Amino Acids & Peptides

University of Anbar/College of Pharmacy
Second semester 2021-2022 / Biochemistry I / 3rd stage

References :

1- Harper’s Illustrated Biochemistry
2- Lehninger Principles of Biochemistry

By
Dr. Muthanna Owaid Hussein

Amino Acids

As their name indicates, amino acids are compounds that contain an amino group and a carboxylic acid group. The amino acids in proteins have the amino group bonded to the α carbon of the carboxylic acid. As a result, they are called α-amino acids.

- Proteins are polymers of amino acids, with each amino acid residue joined to its neighbor by a specific type of covalent bond. (The term “residue” reflects the loss of the elements of water when one amino acid is joined to another.)
- There are about 300 amino acids occur in nature. Only 20 of them occur in proteins.
- The Genetic Code Specifies 20 L-α-Amino Acids

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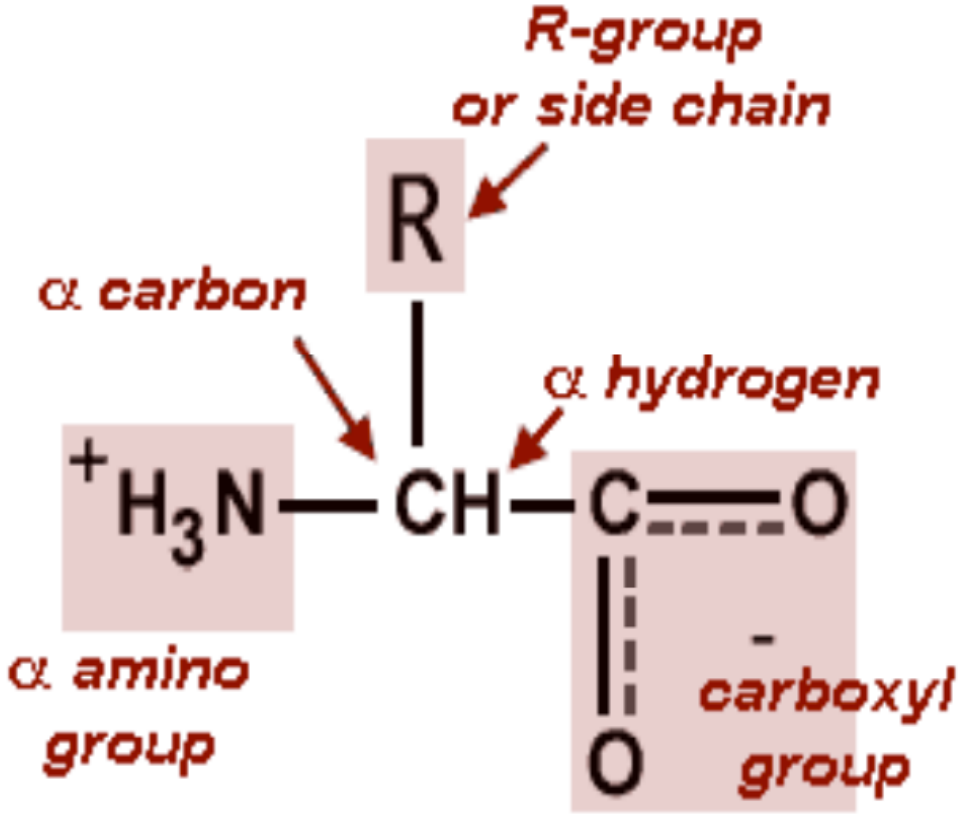
Structure of amino acids:

- Each amino acid has 4 different groups attached to α- carbon (which is C-atom next to COOH). These 4 groups are : amino group, COOH group, Hydrogen atom and side Chain (R).
- At physiological PH (7.4), -COOH group is dissociated forming a negatively charged carboxylate ion (COO-) and amino group is protonated forming positively charged ion (NH3+) forming Zwitter ion.
- Proline is an imino acid not amino acid.



Biomedical Importance

Amino acids and their derivatives participate in cellular functions as

- Diverse as nerve transmission.
- Biosynthesis of porphyrins, purines, pyrimidines, and urea.
- The neuroendocrine system employs short polymers of amino acids called peptides as hormones, hormone-releasing factors, neuromodulators, and neurotransmitters.
- 10 of the L-α-amino acids present in proteins in amounts sufficient to support infant growth or to maintain adult health. Consequently, the human diet must contain adequate quantities of these nutritionally essential amino acids.
- Some peptides are of therapeutic value,

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Nomenclature & Classification of amino acids

Abbreviations and symbols for the commonly occurring amino acid each aa name has either three letters abbreviation or a one-letter symbol.

A- Chemical classification (R function group)

B- Classification according to (polarity of R group)

C- Nutritional classification (Essential & Non essential amino acids)

D- Metabolic classification (Ketogenic, Glucogenic, Mixed ketogenic and glucogenic)

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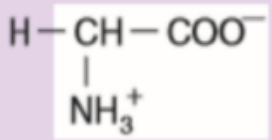
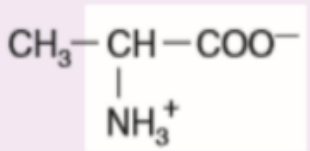
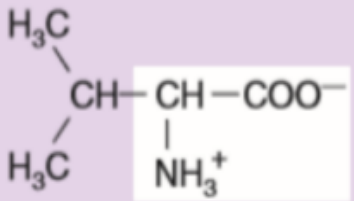
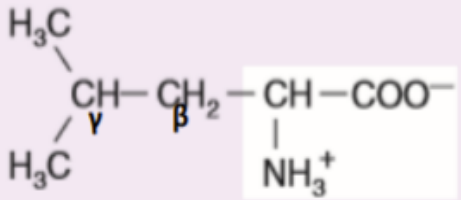
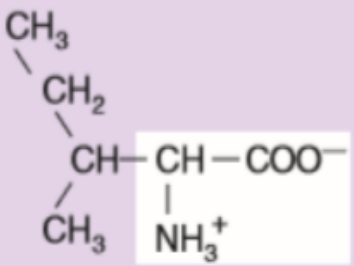
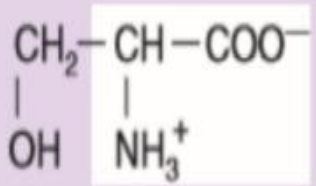
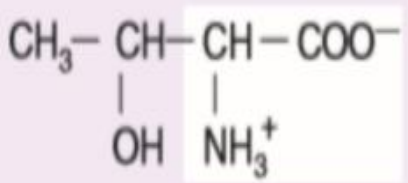
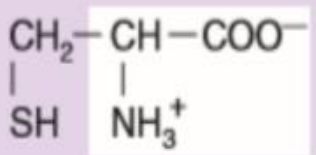
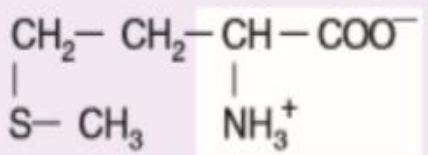
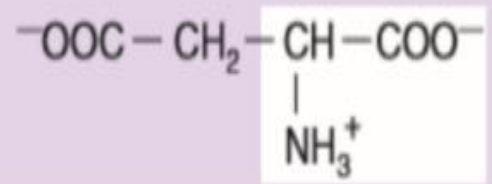
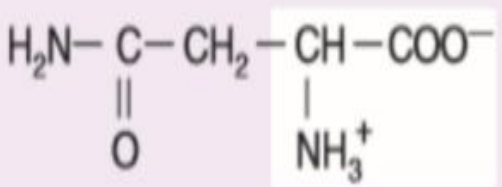
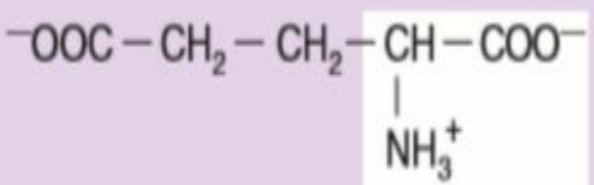
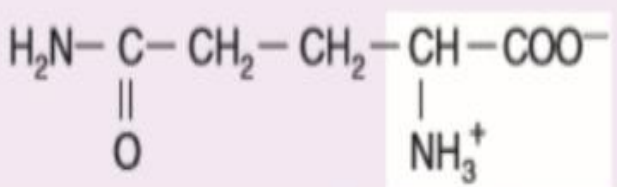
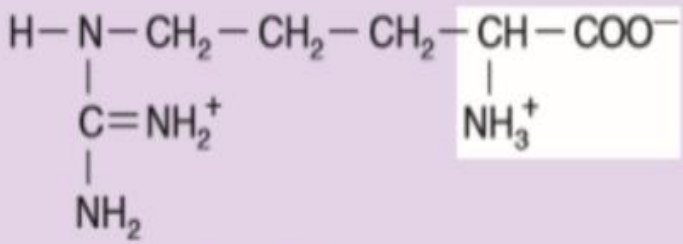
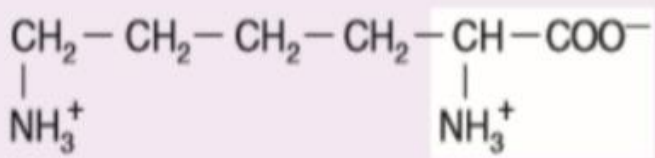
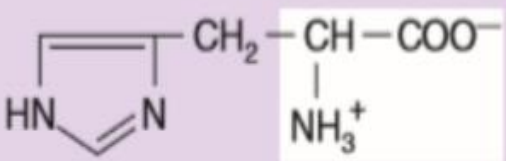
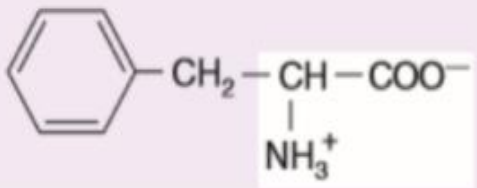
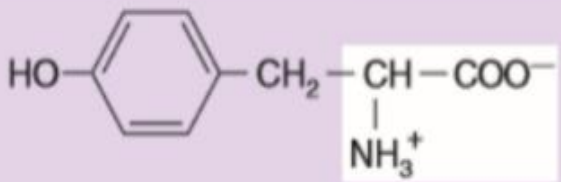
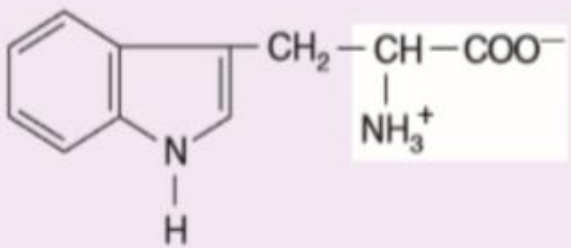
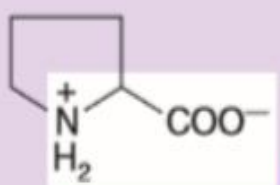
TABLE 3–1 L-α-Amino Acids Present in Proteins

Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Aliphatic Side Chains	**Nonpolar/Hydrophobic**		α-COOH	α-NH_3^+	R Group
Glycine	Gly [G]		2.4	9.8	
Alanine	Ala [A]		2.4	9.9	**Methyl R group**
Valine	Val [V]		2.2	9.7	**Isopropyl R group**
Leucine	Leu [L]		2.3	9.7	**Branching in isobutyl side chain on γ carbon of amino acid**
Isoleucine	Ile [I]		2.3	9.8	**Branching in isobutyl side chain on β carbon of amino acid**

Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Side Chains Containing Hydroxylic (OH) Groups					
Serine **Polar, uncharged-R group**	Ser [S]		2.2	9.2	about 13
		Hydroxymethyl R group			
Threonine **Polar, uncharged-R group**	Thr [T]		2.1	9.1	about 13
		Secondary Alcohol structure			
Tyrosine	Tyr [Y]	Mentioned in amino acids with aromatic rings section			
With Side Chains Containing Sulfur Atoms			**α-COOH**	**α-NH_3^+**	**R Group**
Cysteine **Polar, uncharged-R group**	Cys [C]		1.9	10.8	8.3
		Thiolmethyl/Sulfhydryl R group			
Methionine **Nonpolar**	Met [M]		2.1	9.3	
		Methyl ethyl thiol ether R group			

Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Side Chains Containing Acidic Groups or Their Amides					
Aspartic acid	Asp [D]		2.1	9.9	3.9
Negatively charged R group			**β-COOH R group**		
Asparagine	Asn [N]		2.1	8.8	
Polar, Uncharged-R group					
Glutamic acid	Glu [E]		2.1	9.5	4.1
Negatively charged R group			**γ-COOH R group**		
Glutamine	Gin [Q]		2.2	9.1	
Polar, Uncharged-R group					

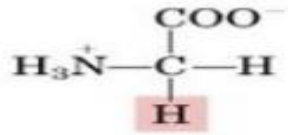
Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Side Chains Containing Basic Groups		**Positively charged R groups**			
Arginine	Arg [R]		1.8	9.0	12.5
			Guanidinium R group		
Lysine	Lys [K]		2.2	9.2	10.8
			ε-NH^+_3 R group		
Histidine	His [H]		1.8	9.3	6.0
			Imidazolium R group		

Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
Containing Aromatic Rings					
Histidine	His [H]	Mentioned in amino acids with basic groups section			
Phenylalanine	Phe [F]		2.2	9.2	
		Benzene ring R group			
Tyrosine	Tyr [Y]		2.2	9.1	10.1
		Phenol R group			
Tryptophan	Trp [W]		2.4	9.4	
		Heterocyclic structure, indole R group			
Imino Acid					
Proline	Pro [P]		2.0	10.6	
		Imino group belongs to a five-member ring			

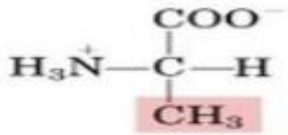
B. Classification of amino acids based On polarity

1. Non-polar amino acids with aliphatic ‘R’ group
2. Non-polar amino acids with aromatic ‘R’ group
3. Polar amino acids with no charge on ‘R’ group
4. Polar amino acids with negative ‘R’ group
5. Polar amino acid with positive ‘R’ group

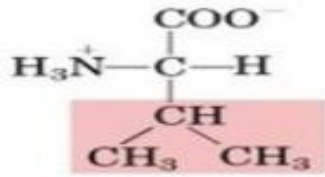
Nonpolar, aliphatic R groups



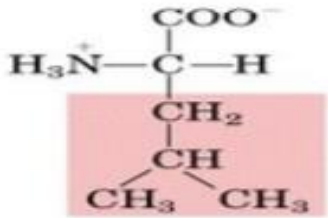
Glycine



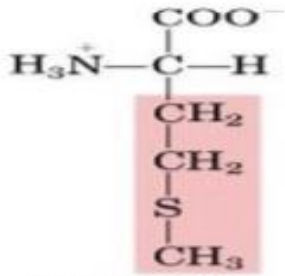
Alanine



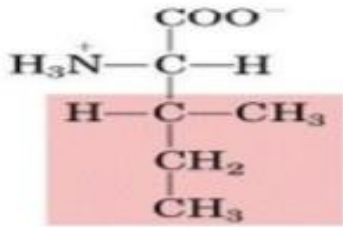
Valine



Leucine

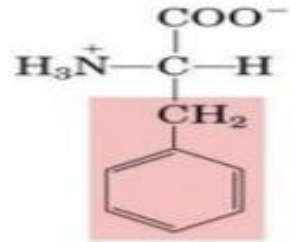


Methionine

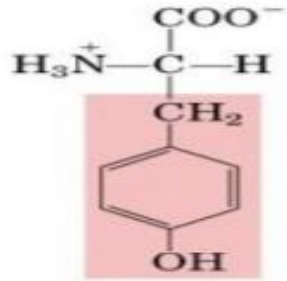


Isoleucine

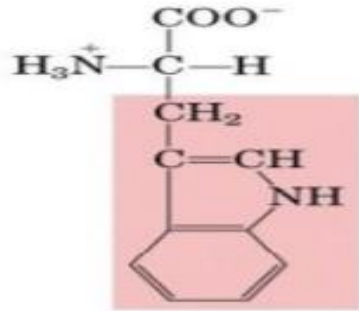
Aromatic R groups



Phenylalanine

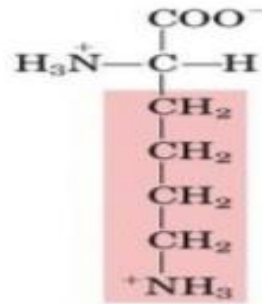


Tyrosine

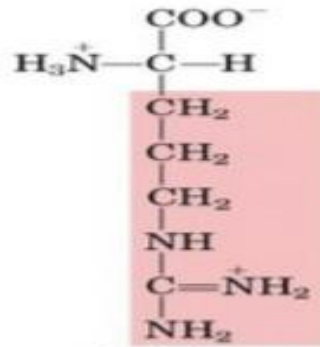


Tryptophan

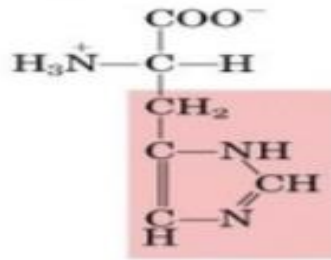
Positively charged R groups



Lysine

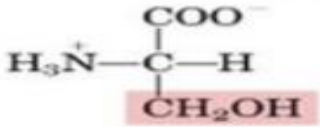


Arginine

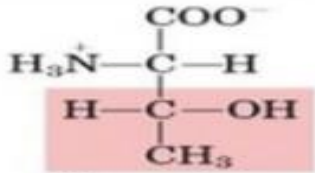


Histidine

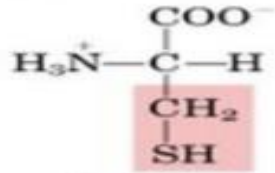
Polar, uncharged R groups



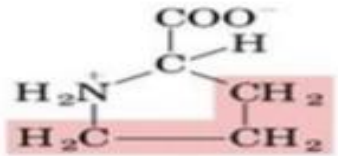
Serine



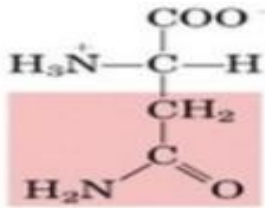
Threonine



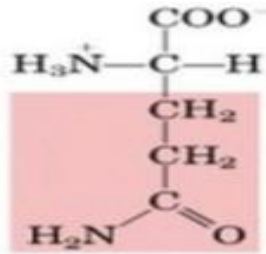
Cysteine



Proline

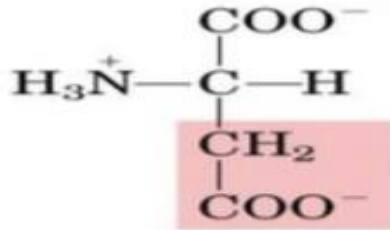


Asparagine

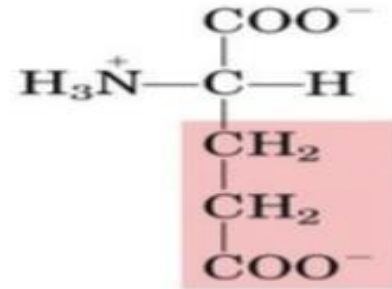


Glutamine

Negatively charged R groups



Aspartate



Glutamate

C- Nutritional classification:

Essential amino acids

- The amino acid which cannot be synthesized by the body and, therefore need to be supplied through the diet is called essential amino acids.

- Ten amino acids comes under this group. Arginine, Valine, Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan

Non-Essential amino acids

- The body can synthesize about 10 essential amino acids to meet the biological needs hence they need not be consumed in the diet.

- Glycine, Alanine, Serine, Cysteine, Aspartate, Asparagine, Asparagine, Glutamate, Glutamine, Tyrosine, and Proline.

Essential Amino acids	Non-Essential Amino acids
Arginine	Glycine
Histidine	Alanine
Isoleucine	Asparagine
Leucine	Aspartate
Lysine	Glutamate
Methionine	Serine
Phenylalanine	Cysteine
Threonine	Glutamine
Tryptophan	Tyrosine
Valine	Proline

D- Metabolic classification: according to metabolic or degradation products of amino acids they may be:

1- Ketogenic amino acids: which give ketone bodies . Lysine and Leucine are the only pure ketogenic amino acids.

2- Glucogenic amino acids: Which give glucose. They include the rest of amino acids. These amino acids by catabolism yields products that enter in glycogen and glucose formation.

3- Mixed ketogenic and glucogenic amino acids: which give both ketonbodies and glucose. These are: isoleucine, phenyl alanine, tyrosine and tryptophan.

