Structure of Amino Acids

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8:00-9:00 AM

Specific Learning Objectives

1. **General Structure of amino acids**
2. **Amino acids classification based on:**

- Standard and Non-standard amino acids (aa)
- Essential and non-essential aa
- Ketogenic and Glucogenic aa
- Side chain functional group

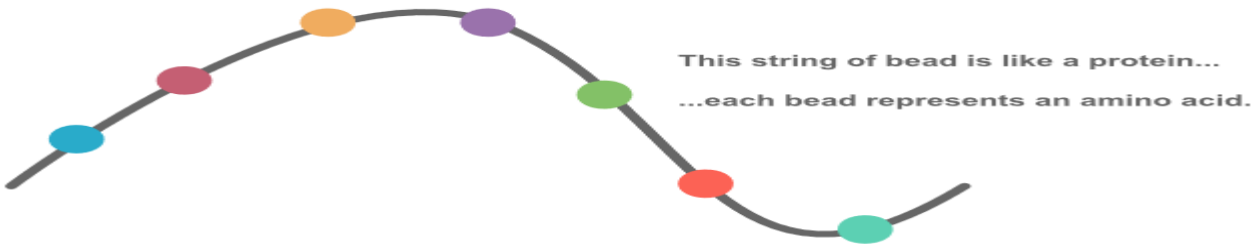
3. Function of essential amino acids

Introduction

- Amino acids as a building blocks of peptides and proteins

- Proteins are made up of hundreds of smaller units called **amino acids** that are attached to one another by peptide bonds, forming a long chain.

- Protein as a string of beads where each bead is an amino acid.



Genetic Code Specifies 20 L-α-Amino Acids

- Proteins are synthesized from the set of 20 L-α-amino acids encoded by nucleotide triplets called codons.

- Common amino acids are those for which at least one specific codon exists in the DNA genetic code.

- Sequences of peptides and proteins represent by using one- and three letter abbreviations for each amino acid.

Genetic information is transcribed from a DNA sequence into mRNA and then translated to amino acid sequence of a protein

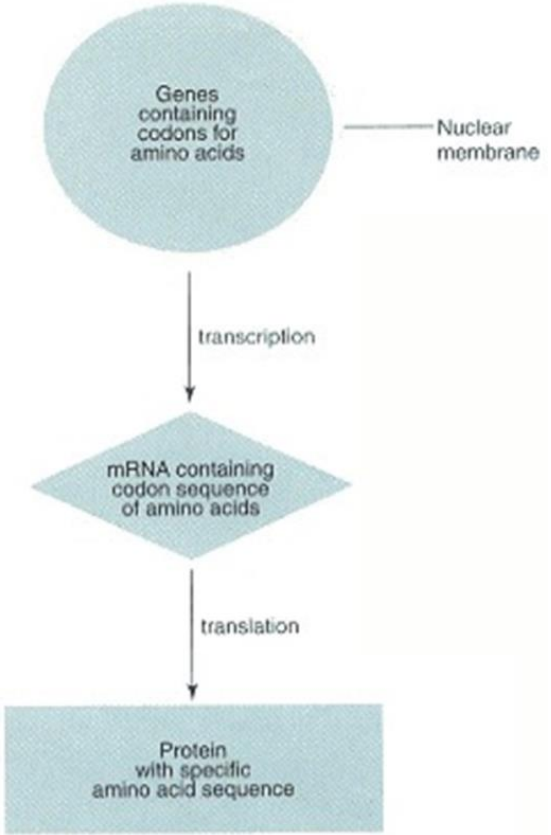


Fig. 2.1. Textbook of Biochemistry with Clinical Correlations, 4th edition by Thomas M Devlin

General Structure of Common Amino Acids

- General structure of amino acids $NH_3^+-CH-COO^-$, group and a variable side chain
- Side chain determines: protein folding, binding to specific ligand and interaction with its environment
- Amino acids consists of a constant $H_2N-CH(R)-COOH$ (R is side chain)
- At neutral pH, H_2N- protonated to H_3N^+-, and –COOH deprotonated to $–COO^-$

