Amino Acids

- Amino Acids are the building units of proteins. Proteins are polymers of amino acids linked together by what is called " Peptide bond" (illustrated below).

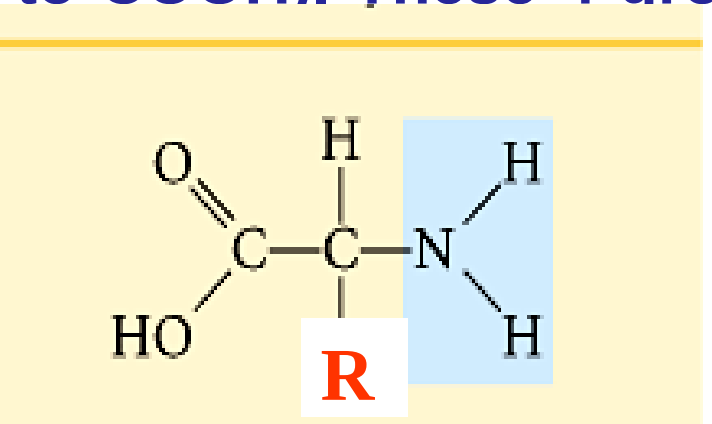
- There are about 300 amino acids occur in nature. Only 20 of them enter in proteins synthesis.

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 gp,

Hydrogen atom and side

Chain (R)



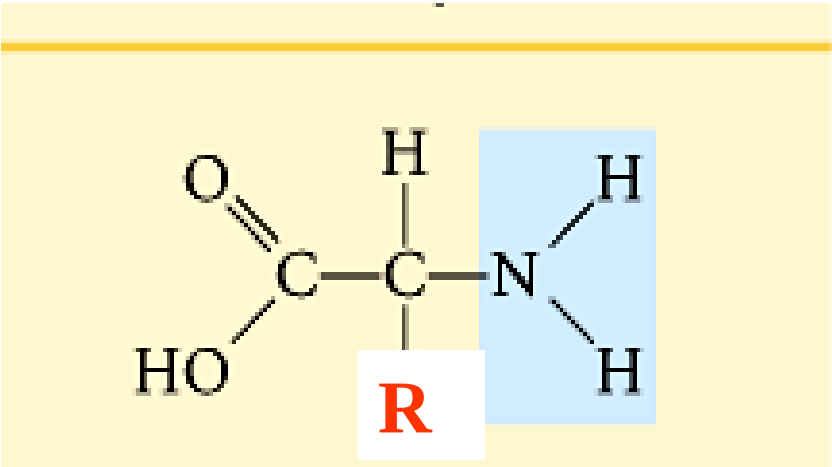
- **At physiological PH (7.4), -COOH gp is dissociated forming a negatively charged carboxylate ion (COO^-) and amino gp is protonated forming positively charged ion (NH_3^+) forming <u>Zwitter ion</u>**

- **N.B. <u>Proline</u> is an <u>imino acid</u> not amino acid <u>(see latter)</u>**

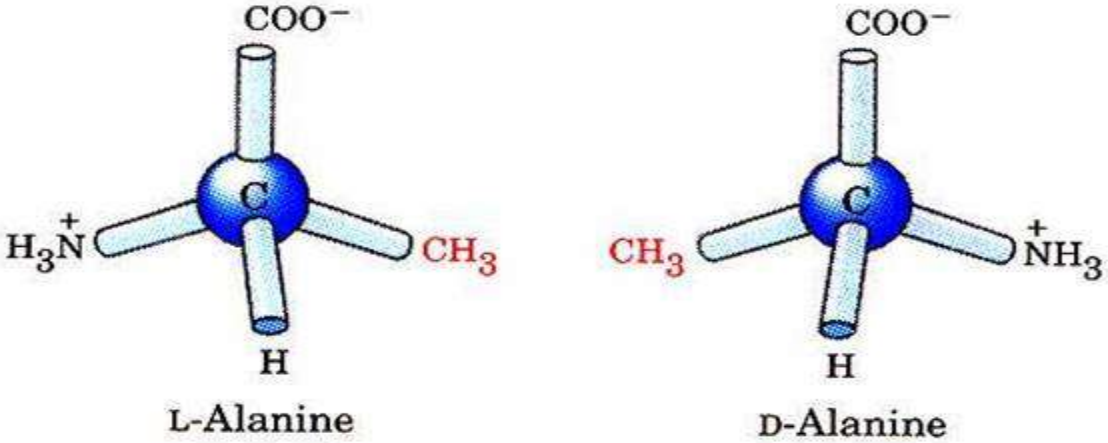
<u>Classification of amino acids</u>

<u>I- Chemical classification:</u> According to number of COOH and NH_2 groups i.e. according to net charge on amino acid.

A- **<u>Monobasic& monocarboxylic amino acids i.e. neutral or uncharged:</u>**



Only L-α amino acid occur in proteins



(a)

Subclassification of neutral amino acids:

1- **Glycine** R= H

2- **Alanine** R= CH_3

3- **Branched chain amino acids:** R is branched such as in:

a - **Valine** R= isopropyl gp

b- **Leucine** R= isobutyl gp

c- **Isoleucine** R = is isobutyl

4- Neutral Sulfur containing amino acids:

e.g. Cysteine and Methionine. Cystine,not involved in proteins. It is dimer of cysteine linked by S-S bond(oxidized form)

5- Neutral, hydroxy amino acids:

e.g. Serine and Threonine

6- Neutral aromatic amino acids:

a- Phenyl alanine

b- Tyrosine: - it is P- hydroxy phenyl alanine

c- Tryptophan:

7- Neutral heterocyclic amino acids:

a- Tryptophan: contains indole ring

b- Proline: In proline, amino group enters in the ring formation being α-imino gp so proline is an α-imino acid rather than α-amino acid

B- Basic amino acids: Contain two or more NH_2 groups or nitrogen atoms that act as base i.e. can bind proton.

