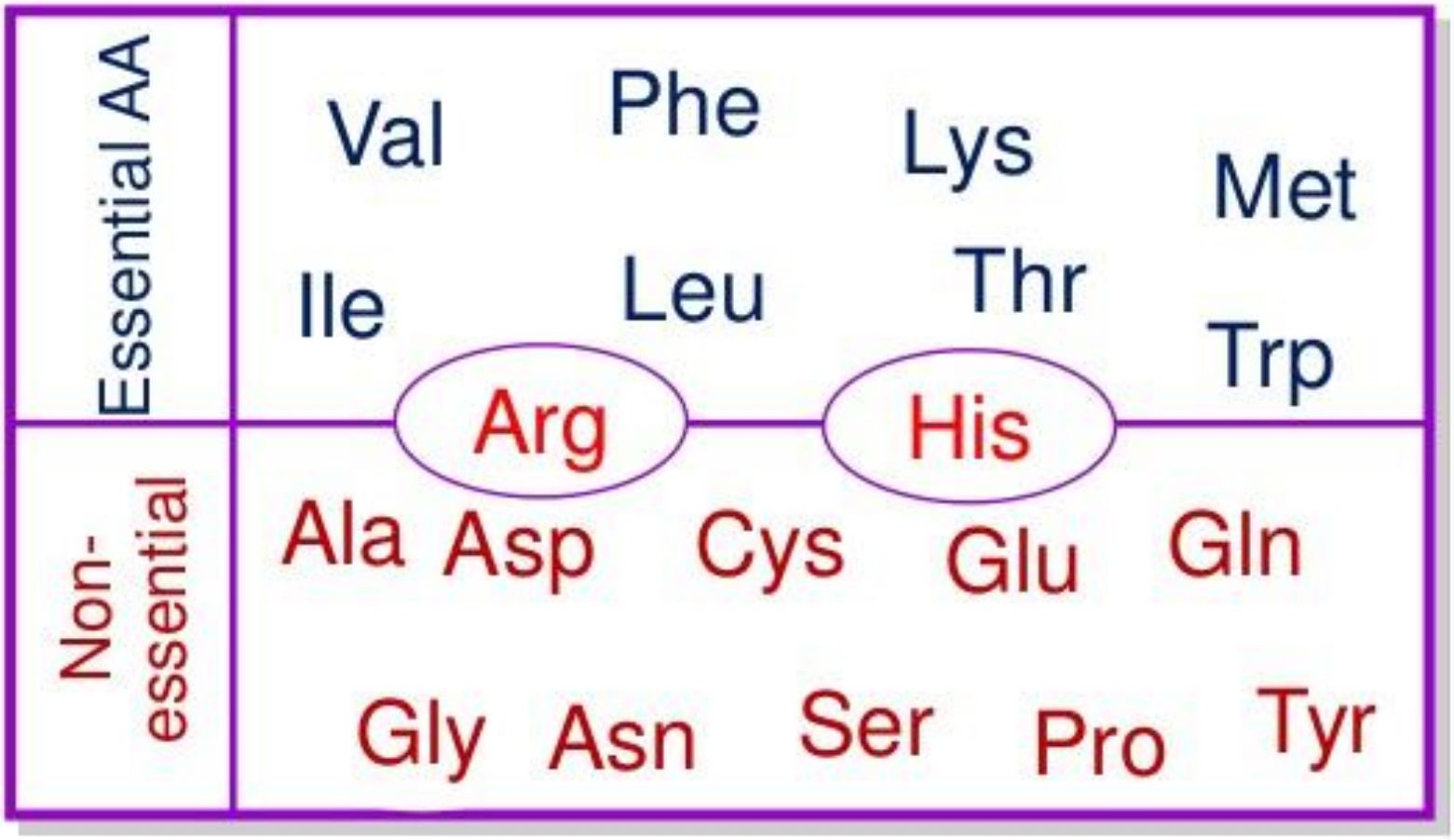
A

	Glucogenic	Glucogenic and Ketogenic	Ketogenic
Nonessential	Alanine Asparagine Aspartate Cysteine Glutamate Glutamine Glycine Proline Serine	Tyrosine	
Essential	Arginine Histidine Methionine Threonine Valine	Isoleucine Phenylalanine Tryptophan	Leucine Lysine

