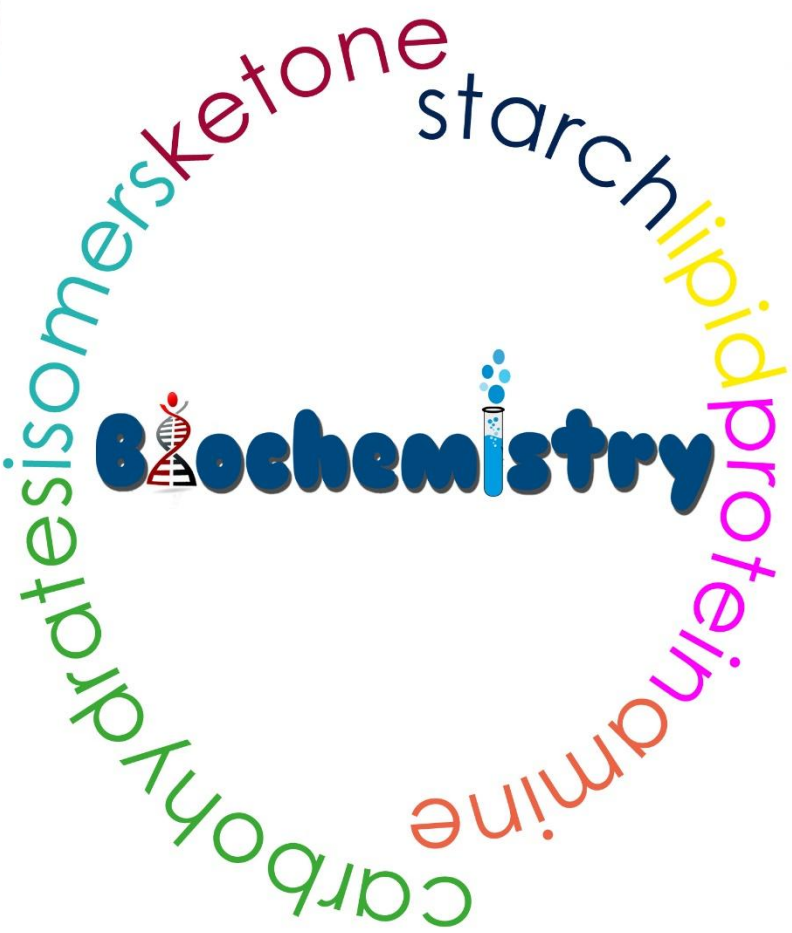


◉Sheet ○Slides

Subject:	**Biochemistry**
Done by:	**Abdullah Nimer**
Corrected by:	**Abdullah Tuffaha**
Number:	**1**

Dr Mamoun Lecture 15

Minutes: 30-52

Peptide bond

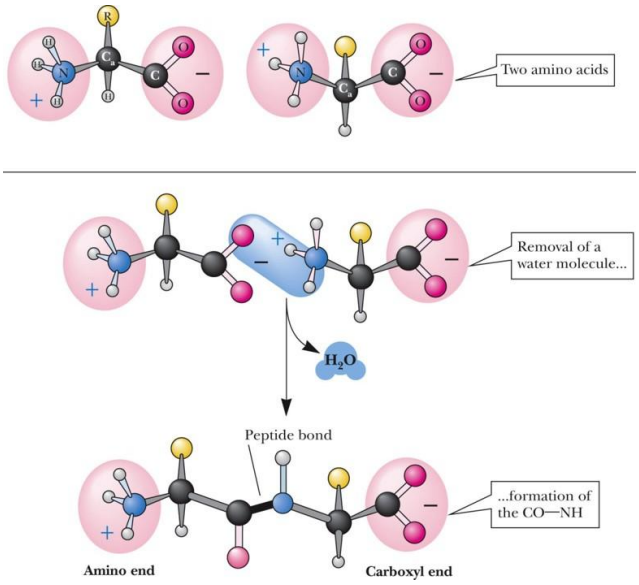
- Amino acid residue → part of a larger structure

- Amino acid (without residue) → means one single amino acid
    - 2 amino acids dipeptide
    - 3 amino acids tripeptide
    - 4 amino acids tetrapeptide
    - Oligopeptide 3 to 10(same as saying peptide)
    - Polypeptide more than 10(long sequence of amino acids)

- **Protein**: polypeptide (or more than one polypeptide) folded into specific 3D structure
    - If we denatured the protein (changed it from the normal structure to the long sequence of amino acids) it will fold back into its original shape.
    - Protein's structure determines <u>its **function**.</u>

