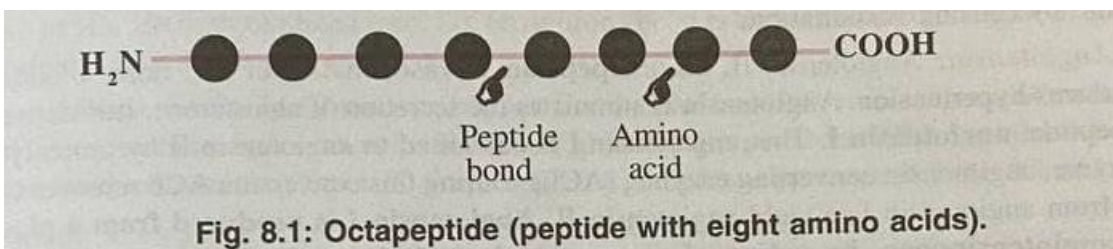


Chemistry of Peptides and Amino Acids

What are Peptides?

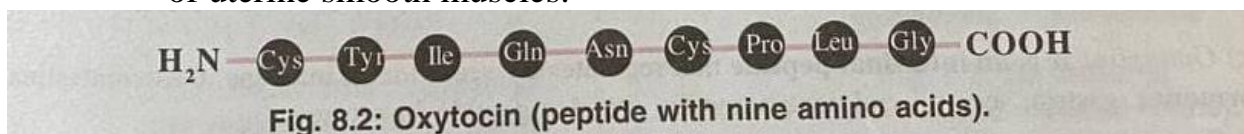
Peptides are unbranched polymers of less than 50 amino acids, which are covalently linked together through peptide bonds (Fig. 8.1). The term protein is used for polymer composed of over 50 amino acids.



Chemistry of peptides: When two amino acids join covalently through a peptide bond, they yield dipeptide. A peptide bond is formed between two adjacent amino acids by elimination of a water molecule from the α -carboxyl group ($-COO$) of one amino acid and a-amino group (NH_2) of other amino acid. Such reaction is known as condensation reaction. Joining of a third amino acid to dipeptide through peptide bond yields tripeptide; similarly amino acids can further join to form tetrapeptide, pentapeptide, hexapeptide, etc. Normally, term 'peptide' is used for a structure containing less than 50 amino acids.

Biologically active peptides and their functions: Many biologically active peptides are present in human body and play important roles. Functions of some biologically active peptides are as given below.

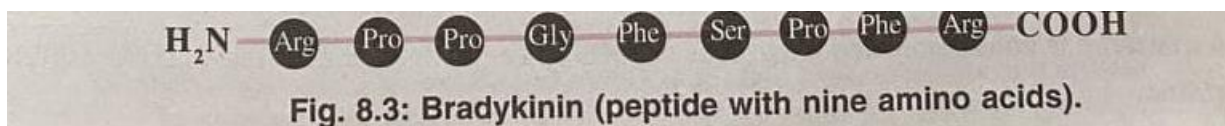
- (i) **Thyrotropin releasing hormone (TRH):** It is a tripeptide secreted by hypothalamus. TRH stimulates the release of hormone, thyrotropin, from the anterior pituitary gland.
- (ii) **Oxytocin:** Oxytocin is a hormone secreted by posterior pituitary gland. It is a nonapeptide (Fig. 8.2) and stimulates the contraction of uterine smooth muscles.



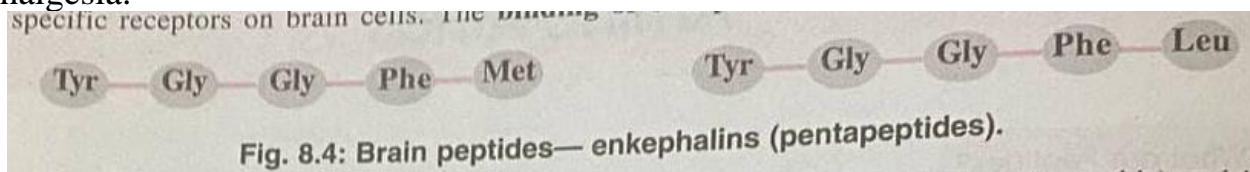
(iii) **Vasopressin**: Vasopressin is also known as antidiuretic hormone (ADH). It is a nonapeptide secreted by posterior pituitary gland and acts on kidney to retain water.

(iv) **Substance P**: It is a decapeptide with neurotransmitter-like activity.

(v) **Bradykinin and Kallidin**: Bradykinin, a nonapeptide, has hormone-like action and inhibits inflammation of tissues. Kallidin, a decapeptide, serves as a powerful vasodilator.

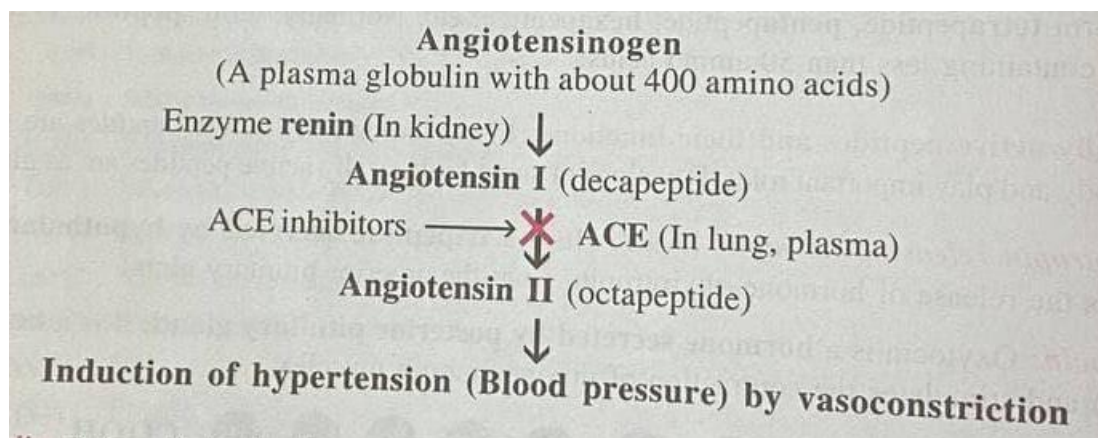


(vi) **Brain peptide**: brain peptide, enkephalins (fig 8-4), have opiate like activity and bind to specific receptor on brain cells. The binding of enkephalins induced analgesia.



(vii) **Atrial natriuretic factor (ANF)**: It is a polypeptide hormone (of 12 amino acids) and is released by specialized cells of right atrium, when it is stretched in response to increased blood volume. ANF acts on kidney where it increases the excretion of Na⁺ and water, which causes lowering of blood pressure. ANF also acts on vascular smooth muscles and further reduced blood pressure by causing vasodilation.