B



Nutritional classification of Amino acids



H. VITTAL, LMP

3.Classification based on metabolic fate:

a: Glucogenic Amino Acids

b: Ketogenic Amino Acids

c: Both Glucogenic & Ketogenic Amino Acids

4. Classification based on structure: (according to their reaction in Solution):

a: <u>Neutral Amino Acids:</u>

» No. of – NH_2 & – COOH groups are equal i.e.,

they are "Mono amino", "Mono carboxylic" acid

» They are largest group of a. acids & can be further sub divided in to

- i: Aliphatic Amino Acids
- ii: Aromatic Amino Acids
- iii: Heterocyclic Amino Acids
- iv: S-Containing Amino Acids

- **i: Aliphatic Amino Acids**
- **Simplest amino acids**
- Glycine , Alanine, Valine, Leucine, Isoleucine
- Valine,leucine,isoleucine are called branched chain amino acids

ii: Aromatic Amino Acids

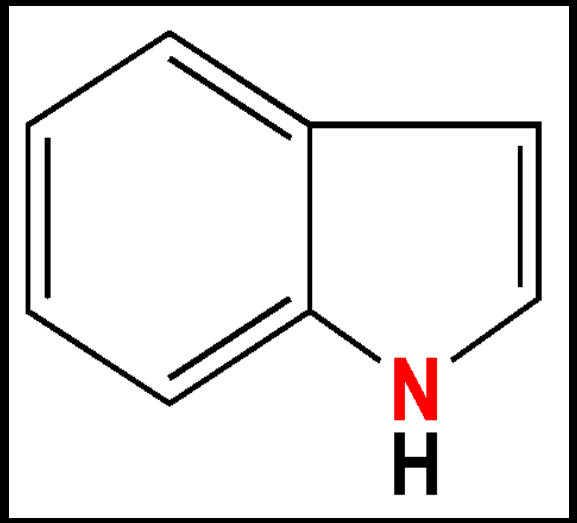
- Containing Benzene Ring
- e.g., Phenylalanine, Tyrosine

iii: Heterocyclic Amino Acids

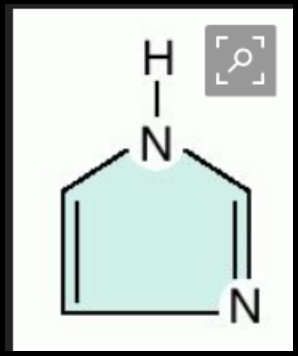
Compounds that has atoms of at least two different elements as members of its ring e.g;

- Tryptophan(indole ring ;often considered aromatic)
- Histidine (considered as Basic a. acid, on account of Imidazole ring)

» Indole ring



» Imidazole ring



iv: S – Containing Amino Acids

Cysteine, & Methionine

Two molecules of Cysteine can make Cystine

b)Acidic Amino Acids:

- These a. acids has two – COOH groups & one $–NH_2$ i.e. **Monoamino dicarboxylic acid**
- Example are aspartic acid, glutamic acid

c)Basic Amino Acids:

- This class of a. acids consists of one –COOH &2 –NH_2 groups **Diamino mono carboxylic acid**
- Examples:
- arginine,
- lysine,
- hydroxylysine,
- histidine

5. **On the Basis of side chain characteristics (Polarity of "R – Group"):**

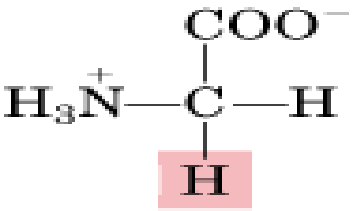
Four sub groups

a: **Non – Polar "R – Group"**

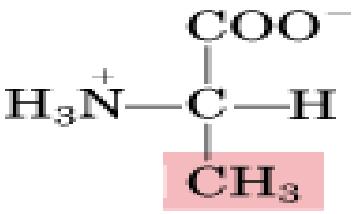
» Hydrophobic in nature

» Includes Alanine, Valine, Leucine, Isoleucine, Proline, Phenyalanine, Tryptophan, Methionine