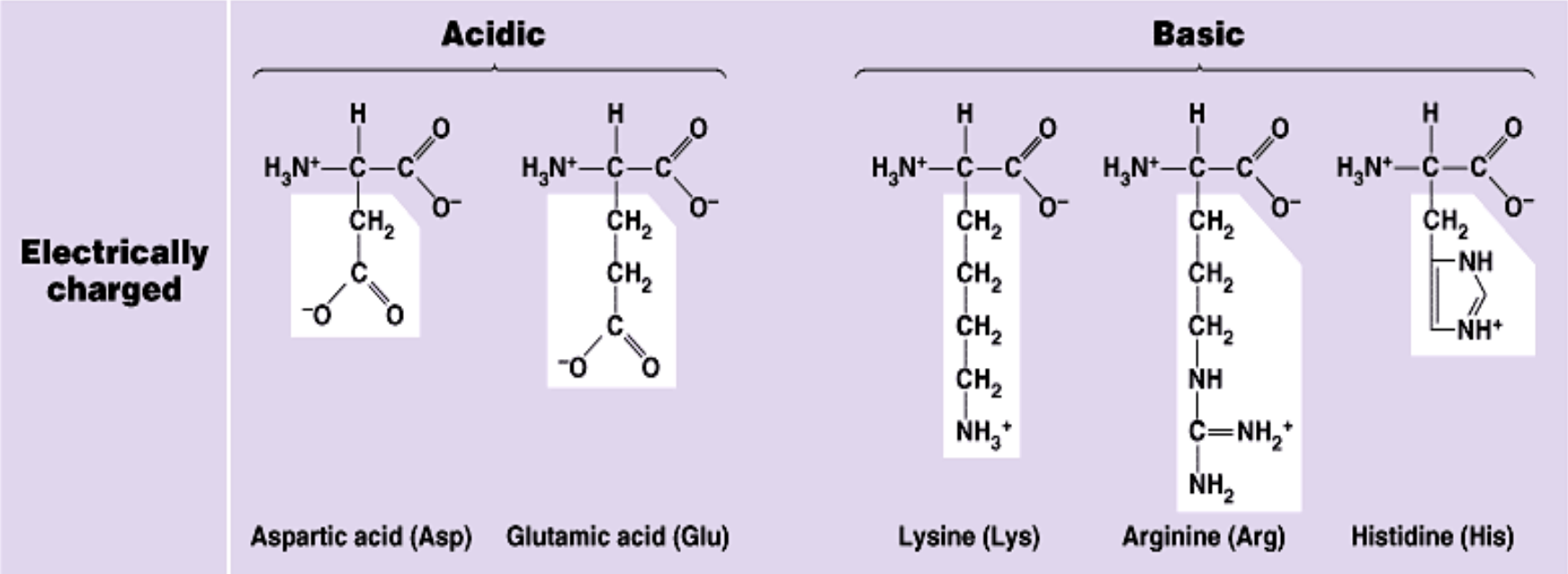
At physiological pH, basic amino acids will be **positively charged**.

e.g.

a- Lysine

b- Arginine: contains guanido group

c- Histidine:



C- Acidic Amino acids: at physiological pH will carry negative charge.

e.g. Aspartic acid (aspartate) and Glutamic acid (glutamate). see structures in hand out.

Aspargine and Glutamine: They are amide forms of aspartate and glutamate in which side chain COOH groups are amidated. They are classified as neutral amino acids.

II- Classification according to polarity of side chain (R):

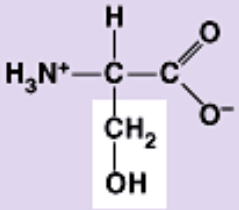
A- Polar amino acids: in which R contains polar hydrophilic group so can forms hydrogen bond with H_2O. In those amino acids, R may contain:

1- OH group : as in serine, threonine and tyrosine
2- SH group : as in cysteine
3- amide group: as in glutamine and aspargine
4- NH_2 group or nitrogen act as a base (basic amino acids): as lysine, arginine and histidine
5- COOH group (acidic amino acids): as aspartic and glutamic .

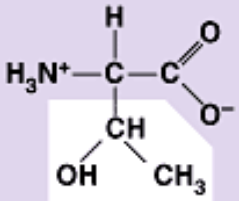
B- Non polar amino acids:

R is alkyl hydrophobic group which can't enter in hydrogen bond formation. 9 amino acids are non polar (glycine, alanine, valine, leucine, isoleucine, phenyl alanine, tryptophan, proline and methionine)

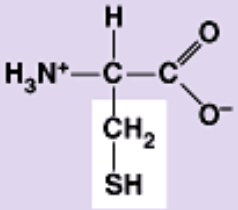
Polar



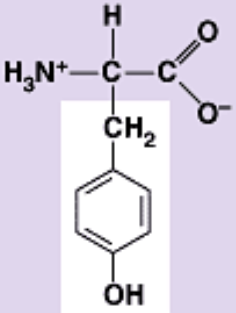
Serine (Ser)



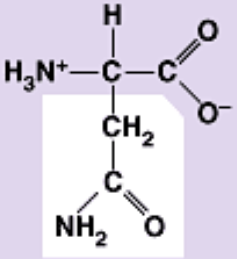
Threonine (Thr)



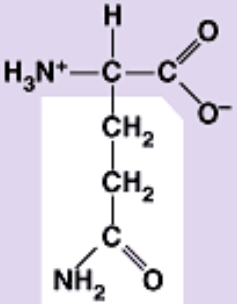
Cysteine (Cys)



Tyrosine (Tyr)

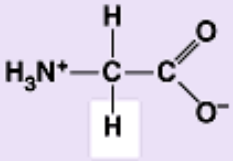


Asparagine (Asn)

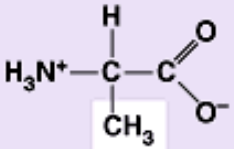


Glutamine (Gln)

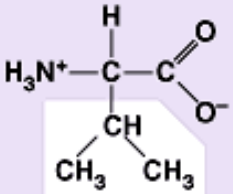
Nonpolar



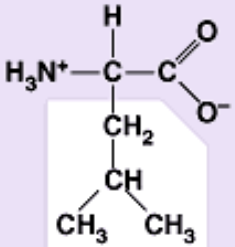
Glycine (Gly)



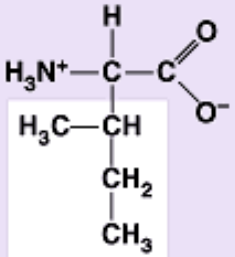
Alanine (Ala)



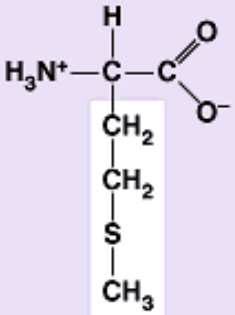
Valine (Val)



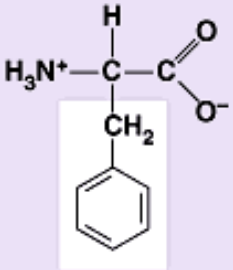
Leucine (Leu)



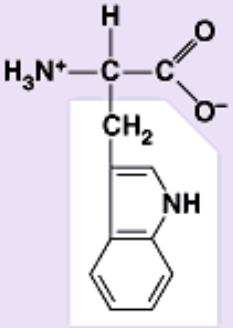
Isoleucine (Ile)



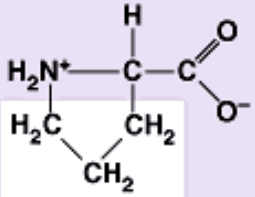
Methionine (Met)



Phenylalanine (Phe)



Tryptophan (Trp)



Proline (Pro)

III- Nutritional classification:

1- Essential amino acids: These amino acids can't be formed in the body and so, it is essential to be taken in diet. Their deficiency affects growth, health and protein synthesis.