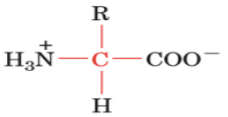


Fig.4.2. Biochemistry. 4th edition by Donald Voet and Judith G. Voet

Amino-Acids Classification Based on Standard and Non-Standard Amino Acids

1. **Standard amino-acids:** Those 20 amino acids are encoded by universal genetic code
2. **Non-Standard amino-acids:** Two amino acids incorporated into proteins by unique synthetic mechanism

- **Selenocysteine:** Incorporated when mRNA translated included SECIS (selenocysteine insertion seq) element, causes the UGA codon to encode selenocysteine instead of stop codon)
- **Pyrrolysine:** used by methanogenic archaea in enzyme that they use to produce methane. It is coded for UAG stop codon.

Standard amino acids

- All proteins are composed of the 20 “standard "amino acids.
- Common central alpha (α)-carbon atom bound to a carboxylic acid group, an amino group and a hydrogen atom are covalently bonded.
- They have a primary amino group and a carboxylic acid group substituent on the same carbon atom, with the exception of proline, (has a secondary amino group).

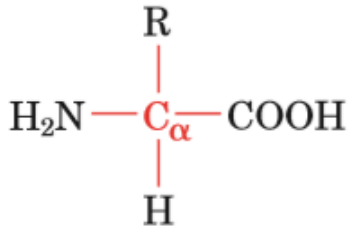
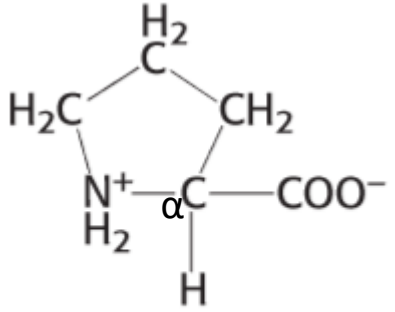


Fig.4.1. Biochemistry. 4th edition by Donald Voet and Judith G. Voet

How Proline gives conformational rigidity?

- Proline classified as an imino acid, its α-amine is a secondary amine with its a nitrogen having two covalent bonds to carbon (to the α-carbon and side chain carbon), rather than primary amine

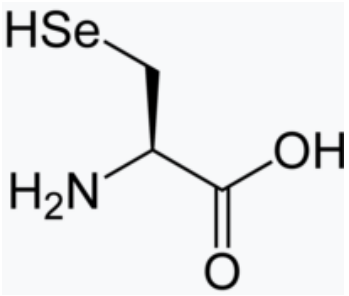


Proline
(Pro, P)

- Incorporation of amino nitrogen into a five membered ring constrains rotational freedom around $–N_{\alpha}$-C_{α}-bond in proline to specific rotational angle, reduces structural flexibility of polypeptide regions containing proline.

Non-Standard Amino Acids

- Selenocysteine, 21st protein L-α amino acids



- Selenium atom replaces the sulfur of its elemental analog, cysteine

- Selenocysteine is not the product of a posttranslational modification, but is inserted directly into a growing polypeptide during translation.

- Selenocysteine is charged on a special tRNA called $tRNA_{Sec}$ specific for UGA (STOP)codon inserted into growing polypeptide during translation

Other Classification of Amino Acids

- Non-protein aa: Not naturally encoded by genetic code but found in free state as intermediates of metabolic pathway for standard aa: Ornithine and citrulline are intermediates in urea biosynthesis.

- Non α-aa: -NH_2 group not attached to α-carbon atom but some other carbon atom. Ex. γ-aminobutyric acid (GABA) and β-alanine.

- Modified protein aa: Amino acids modified after they incorporated into protein. Proline and lysine undergo hydroxylation to become hydroxyproline and Hydroxylysine. Essential for formation of mature collagen.