(viii) **Angiotensin**: Angiotensin II, an octapeptide, is vasoconstrictor and raises blood pressure, i.e. induced hypertension. Angiotensin II stimulates the secretion of aldosterone. It is derived from a decapeptide, angiotensin I. The angiotensin I is converted to angiotensin II by proteolytic action of enzyme, angiotensin converting enzyme, (ACE). During this conversion ACE removes two amino acids from angiotensin I to yield angiotensin II. Angiotensin I is produced from plasma protein, angiotensinogen, by action of enzyme renin in kidney. Angiotensinogen is a globulin containing about 400 amino acids. Angiotensin III is a heptapeptide.



(ix) **Guanylin**: It is an intestinal peptide that regulates Cl^- secretion in intestinal. Gastrointestinal hormones, gastrin, secretin and pancreaticozym, are also peptide in nature.

(x) **Carnosine**: It is a dipeptide, composed of β -alanine and histidine, and is present in muscles. It activates myosin ATPase activity, chelates copper and enhances copper uptake.

(xi) **Hormonal peptides**: Several hormones are peptide in nature, e.g. corticotropin, insulin, glucagon, calcitonin, etc.

(xii) **Aspartame**: It is a commercially synthesized dipeptide (Fig 8.5) and used as an artificial sweetening agent by the diabetics and obese persons. It is a non-carbohydrate and has almost no caloric value.

(xiii) **Glutathione**: It is a tripeptide (known as γ -glutamylcysteinylglycine) composed of 3 amino acids namely γ -glutamic acid, cysteine, and glycine. It is widely distributed both in plants and animals. Glutathione exists in oxidized (GS-SG) and reduced (GSH) states and participates in oxidation-reduction reaction. Reduced glutathione molecule contains a free -SH group (sulfhydryl group), whereas oxidized glutathione contains two glutathione molecules linked together by a disulfide linkage (Figs. 8.6 and 8.7). Glutathione is an important tripeptide and takes part in many cellular functions, which are described below in brief.

- 1- **Reduced glutathione**, an intracellular reductant, prevents the oxidation of sulfhydryl groups of cellular proteins and thus helps to keep them in reduced state.
- 2- **It maintains heme-iron (of Hb) in ferrous state (Fe^{2+})**, which is necessary for normal functioning of Hb. Hb with oxidized iron, i.e. ferric iron (Fe^{3+}) is termed as methemoglobin (Hb M) and is physiologically non-functional.
- 3- Oxidative damage of RBC membranes by oxygen free radicals and H_2O_2 results in loss of membrane integrity leading to hemolytic anaemia. Reduced glutathione protects RBC membrane from H_2O_2 since glutathione decomposes H_2O_2 in presence of glutathione peroxidase (Figs. 8.7 and 5.10).

- 4- **Glutathione takes part in detoxication of xenobiotics** (see chapter 28).
- 5- Deoxyribonucleotides, the monomeric units of DNA, are derived by reduction of D-ribose of ribonucleotides. Glutathione is required for reduction of ribonucleotides to deoxyribonucleotides; [his reaction js catalysed by ribonucleotide reductase.
- 6- Role of glutathione has been suggested in transport of amino acids across the plasma membrane of renal tubular cells via ' γ -glutamyl cycle.
- 7- **Glutathione scavenges the cells from oxidative stress** caused by superoxide, peroxy radicals ($\text{ROO}\cdot$), hydrogen peroxide and hydroxyl radicals ($\text{HO}\cdot$) (see chapter 30).
- 8- **Glutathione** is required for synthesis of prostaglandins (Fig. 11.27).

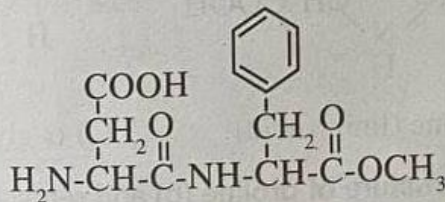


Fig. 8.5: Aspartame (L-aspartyl-L-phenyl-alanine methyl ester).

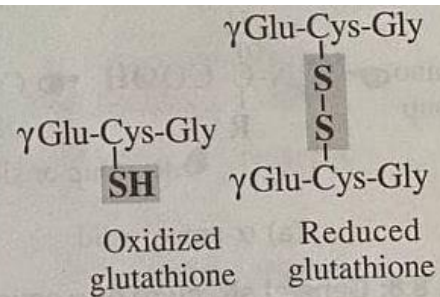


Fig. 8.6: Glutathione (oxidized and reduced forms).

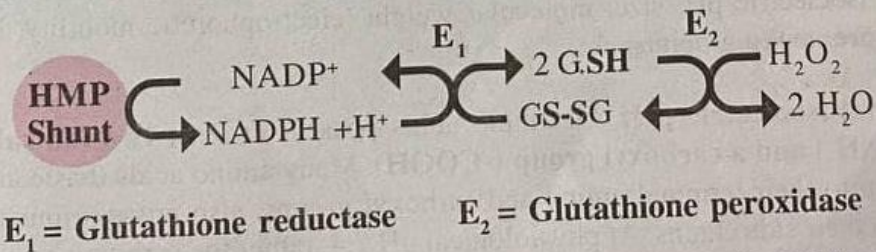
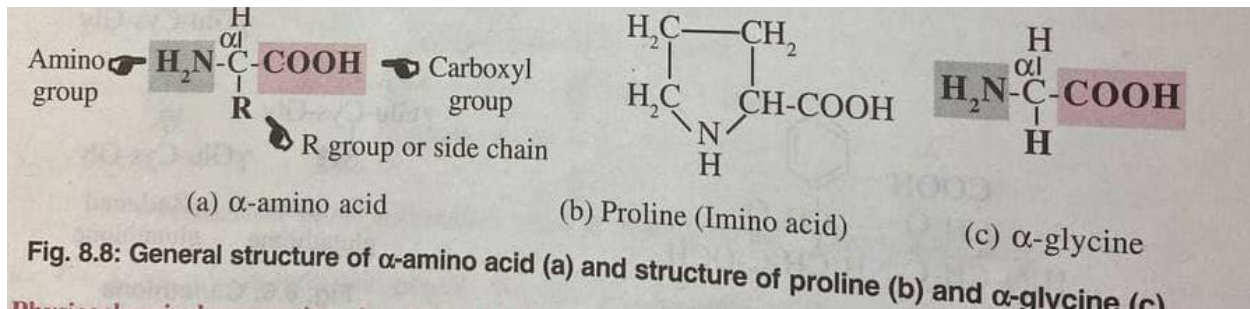


Fig. 8.7: Formation of GSH (reduced glutathione) and GS-SG (oxidized glutathione). Glutathione is reduced by enzyme glutathione reductase in presence of $\text{NADPH} + \text{H}^+$, which is provided by HMP shunt.

