Lecture : 4

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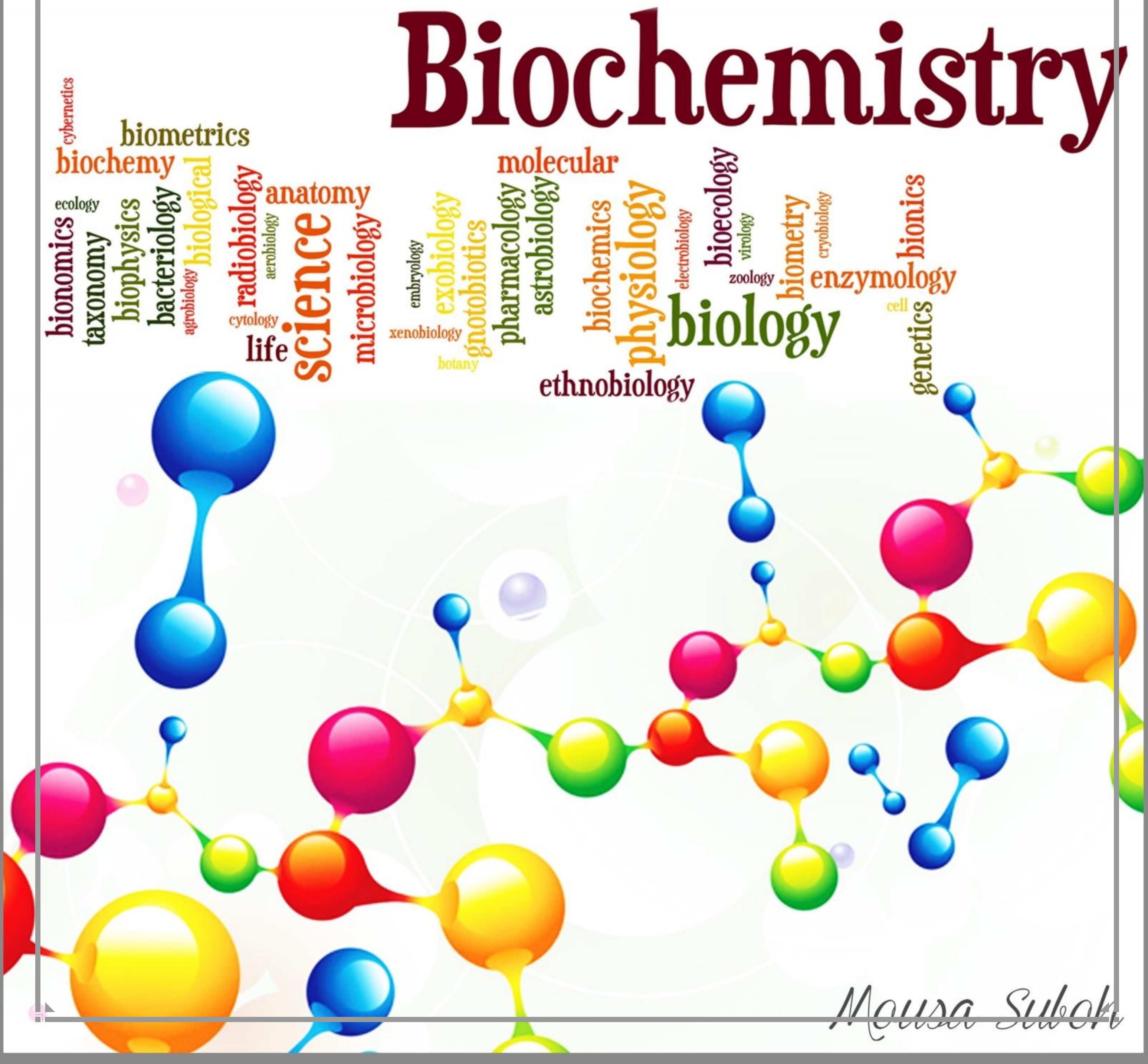
Medical Committee
The University of Jordan

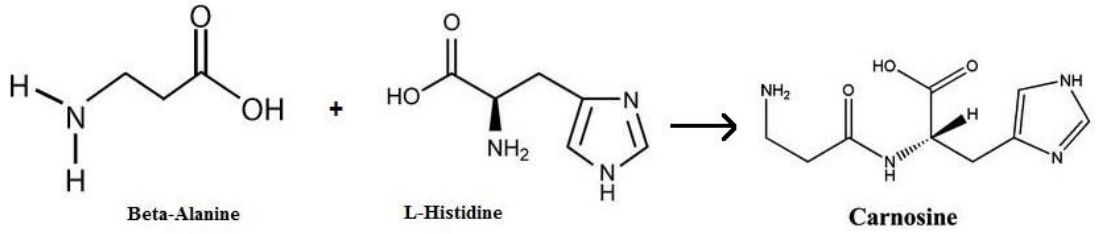


Small Peptides with Physiological Activity

These are certain peptides produced by the body or from outside with a physiological relevance.