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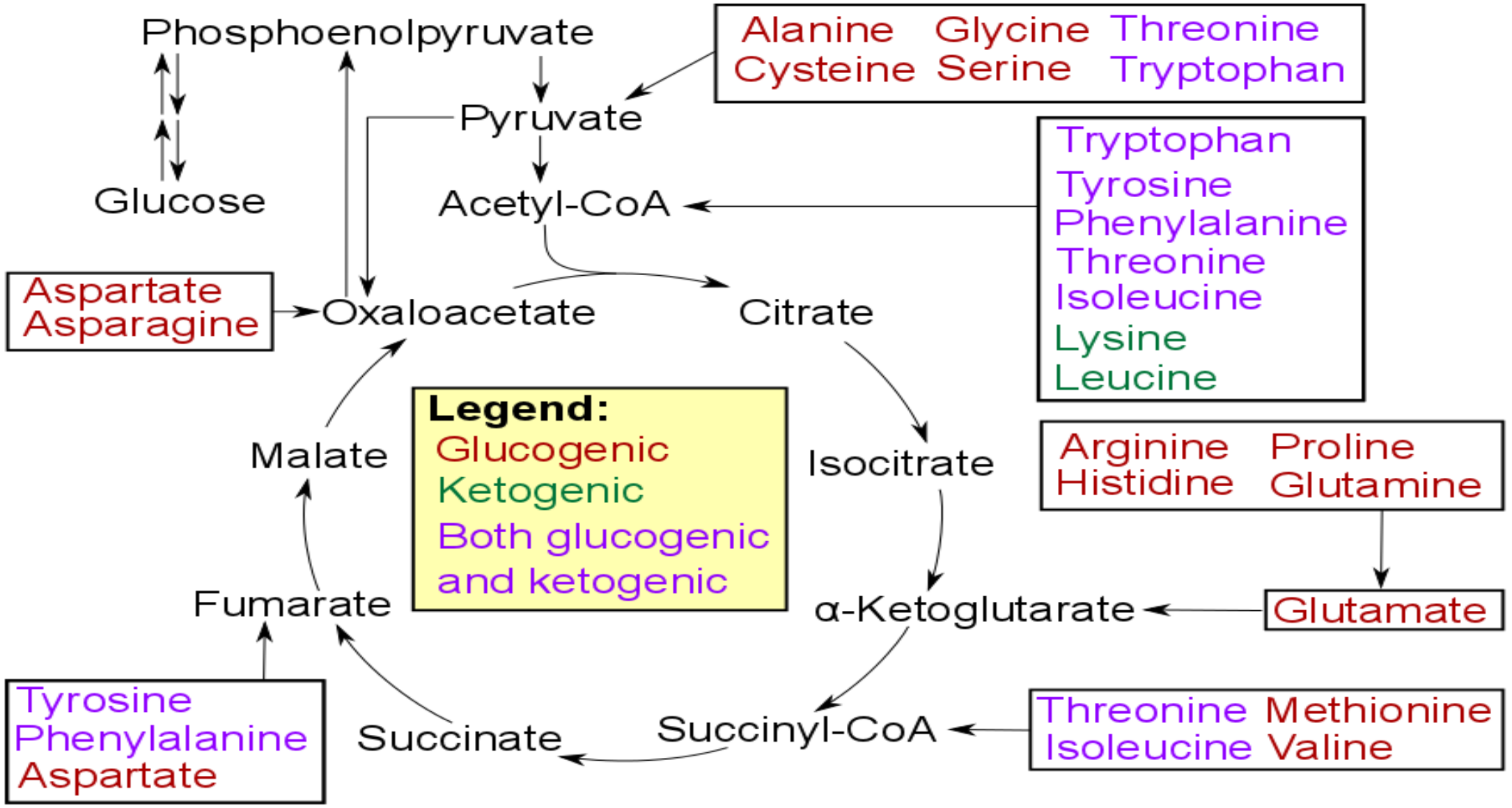
Metabolic Catabolism of Amino Acids



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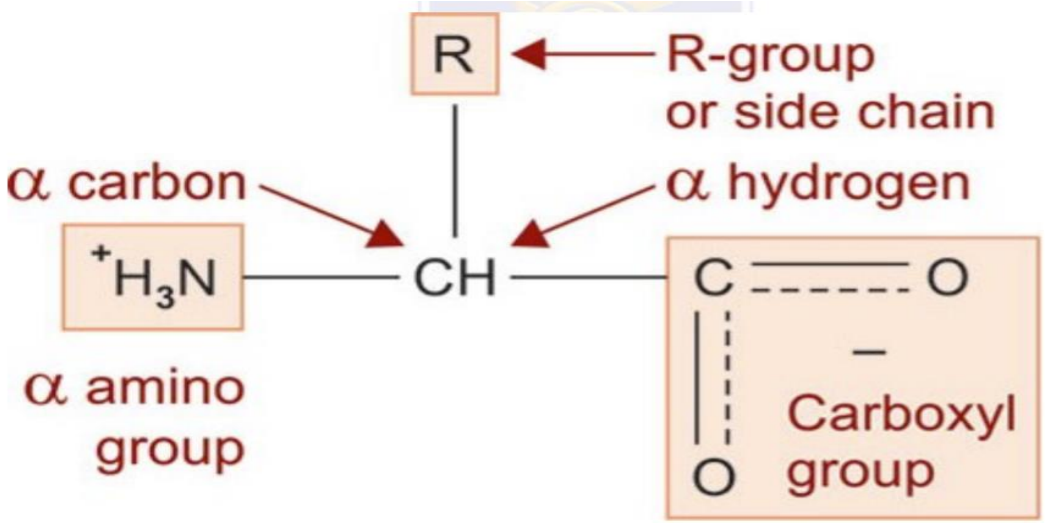
Properties of amino acids:

The amino acids differ in their physiochemical properties which determine the characteristic of protein.



A. Physical properties B. Chemical properties

A. Physical properties

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

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

3-Taste : Amino acids may be sweet (Gly, Ala, Val), tasteless (Leu) or bitter (Arg, Ile), Monosodium glutamate (MSG) is used as a flavoring agent in food industry.

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

5- Amino acids as ampholytes : amino acid contains both acidic(-COOH) and basic (-NH2) groups. They can donate a proton or accept a proton , hence amino acids are regarded as ampholytes.

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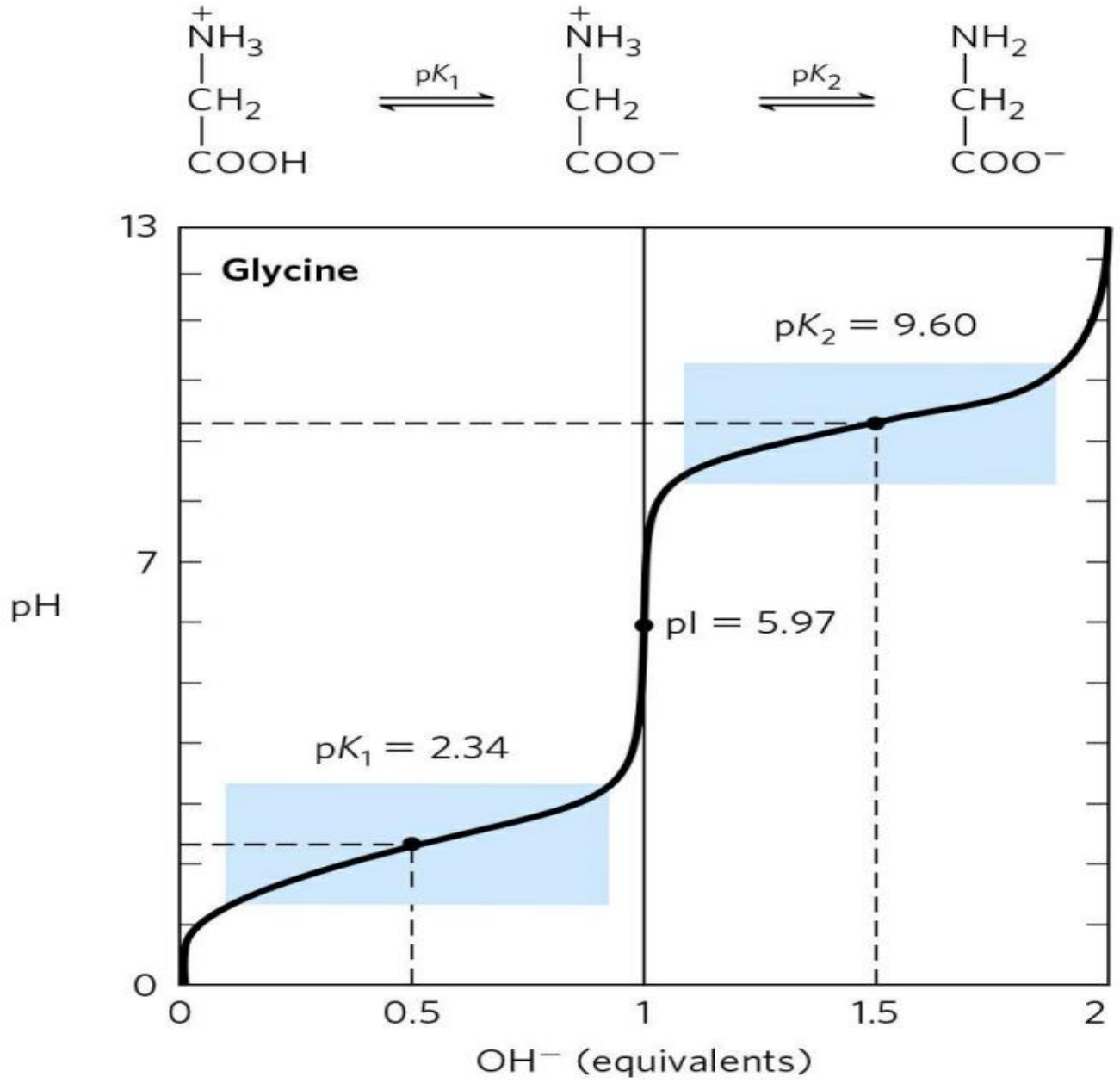
TABLE 3–2 Hydrophilic & Hydrophobic Amino Acids

Hydrophilic	Hydrophobic
Arginine	Alanine
Asparagine	Isoleucine
Aspartic acid	Leucine
Cysteine	Methionine
Glutamic acid	Phenylalanine
Glutamine	Proline
Glycine	Tryptophan
Histidine	Tyrosine
Lysine	Valine
Serine	
Threonine	

6. Zwitter ion or dipolar ion: It is a hybrid molecule containing positive and negative groups. The amino acids rarely exist in a neutral form with free carboxylic (-COOH) and free amino (-NH) 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. glycin, pH 5.97) at which it carries both positive and negative charge and exist as a zwitter ion.