What are Amino Acids?

Amino acids are monomer units of proteins and peptides. In a protein or peptide molecule, amino acids are held together via peptide bonds. Amino acids are also called 'building blocks' of proteins. On hydrolysis, the proteins and peptides yield free amino acids.

Chemistry of amino acids: Although about 300 amino acids exist in nature, only 20 amino acids (Known as 'standard amino acids') commonly constitute the human and other mammalian proteins. All the 20 standard amino acids present in mammalian proteins are α -amino acids. A typical α -amino acid (except proline; Fig. 8.8b) has an amino group (-NH), a carboxyl group (-COOH), a hydrogen atom (-H) and a side chain (-R group) bonded covalently to a central α -carbon atom (Fig. 8.8a). All the 20 standard amino acids differ from each other in their side chains (-R group). Glycine is the simplest α -amino acid where -R group is a hydrogen atom (Fig. 8.8c). Some amino acids like alanine, valine, leucine and isoleucine, etc. have aliphatic side chains, whereas phenylalanine, tyrosine and tryptophan have aromatic side chains. There are some amino acids, e.g. glutamic acid and aspartic acid which contain side chains with carboxyl groups and some with side chains containing amino groups, e.g. arginine and lysine. Cysteine contains sulfhydryl (-SH) whereas threonine and serine contain hydroxyl group (OH) in their side chains. Hydroxyproline, hydroxylysine and γ -carboxyglutamate present in mammalian proteins are not standard amino acids, however, they are formed by hydroxylation of proline and lysine and γ -carboxylation of glutamate during post-translational modification of proteins. Ornithine, citrulline and argininosuccinate are amino acids that are present in our body but they are not constituents of proteins. These amino acids participate in urea synthesis in liver. β -alanine and γ -aminobutyric acid (GABA) are also non-protein amino acids. β -alanine is a constituent of pantothenic acid (a member of vitamin-B-complex) and carnosine, whereas aminobutyric acid (GABA) is a neurotransmitter.



Physicochemical properties of amino acids: On the basis of different -R groups present in twenty standard amino acids, these amino acids differ in their physicochemical properties such as electric charge, isoelectric pH, size, molecular weight, electrophoretic mobility, hydrophilic and hydrophobic nature, melting points, etc.

1- **Ionization and isoelectric pH:** All amino acids possess at least two ionizable groups, an amino group ($-\text{NH}_2$) and a carboxyl group ($-\text{COOH}$). Many amino acids (basic and acidic amino acids) in addition to their terminal amino and carboxyl groups, also possess ionizable $-\text{NH}_2$ and COOH groups in their side chains. At physiological pH 7.4, either the carboxyl group dissociate: COO^- or the amino group is protonated to $-\text{NH}_3^+$. At pH 7.4, most of amino acids exist in ionized form (Fig. 8.9). However, at isoelectric pH (pI), an amino acid exists as zwitter ion or dipolar ion. The isoelectric pH of an amino acid is pH at which amino acids possess equal positive and negative charges and are electrically neutral (Fig. 8.10). An amino acid does not migrate in electric field at its pI . The amino acids are also least soluble at their isoelectric pH. Each amino acid has a specific isoelectric pH, e.g. aspartic acid and lysine have pI 2.9 and 9.7, respectively. Fig. 8.9: General structure

2- **Ampboteric nature:** Depending on their isoelectric pH, amino acid of an ionized α -amino acid. acids can either donate or accept protons because of their ionizable $-\text{NH}_2$ and $-\text{COOH}$ groups. An amino acid accepts proton when

pH of solution is less than pI and donates proton when pH of solution is more than pI (Fig. 8.10). Therefore, on acidic side of its pI , an amino acid acts as base and accepts proton to become positively charged (cation), whereas on alkaline side of its pI , an amino acid acts as an acid and donates proton to become negatively charged (anion)- Fig. 8.10. Thus an amino acid

acts as both acid and base and is called ampholyte. This property of amino acid is known as amphoteric nature.

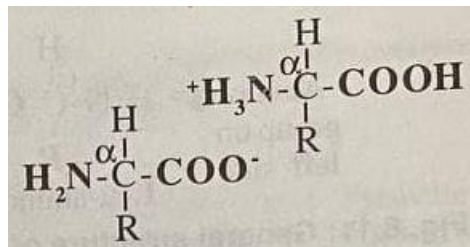
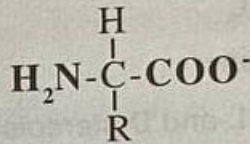
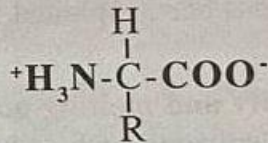
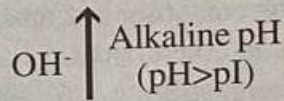


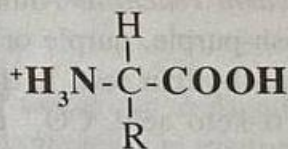
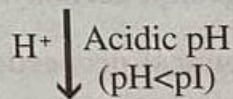
Fig. 8.9: General structure of an ionized α -amino acid.



