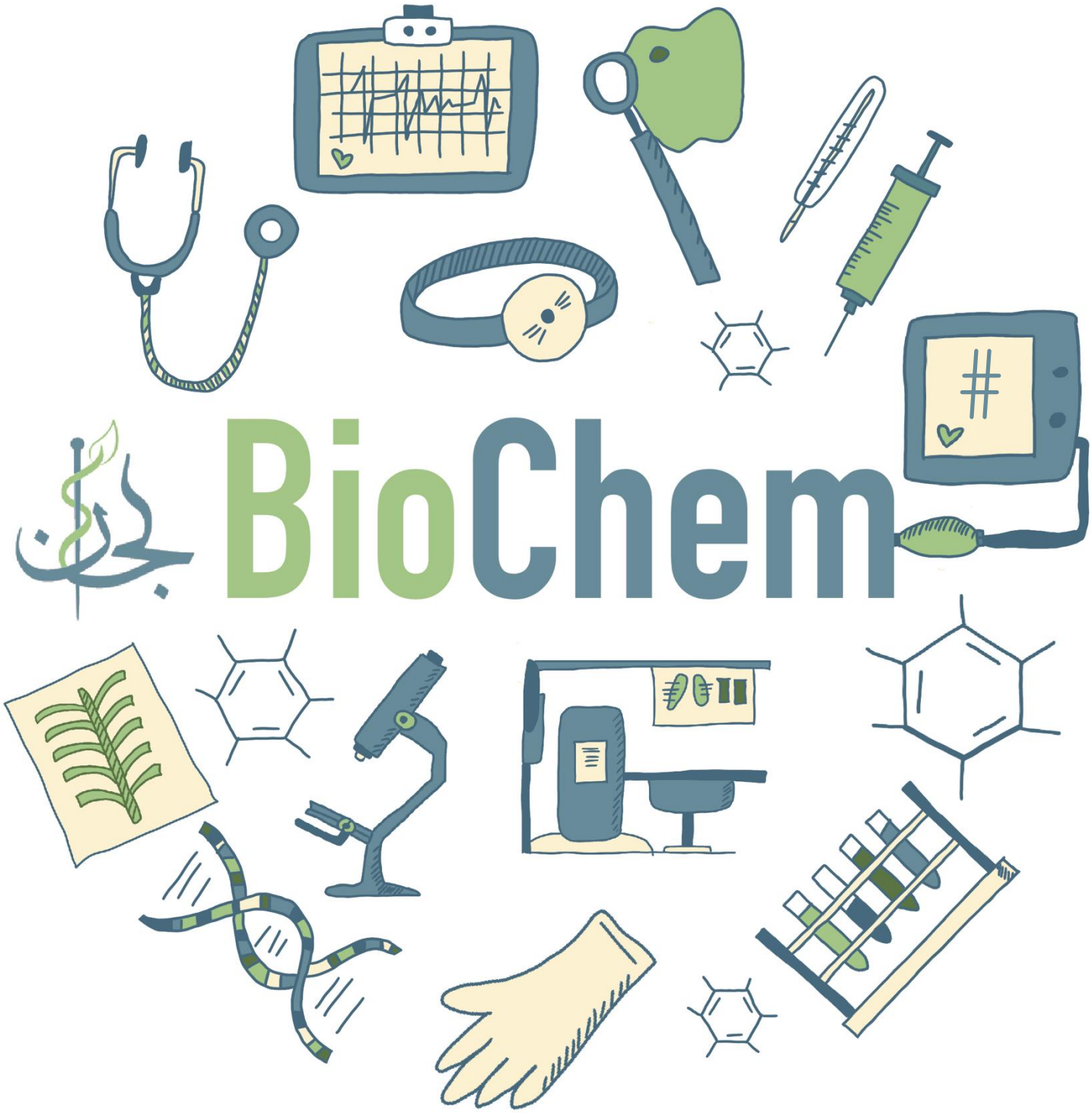

BioChem

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After we had taken the Amino acids and we know their types and classes so in the following lecture we will talk about how amino acids assemble into peptides and proteins and how proteins have a three dimensional structure and how this structure is related to its function.

Some important Definitions and concepts: -

- A **residue**: **each amino acid in a (poly)peptide** (if we say amino acid we are talking about one single amino acid molecule like glycine, tryptophan, etc. but if we say an amino acid residue it means it's an amino acid that makes a part of a larger structure like polypeptide or protein).
- **Di**peptide (**two** amino acids linked together by **peptide bond**), **tri**peptide (**three** ….), **tetra**peptide(**four**….), etc.
- **Oligopeptide (peptide): a short chain of 20-30 amino acids** or it can be 10 or 13
- **Polypeptide: a longer peptide with no particular structure (more than 30 amino acids)**
- **Note: The number of peptide bond in any peptide is (n-1) where n is the number of amino acids.**

*It's all relative, there isn't a certain line that defines the oligopeptides from a polypeptide.