2- Semiessential amino acids: These are formed in the body but not in sufficient amount for body requirements especially in children.

Summary of essential and semiessential amino acids:

Villa HM = Ten Thousands Pound

V= valine i= isoleucine l= lysine l= leucine

A = arginine* H= histidine* M= methionine

T= tryptophan Th= threonine P= phenyl alanine

*= arginine and histidine are semiessential

3- Non essential amino acids: These are the rest of amino acids that are formed in the body in amount enough for adults and children. They are the remaining 10 amino acids.

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

3- 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.

Amphoteric properties of amino acids: that is 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

NITROGEN BALANCE

Nitrogen balance = nitrogen ingested - nitrogen excreted

(primarily as protein) (primarily as urea)

Nitrogen balance = 0 (*nitrogen equilibrium)*

protein synthesis = protein degradation, as in normal healthy adult

Positive nitrogen balance

protein synthesis > protein degradation , as during growth, convulaesence, lactation, and pregnancy

Negative nitrogen balance

protein synthesis < protein degradation, as during illness, surgery.

peptides and Proteins

20 amino acids are commonly found in protein.

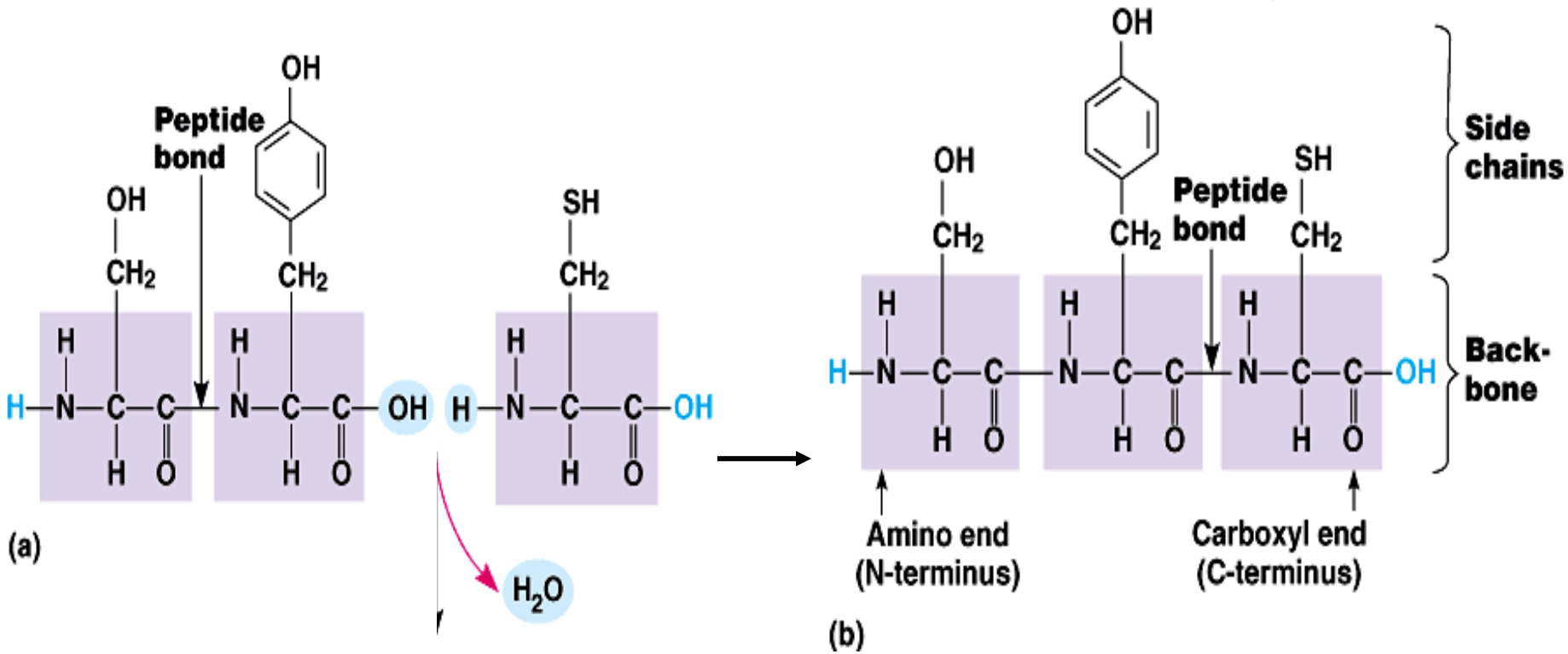
These 20 amino acids are linked together through "peptide bond forming peptides and proteins (what's the difference?).

- The chains containing less than 50 amino acids are called **"peptides",** while those containing greater than 50 amino acids are called **"proteins".**

Peptide bond formation:

α-carboxyl group of one amino acid (with side chain R1) forms a covalent peptide bond with α-amino group of another amino acid (with the side chain R2) by removal of a molecule of water. The result is : **Dipeptide** (i.e. Two amino acids linked by one peptide bond). By the same way, the dipeptide can then forms a second peptide bond with a third amino acid (with side chain R3) to give **Tripeptide.** Repetition of this process generates a polypeptide or protein of specific amino acid sequence.

Peptide bond formation:



- Each polypeptide chain starts on the left side by free amino group of the first amino acid enter in chain formation . It is termed (N- terminus).

- Each polypeptide chain ends on the right side by free COOH group of the last amino acid and termed (C-terminus).

Examples on Peptides:

1- Dipeptide (tow amino acids joined by one peptide bond):

Example**:** **Aspartame** which acts as sweetening agent being used in replacement of cane sugar. It is composed of aspartic acid and phenyl alanine.

2- Tripeptides (3 amino acids linked by two peptide bonds).