Anionic form of α -amino acid



Zwitter ion form of α -amino acid



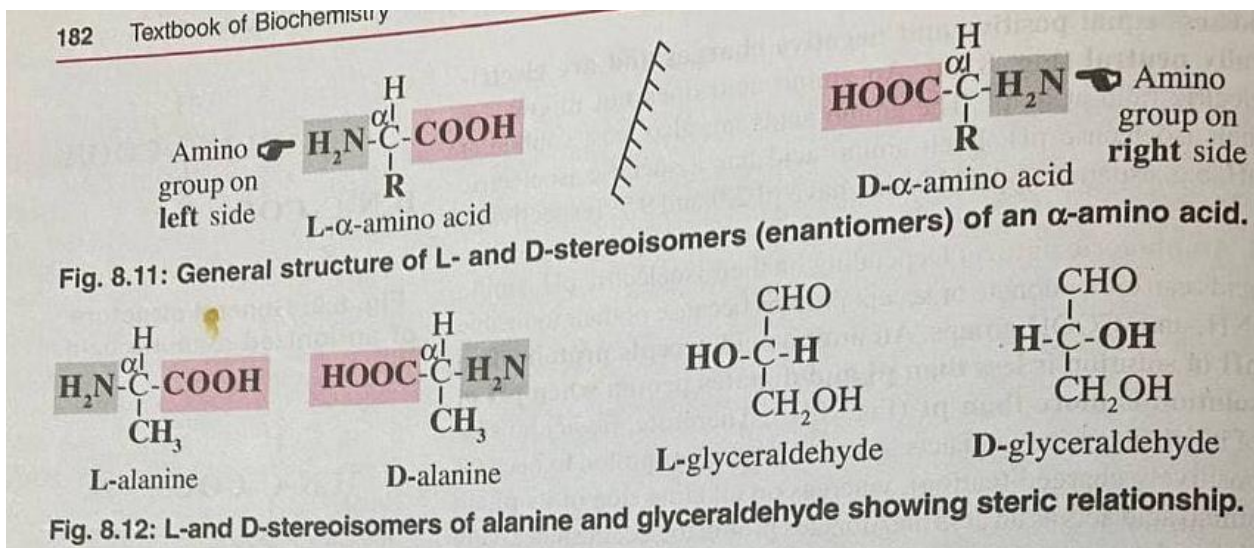
Cationic form of α -amino acid

Fig. 8.10: Amphoteric nature of amino acid.

3. **Isomerism:** The α -carbon atom in standard amino acids Zwitter ion form (except glycine) is a chiral carbon (asymmetric carbon) to which four different groups are covalently attached (Fig. 8.8a). The spatial arrangement of these four different groups on asymmetric carbon atom allows the formation of isomers (both stereoisomers and optical isomers).

(i) **Stereoisomerism:** Depending on orientation of -OH group on α -carbon atom, two stereoisomers (L- and D- isomers) of each -amino acid exist. An amino acid is said to be L-isomer and D-isomer if the -OH group on the α -carbon atom is on left side and on right side, respectively (Fig. 8.11). The two stereoisomers, L- and D-isomers, of an amino acid are non-superimposable mirror images of each other and are termed as enantiomers (Fig. 8.11). There is steric relationship between stereoisomers of amino acids and L- and D- glyceraldehyde (Fig. 8.12). Only L- α -amino acids are present in mammalian proteins. D-amino acids are found in bacterial cell walls, some non-mammalian peptides and certain peptide antibiotics (Actinomycin-D, gramicidin, etc.). D-serine and D-glutamate are suggested to be present in brain tissue.

(iii) **Optical isomers:** Amino acids with chiral carbon atom are also optically active and have ability to rotate the plane-polarized light. They exist as dextrorotatory (d) and laevorotatory (l) isomers. Similar to saccharides, the dextrorotatory and laevorotatory amino acids rotate the plane-polarized light to right and left, respectively. Glycine is optically inactive due to lack of chiral carbon.



4. Solubility and melting point: Amino acids are usually soluble in water but they are insoluble in organic solvents such as benzene and ether. Amino acids have melting point $>200^{\circ}\text{C}$.

(A) Chemical properties due to amino group (-NH)

5. Chemical properties of amino acids: Chemical properties of amino acids are due to their amino group, carboxyl group and side chain R.

(i) Ninhydrin reaction: Amino acids containing α -amino group reacts with ninhydrin reagent to give bluish-purple, purple or Ruhemann's blue colour (λ -max 540 nm). This reaction forms the basis of ninhydrin test. In this reaction, ninhydrin causes oxidative-deamination of α -amino acid yielding α -keto acid, CO, and ammonia. The reduced ninhydrin molecule (hydrindantin) then reacts with ammonia and another molecule of ninhydrin to form blue-coloured complex. Ninhydrin gives yellow colour (λ -max 440 nm) with proline.

Heat

Ninhydrin + α -amino acid $\xrightarrow{\text{heat}}$ α -keto acid + NH_3 + hydrindantin + CO_2
 Ninhydrin + NH_3 + hydrindantin $\xrightarrow{\text{heat}}$ Purple or Ruhemann's blue colour complex

(ii) Transamination reaction: In transamination reaction, α -amino group of an α -amino acid, and is transferred to an α -ketoacid₂ resulting in formation of a new α -amino acid, and another α -ketoacid, (derived from original α -amino acid,). Transamination reaction is reversible and is catalyzed by transaminases.

L-alanine + α -ketoglutarate $\xrightarrow[\text{Pyridoxal phosphate}]{\text{Glutamate-pyruvate transaminase}}$ L-glutamate + Pyruvate
 (α -amino acid₁) (α -keto acid₁) (α -amino acid₁) (α -keto acid₁)

(iii) The basic amino group of amino acid reacts with mineral acids to form salts

(iv) Amino acids are reduced to amino alcohol in presence of lithium aluminium hydride.

(B) Chemical properties due to carboxyl group (-COOH)

- (i) Amino acids react with alcohol to form esters.
- (ii) Amino acids form salts (-COONat), when react with alkali (like NaOH) or base.
- (iii) **Decarboxylation:** Amino acids are decarboxylated to corresponding amines. The most important example is histamine and tyramine derived from decarboxylation of histidine and tyrosine, respectively. In humans, decarboxylation of histidine and tyrosine is catalysed by a broad-specificity aromatic L-amino acid decarboxylase.

(C) Chemical properties due to side chain R: Because of their specific side chains, amino acids react with variety of reagents to give specific colour reactions. Some of the specific colour reactions are given below.

(i) **Xanthoproteic reaction:** It is specific for aromatic amino acids (tyrosine, phenylalanine and tryptophan) containing aromatic ring in their side chains. When concentrated nitric acid reacts with aromatic amino acid, a yellow colour develops due to formation of certain nitro-derivatives. When strong alkali is added to it, the colour turns into orange due to salt formation of nitro-derivatives.

(ii) **Millon's reaction:** It is specific for tyrosine containing phenylhydroxy group in its side chain. Tyrosine reacts with Millon's reagent to give hydroxyphenyl mercuric complex. On treatment with sodium nitrite the Hg-complex forms nitrohydroxyphenyl mercuric complex, which is red in colour.

(iii) **Sakaguchi reaction:** It is specific for arginine which contains guanidino group in its side chain. Arginine reacts with α -naphthol in alkaline medium and oxidizing agent such as sodium hypobromite (or sodium hypochlorite) to give a pink or red colour.

(iv) **Hopkins-Cole reaction:** It is specific for tryptophan which contains indole ring in its side chain. Tryptophan condenses with aldehydes in presence of strong H_2SO_4 and traces of some oxidizing substance to give purple coloured complex

(v) **Nitroprusside reaction:** It is specific for cysteine which contains free -SH group in its side chain. Sodium nitroprusside reacts with -SH group of cysteine to form sodium thionitroprusside, which is red/magenta in colour.