- **Protein: a polypeptide chains with an organized 3D structures, and can perform a specific function.**

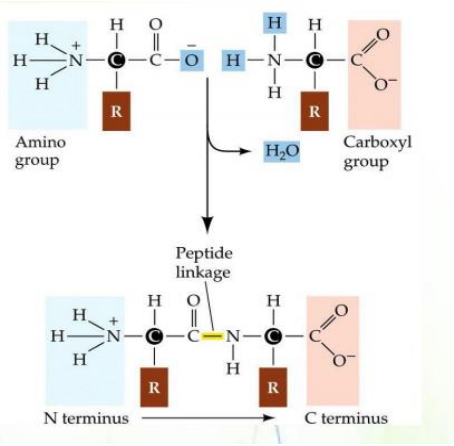
The difference between polypeptide and protein is that the protein has a specific 3D structure with a defined function but polypeptide its large number of amino acid without a 3D structure, so if the polypeptide folds and form a 3D structure it will turn into a protein.

- **The average molecular weight of an amino acid residue is about 110**
- **The molecular weights of most proteins are between 5500 and 220,000** (*calculate how many amino acids*) (number of amino acids 5500/110 =50 and 220000/110=2000)

*We can estimate the size of protein by knowing the number of amino acids that make up the protein)

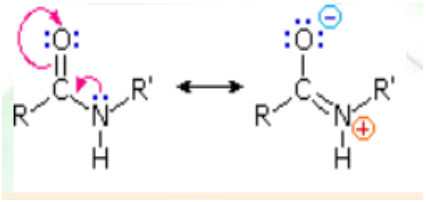
- **We refer to the mass of a polypeptide in units of Daltons**
  - **A 10,000-MW protein has a mass of 10,000 Daltons (Da) or 10kilodaltons (kDa)**

Peptide bond: -

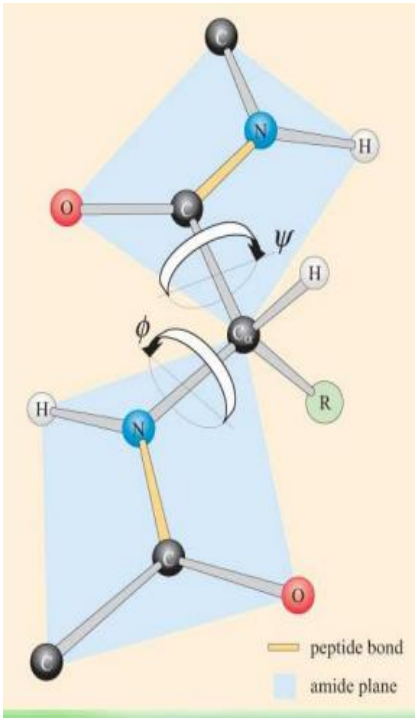


- It is called an amide bond formed via a condensation reaction. (**Dehydration reaction**)
- It's a bond between an **amino group** (N terminus) and a **carboxyl group** (C terminus).
- ❖ Amide bond in organic chemistry and peptide bond in biochemistry it's the same.
- ❖ Its formed through condensation reaction because there is a release in water.

Features for peptide bond: -

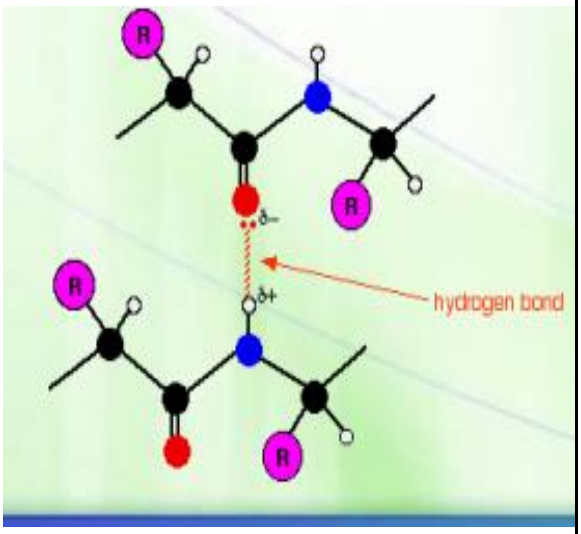


- ➢ **It has a resonance structure** (there is a convergence of the double bond, normally we have the carbonyl group c=o and when the electrons on the double bond move to the Oxygen it will become negative and the electrons on the nitrogen will form a double bond between carbon and nitrogen that's results in appearing a negative charge on Oxygen and positive charge on Nitrogen so peptide bond keeps on changing from the left form to the right form.



- ➢ **Double bond** makes the amide bond →**Planar**, **charged**, **Rigid, Un-rotatable** (due to double bond characteristics in the peptide bond which makes the carbonyl and the amine groups planner meaning it's flat and also due to the double bond the bond is rigid and can't rotate but the bonds within the amino acid itself can rotate and these bonds which can rotate gives the protein the 3d structure).

