University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

Introduction to

BIOCHEMISTRY

Lecture #: (.....11.....)

■ Sheet ☐ Slides ☐ Other

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Continuation of amino acids applications in life other than tryptophan and tyrosine:

1. **Glutamate (glutamic acid):** it's modified to give monosodium glutamate (MSG), which is a flavoring agent used widely in restaurants. On the short run, MSG affects some people causing headaches especially for those eating Chinese food a lot at restaurants, so these symptoms are called Chinese restaurant syndrome. Its effects on the long run are under studies.
2. **Histidine**: produces histamine by decarboxylation reaction (taking CO_2 from $-COO^-$ in the backbone) that causes vasodilation by increasing intercellular space of the lining cells of the nose for example to increase filteration, and thus increases flu effects (this what makes us blow our noses with tissues). In inflammatory processes patients are given antihistamine.
3. **Aspartame**: sweetener, it's the methyl ester of the dipeptide composed of aspartic acid and phenylalanine (BOTH MUST be of the L type, if one or both are of D configuration aspartame will give bitter taste). Aspartame's sweetness is 200 times that of sugar.
   Some people have genetic errors in amino acids metabolism; they may lack phenylalanine hydroxylase, as in phenylketonuria, which is the enzyme responsible for conversion of phenylalanine into tyrosine, so Phe is transformed into other derivative which can build up in the nervous system causing mental retardation.
   In patients' diet books aspartame is forbidden, could instead take another sweetener such as alatame in which Phe is replaced by alanine.

Small polypeptides with physiological activity (functional modification of peptides):

1. **Carnosine**: the body produces this dipeptide as an anti-oxidant, and it's composed of β-alanine and L-Histidine.
2. **Glutathione**: is a tripeptide of glutamate, cysteine, and glycine. It works as an anti-oxidant as well and it can be as a dimer structure by a disulfide bridge between 2 thiol groups of cysteine.
   ~ Oxygen derivatives are toxic to the body like $O^{\cdot}$, O_2^{-} , $O_2^{\cdot}$, $OH^{\cdot}$, and H_2O_2 so enzymes fight them by anti-oxidants~
3. **Enkephalins**: are pentapeptides produced as analgesics (مسكنات الألم)
   ~ our body produces analgesics that are not of high potency in order to give alarm of tissue damage~
   Enkephalins are of two types that differ in the last amino acid: leucine Enkephalins (Tyr-Gly- Gly- Phe- Leu) and methionine Enkephalins (Tyr-Gly- Gly- Phe- Met)
   Their structure is similar to those of opiates (المخدرات) like morphine.
4. Peptides of cyclic structures like **oxytocin and vasopressin:** they are both secreted from the posterior pituitary gland and are similar in structure; (9 amino acids) 6-membered ring with a disulfide bone between cysteines and 3 free amino acids (out of these oxytocin is different from vasopressin by amino acid number 8 in which leucine is in the first and arginine in the second).

This small difference in structure gives very huge difference in function and effect; oxytocin causes control of uterus during delivery and of mammary glands after to give milk whereas vasopressin causes reabsorption of water in the kidneys.
People with diabetes insipidus (السكري الكاذب) have errors in vasopressin secreting hormones so no water absorption is there, and nocturnal urination (التبول الليلي) occurs.

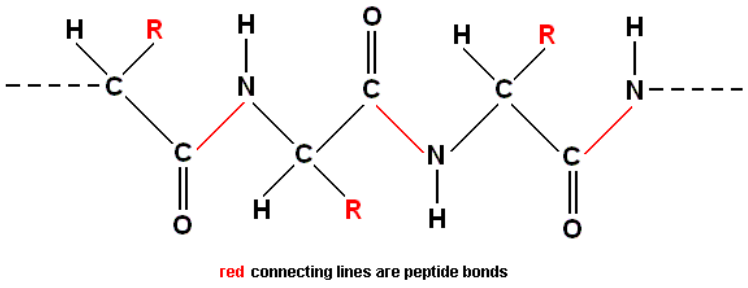
Polypeptides and proteins:

Protein is a three dimensional structure. In reality a protein may have multiple structures that are slightly different; these are called conformations of a protein. The functional active conformation is called the native conformation of protein.