(vi) **Lead acetate reaction:** It is specific for sulphur containing amino acids, cysteine and cystine. Cysteine and cystine react with lead acetate in alkaline medium (NaOH) and form a black or brown precipitate of lead sulphide.

(6) **Chelating property of amino acids:** Amino acids chelate certain metal ions such as Ca^{2+} and Mn^{2+} to form chelated coordination complexes, which are non-ionic in nature. The chelating property of an amino acid is found to be due to both amino ($-\text{NH}_2$) and carboxyl ($-\text{COOH}$)

Classification of amino acids: The 20 standard amino acids have been classified in several ways.

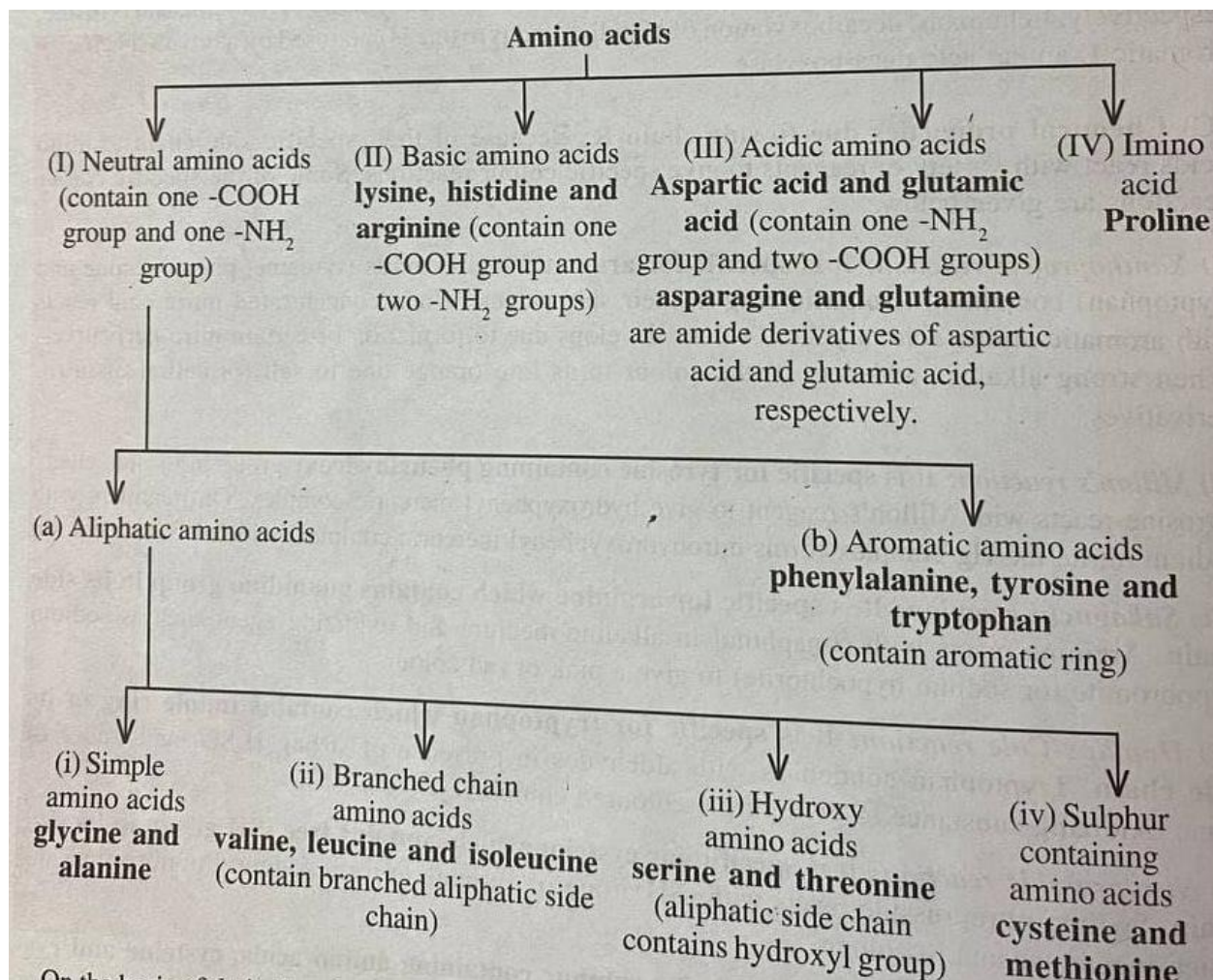
(A) Classification of amino acids on the basis of their chemical nature and structure.

(B) Classification of amino acids on the basis of their nutritional importance.

(C) Classification of amino acids on the basis of their catabolic end products.

(D) Classification of amino acids on the basis of their polarity.

CA) Classification of amino acids on the basis of their chemical nature and structure.



On the basis of their chemical nature and structure, amino acids have been classified into four groups:

(I) Neutral amino acids, (II) Basic amino acids, (III) Acidic amino acids and (IV) Imino acid.

(I) Neutral amino acids: These amino acids are monoamino monocarboxylic acids containing one -COOH group and one -NH₂ groups and are neutral in reaction. On the basis of their side chains, the neutral amino acids have been subdivided in two main categories: **(a) Aliphatic amino acids and (b) Aromatic amino acids.**

(a) Aliphatic amino acids: These amino acids contain aliphatic side chain and can be subdivided into three groups.

(i) **Simple amino acids:** Glycine and alanine are simple amino acids containing -H and -CH₃ group in their side chains, respectively (Fig. 8.13). Glycine is the smallest amino acid with the simplest structure. Glycine has no chiral carbon atom, therefore, it does not exhibit isomerism.

(ii) **Branched chain amino acids:** Valine, leucine and isoleucine are branched chain amino acids containing branched aliphatic side chain (Fig. 8.13).

(iii) **Hydroxy amino acids:** Serine and threonine are hydroxy amino acids containing hydroxyl group (-OH) in their side chains (Fig. 8.13).

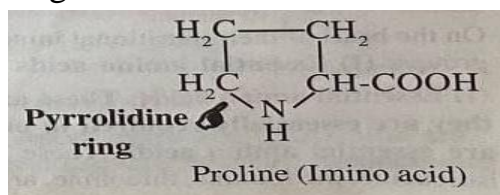
(iv) **Sulphur containing amino acid:** Cysteine and methionine are sulphur containing amino acids. Cysteine has free -SH group in its side chain (Fig. 8.13). The two molecules of cysteine may join together through disulfide linkage to form cystine. Methionine does not contain free-SH group, however, S is part of its side chain (Fig. 8.13).