- **Zigzag structure** (peptide bonds make the peptide have a zigzag structure).

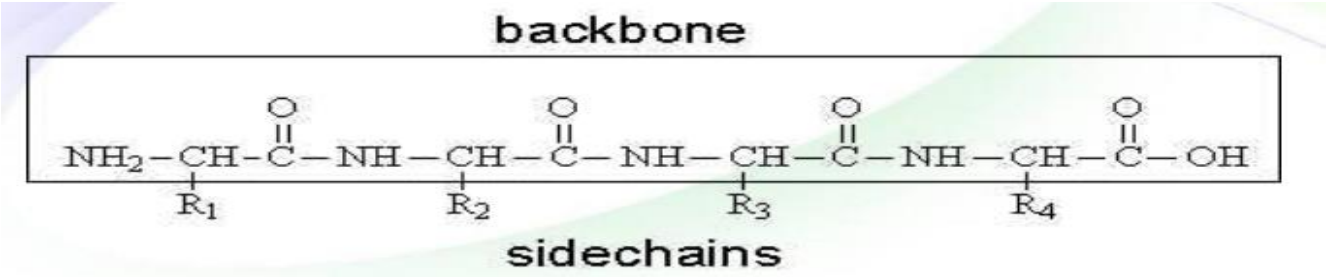


- **Hydrogen bonding** (**Except proline**) (because of the presence of the carbonyl group, amine group and the negative and positive charges the groups of the peptide bonds can form a hydrogen bonding).

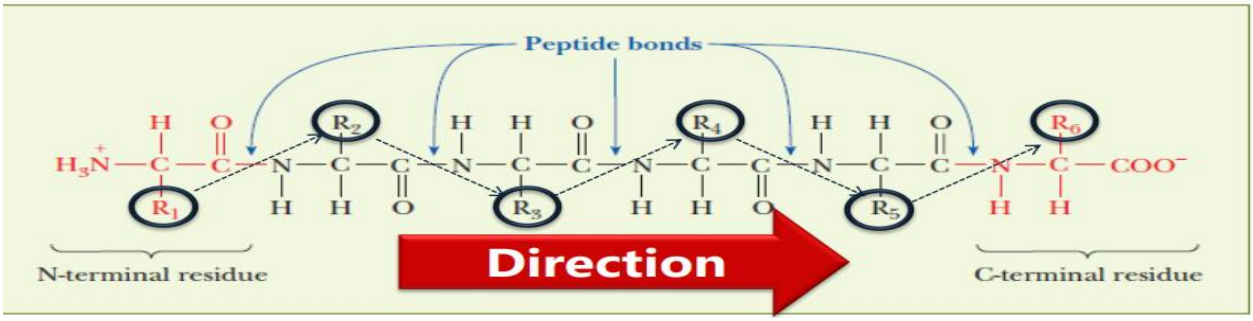
- Remember that certain amino acids like the polar and charged amino acids can form a non-covalent interactions that are important in formation in a 3D structure of the protein
- When the amino acid groups rotate they will form a repulsion and this is very important to the 3D structure.

Backbone, orientation and directionality

- **α-amide N, the α-C, and the α carbonyl C atom**



- This is the peptide backbone its formed by amide bond, central carbon, carbonyl group amide, central carbon, carbonyl and so on. On each center carbon we have side chain (R group) which define the amino acid.



Notice that the **side chains** (R groups) in a **trans** orientation in another words one R up and one Down up, Down and so on. And that is an outcome of the ZIGZAG structure.

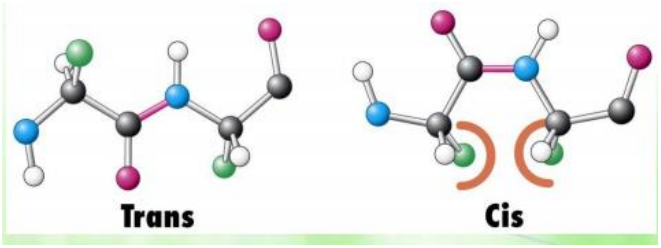
The peptide has a **polarity** (two different ends) the first end is known as a **N terminus** and the last end **C terminus** so we have two opposite ends because the **N** end is **positively** charged and the **C** end is **negatively** charged.

The **N terminus** that has the amine group it's the **first** amino acid and the **C terminus** that has the carboxyl group is the **last** amino acid so whenever we want to add an amino acid we **add** it to the **carboxy terminus** so polypeptides or proteins goes from N terminus to C terminus.