AA Classified on Basis of Nutritional Requirement

- **Essential amino acids:** Not synthesised in the body and must be supplied in diet
- **Non-essential amino acids:** Synthesized in body and there is no diet dependency for them
- Semi-essential amino acids: Not synthesised in the body in adequate amounts and requires dietary supplementation.

Amino-Acid Requirements of Humans

Nutritionally Essential	Nutritionally Nonessential
Arginine[1]	Alanine
Histidine	Asparagine
Isoleucine	Aspartate
Leucine	Cysteine
Lysine	Glutamate
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Hydroxyproline[2]
Tryptophan	Hydroxylysine[2]
Valine	Proline
	Serine
	Tyrosine

Table 28.1. Harper's Illustrated Biochemistry 26th edition

AA Classified on Basis of metabolic classification

- **Ketogenic amino acids:** Only two aa are ketogenic, ex. Lysine and leucine. They catabolically give intermediates convertible into acetyl-CoA or acetoacetyl-CoA

- **Glucogenic amino acids:** Those aa give rise to intermediates of glycolysis or Kreb's cycle convertible by gluconeogenesis into glucose. Ex. Arg, His etc.

- **Mixed amino acids:** There are aa, carbon skeleton of which catabolized to produce the glycolytic intermediates as well as acetyl-CoA derivatives. Ex. Phe, Try etc.

Amino-Acids Classification Based on Side Chain Groups

- Based on **type of functional group (R group)** present amino acids are classified as: Aliphatic, aromatic, acidic, basic, acid amide, sulfur and cyclic amino acids.

- Based on **characteristic of functional group** amino acids are classified as: polar and non-polar amino acids.

- Based on **site of attachment of functional group**. They are also classified as: alpha, beta, gamma and delta amino acids.