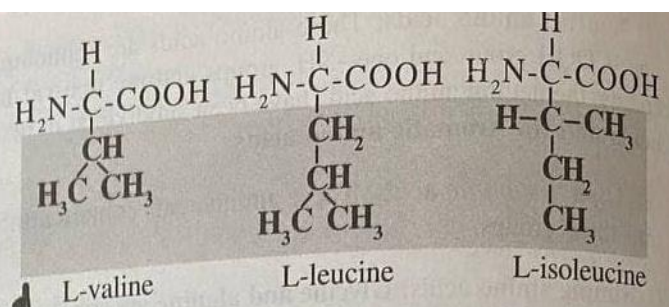
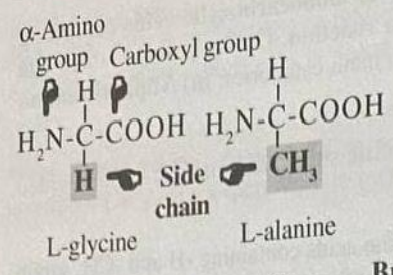
(b) **Aromatic amino acids:** These amino acids contain aromatic ring in their side chains. Three aromatic amino acids are constituents of mammalian proteins. These amino acids are phenylalanine (benzene ring in side chain), tyrosine (phenyl group in side chain) and tryptophan (indole ring in side chain) (Fig. 8.13).

(II) **Basic amino acids:** These amino acids are diamino monocarboxylic acids containing one -COOH group and two -NH₂ groups and are basic in reaction. Lysine, arginine and histidine are basic amino acids (Fig. 8.15). Arginine and histidine contain guanidino group and heterocyclic imidazole ring, respectively (Fig. 8.15).

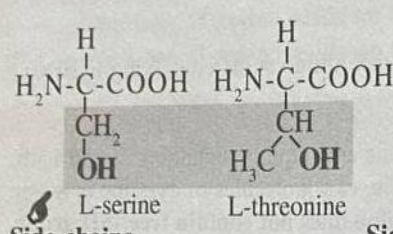
(III) **Acidic amino acids:** These amino acids are monoamino dicarboxylic acids containing two -COOH groups and one -NH₂ group and are acidic in reaction. Aspartic acid and glutamic acid are acidic amino acids (Fig. 8.15). Asparagine and glutamine are, however, amide derivatives of aspartic acid and glutamic acid, respectively (Fig. 8.15).

(IV) **Imino acid:** Proline is an imino acid. It does not possess a primary α -amino group but contains a secondary imino group (-NH-) in its pyrrolidine ring.

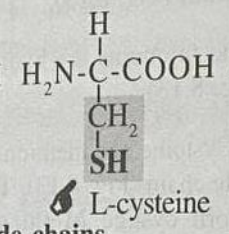




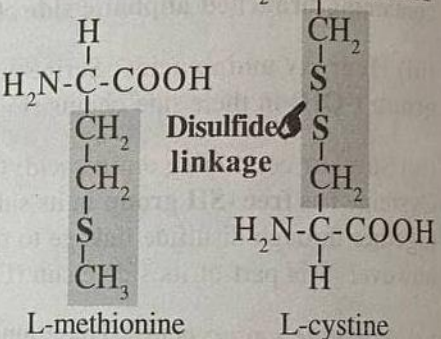
Branched chain amino acids



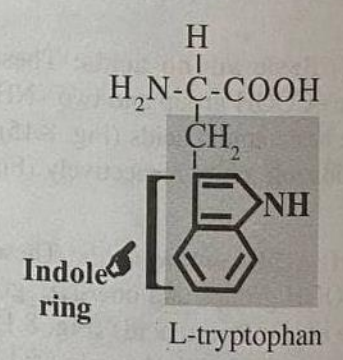
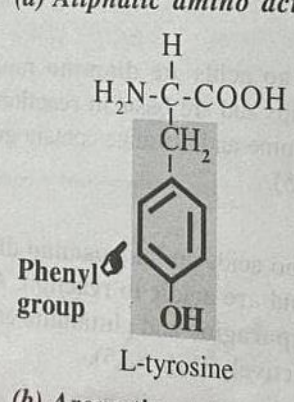
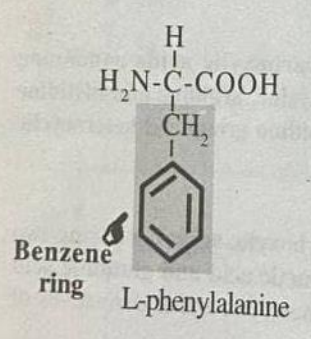
Hydroxy amino acids



Sulphur containing amino acids



(a) Aliphatic amino acids

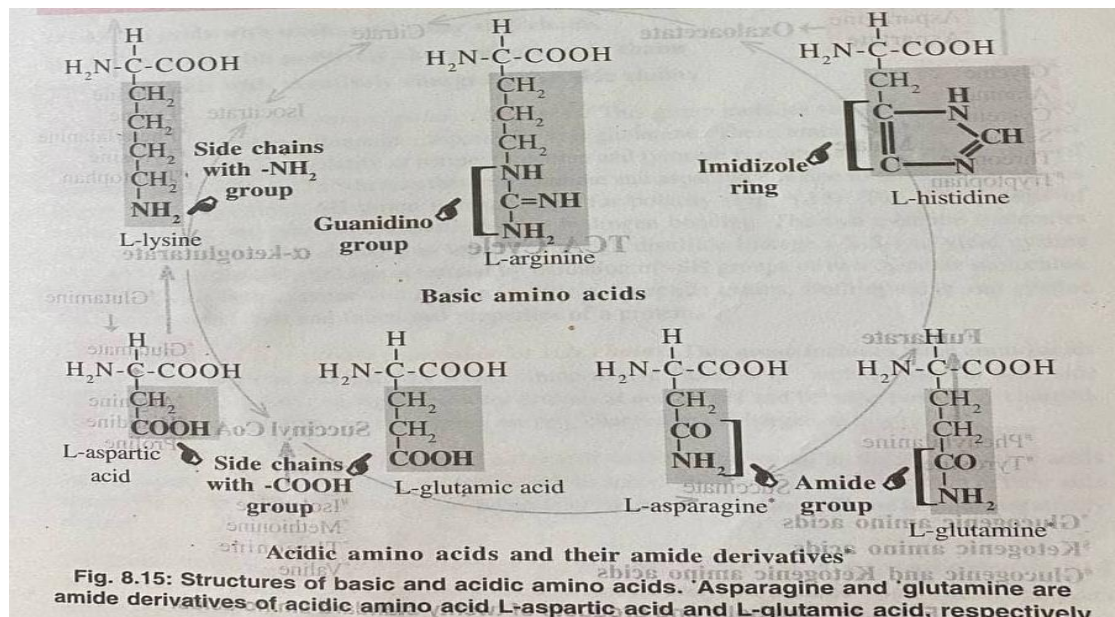
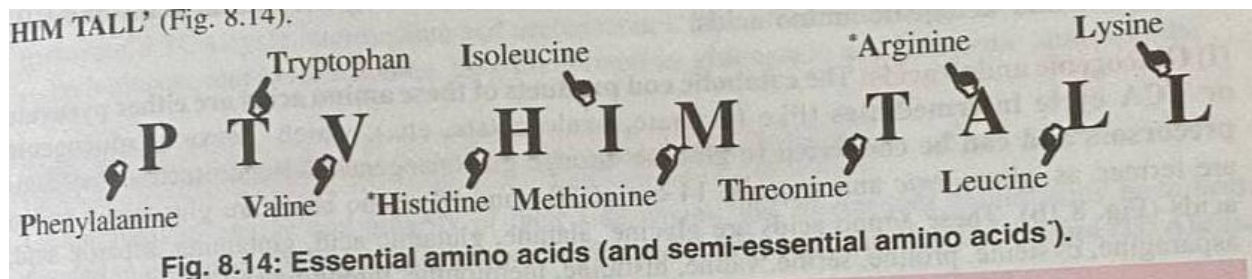