Except for Proline: -

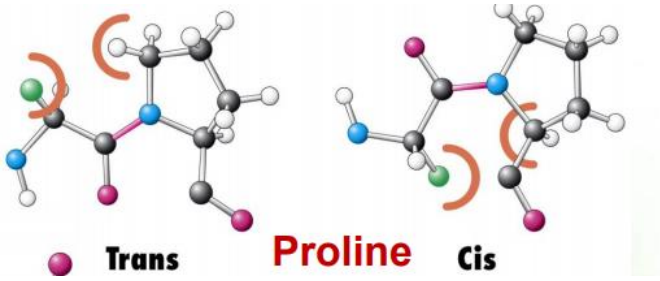
As we said R groups are oriented in trans form to avoid the repulsion between R groups so all amino groups –except proline - prefer trans form because in cis form they have repulsion.

ALL AMINO GROUPS



- Steric hindrance between the functional groups attached to the Cα atoms will be greater in the cis configuration.

- In Proline, both cis and trans conformations have about equivalent energies.
  - So proline doesn't have any preference for cis or trans orientation because in both ways there is repulsion.



- **Proline is thus found in the cis configuration more frequently than other amino acid residues.**

✓ Another specialty about **Proline that it can't form hydrogen bonding** because its doesn't have an amide group because the nitrogen of Proline is occupied by three covalent bond so it doesn't have hydrogen that can donate into hydrogen bonding.

✓ **Note: The only amino acid that doesn't have H-bond donor is Proline.**

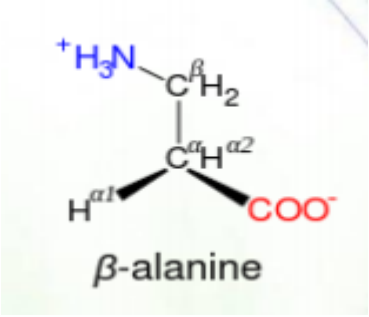
Examples of functional and exceptional peptides: -

We will discuss six examples: - 1- Carnosine 2-Glutathione 3- Enkephalins 4- Oxytocin and vasopressin 5- Gramicidin S and tyrocidine A 6- Aspartame

1-Carnosine (β-alanyl-L-histidine)

- A **di**peptide of **β-alanine and histidine**
- **The amino group is bonded to the β -carbon of alanine**

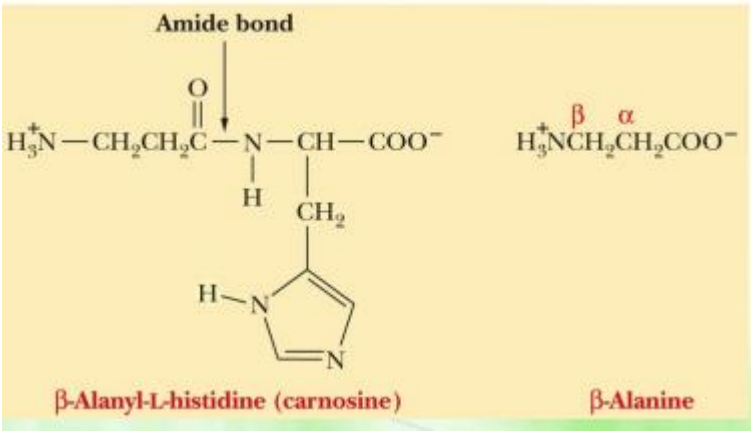
*This is an alpha Alanine
Alanine has atoms or groups attached to it: amine group, carboxyl group, hydrogen atom, and side chain (R group) which is methyl in Alanine.



*This is Beta Alanine notice that the amine group is attached to the beta carbon (carbon no.2 or carbon of the methyl)

*alpha carbon is central carbon or carbon no.1
*beta carbon is methyl carbon or carbon no.2
Again Carnosine is made of Beta alanine and histidine.

- It is highly concentrated in muscles and brain tissues.
  - Protection of cells from ROS (radical oxygen species) and peroxides
  - Contraction of muscle



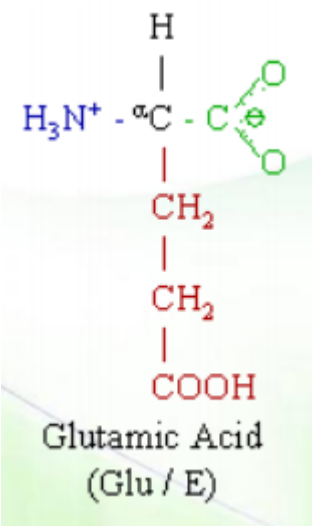
2-Glutathione (γ-glutamyl-L-cysteinylglycine)