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Amphoteric properties of amino acids: They have both basic and acidic groups and so can act as base or acid.
Neutral amino acids (monobasic, monocarboxylic) exist in aqueous solution as " Zwitter ion" i.e. contain both positive and negative charge. Zwitter ion is electrically neutral and can't migrate into electric field.

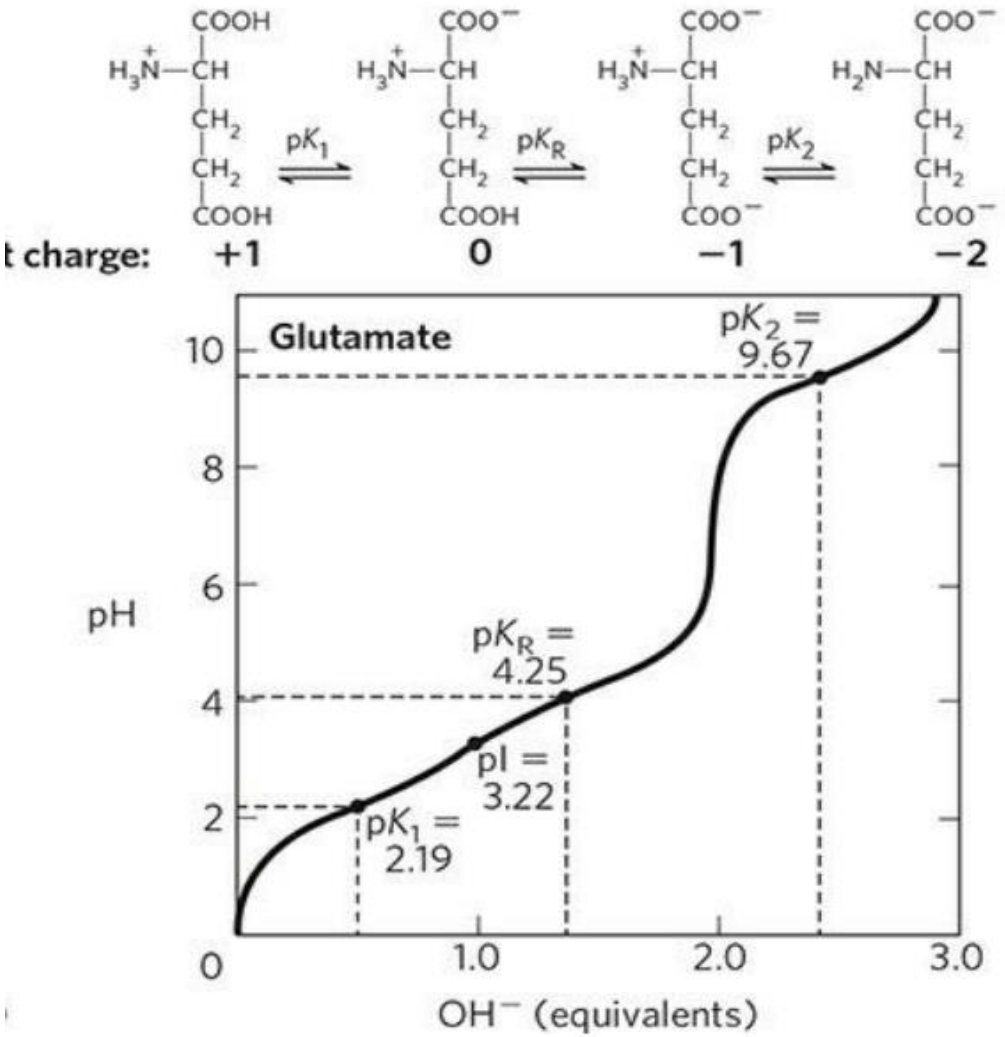
Isoelectric point (IEP) = is the pH at which the zwitter ion is formed.
e.g IEP of alanine is 6

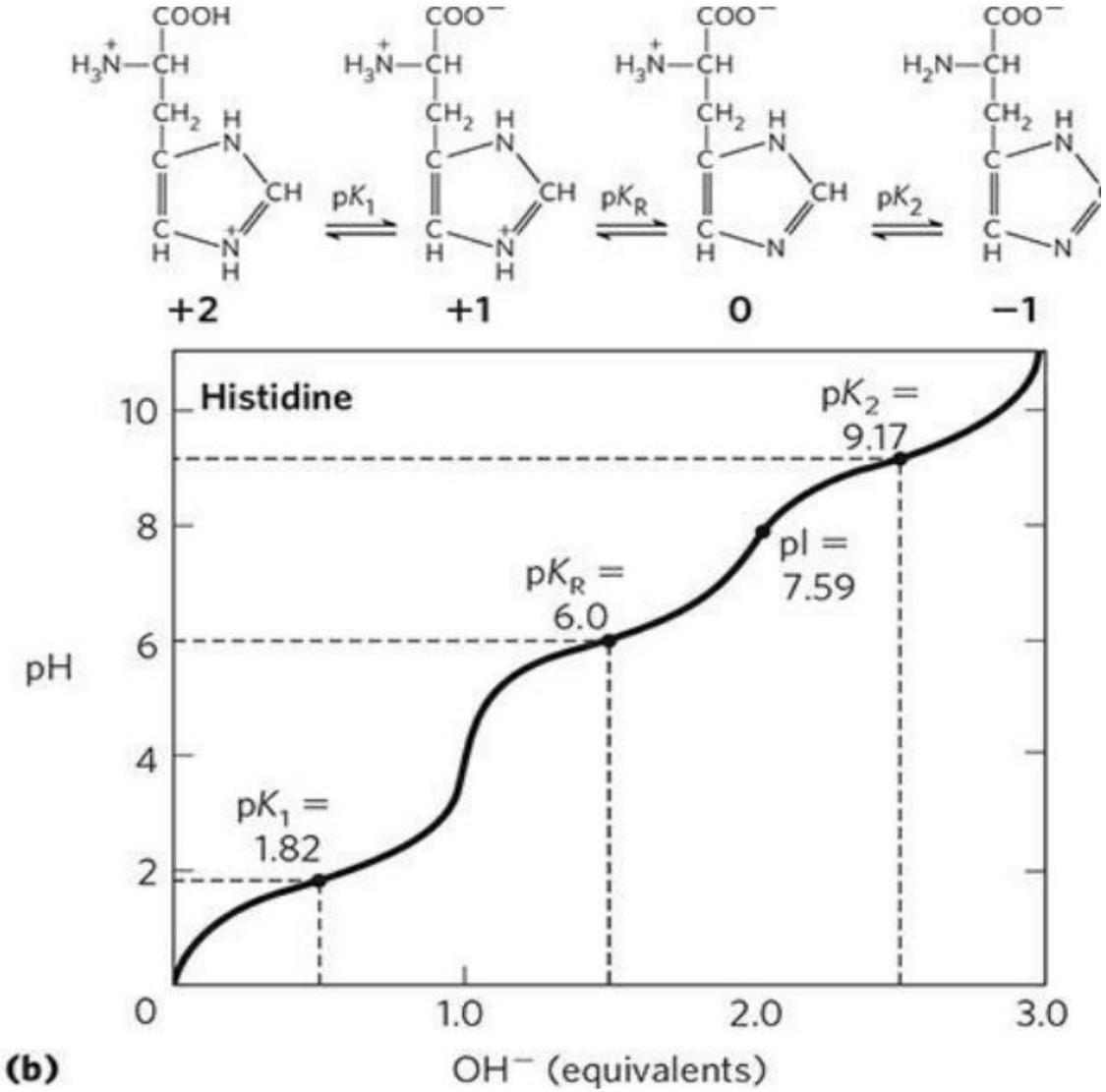
The characteristic pH at which the net electric charge is zero is called the isoelectric point or isoelectric pH, designated pI. For glycine, which has no ionizable group in its side chain, the isoelectric point is simply the arithmetic mean of the two pKa values:

$$\mathrm{pI} = \frac{1}{2}(\mathrm{p}K_1 + \mathrm{p}K_2)$$

Titration curves for Glutamate and Histidine.

The pKa of the R group is designated here as pKR.





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Chemical properties of amino acids:

1- Reactions due to COOH group:

Salt formation with alkalis, ester formation with alcohols, amide formation with amines and decarboxylation.

2- Reactions due to NH2 group:

deamination and reaction with ninhydrin reagent. Ninhydrin reagent reacts with amino group of amino acid yielding blue colored product. The intensity of blue color indicates quantity of amino acids present.

3- Millon reaction: for tyrosine, it gives red colored mass

4- Rosenheim reaction: for tryptophan, it gives violet ring.

5- Pauly reaction: for imidazole ring of histidine, it gives yellow to reddish product

6- Sakagushi test: for guanidine group of arginine, it gives red color.

7- Lead sulfide test (sulfur test): for sulfur containing amino acids as cysteine give brown color.