1. Carnosine (β-alanyl-L-histidine):

Is a **dipeptide** of the amino acids beta-alanine and histidine. Carnosine acts as a **natural antioxidant** secreted by the body. It is highly concentrated in **muscle** and **brain tissues**.



Alanine is connected through its β-carbon. It has 3 carbon atoms (α carbon, the carboxylic group carbon and the carbon in the methyl side chain).

What are antioxidants ?

Antioxidant is a molecule that inhibits the oxidation of other molecules. It is a **reducing agent**, that **removes free radical intermediates** by providing them with the extra electron needed to make the pair. So they are materials that have the capability to fight radicals (oxidants).

So that, antioxidants are also known as "free radical scavengers".

What are free radicals ?

Free radical is a **harmful molecule** that contains **unpaired electrons**-which is unusual because electrons typically come in pairs. The unpaired electrons make free radicals **highly reactive**, and in this state, they **can cause damage** (cancer) by attacking the components of our cells like: DNA and this leads to mutations, proteins and disabling their functions or lipids in the cell membrane.

Paired electrons spin in opposite directions, one spins clockwise (downward) and the other spins counter-clockwise (upward), so the positive

and negative spins will cancel each other. **Single electron spinning by itself** attempts to find another electron and attacks any structure around it in order to reach stability and saturation state and this damages the cells.

Antioxidants become free radicals themselves upon donation of an electron, how do they solve this problem ?

Its structure is a ring structure as in carnosine. Ring structures always can stabilize electrons better than aliphatic structures because of its high resonance. It has shortage of electrons and can be saturated.

When we don't have ring structures there are another mechanisms, consider glutathione.

2) Glutathione :

The most important antioxidant produced in human body.

It is a tripeptide consisting of three amino acids connected together:

γ - glutamic acid, cysteine, and glycine.

Glutamate is connected to cysteine and glycine through its **γ-carbon** (through the side chain).

It does not have a ring structure, so how will it stabilize?

It connects with itself. How? Via disulfide bond.

Cysteine through its thiol group, in the presence of free radicals, can donate the hydrogen with its electron (HS- hydrogen), so we have done stabilization and saturation to the free radical, leaving the S atom alone, another glutathione molecule will donate the H-atom and its electron to another free radical leaving another S atom. The two S atoms from both molecules can form disulfide bond with each other.

3) Enkephalins :

Another small peptides produced by the human body.

Enkephalins work mainly as naturally occurring analgesics.

An **analgesic**, or **painkiller**, is any member of the group of drugs used to achieve analgesia – relief from pain like panadol or brufen.

Enkephalins are pentapeptides, five amino acids connected together. There are two types of enkephalins according to the 5^{th} amino acid :

Tyr- Gly- Gly- Phe- Leu → (Leucine enkephaline).

Tyr-Gly-Gly-Phe- Met → (Methionine enkephaline).

These two types differ in tissue localization (found in different places within tissues). But they have the same function. The functional amino acids are the aromatic ones: Tyrosine and Phenylalanine. (Their side chains).

Enkephalines are found in the brain and they are structurally similar with morphine (a pain reliever). They are secreted to feel pain when it exceeds a certain threshold.

3)Oxytocin and vasopressin :

They are hormones secreted from the posterior pituitary gland.

Oxytocin regulates the contraction of smooth muscles in the uterine wall to induce labor/ delivery. Oxytocin also induces contraction of smooth muscles in the mammary glands to induce lactation.

Vasopressin, antidiuretic hormone (ADH) , has a circadian secretion which means it is secreted at night more than daytime. It is an osmoregulation hormone that increases the reabsorption of water after it is secreted to urine, preventing water loss and increasing the blood volume which increases the blood pressure so it is a vasopresser. It presses the blood vessels.