It's a **tripeptide** made of three amino acids: -

1-Glutamate 2- Cysteine 3- Glycine

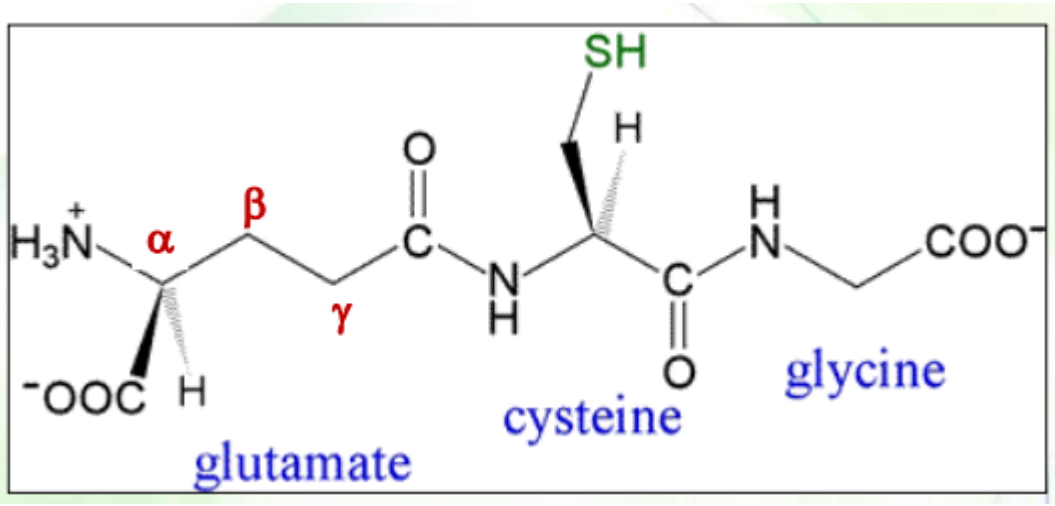
Notice that Glutamate in the Glutathione is GAMA Glutamate.

Side note: gluta means five.



This is a normal glutamate.

*Again central carbon alpha, the second is beta, the third is Gama and on Gama carbon there is a carboxyl group and this carboxyl group that form an amide bond with the amino group from Cysteine because of that it's called Gama Glutamate.



Function of glutathione: -

- **The main function of glutathione is to protect our cells from oxidizing agents that is reactive oxygen species and free radicals.**
- Remember free radical are molecules that are missing an electron and they are very reactive they **want an electron from ANY GROUP so they attack other groups** and extract this electron from them so they get reduced and the other molecules get oxidized that's why they are known as oxidizing agents, now when they oxidize other molecules these molecules are damaged like DNA, lipids in plasma membrane, sugars, proteins and so on.
- Damaging DNA will cause mutations, while damaging the plasma membrane will destroy the cells.

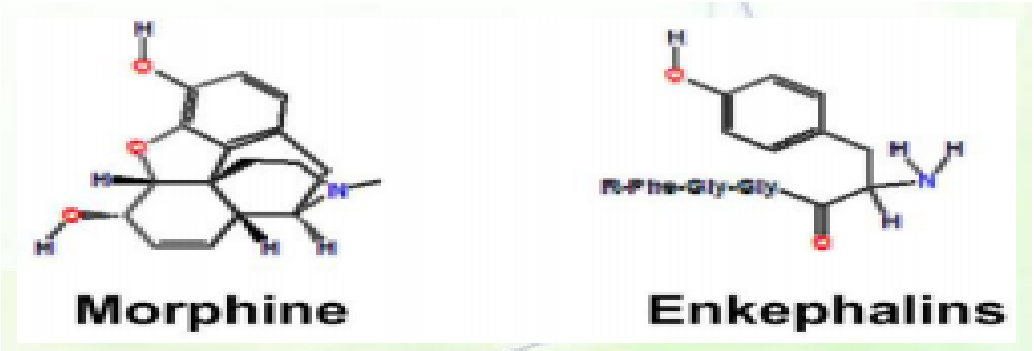
To protect these molecules Glutathione, get oxidized rather than them (commit suicide).

What happens that the (sulfhydryl group SH) of Cysteine is reduced originally and it gets oxidized so we have a formation of two molecules of glutathione which are connected to each other **via a disulfide bond** so the molecule gets oxidized and the active molecule gets reduced.

- **The oxidized form of the glutathione can revert to the reduced form enzymatically.**
- **It scavenges oxidizing agents by reacting with them**.
- **Two molecules of the reduced glutathione molecules form the oxidized form of glutathione by forming a disulfide bond between the —SH groups of the two cysteine residues.**

3-Enkephalins: -

- Two **penta**peptides found in the **brain** known as enkephalins, and function as **analgesics** (**pain relievers). (penta= five)**
- There are two forms of Enkephalins and they **differ only in their C terminal** amino acids: -
  - **Met-enkephalin: Tyr**-Gly-Gly-**Phe-Met**
  - **Leu-enkephalin: Tyr-**Gly-Gly-**Phe-Leu**
- The aromatic side chains of **tyrosine** and **phenylalanine** play a role in their activities
- **Tyrosine and phenylalanine act similar to morphine (addictive substance)**
- **There are similarities between the three-dimensional structures of opiates, such as morphine, and enkephalins.**