Example: **GSH** which is formed from 3 amino acids: glutamic acid, cysteine and glycine. It helps in absorption of amino acids, protects against hemolysis of RBC by breaking H_2O_2 which causes cell damage.

3- octapeptides: (8 amino acids)

Examples: Two hormones; oxytocine and vasopressin (ADH).

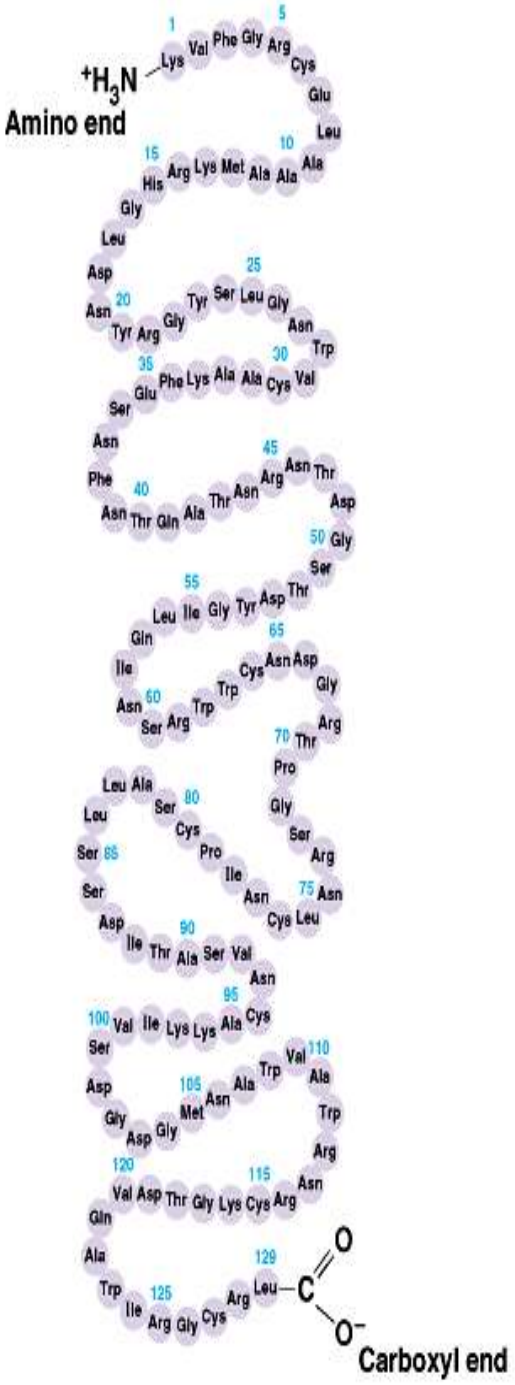
4- polypeptides: 10- 50 amino acids: e.g. Insulin hormone

Protein structure:

There are four levels of protein structure (primary, secondary, tertiary and quaternary)

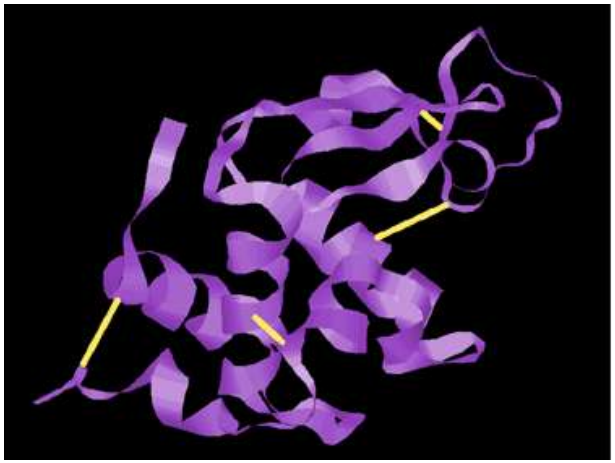
Primary structure:

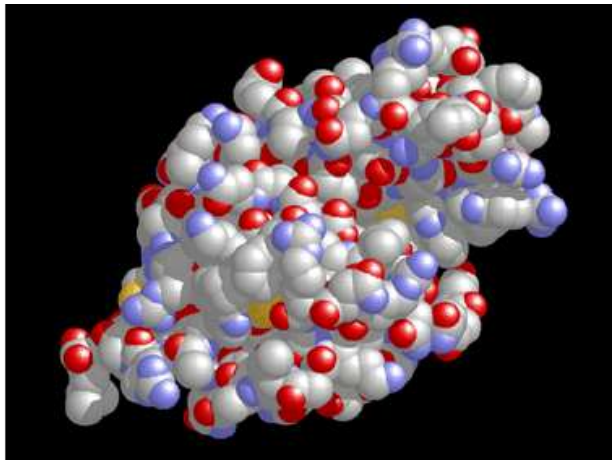
- The **primary structure** of a protein is its unique sequence of amino acids..
  - The precise primary structure of a protein is determined by inherited genetic information.
  - At one end is an amino acid with a free amino group the (the N-terminus) and at the other is an amino acid with a free carboxyl group the (the C-terminus).



High orders of Protein structure

- **A functional protein** is **not just** a polypeptide chain, but **one or more** polypeptides precisely **twisted, folded and coiled** into a molecule of unique shape (**conformation).** This conformation is essential for some protein function e.g. Enables a protein to recognize and bind specifically to another molecule e.g. hormone/receptor; enzyme/substrate and antibody/antigen.
-