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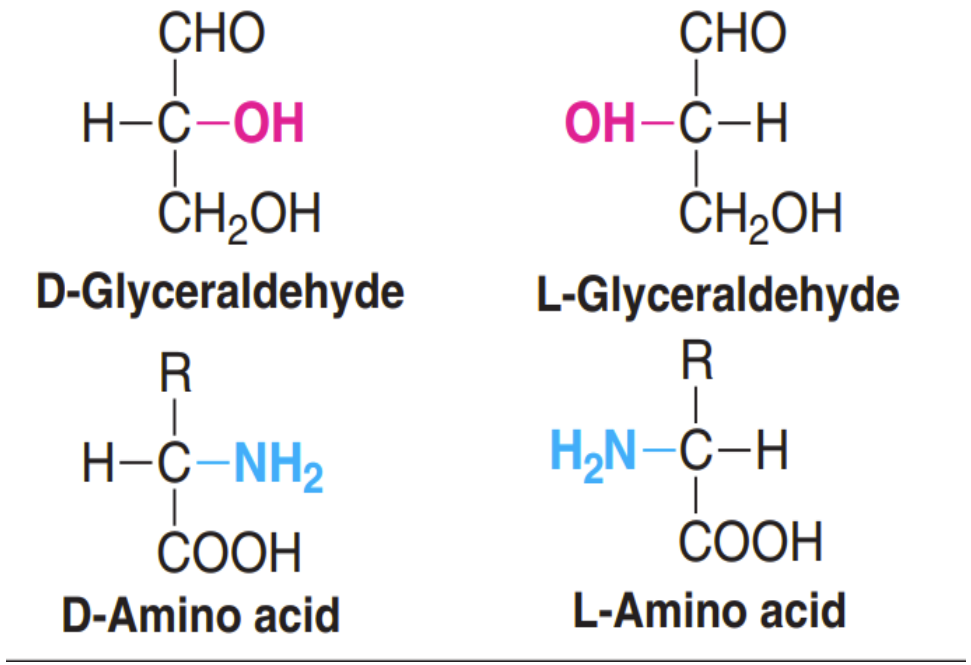
Optical isomers of amino acids:

If a carbon atom is attached to four different groups, it is asymmetric and therefore exhibits optical isomerism. The amino acids (except glycine) possess four distinct groups (R, H, COO–, NH3+) held by D-carbon.
Thus all the amino acids (except glycine where R = H) have optical isomers.

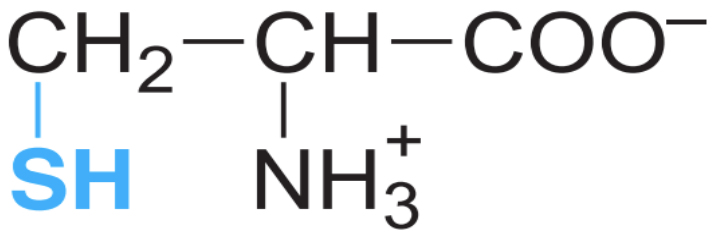
The structures of L- and D-amino acids are written based on the configuration of L- and D-glyceraldehyde

The proteins are composed of L-D-amino acids.

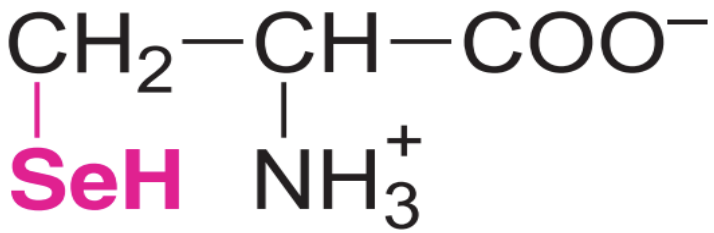


Selenocysteine – the 21st amino acid

As already stated, 20 amino acids are commonly found in proteins. In recent years, a 21st amino acid namely selenocysteine has been added. It is found at the active sites of certain enzymes/proteins (selenoproteins). e.g. glutathione peroxidase, glycine reductase, 5c-deiodinase, thioredoxin reductase. Selenocysteine is an unusual amino acid containing the trace element selenium in place of the sulfur atom of cysteine.



Cysteine



Selenocysteine

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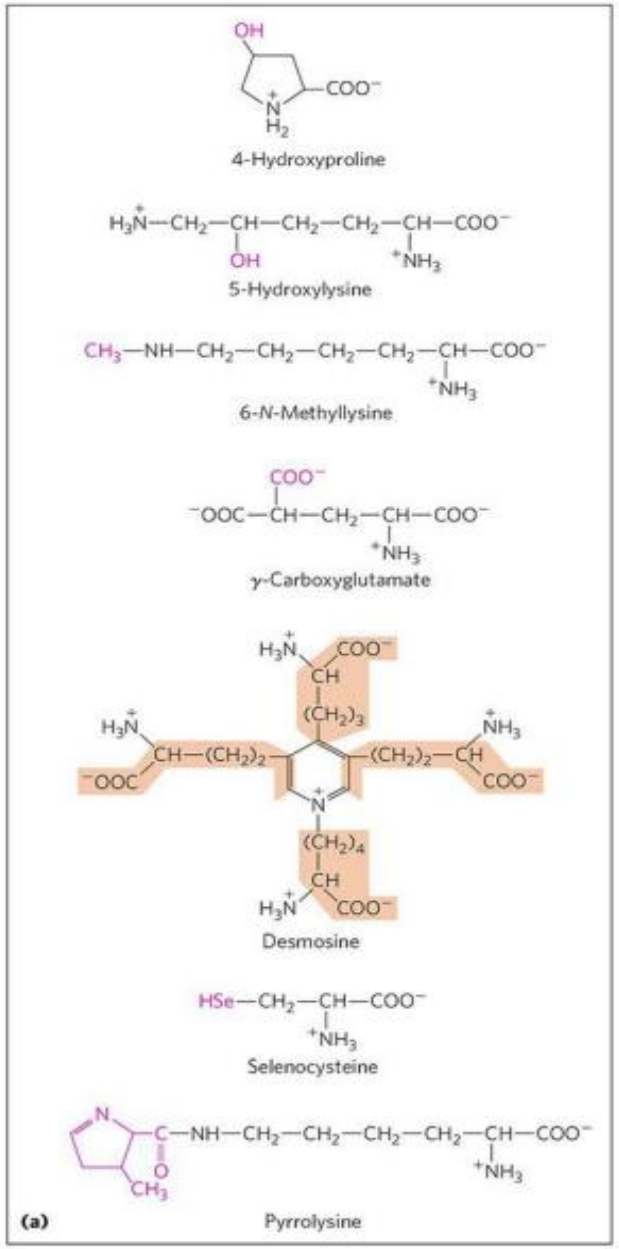
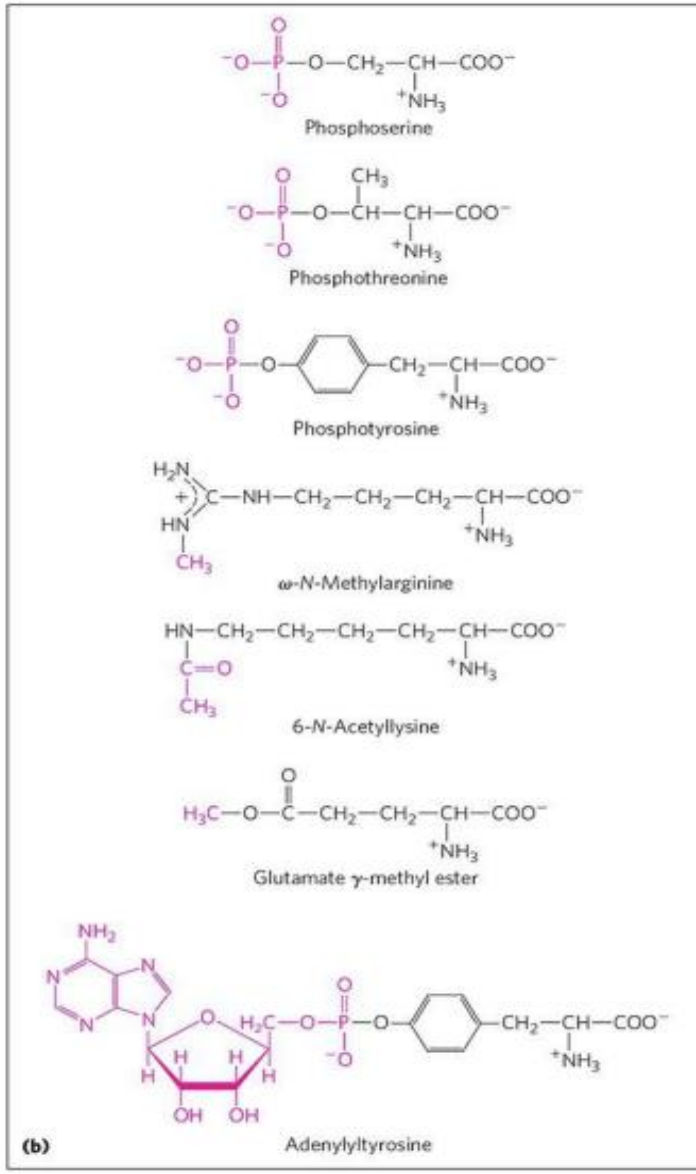
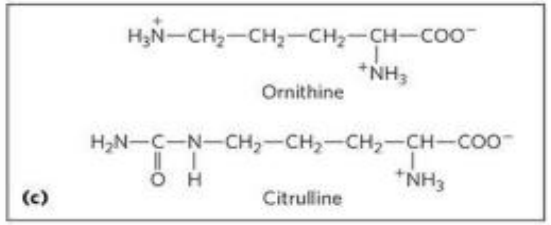
NON-STANDARD AMINO ACIDS

Besides the 20 standard amino acids present in the protein structure, there are several other amino acids which are biologically important. These include the amino acid derivatives found in proteins, non-protein amino acids performing specialized functions and the D-amino acids.

Some other amino acids are derivatized once incorporated into proteins for example, Hydroxyproline and hydroxylysine found in collagen, the principal component of connective tissue. Proline and lysine modified after incorporation modifications essential for maintaining normal connective tissues in tendons, cartilage, bones, teeth, skin.