(b) Aromatic amino acids

Fig. 8.13: Structures of neutral amino acids: (a) aliphatic and (b) aromatic amino acids.

(B) Classification of amino acids on the basis of their nutritional importance
 On the basis of their nutritional importance, the 20 standard amino acids have been divided into two groups: **(I) Essential amino acids and (II) Non-essential amino acids.**

(I) Essential amino acids: These amino acids cannot be synthesized in human body, therefore they are essentially required in our diet. Out of the 20 standard amino acids, ten amino acids are essential amino acids. These amino acids are phenylalanine, tryptophan, valine, histidine, isoleucine, methionine, threonine, arginine, leucine and lysine. Among the ten essential amino acids, arginine and histidine are known as semi-essential amino acids since these amino acids are synthesized partially in human body. The arginine and histidine are not essentially required in adult diet because the quantities of these amino acids synthesized in adults are adequate to fulfil their body requirement. However, the quantities of arginine and histidine synthesized in growing children, pregnant women and lactating mothers are not adequate to meet the requirement of their body, therefore, the arginine and histidine become essential in diet of children, teenagers, pregnant women and lactating mothers. Essential amino acids can be remembered by using abbreviation PTV HIM TALL (Fig. 8.14).

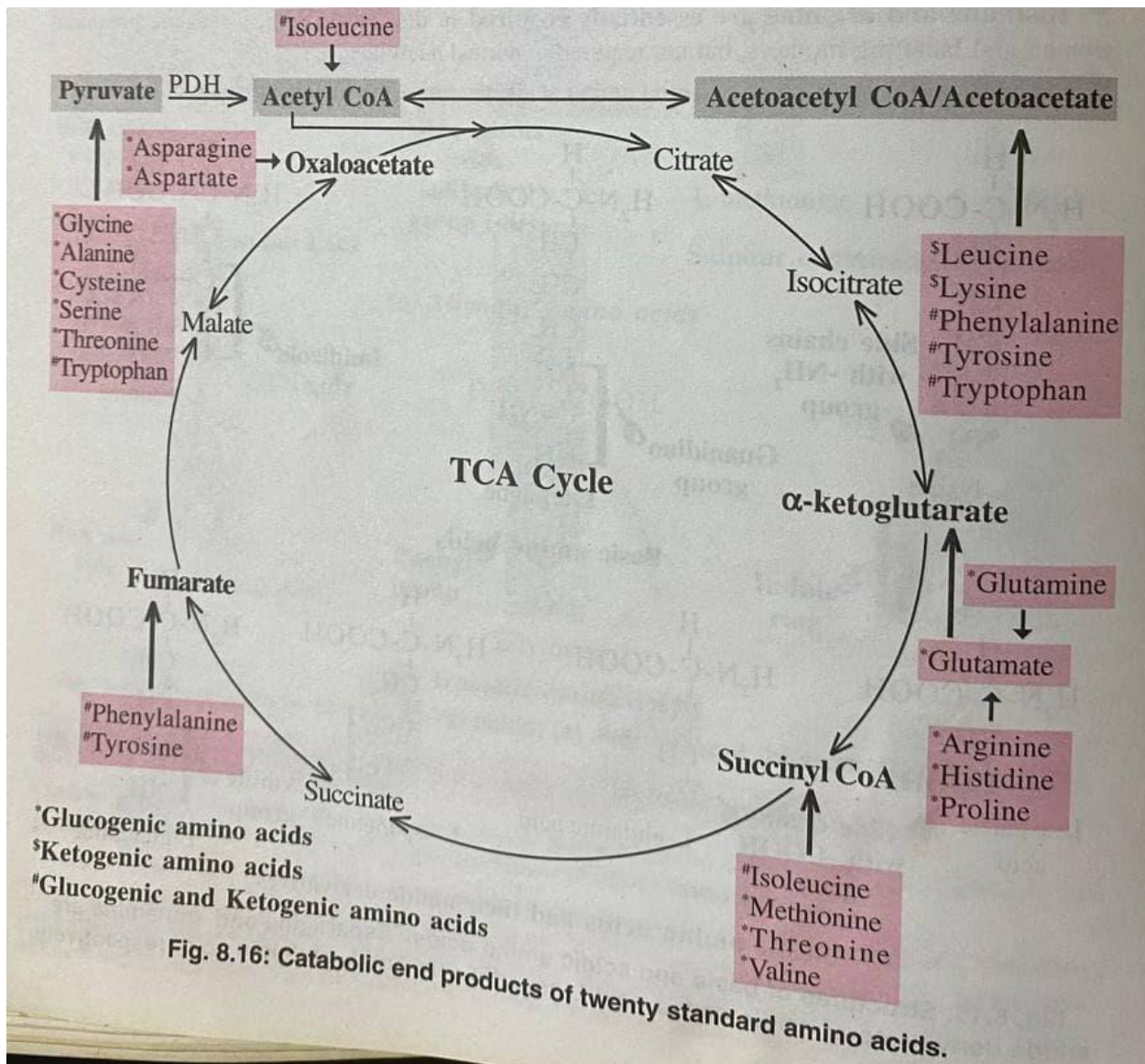


(II) Non-essential amino acids: Amino acids which are synthesized in human body are required in diet are called non-essential amino acids. They are also ten in number and include alanine, glutamic acid, glutamine, aspartic acid, asparagine, cysteine, proline, serine and tyrosine.