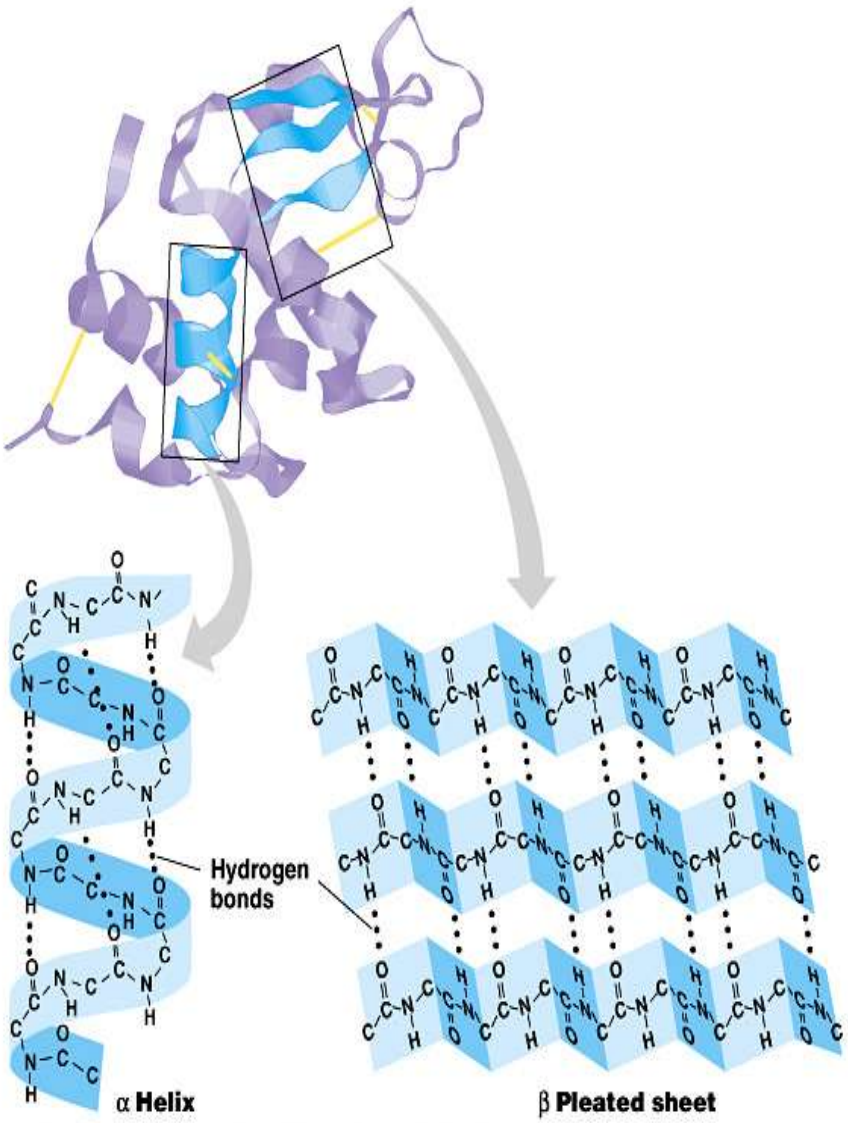


2- Secondary structure:

Results from hydrogen bond formation between hydrogen of –NH group of peptide bond and the carbonyl oxygen of another peptide bond. According to H-bonding there are two main forms of secondary structure:

α-helix: It is a spiral structure resulting from hydrogen bonding between one peptide bond and the fourth one

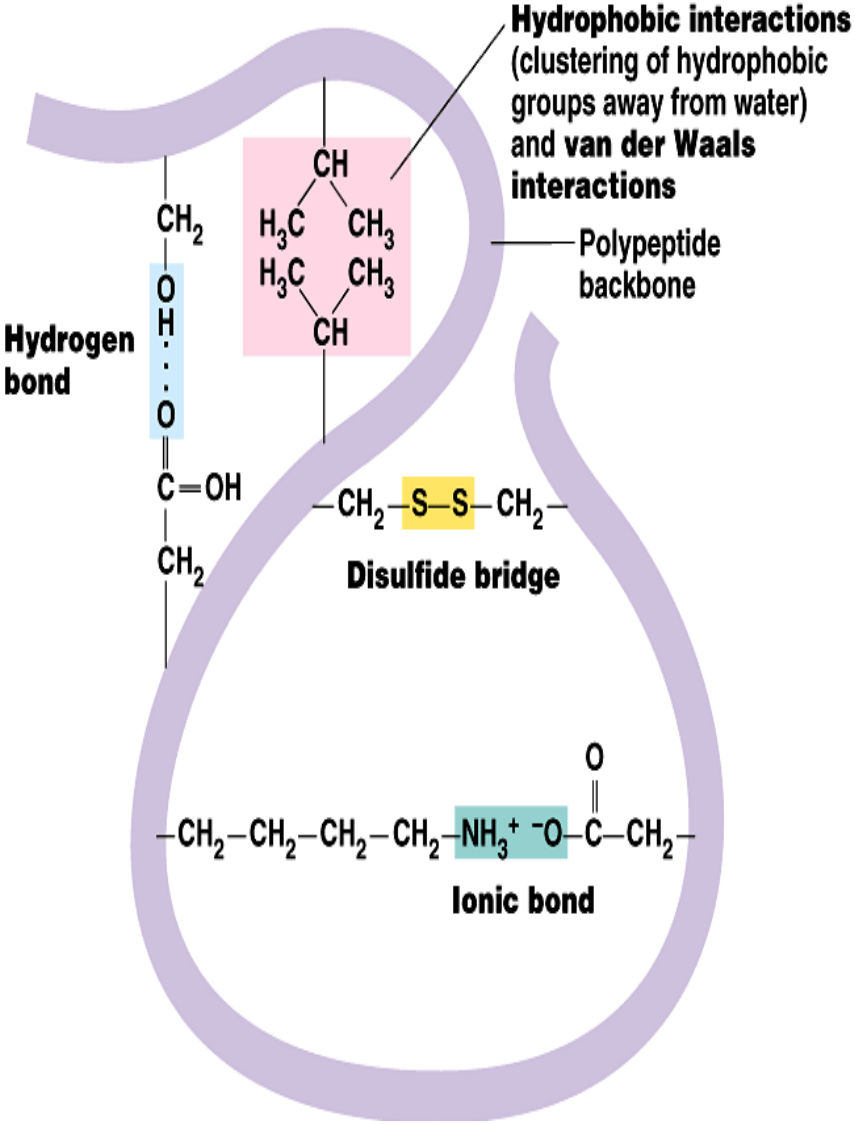
β-sheets: is another form of secondary structure in which two or more polypeptides (or segments of the same peptide chain) are linked together by hydrogen bond between H- of NH- of one chain and carbonyl oxygen of adjacent chain (or segment).