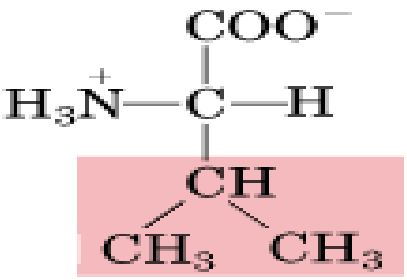
Nonpolar, aliphatic R groups



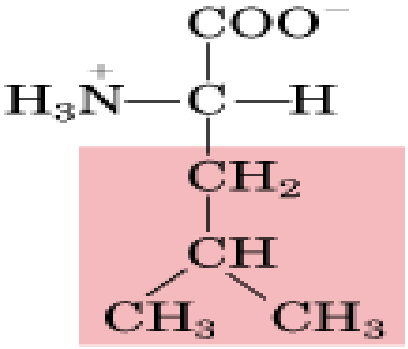
Glycine



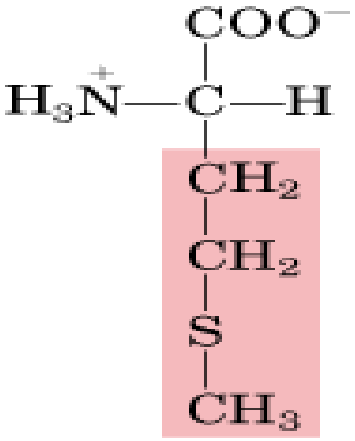
Alanine



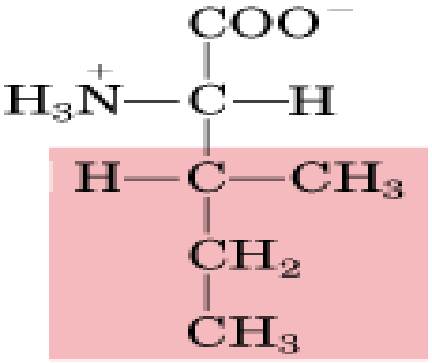
Valine



Leucine



Methionine

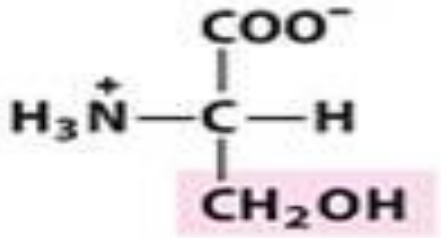


Isoleucine

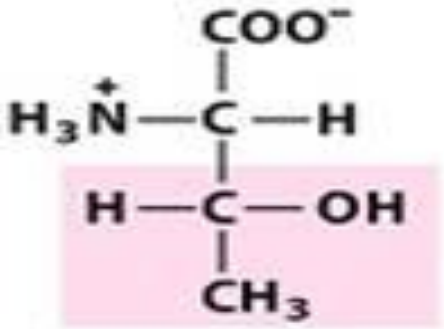
b: Polar with uncharged or non ionic R-group:

- no charge on R-group
- Have hydroxyl, sulfhydryl, amide ,acid, alcohol groups
- These groups take part in H-bonding
- e.g., Glycine, Serine, Threonine, Cysteine, Tyrosine, Asparagine, & Glutamine