Amino Acids Classification based on hydrophobic and hydrophilic property

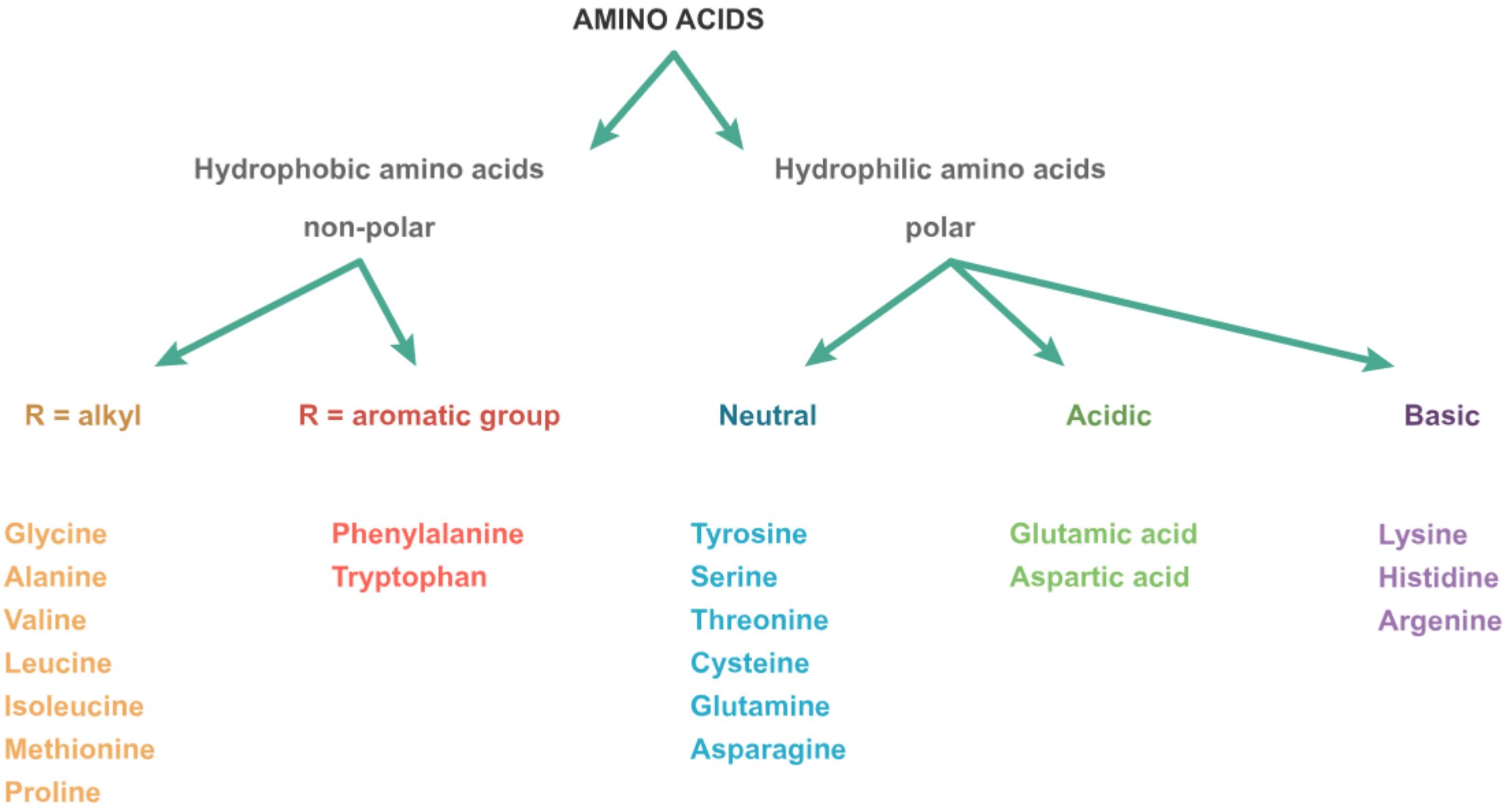


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TABLE 3–1 L-α-Amino Acids Present in Proteins

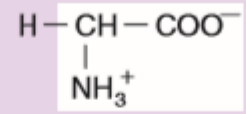
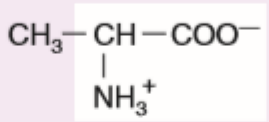
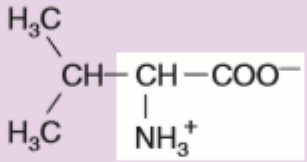
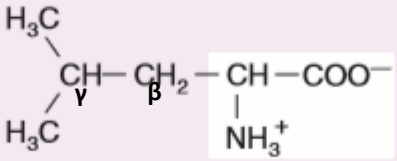
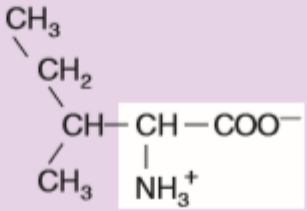
Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Aliphatic Side Chains	**Nonpolar/Hydrophobic**		α-COOH	α-NH_3^+	R Group
Glycine	Gly [G]		2.4	9.8	
Alanine	Ala [A]		2.4	9.9	**Methyl R group**
Valine	Val [V]		2.2	9.7	**Isopropyl R group**
Leucine	Leu [L]		2.3	9.7	**Branching in isobutyl side chain on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

Table 3.1. Harper's Illustrated Biochemistry 30 edition

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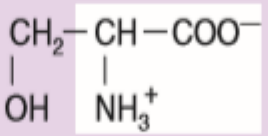
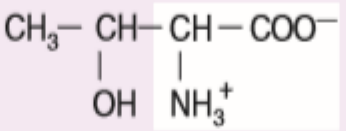
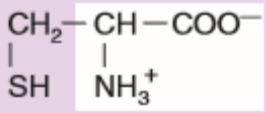
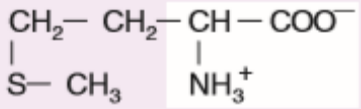
Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Side Chains Containing Hydroxylic (OH) Groups					
Serine **Polar, uncharged-R group**	Ser [S]		2.2	9.2	about 13
Threonine **Polar, uncharged-R group**	Thr [T]		2.1	9.1	about 13
Tyrosine	Tyr [Y]	Mentioned in amino acids with aromatic rings section			
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
Methionine **Nonpolar**	Met [M]		2.1	9.3	