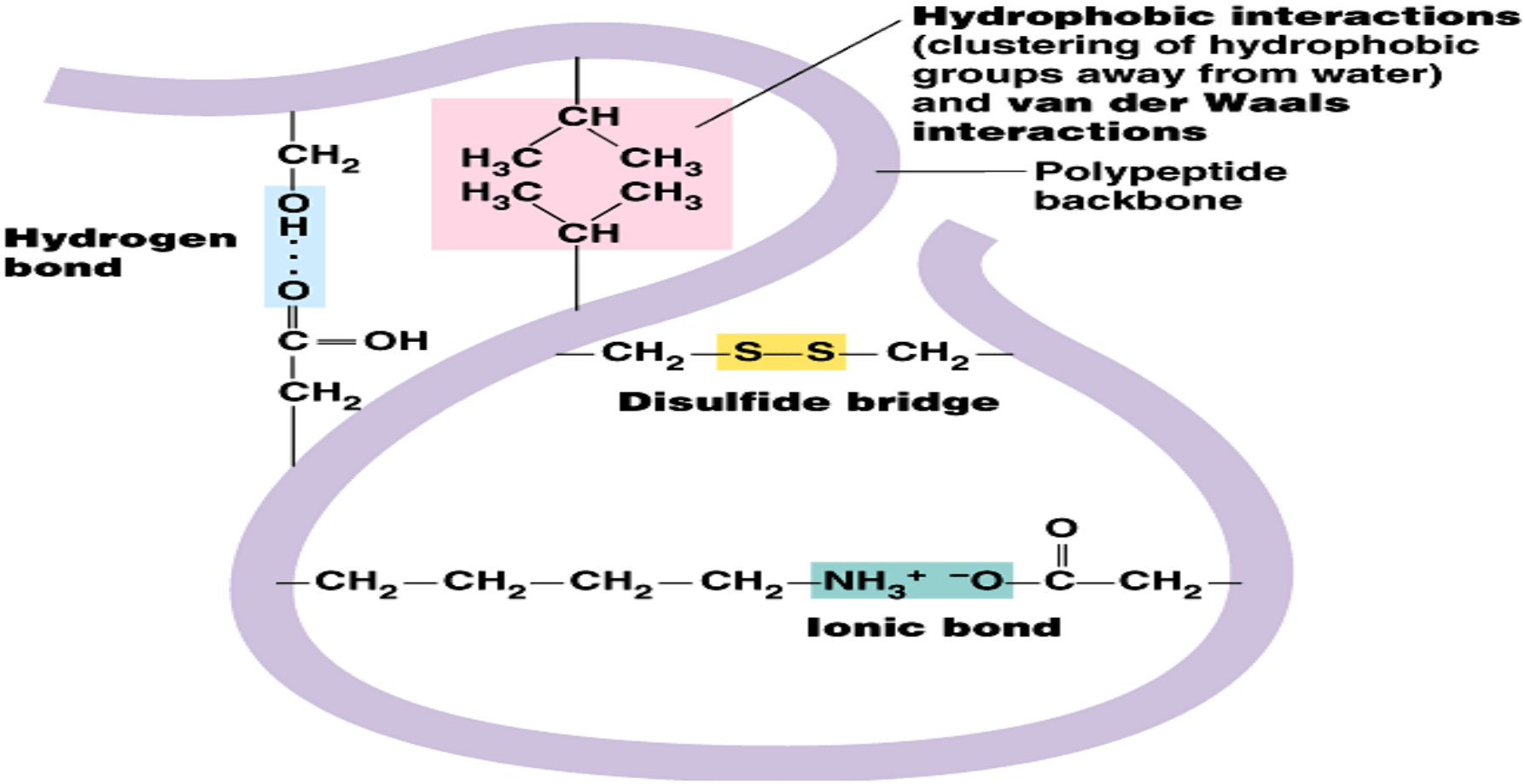
- **Tertiary structure** is determined by a variety of interactions (bond formation) among R groups and between R groups and the polypeptide backbone.

  a. **The weak interactions** include:

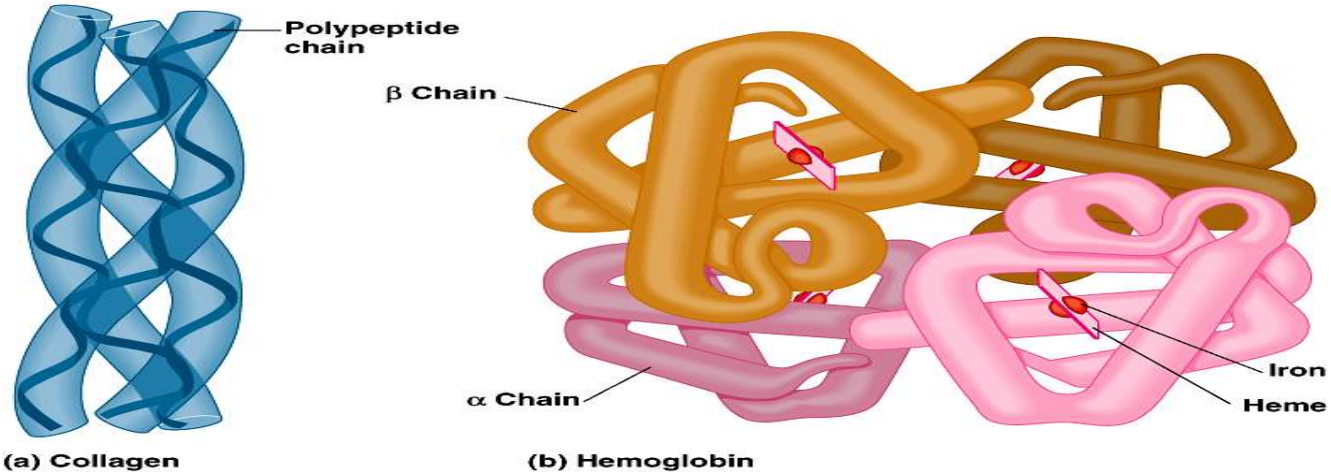
  - **Hydrogen bonds** among polar side chains
  - **Ionic bonds** between charged R groups (basic and acidic amino acids)
  - **Hydrophobic interactions** among hydrophobic (non polar) R groups.



b. **<u>Strong covalent bonds</u>** include **disulfide bridges**, that form between the sulfhydryl groups (SH) of cysteine monomers, stabilize the structure.