- Average molecular weight for an amino acid is 110 Daltons while proteins molecular weight can be 20000 Daltons
    - how many amino acids in that? 20000 = about 182 amino acids
      * 1 Dalton = atomic weight of hydrogen H *

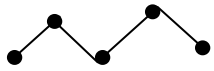
- Two amino acids can link to each other via what we call (**peptide bound**) or chemically (**amide bond**) because it looks like an **amide**
    - We call the reaction (**condensation** reaction)
      Why? Because it involves the **release** of a water molecule (H_2O)

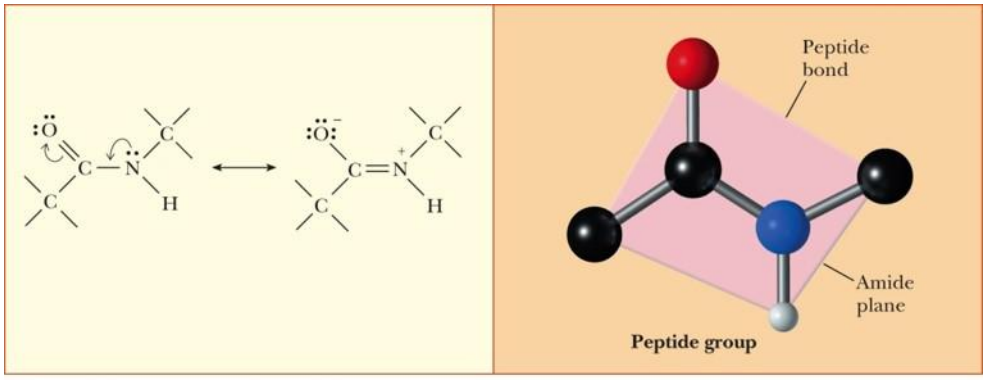


- If we have a dipeptide and we want to make a tripeptide, where do we add the Amino Acid? to the Amino end the carboxyl end?
  Answer: (**carboxyl end**)

Student's Question: Why? Because it is driven **enzymatically** and there are no enzymes that can add Amino Acids to amino end.

Peptide bone features:

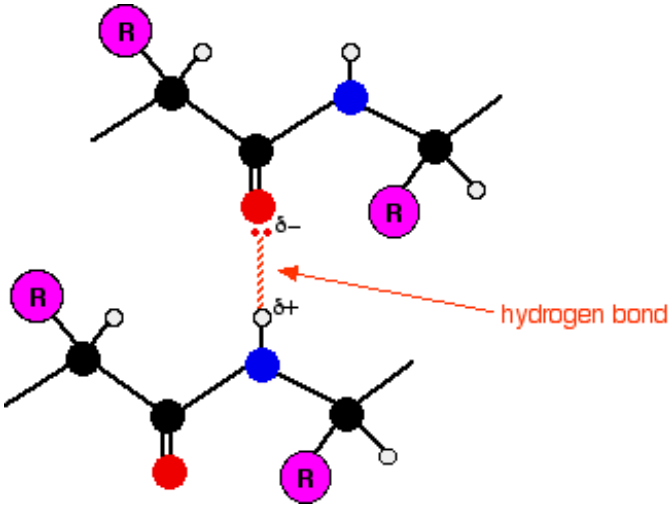
1- **Zigzag structure**: 
2- Peptide bond is **planner** (flat)
   Why is it planner? Because it can form **a double bond**.
   How: by **resonance structure**.

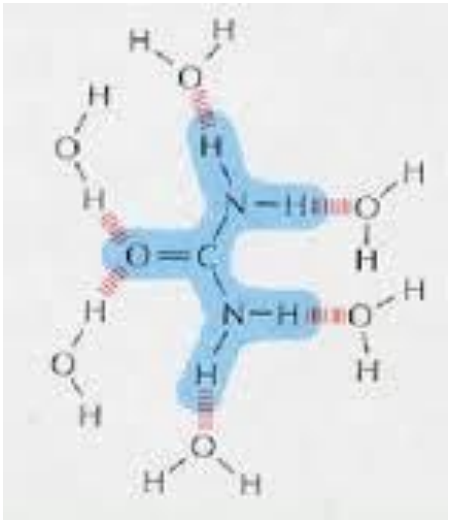


A Resonance structures of the peptide group.

B The planar peptide group.

3- **Rigid**: because of the double bond, it is not flexible.
4- **Non-rotatable**: cannot rotate, because of the double bond
5- **(Un)charged**: but in the cause of resonance (O) becomes Negative, (N) becomes positive
6- Can form **hydrogen bonds** (except for **proline**) how?
Nitrogen has higher electronegativity than hydrogen **($N^{\delta-}$ – $H^{\delta+}$)** hydrogen bond donor.
And (O) has higher electronegativity than (C). **($O^{\delta-}$=$C^{\delta+}$)** hydrogen bond acceptor.