When ADH is low especially in children, they can't hold urination at night and they suffer from nocturnal enuresis. (السلس البولي الليلي) They can be treated by giving them ADH.

Vasopressin and oxytocin both consist of the same nine amino acids' sequence except for two amino acids:

In <u>oxytocin</u> the third amino acid is <u>isoleucine</u> and the eighth is <u>leucine.</u>

In <u>vasopressin</u> the third amino acid is <u>phenyl alanine</u> and the eighth is <u>arginine.</u>

They have a cyclic structure because of disulfide bond , cysteine is present in the first and the sixth positions so they are linked via disulfide bond.

As we see, simple changes in amino acids create great changes in function.

4)Gramicidin S and tyroicidine A :

They are two antibiotics. (antibacterial substances secreted from bacteria and other living cells).

They are decapeptides (10 amino acids) that have cyclic structure connected at both ends. (Like a rectangle). They contain D and L amino acids.

They contain the basic amino acid ornithine (ORN) that is used in the first step in urea cycle to form urine. It is not encoded by the genetic code and this means that it doesn't occur in proteins though it is produced in the body.

5) Aspartame :

A dipeptide, as the name implies, it consists of aspartic acid and followed by phenyl alanine. Both of them have the L- configuration.

It functions as a sweetener that has 200 times more sweet effect than regular sugar. It is considered a sugar substitute for diabetic patients. It is a methyl ester derivative.

Phenylketonuria :

It is one of the inborn errors of metabolism which are congenital group of diseases caused by deficient, insufficient or problematic enzymes in one of the pathways in the human body.

Phenylketonuria is present in Jordan and some countries screen the newborn immediately after birth to check for the disease.

Phenylketonuria is characterized by the increase of the secretion of Phenyl ketones in urine.

Phenylalanine must be converted to tyrosine via hydroxylation process and catalyzed by enzyme phenylalanine hydroxylase.

Sometimes this enzyme will be deficient genetically, or a mutation occurs in the gene so that the enzyme won't function properly or it might be absent and the phenylalanine will accumulate resulting in the deficiency of tyrosine.

How is it treated ?

By a special diet, we reduce the amount of phenyl alanine and give supplements of tyrosine so the child will live happily and normally on his diet.

The problem is we do not do screening, the phenyl alanine will be in a high concentration, and its metabolites through ketone routes will increase such as ; phenyl lactate, phenyl pyruvate, and phenyl acetate and accumulate within the brain cells and after a year the child will have a mental retardation.

So people with Phenylketonuria can take aspartame?

No, because it contains phenyl alanine. They are given Alatame as subsitute which is 2000 times sweeter than sucrose.

Q1) Which of the following amino acids are polar ?

A) Serine B) Tyrosine C) Arginine D) All of the above

Q2) Which two of the following amino acids could form an ionic bond ?

A) Aspartic acid and Lysine

B) Arginine and Glutamine

C) Glutamic acid and Valine

D) Proline and Glycine

Q3) Which of the following amino acids' side chains is a single methyl group ?

A) Valine B) Alanine C) Leucine D) Isolecine

Q4) The three letter abbreviation "asn" corresponds to which amino acid ?

A) Aspartic acid B) Asparagine C) Arginine D) Alanine

Q5) Of the amino acids abbreviated "Lys", "Glu", "Trp", and "Gln", which is a basic amino acid with a positive charge ?

A) Lysine B) Tryptophan C) Glutamic acid D) Glutamine

Q6) Which of the following amino acids is NOT positively charged ?

A) Histidine B) Lysine C) Aspartic acid D) Arginine

Q7) Which of the following amino acids is the largest of all amino acids ?

A) Tryptophan B) Histidine C) Tyrosine D) Glutamic acid

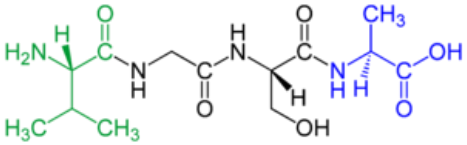
Q8) Which of the following amino acids is actually an imino acid ?

A) Alanine B) Proline C) Tryptophan D) Glutamic acid

Q9) Which of the following amino acids can form a special covalent bond called a disulfide bond ?

A) Tyrosine B) Methionine C) Cysteine D) Lysine

Q10) What is the amino acid sequence for the following tetrapeptide ?



Ans : Val-Gly-Ser-Asp