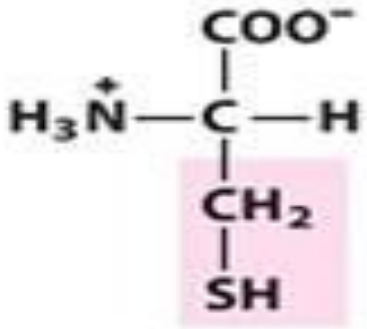
Polar, uncharged R groups



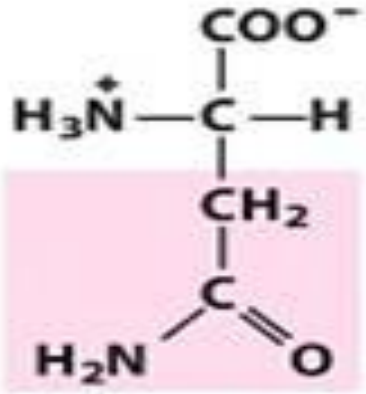
Serine



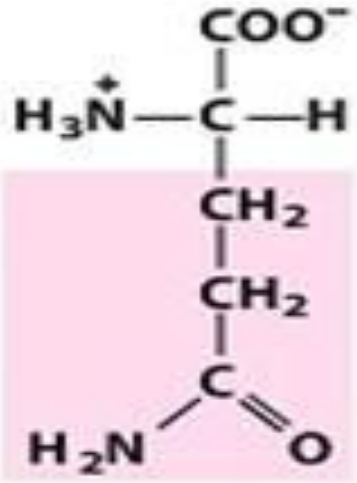
Threonine



Cysteine



Asparagine



Glutamine

C: A.A with charged or ionic R-Groups:

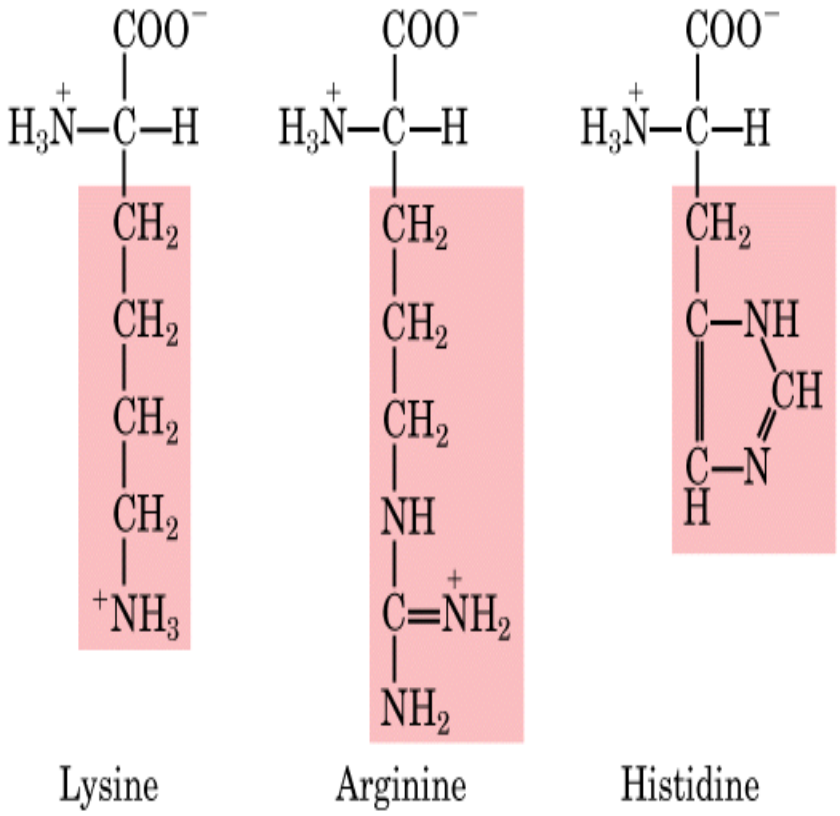
i: A A with – vely Charged "R – Group"

- Having Acidic "R – Group"
- This class includes, Aspartic acid, & Glutamic acid

ii: A A with + vely Charged "R – Group"