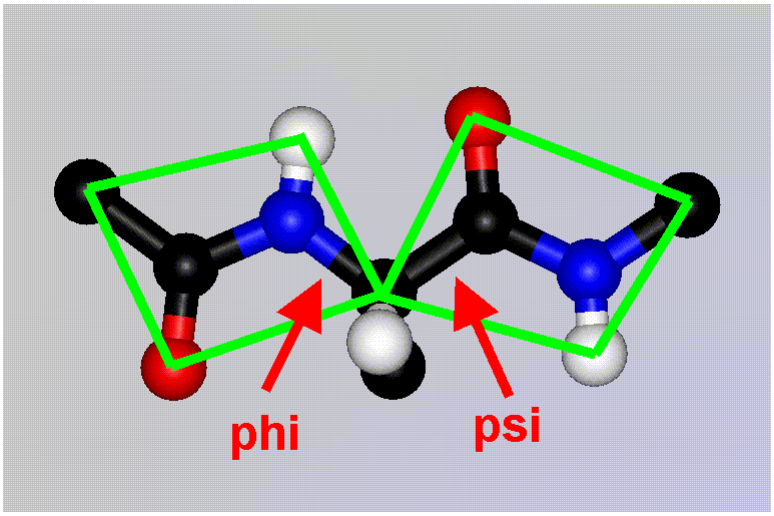
Why proline can't form H-bond?
The amino group in proline is **secondary** and it is called **Imino** group and is missing the hydrogen Atom so there **is no hydrogen bond donor.**

Is proline a hydrogen acceptor? Yes, it is **($O^{\delta-}$=$C^{\delta+}$)**

*The peptide bond is rigid, but the protein's structure contains many rotations, loops, turns, etc. How is that possible?
Because the bond between the (Alpha-C) and the (carboxyl carbon), and the bond between the (Alpha-C) and the (N) are flexible. *

(**Phi** bond ϕ) → the bond between (Alpha-C) and the amino nitrogen of the same reside

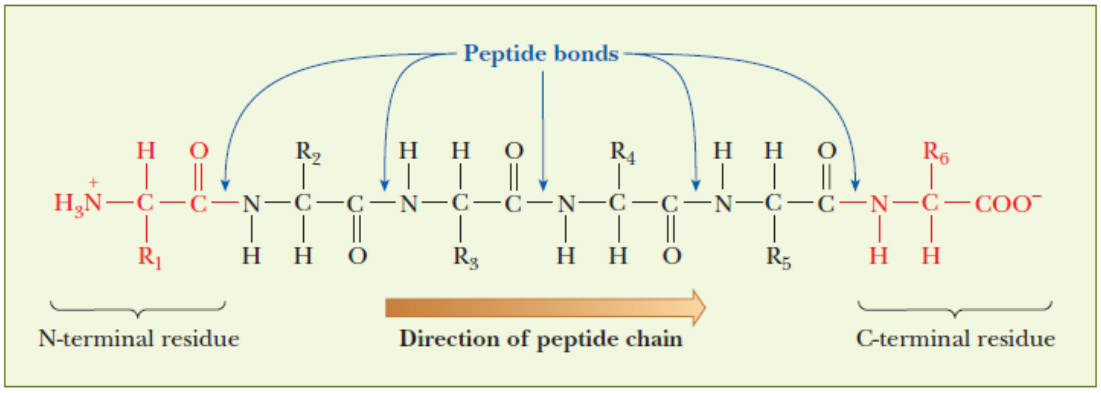
(**Psi** bond ψ) → the bond between (Alpha-C) and the carboxyl carbon of the same reside



(phi and psi bonds can rotate) giving more flexibility to structure

BUT this rotation is not free, why? Because of the **steric hindrance** which is a repulsion force.