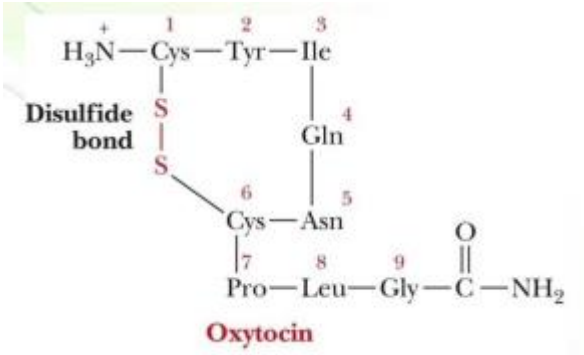


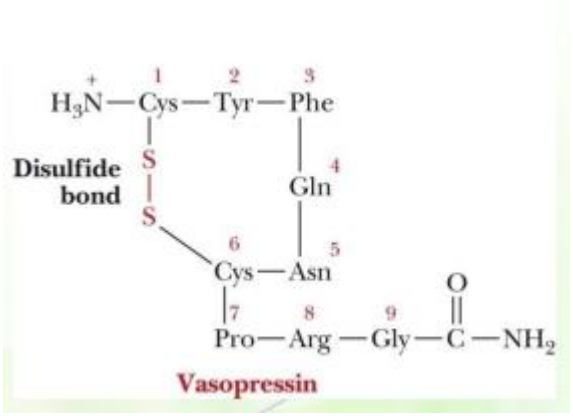
4-Oxytocin and Vasopressin: -

- **Hormones with cyclic structures due to S-S link between Cysteine(Cys).**
- **Both have amide group at the C-terminus.**
- **Both contain nine residues, but:**
  - **Oxytocin has isoleucine and leucine.**
  - **Vasopressin has phenylalanine and arginine.**

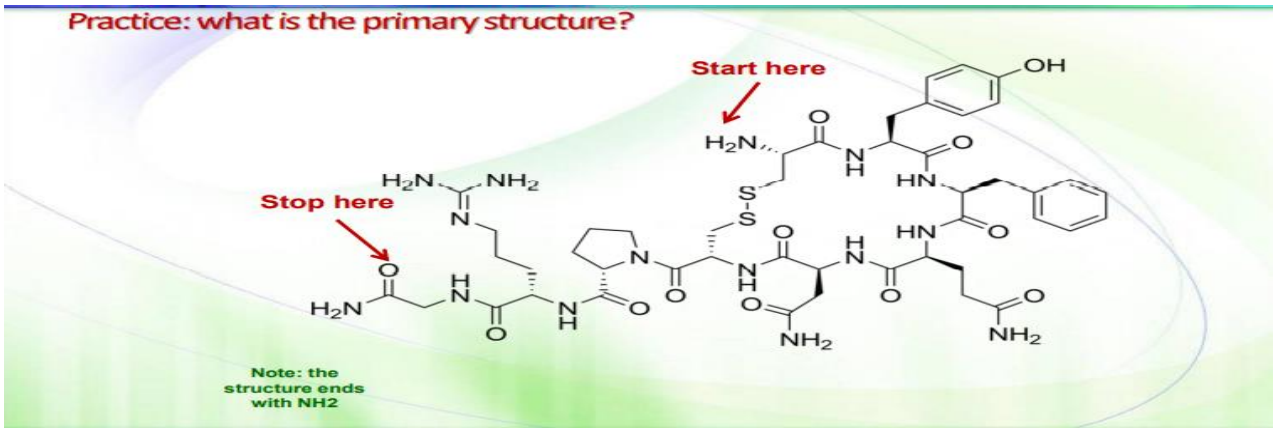
Functions of Oxytocin and Vasopressin: -

- **Oxytocin regulates contraction of uterine muscle (labor contraction)**. (It's the hormone that induce the contractions in the uterus of the pregnant female)
- **Vasopressin regulates contraction of smooth muscle, increases water retention, and increases blood pressure.**