(C) Classification of Amino Acids on the Basis of their Catabolic End Products

On the basis of their catabolic end products (Fig. 8.16), the 20 standard amino acids have divided in three groups: **(I) Glucogenic amino acids, (II) Ketogenic amino acids and (III) Glucogenic and ketogenic amino acids.**

(I) Glucogenic amino acids: The catabolic end products of these amino acids are either pyruvate or TCA cycle intermediates (like fumarate, Oxaloacetate, etc.), which serve as glucogenic precursors and can be converted to glucose through gluconeogenesis. Hence such amino acids are termed as glucogenic amino acids. 14 out of 20 standard amino acids are glucogenic amino acids (Fig. 8.16). These amino acids are glycine, alanine, glutamic acid, glutamine, aspartic acid, asparagine, cysteine, proline, serine, valine, histidine, methionine, threonine and arginine.



(II) Ketogenic amino acids: The catabolic end products of few amino acids are either acetoacetate or one of its precursors (acetyl CoA or acetoacetyl CoA). Acetoacetate is one of the three ketone bodies and the catabolic end products, acetyl CoA and acetoacetyl CoA, can be easily converted to ketone bodies. Since such amino acids are metabolized to ketone bodies, they are termed as ketogenic amino acids. Leucine and lysine are the only exclusive ketogenic amino acids.

(III) Glucogenic and ketogenic amino acids: The catabolism of isoleucine and aromatic amino acids, phenylalanine, tyrosine and tryptophan, yield both glucogenic and ketogenic precursors (pyruvate, a TCA cycle

intermediate and acetoacetate). Since these amino acids can be metabolized to both glucose and ketone bodies, they are termed as glucogenic and ketogenic amino acids.

(D) Classification of Amino Acids on the Basis of their Polarity

On the basis of charge and polarity of their side chains, the 20 standard amino acids have been divided in two main groups: **(I) Amino acids with polar (hydrophilic) side chains and (II) Amino acids with non-polar (hydrophobic) side chains.**

(I) Amino acids with polar (hydrophilic) side chains: Among 20 standard amino acids, 11 amino acids have polar side chains. These amino acids have been further subdivided in following three groups.

- (a) Amino acids with uncharged polar side chains.
- (b) Amino acids with positively charged polar side chains.
- (c) Amino acids with negatively charged polar side chains.

(a) Amino acids with uncharged polar side chains: This group includes six amino acids namely cysteine, tyrosine, serine, threonine, asparagine and glutamine. These amino acids have zero net charge at neutral pH. The polarity of serine, threonine and tyrosine is contributed by -OH groups of their side chains (Fig. 8.13), whereas that of glutamine and asparagine is due to their amide groups (Fig. 8.15). In cysteine, -SH group is responsible for polarity (Fig. 8.13). The -OH groups of serine, threonine and tyrosine can participate in hydrogen bonding. The two cysteine molecules (with -SH group) can covalently join together through disulfide linkage (-S-S-) to yield cystine (Fig. 8.13). The disulfide linkage is formed by oxidation of -SH groups of two cysteine molecules. Proteins contain both cysteine and cystine in their polypeptide chains. Both cysteine and cystine determine the structural and functional properties of a protein.

(b) Amino acids with positively charged polar side chains: This group includes three amino acids namely lysine, arginine and histidine (basic amino acids). Because of amino group in their side chains (Fig. 8.15), lysine and arginine accept protons at neutral pH and become positively charged. The side chain of histidine can be either positively charged or uncharged at neutral pH.

(c) **Amino acids with negatively charged polar side chains:** This group includes two amino acids namely aspartic acid and glutamic acid (acidic amino acids). Because of carboxyl group in their side chains (Fig. 8.15), aspartic acid and glutamic acid donate protons at neutral pH and become negatively charged.

(II) **Amino acids with non-polar (hydrophobic) side chains:** Among 20 standard amino acids, 9 amino acids have non-polar side chains. This group includes 7 aliphatic amino acids (glycine, alanine, valine, leucine, isoleucine, methionine and proline) and 2 aromatic amino acids (phenylalanine and tryptophan). These amino acids are hydrophobic in nature because of their non-polar side and do not take part in hydrogen bonding and ionic interactions. These amino acids, however, participate in hydrophobic interactions in stabilizing protein structure.

Abbreviations and symbols used for the standard amino acids: The standard amino acids have been assigned three-letter abbreviations and one-letter symbol (table 8.1). These abbreviation and symbols have been used as shorthand script to describe the composition and sequence of amino acids in polypeptide/peptide chains.

Table 8.1: One-letter symbol and three-letter abbreviation of standard amino acids.

Name of amino acid	Three-letter abbreviation	One-letter symbol
Cysteine	Cys	C
Histidine	His	H
Isoleucine	Ile	I
Methionine	Met	M
Serine	Ser	S
Valine	Val	V
Alanine	Ala	A
Glycine	Gly	G
Leucine	Leu	L
Proline	Pro	P
Threonine	Thr	T
Arginine	Arg	R
Asparagine	Asn	N
Aspartate	Asp	D
Glutamate	Glu	E
Glutamine	Gln	Q
Phenylalanine	Phe	F
Tyrosine	Tyr	Y
Tryptophan	Trp	W
Lysine	Lys	K

Non-standard amino acids present in mammalian proteins: Some non-standard amino acids exist in mammalian proteins, These amino acids are 4-hydroxyproline, 5-hydroxylysine, γ -carboxyglutamate, 6-N-methyl-serine, cystine and selenocysteine. The 4-hydroxyproline and 5-hydroxylysine are present in collagen and are derived from hydroxylation of proline and lysine residues during Post-translational modification of collagen. The γ -carboxyglutamate (Gla residue) is found in many proteins such as, blood-clotting factors, prothrombin, osteocalcin, etc. and is derived from gamma-carboxylation of glutamate residues during post-translational modification. 6-N-methyl-serine is a constituent of contractile protein myosin. The two cysteine molecules are covalently joined together through disulfide linkage (-S-S-) to yield cystine. Selenocysteine occurs at catalytic sites of many

enzymes, e.g. glutathione peroxidase, deiodinase, etc. Selenocysteine contains selenium in place of sulphur and is derived from serine.

Sources and Functions of Amino Acids in Human Body

There are two sources of amino acids.

1. **Exogenous source of amino acids:** Exogenous source includes amino acids derived from digestion and absorption of dietary proteins.
2. **Endogenous source of amino acids:** The endogenous source includes amino acids obtained from breakdown of tissue proteins and from endogenous synthesis.

Amino acids are required for variety of functions in human body (see below).