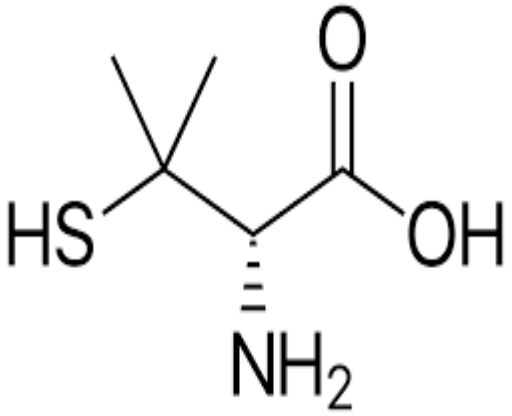




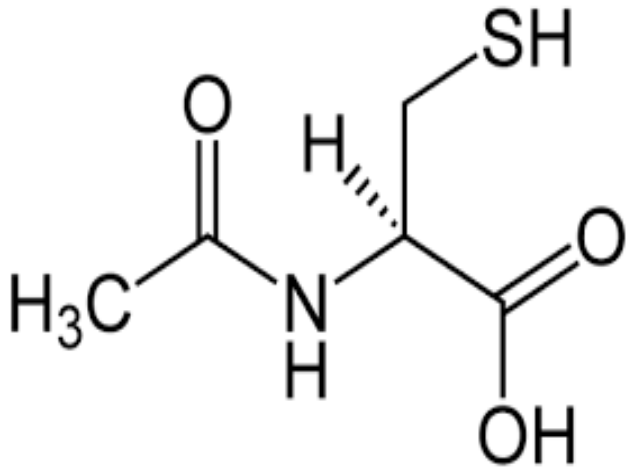


Amino acids useful as drugs:

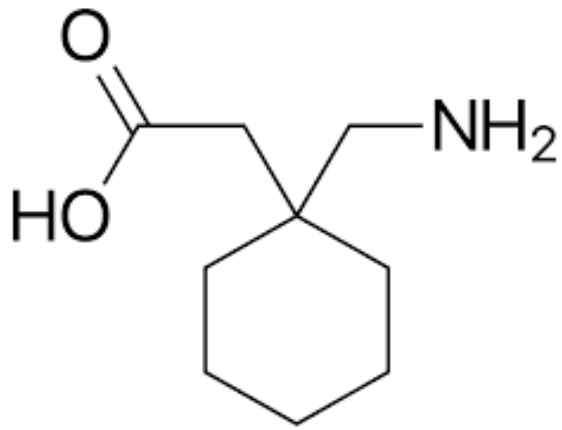
There are certain non-standard amino acids that are used as drugs.



D-Penicillamine therapy of Wilson's disease



N-Acetylcysteine is used in cystic fibrosis, and chronic renal insufficiency, as it can function as an antioxidant.



Gabapentin (J-aminobutyrate linked to cyclohexane) is used as an anticonvulsant.

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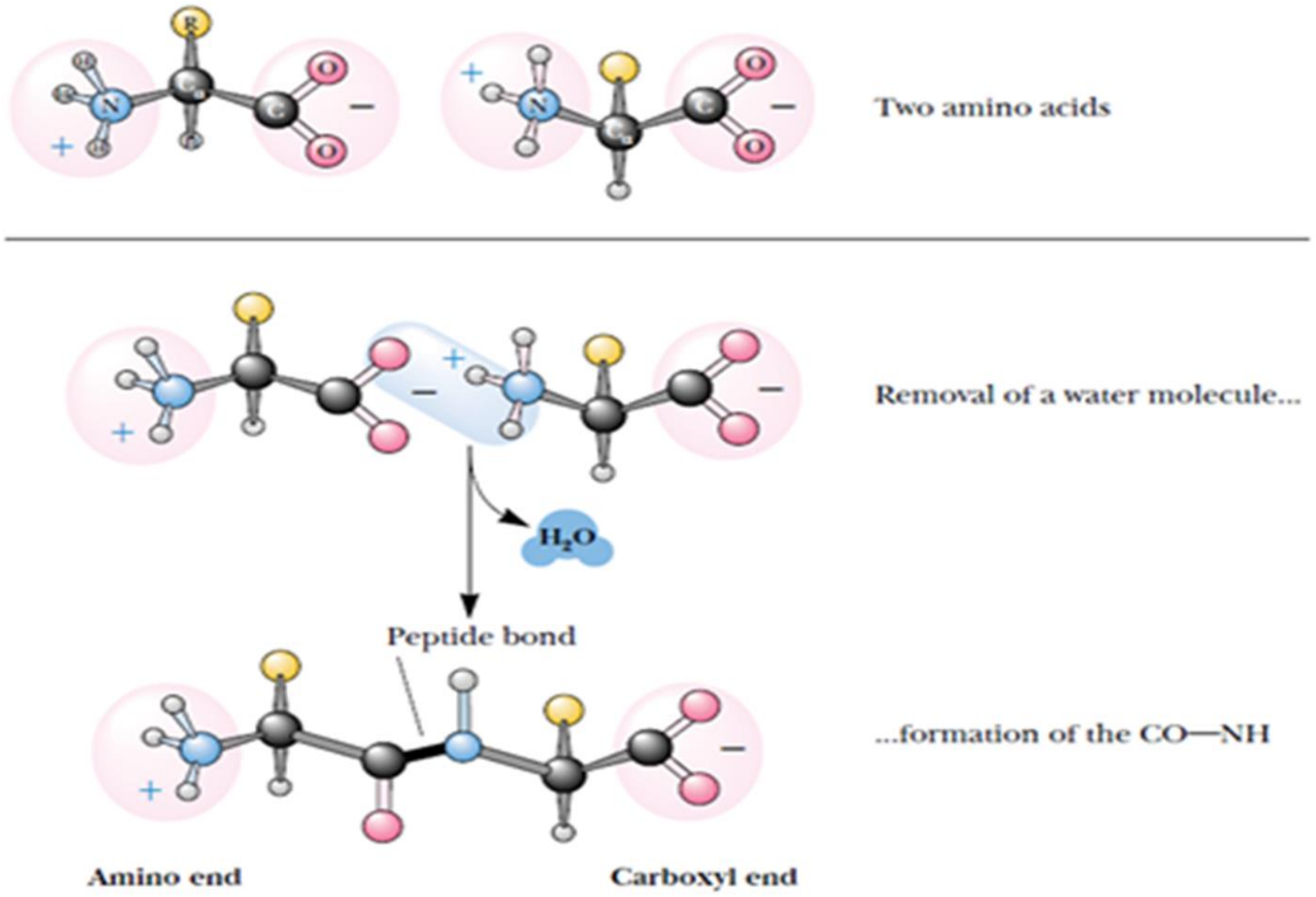
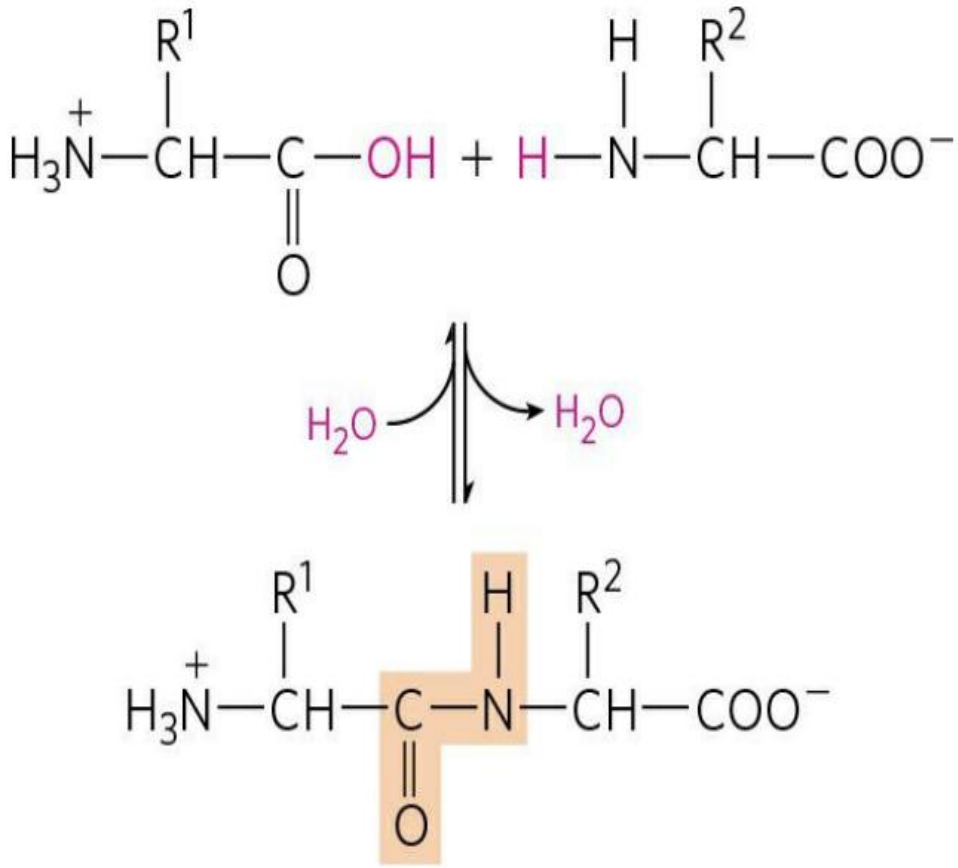
Peptides:

The polymers of amino acids are peptides and proteins. Biologically occurring polypeptides range in size from small to very large, consisting of two or three to thousands of linked amino acid residues.





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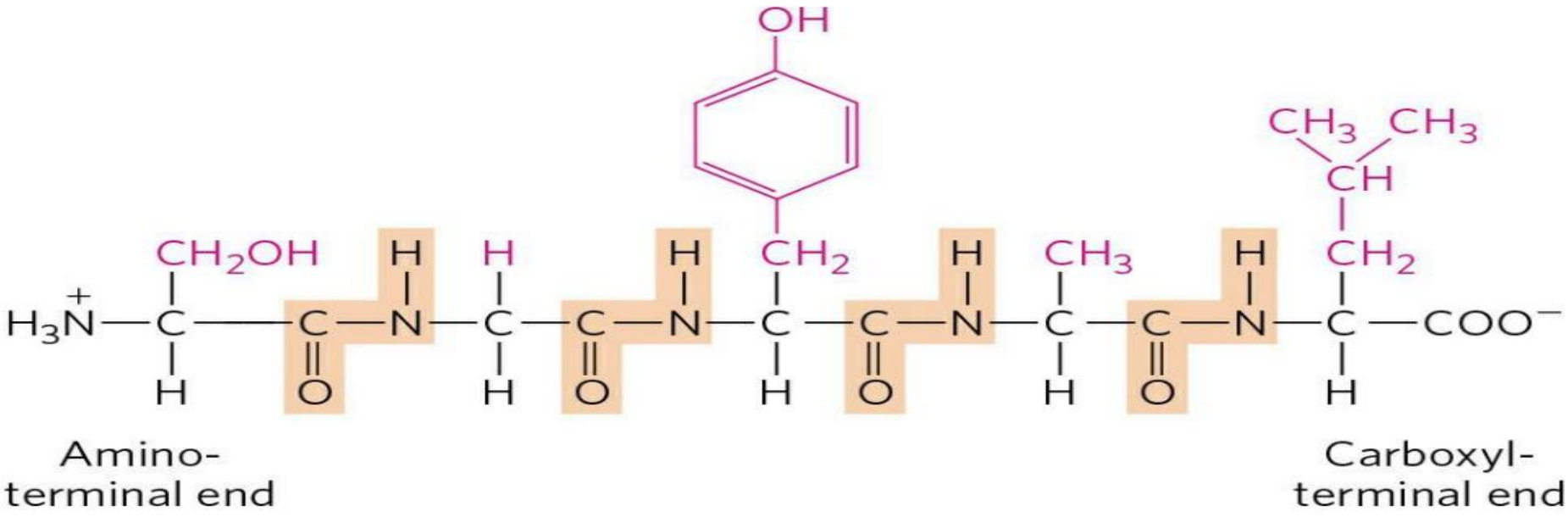
- Three amino acids can be joined by two peptide bonds to form a tripeptide
- When a few amino acids are joined in this fashion, the structure is called an oligopeptide.
- When many amino acids are joined, the product is called a polypeptide.
- The pentapeptide serylglycyltyrosylalanylleucine, Ser–Gly–Tyr–Ala–Leu, or SGYAL.
- Peptides are named beginning with the amino-terminal residue, which by convention is placed at the left. The peptide bonds are shaded in light red; the R groups are in purple.