Hydroxymethyl R group

Secondary Alcohol structure

Thiolmethyl/Sulfhydryl R group

Methyl ethyl thiol ether R group

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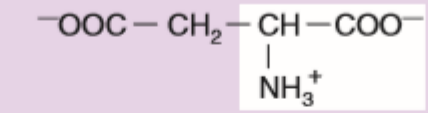
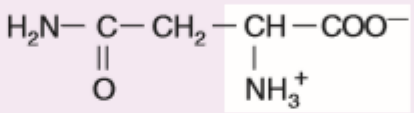
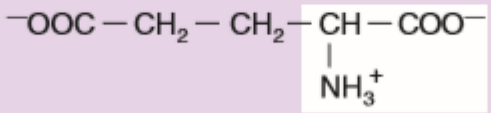
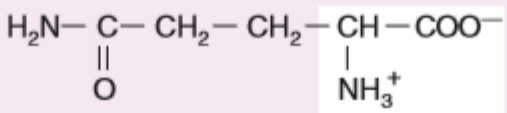
Name	Symbol	Structural Formula	pK_1	pK_2	pK_3
With Side Chains Containing Acidic Groups or Their Amides					
Aspartic acid	Asp [D]		2.1	9.9	3.9
Asparagine	Asn [N]		2.1	8.8	
Glutamic acid	Glu [E]		2.1	9.5	4.1
Glutamine	Gin [Q]		2.2	9.1	

Negatively charged R group

β-COOH R group

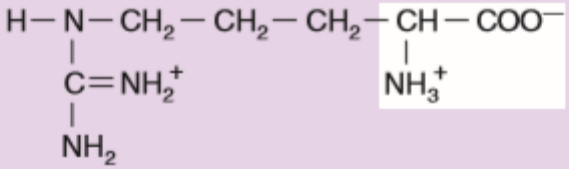
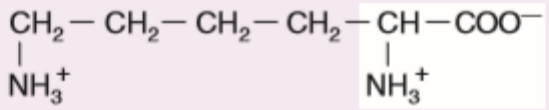
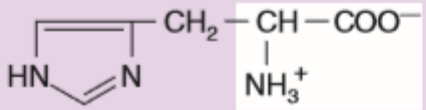
Polar, Uncharged-R group

Negatively charged R group

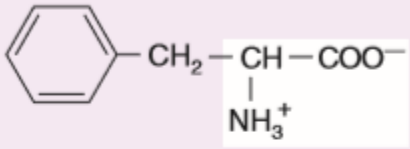
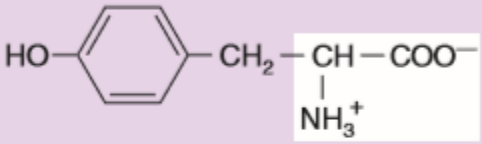
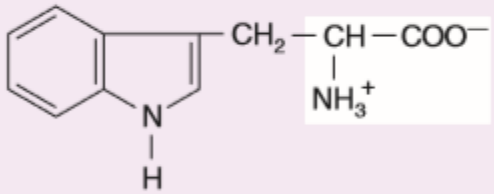
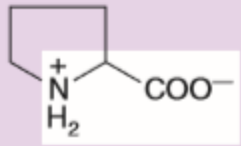
γ-COOH R group

Polar, Uncharged-R group

Cont--

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

Cont--

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			

Function of Essential Amino acids

Non-polar amino acids:

1. **Aromatic aa:**

a) **Phenylalanine:** precursor for tyrosine, dopamine, nor-epinephrine, epinephrine and melanin.