Levels of proteins:

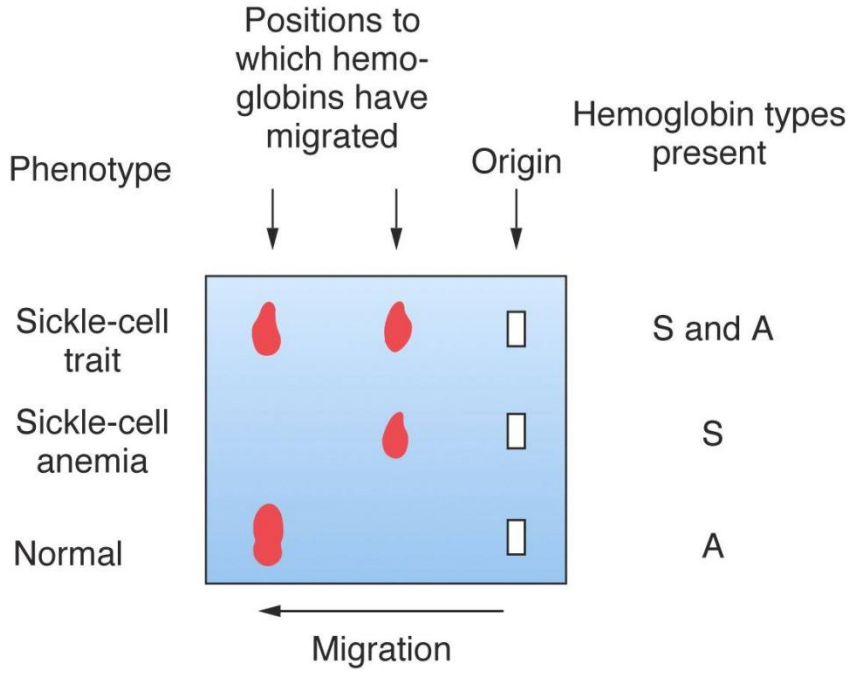
☞*Primary structure:*

It is the linear arrangement of amino acids with each other (sequence, number, and type of amino acids). R groups are generally bulky so when forming an amino acid chain –for steric reasons- they locate in zigzag arrangement.



- How can we determine the 1ry structure of the protein; how can we know the amino acids arrangement? By knowing the codon arrangements in the genetic code.
- Is the sequence important? Yes, if any amino acid is changed the whole interactions are affected. Taking the case of **sickle cell anemia**, a genetic mutation changes the sixth amino acid from glutamate into valine so a negative charge (extremely polar) is replaced by a nonpolar amino acid. In normal case each hemoglobin molecule repels the other (–ve –ve interaction) so the cell maintains its spherical shape whereas in sickle cell hemoglobin molecules stick together in a linear way by hydrophobic interactions so the cell will have irregular shape (crescent-shaped). Red blood cells will be clogging the capillaries leading to ischemia (restriction in blood supply to tissues)
  Sickle cell anemia is common in KSA because of inbreeding.
  Other than examining genes, sickle cell anemia can be examined by putting hemoglobin in gel electrophoresis. The hemoglobin molecule of sickle cell anemia will move towards anodes slower than normal ones, this is because of having one less negative charge.

A question in an exam was about choosing which of the following hemoglobin of a sickle cell is:



The third row above indicates a normal human. The second is for a patient. And the first one is a trait holder (حامل الصفة) and both sickle cell and normal hemoglobin molecules are found in his blood.

-Shape determining interactions in Proteins:

Folding in proteins is not random like in spaghetti. It's specific because of interactions between amino acids like H bonding, covalent bonding (cysteine residues), hydrophobic interactions and van de Waals forces and ionic interactions. Insulin for example is composed of two amino acids chains (A and B) via 2 disulfide bridges between cysteine residues and they include one intra-chain and two inter-chain disulfide bridges.

☞ ***Secondary structure:***

It is the three-dimensional arrangement of close amino acids together, it involves the backbone only. (Bonds in side chains are never included here; they are in higher structural levels). Close amino acids interact by H-bonding (presence of nitrogen and oxygen). While tertiary structure is the 3D arrangement of all amino acids in the polypeptide chain. Peptide bond can exist as either as a single bond or double bond due to resonance, so rotation is restricted. While bonds around the alpha carbon have a degree of rotation giving the zigzag arrangement in the chain, which leads to alpha helix or beta sheets. In alpha helix, hydrogen bonding between the amino acids is parallel to the long axis of the chain. Each turn in the helix has 4 amino acids or more correctly 3.6. Sequence and types of amino acids affect the structure of the helix. Proline causes kinking

ending the helix most usually and forming turns. The R groups are directed away from the axis of the helix.

Beta sheets have hydrogen bonds between anti-parallel segments, and hydrogen bonding is perpendicular to the long axis of the sheet. R groups are on the either side of each segment (above and below) for steric reasons. The segments could be parallel or anti-parallel.