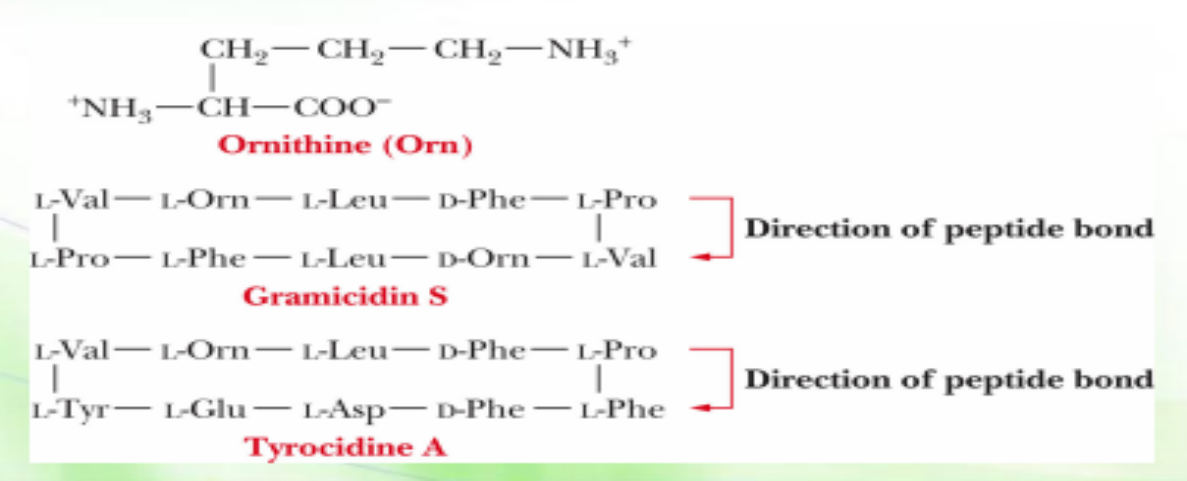
Vasopressin: -



- ✓ In this figure you should know the beginning of the peptide and the end. And the sequence of amino acids with their names. So you should memorize the amino acids with their structure (الصورة طبعا مش حفظ لكن ممكن يجي سؤال تكون الصورة موجودة بس لازم تعرف البداية و النهاية و ايش اسماء الحموض الأمينية :)

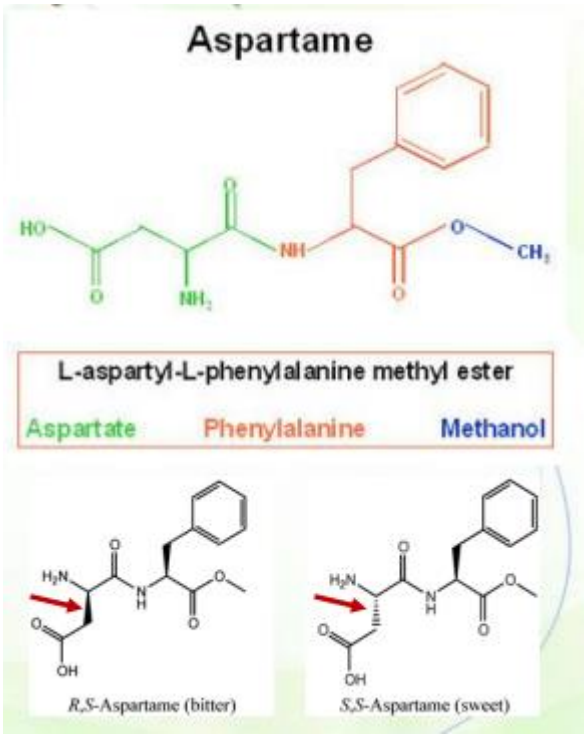
5-Gramicidin S and tyrocidine A:-

- **They are cyclic decapeptides formed by peptide bonds. (deca=10)**
- They are produced by the bacterium Bacillus brevis and act as antibiotics.
- Both contain D- and L-amino acids.
- Normally in our bodies we have amino acids in L form but in bacteria there are exceptions
- Both contain the amino acid **ornithine (Orn**), **which is not found in our proteins.**
- Ornithine is a derivative of arginine and it doesn't naturally exist in peptides but in these two peptides it exists because they are produced by bacterial cells.
- (Orn) is similar to (lys) except of that (lys) has additional (CH2) group.