- **Quaternary structure:** results from the aggregation (combination) of two or more polypeptide subunits held together by non-covalent interaction like H-bonds, ionic or hydrophobic interactions.
- Examples on protein having quaternary structure:
  - **Collagen** is a fibrous protein of three polypeptides (trimeric) that are supercoiled like a rope.
  - This provides the structural strength for their role in connective tissue.
  - **Hemoglobin** is a globular protein with four polypeptide chains (tetrameric)
  - **Insulin** : two polypeptide chains (dimeric)



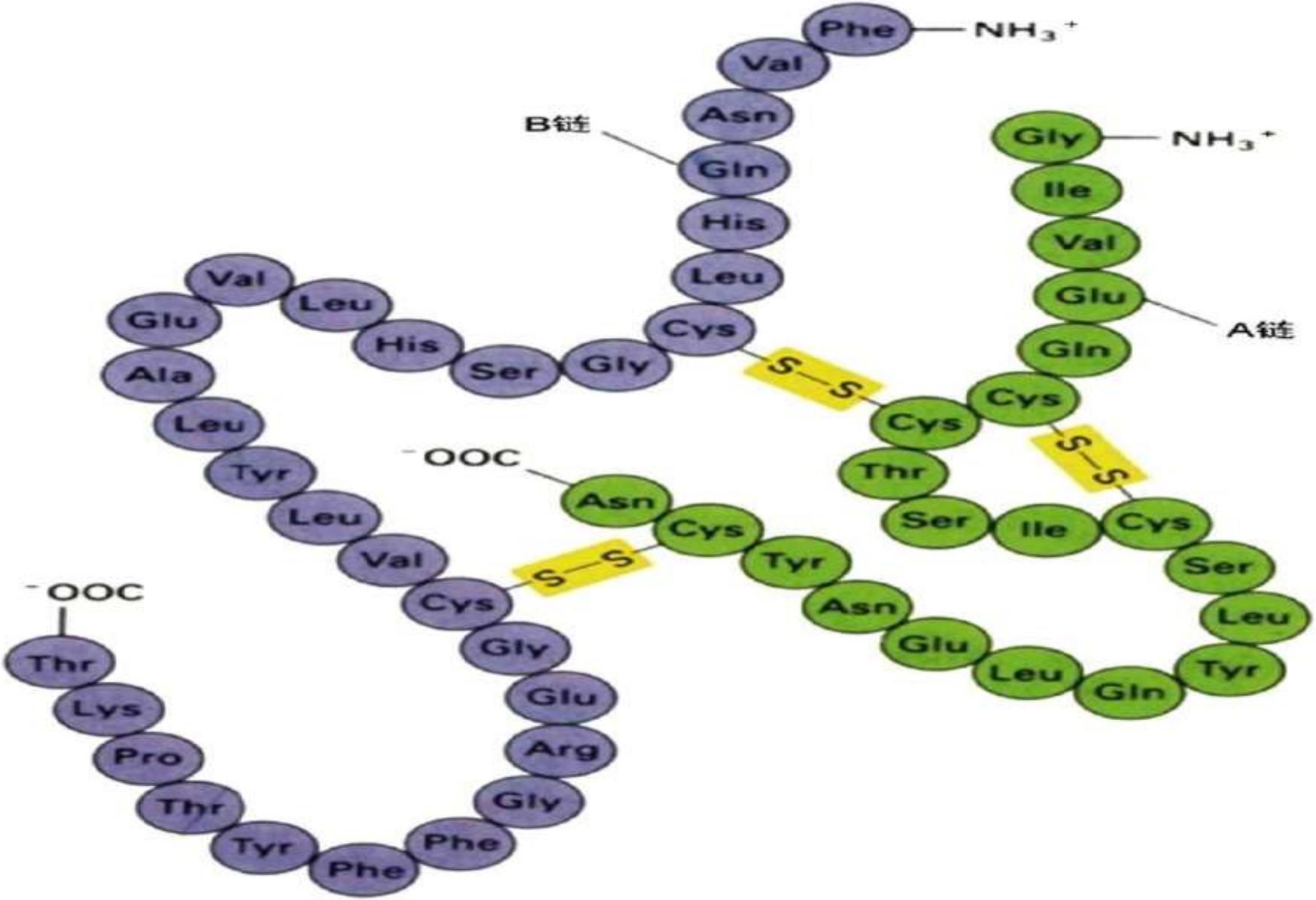
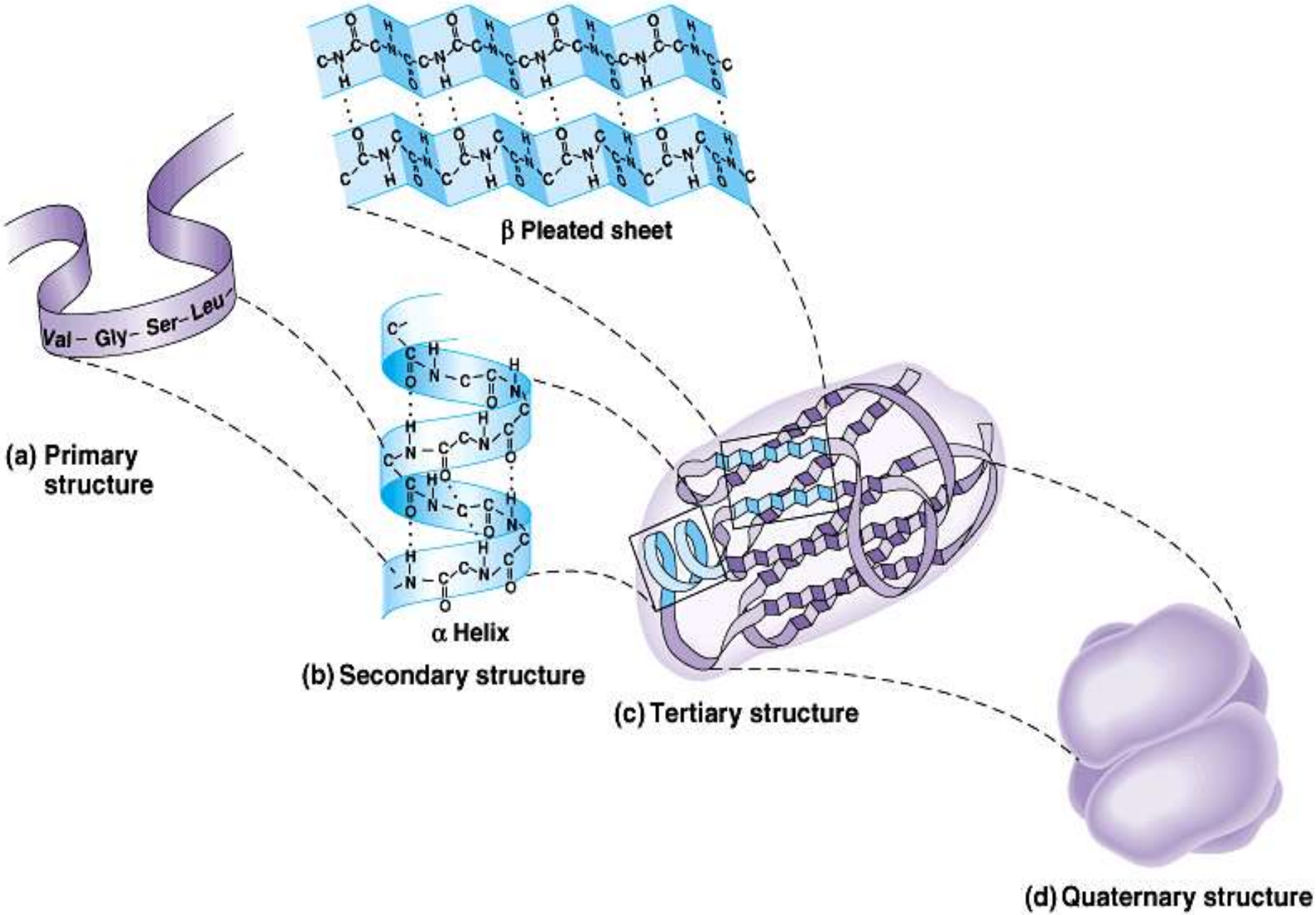