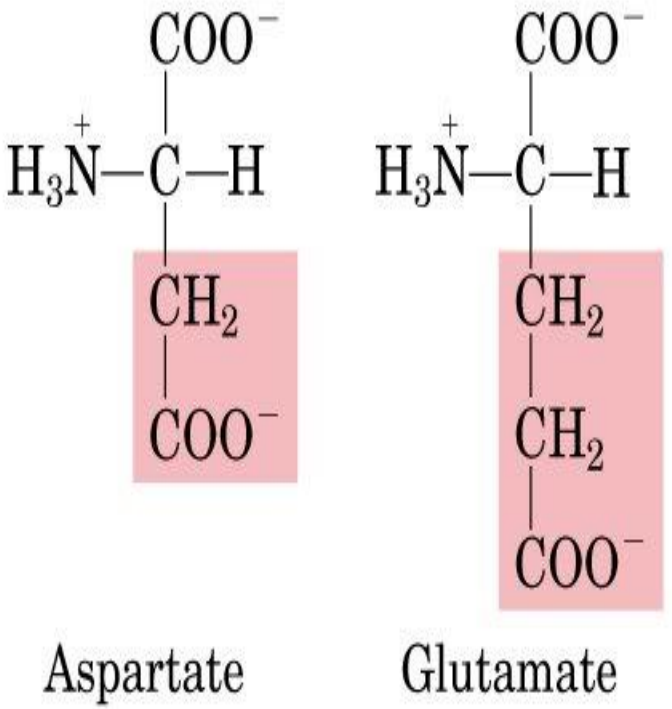
- Having Basic "R – Group"
- e.g., Lysine, & Arginine

Positively charged R groups



Lysine Arginine Histidine

Negatively charged R groups



Aspartate Glutamate

New Amino Acids

» In addition to 20 – L amino acids that take part in protein synthesis, recently Two more new amino acids are described.

They are;

i. Selenocysteine……21st A A

ii. Pyrrolysine……22nd A A

Selenocyteine:

- It has antioxidant properties.
- Occurs at “active site” of several enzymes

e.g.,

a): Glutathione Peroxidase

b): 5-deiodinase

Pyrrolosine :not present in humans

Functions Of Amino Acids

- A part from being monomeric constituent of proteins and peptides, amino acids serves a variety of functions.

1. Glucogenic & Ketogenic

2. Specific A A give rise to specialized products

- Tyrosine …… T3, T4, Epinephrine Nor epinephrine, & a pigment called Melanin
- Gly + Glutamate + Cyst (Glutathione)

- Aspartate, Glutamate & Glycine help in the formation of Purine & Pyrimidine
- Methionine acts – CH_3 group donor
- Cysteine & Methionine are sources of “S”
- Histidine (histamine)

Formation of amines by decarboxylation

Histidine ⟶ Histamine

- increase formation as a result of stings of Bees
- causes Vasodilation, redness & Swelling
- Involved in inflammatory response

- Tryptophan can synthesize a Vitamin called Niacin (Vit. B_1) ,and serotoninn (vasoconstrictor)
- Glycine & Cysteine help in the synthesis of Bile Acids
- Glycine present in heme

Some peptides & their Properties:

GLUTATHIONE:

- It is combination of Glutamic acid, Cysteine& Glycine.
- Protect the cell wall from Toxic effects of

  H_2O_2 by converting it to H_2O……*Antioxidant*

BRADYKININ & KALLIDIN:

- Both have 9 – 10 a. a residues.
- Vasodilator
- Mediator of inflammation, drops B.P & mediates pain
- Role in coagulation .

MANY HORMONES ARE PEPTIDES:

e.g., Gastrin, Pancreatic Hormones, PTH, GH,Oxytocin & Vasopressin

ANTIBIOTIC PEPTIDES:

Penicillin, chloramphenicol, Actinomycin etc.

Take home message

- Proteins are polymers of L-α-amino acids
- All standard amino acids are L- alpha
- Neutral amino acids are most abundant
- Aliphatic are simplest amino acids eg glycine
- Proline has secondary amine

- S-containing amino acids include cystein,methionine
- Aromatic amino acids include phenylalanine , tyrosine and tryptophan
- Tryptophan and histidine are heterocyclic
- Neutral amino acids exist as zwitter ions

THANK YOU