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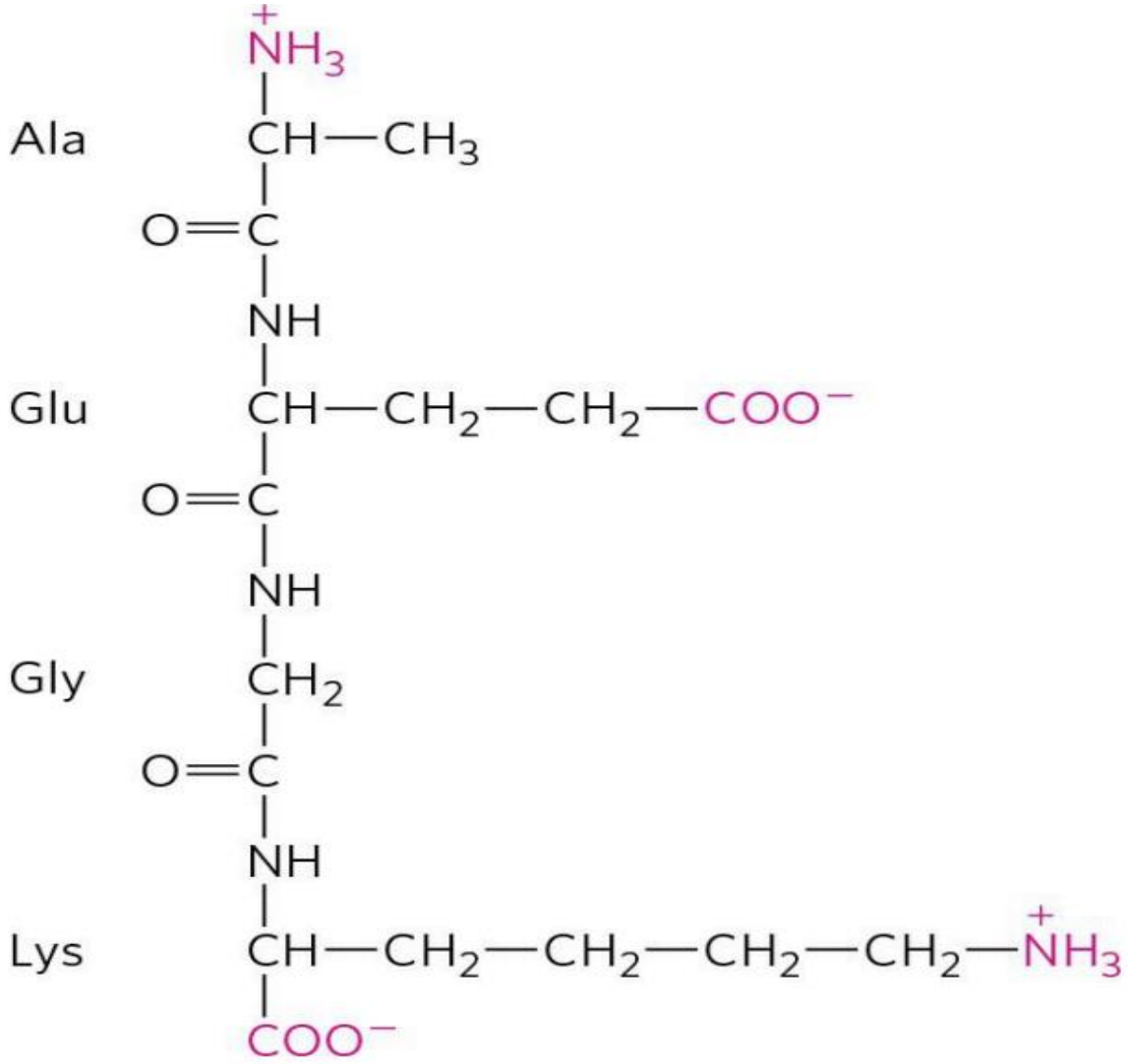
Peptides Can Be Distinguished by Their Ionization Behavior

Alanylglutamylglycyllysine.
This tetrapeptide has one free α-amino group, one free α-carboxyl group, and two ionizable R groups. The groups ionized at pH 7.0 are in red.



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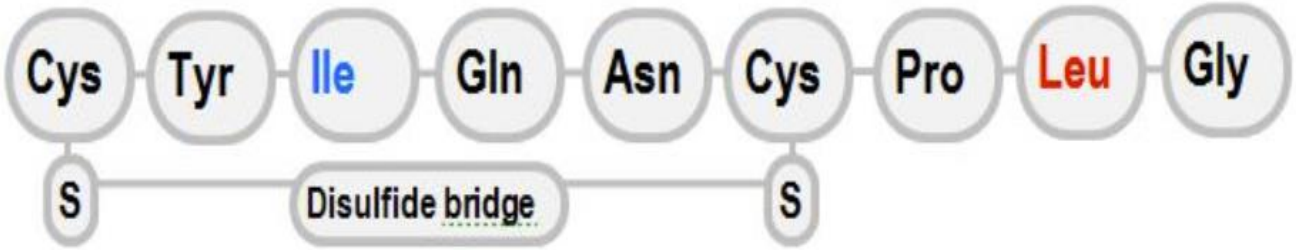
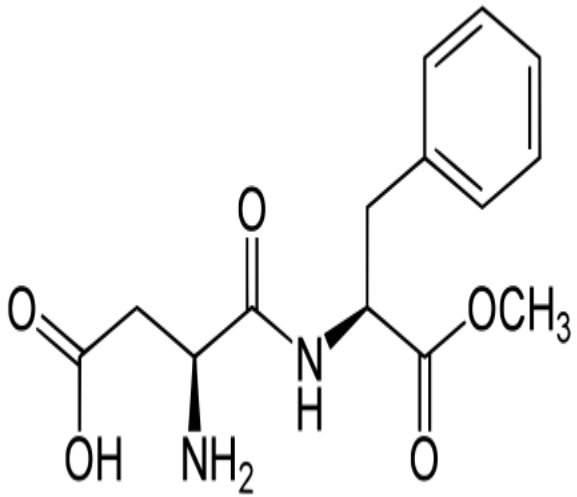
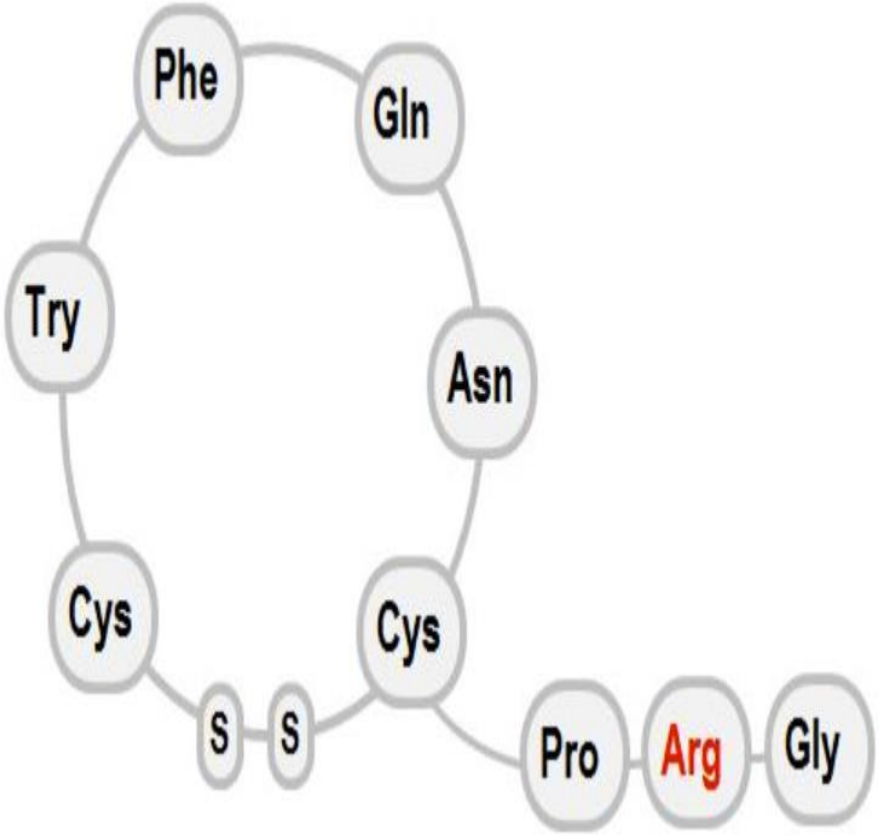
Biologically Active Peptides and Polypeptides Occur in a Huge Range of Sizes and Compositions