6-Aspartame

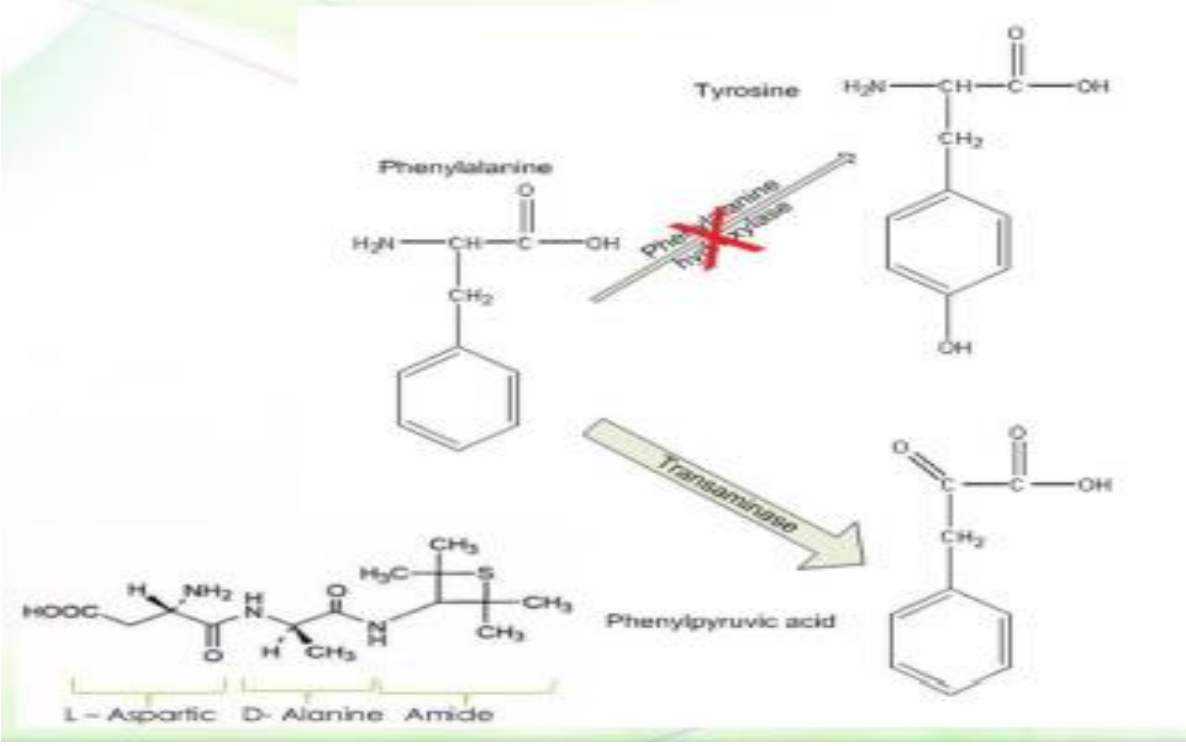
- A **di**peptide that is 200 times sweeter than sugar.
- Made of: **L-Aspartyl-L-phenylalanine (methyl ester)**
- It's an **artificial sweetener** and its used as a substitute for sugar.
- It has a **methanol group** on the **C terminus** of the dipeptide.
- If a D-amino acid is substituted for either amino acid or for both of them, the resulting derivative is bitter rather than sweet.



Aspartame should not be given to individuals with a condition known as Phenylketonuria (PKU).

Phenylketonuria (PKU): -

- **PKU is a hereditary "inborn error of metabolism" caused by defective enzyme, phenylalanine hydroxylase.**
  - **Phenylalanine hydroxylase convert phenylalanine to tyrosine.**
- So people which have a problem in Phenylalanine hydroxylase cannot do this reaction so phenylalanine accumulates and it gets converted to phenylpyruvic acid and this acid accumulate in CNS and cause mental retardation and that why people with PKU shouldn't take Aspartame.
- **It causes accumulation of phenylpruvate, which causes mental retardation.**
- Sources of phenylalanine such as aspartame must be limited.
- A substitute for aspartame, known as alitame, contains alanine rather than phenylalanine.



THE END

TEST YOUR KNOWLEDGE

1- Aspartame is a sugar substitute used to reduce weight but it's not recommended

For people with ..... due to .....?

A) diabetes. / being 200 times sweeter than sugar

B) phenylketonuria / containing phenyl alanine

C) phenylketonuria (PKU) / containing aspartate

D) none of the above is correct

Ans:B

2- What are the structural differences between the peptide hormones oxytocin and vasopressin?

a)Oxytocin has disulfide bonds but vasopressin doesn’t.

b)Vasopressin has disulfide bonds but oxytocin doesn’t

c)Oxytocin has phenylalanine and arginine

d)Vasopressin has leucine and isoleucine

e)All of the above are incorrect

Ans:E

3- What's the function of enkiphalins / oxytocin / vasopressin respectively ?

A) anti oxidant / ADH / muscle contraction

B) analgesics / labor hormone / anti oxidant

C) anti oxidant / Muscle contraction/ labor hormone

D) analgesics / Labor hormone / ADH

Ans:D

4- What do carnosins and glutathions have in common:-

A) they both contain histidine

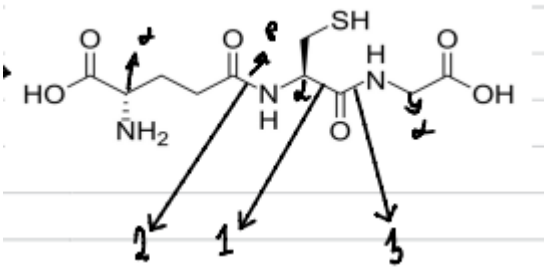
B) they both contribute to muscle contraction

C) they have a similar function of being anti oxidants

D) none of the above is correct

Ans:C

5-regadrind to this molecue :



1- what's the function of this molecule?

A) anit oxidant

B) structural poly peptide

C) analgesic

D) antidiuretic

Ans:A

2- what's the functional amino acid in this peptide?

A) glutamate

B) cysteine

C) glycine

D) serine

Ans:B

3- which of the following is correct regarding its bonds (labeled 1 , 2 , 3)

A) its unrotatable around all 3 bonds

B) its rotatable around only bond number 1

C) its rotatable around bonds 2 and 3

D) its unrotatable around all bonds

Ans:B

Good luck

THE REAL END