- Genetic disorder phenylketonuria is the inability to metabolize phenylalanine because of a lack of phenylalanine hydroxylase.

a) **Tryptophan:** precursor for neurotransmitter (serotonin), hormone (melatonin) and vitamin niacin. Trp and Tyr residues anchoring membrane proteins within cell membrane.

- Fructose malabsorption causes improper absorption of Trp in intestine causes reduced level of Trp in blood.

2. Aliphatic amino acids:

a) **Alanine:** Alanine synthesized from pyruvate and branched chain aa. It plays an imp. role in glucose-alanine cycle between tissues and liver.

- This cycle enables pyruvate and glutamate to be removed from muscle and safely transported to liver.
- Alteration in alanine cycle increase the level of ALT (Alanine transferases) which linked to the development of type II diabetes.

b) Valine: Essential for hematopoietic stem cell (HSC) self-renewal.

- In sickle-cell disease, a single glutamic acid in β-globin replaced with valine because valine is hydrophobic, whereas glutamic acid is hydrophilic, this change makes the Hb prone to abnormal aggregation.

c) Leucine: Primary metabolic end products of leucine metabolism are acetyl-CoA and acetoacetate. It is also a imp ketogenic aa.

- Adipose and muscle tissue use leucine in the formation of sterols.
- MSUD caused by deficiency of branched chain α-keto acid dehydrogenase complex leading to build-up branched chain aa and their toxic product ketoacids present in blood and urine.

c) Isoleucine: diverse physiological functions, such as assisting wound healing, detoxification of nitrogenous wastes, stimulating immune function, and promoting secretion of several hormones.

3. Sulfur-containing aa:

a) **Methionine:** Substrate for other amino acids such as cysteine and taurine, versatile compounds such as S-adenosyl methionine and antioxidant glutathione.

- Homocysteine can be used to regenerate methionine or to form cysteine.
- Improper conversion of methionine can lead to atherosclerosis due to accumulation of homocysteine.

Polar uncharged aa:

1. **Threonine:** Its residue ssusceptible to numerous posttranslational modifications.

- The hydroxyl side-chain undergo *O*-linked glycosylation.
- Threonine residues undergo phosphorylation through the action of a threonine kinase. In its phosphorylated form, it can be referred to as phosphothreonine. Its role in cell signal transduction and neural activity.

Polar Charged amino-acids:

1. **Positive charge/Basic aa:**

a) **Histidine:** precursor for histamine, an amine produced in the body necessary for inflammation.

- Histidine ammonia-lyase converts histidine into ammonia and urocanic acid. deficiency in this enzyme in rare metabolic disorder histidinemia.

b) Lysine: Lysine can also contribute to protein stability as its ε-amino group often participates in hydrogen bonding, salt bridges and covalent interactions to form a Schiff base.

- A second major role of lysine is in epigenetic regulation by means of histone modification.
- It plays a key role in other biological processes including; structural proteins of connective tissues, calcium homeostasis and fatty-acid metabolism.
- Due to a lack of lysine catabolism, the amino acid accumulates in plasma and patients develop hyperlysinaemia.

Summary

- Both α-amino acids and non-α-amino acids occur in nature, but proteins are synthesized using only L-α-amino acids.
- The R groups of amino acids determine their unique biochemical functions.
- Amino acids are classified as basic, acidic, aromatic, aliphatic, or sulfur-containing based on the composition and properties of their R groups.

Interaction with students

Distributed subtopics of today's lecture to students for participate in group discussion in next lecture.

Reference Books

1) Harper’s Illustrated Biochemistry-30th edition
2) Textbook of Biochemistry with Clinical Correlations. 4th edition. Thomas M. Devlin.
3) Biochemistry. 4th edition. Donald Voet and Judith G. Voet.
4) Biochemistry 7th edition by Jeremy M. Berg, John L. Tymoczko and Lubert Stryer
5) Lehninger Principles of Biochemistry
6) Netter's essential biochemistry 1st Ed
7) https://en.wikipedia.org/wiki/aminoacids

THANK YOU