Oxytocin



Aspartame



Vasopressin

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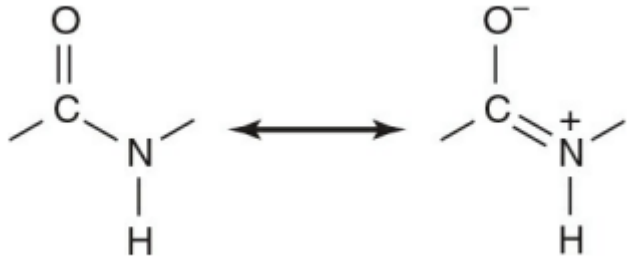
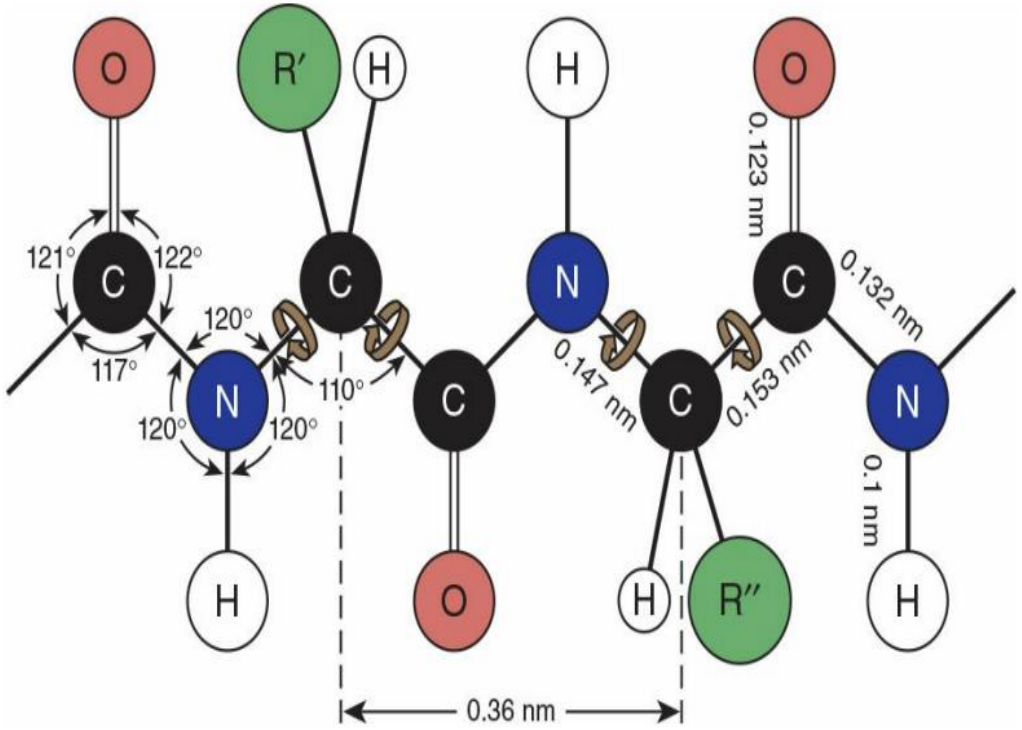
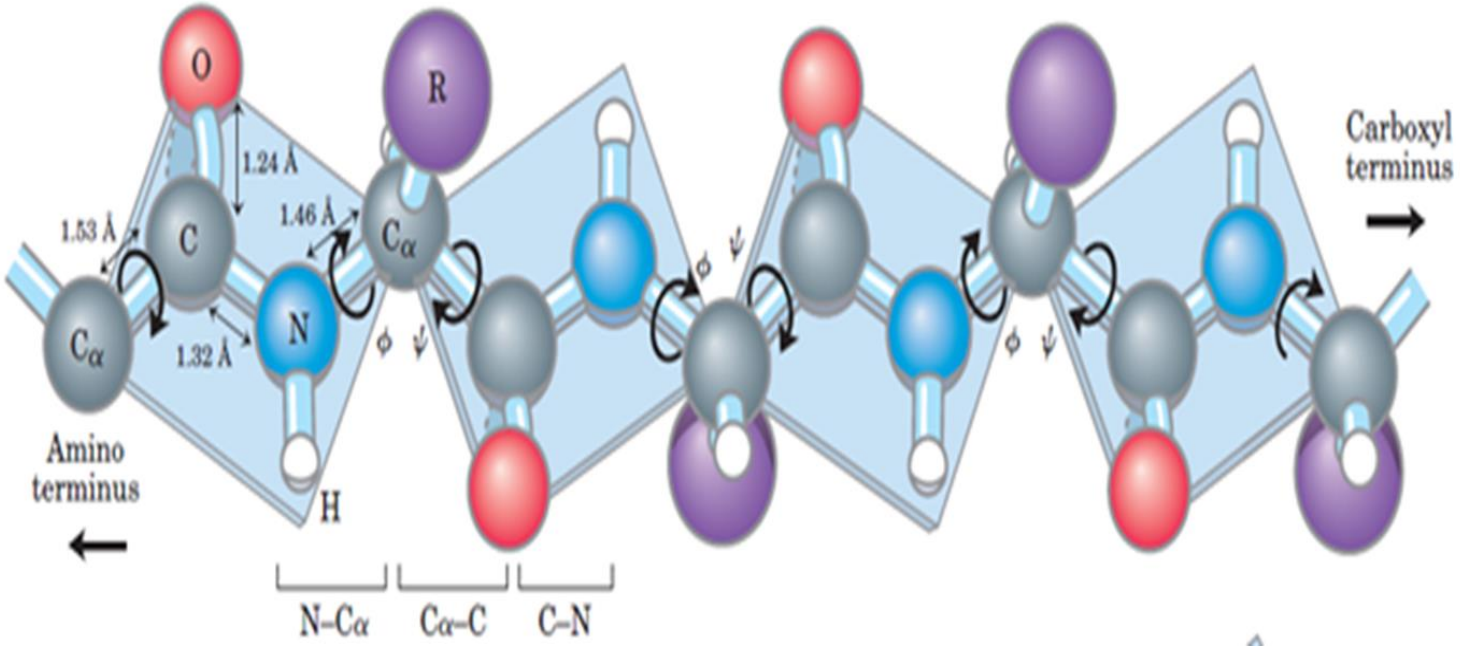
The Peptide Bond Has Partial Double-Bond Character

- peptide structures are written as if a single bond linked the α-carboxyl and α-nitrogen atoms, this bond in fact exhibits partial double bond character.
- The O, C, N, and H atoms of a peptide bond are coplanar.



- Peptide bonds help peptides and proteins to fold and rotation.





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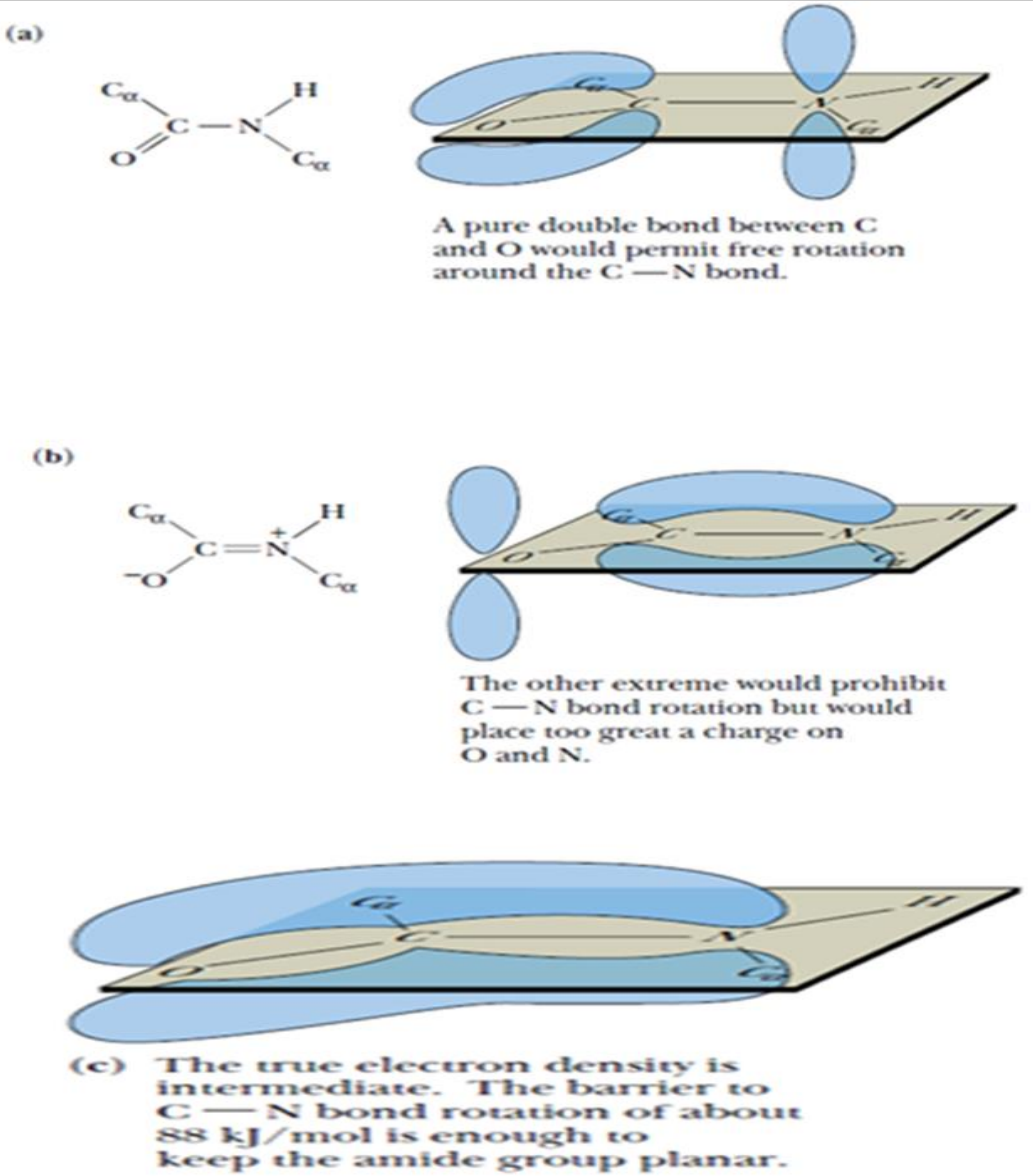
The peptide linkage is usually described by a single bond between the carbonyl carbon and the amide nitrogen .Therefore, in principle, rotation may occur about any covalent bond in the polypeptide backbone because all three kinds of bonds N-Cα , C-Cα , C-N bonds.

In this representation, the C and N atoms of the peptide grouping are both in planar sp2 hybridization and the C and O atoms are linked by a bond, leaving the nitrogen with a lone pair of electrons in a 2p orbital. However, another resonance form for the peptide bond is possible in which the C and N atoms participate in a bond, leaving a lone e-pair on the oxygen.



Thanks for listening