图2-5　人胰岛素的一级结构


β Pleated sheet
Val – Gly – Ser – Leu
(a) Primary structure
α Helix
(b) Secondary structure
(c) Tertiary structure
(d) Quaternary structure

Classification of proteins

I- Simple proteins:

i.e. on hydrolysis gives only amino acids

Examples:

1- Albumin and globulins: present in egg, milk and blood

They are proteins of high biological value i.e. contain all essential amino acids and easily digested.

Types of globulins:

α1 globulin: e.g. antitrypsin: see later

α2 globulin: e.g. hepatoglobin: protein that binds hemoglobin to prevent its excretion by the kidney

β-globulin: e.g. transferrin: protein that transport iron

γ-globulins = **Immunoglobulins** (antibodies) : responsible for immunity.

2- Globins (Histones): They are basic proteins rich in histidine amino acid.

They are present in :
a - combined with DNA
b - combined with heme to form hemoglobin of RBCs.

3- Gliadines are the proteins present in cereals.

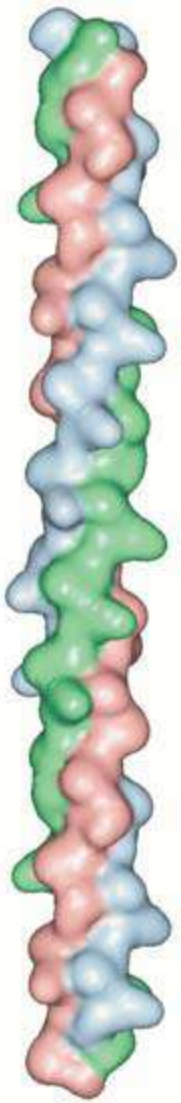
4- Scleroproteins: They are structural proteins, not digested. include: keratin, collagen and elastin.

a- α-keratin: protein found in hair, nails, enamel of teeth and outer layer of skin.

- It is rich in cysteine and hydrophobic (non polar) amino acids so it is water insoluble.

b- collagens: protein of connective tissues found in bone, teeth, cartilage, tendons, skin and blood vessels.

- Collagen may be present as gel e.g. in extracellular matrix or in vitreous humor of the eye.
- Collagens are the most important protein in mammals. They form about 30% of total body proteins.
- There are more than 20 types of collagens, the most common type is **collagen I** which constitutes about 90% of cell collagens.



- **Structure of collagen:** three helical polypeptide chains (trimeric) twisted around each other forming triplet-helix molecule.
- ⅓ of structure is glycine, 10% proline, 10% hydroxyproline and 1% hydroxylysine. Glycine is found in every third position of the chain. The repeating sequence –Gly-X-Y-, where X is frequently proline and Y is often hydroxyproline and can be hydroxylysine.

Solubility: collagen is insoluble in all solvents and not digested.

- When collagen is heated with water or dil. HCl it will be converted into **gelatin** which is soluble , digestible and used as diet (as jelly). Gelatin is classified as derived protein.

Some collagen diseases:

1- Scurvy: disease due to deficiency of vitamin C which is important coenzyme for conversion of proline into hydroxyproline and lysine into hydroxylysine. Thus, synthesis of collagen is decreased leading to abnormal bone development, bleeding, loosing of teeth and swollen gum.

2- Osteogenesis Imperfecta (OI): Inherited disease resulting from genetic deficiency or mutation in gene that synthesizes collagen type I leading to abnormal bone formation in babies and frequent bone fracture in children. It may be lethal.

C- Elastin: present in walls of large blood vessels (such as aorta). It is very important in lungs, elastic ligaments, skin, cartilage, ..

It is elastic fiber that can be stretched to several times as its normal length.

Structure: composed of 4 polypeptide chains (tetramer), similar to collagen being having 33% glycine and rich in proline but in that it has low hydroxyproline and absence of hydroxy lysine.

Emphysema: is a chronic obstructive lung disease (obstruction of air ways) resulting from deficiency of α1-antitrypsin particularly in cigarette smokers.

Role of α1-antitrypsin: Elastin is a lung protein. Smoke stimulate enzyme called elastase to be secreted form neutrophils (in lung). Elastase cause destruction of elastin of lung.

α1-antitrypsin is an enzyme (secreted from liver) and inhibit elastase and prevent destruction of elastin. So deficiency of α1-antitrypsin especially in smokers leads to degradation of lung and destruction of lung (loss of elasticity of lung, a disease called emphysema.

Conjugated proteins

1- Lipoproteins:

These are proteins conjugated with lipids.

2- Phosphoproteins: protein+ phosphate

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3- Glycoproteins:

proteins conjugated with sugar (carbohydrate)

e.g. – Mucin

- Some hormones such as erythropoeitin
- present in cell membrane structure
- blood groups.

4- Nucleoproteins: These are basic proteins (e.g. histones) conjugated with nucleic acid (DNA or RNA).

e.g. a- chromosomes: are proteins conjugated with DNA

b- Ribosomes: are proteins conjugated with RNA

5- Metalloproteins: These are proteins conjugated with metal like iron, copper, zinc, ……

a- Iron-containing proteins: Iron may present in heme such as in

- hemoglobin (Hb)
- myoglobin (protein of skeletal muscles and cardiacmuscle),
- cytochromes,
- catalase, peroxidases (destroy H2O2)

b- Copper containing proteins:

e.g. - Ceruloplasmin which oxidizes ferrous ions into ferric ions.

- Oxidase enzymes such as cytochrome oxidase.

6-Chromoproteins: These are proteins conjugated with pigment. e.g.

- All proteins containing heme (Hb, myoglobin, ……..)
- Melanoprotein:e.g proteins of hair or iris which contain melanin.