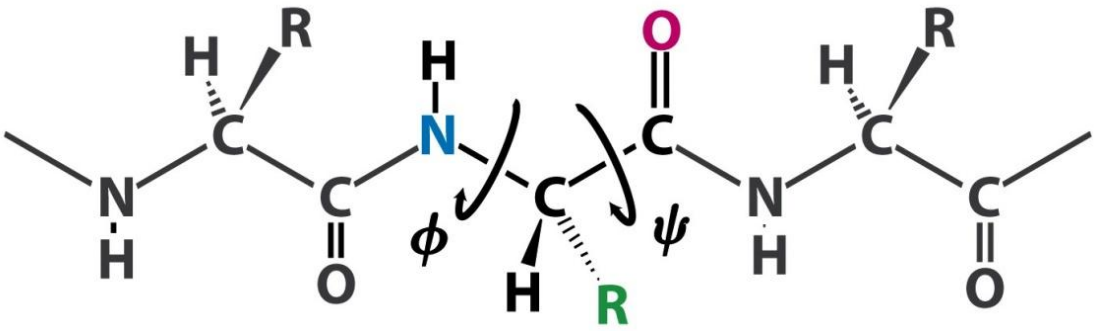
- When groups are close to each other it will cause more repulsion force.
- But if they are at a certain distance there will be an attraction force known as (Van der Waals interaction)



When we want to extend polypeptide we add to the (carboxyl end).

Remember that: carboxyl end →C-terminus, Amino end → N-terminus.

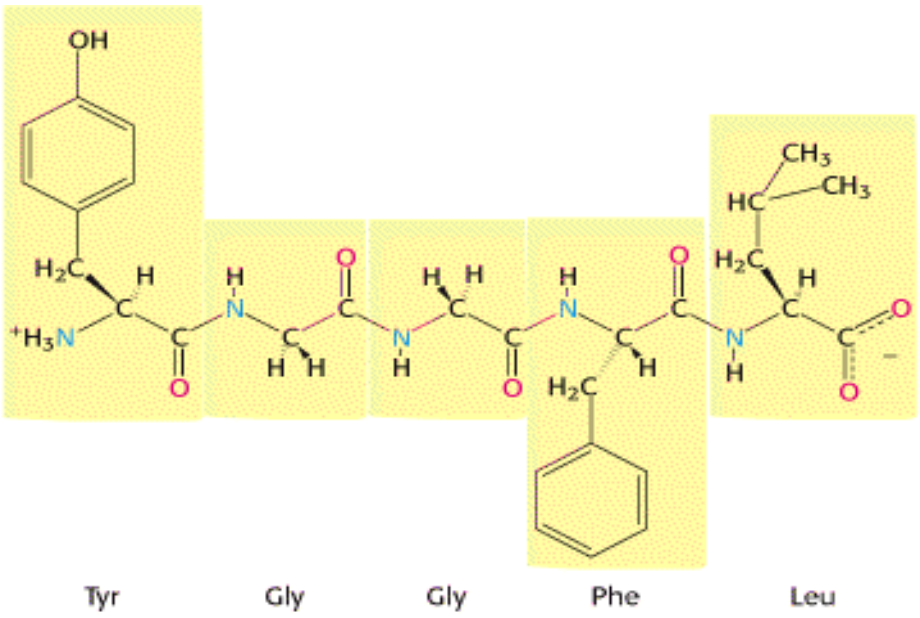
The back bone is the common atoms in all Amino Acid residues (**N, Alpha-**



C, carboxyl C).

The backbone forms a zig-zag structure while the (R) groups extends outside in **(Trans)** orientation. Why? Because of the steric hindrance (repulsion).

Except for proline, whether it is in (**cis or Trans)** orientation there will



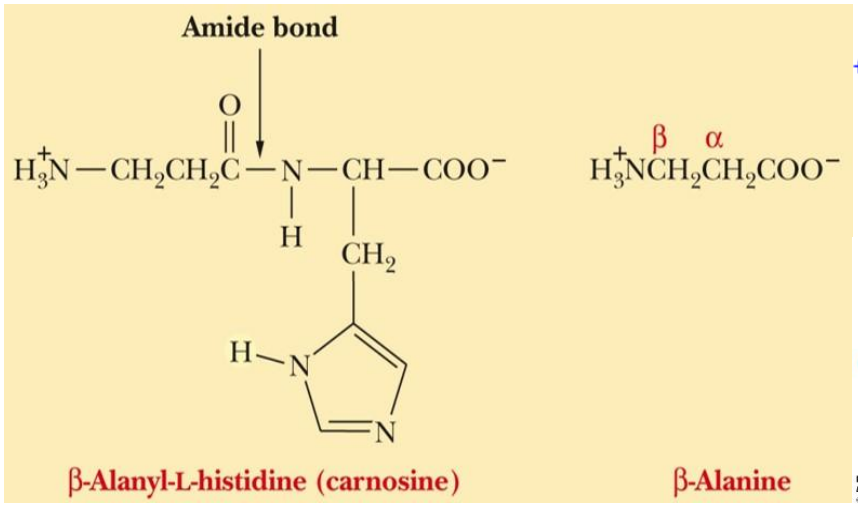
be repulsion so it doesn't matter if it was **(cis or Trans)**.

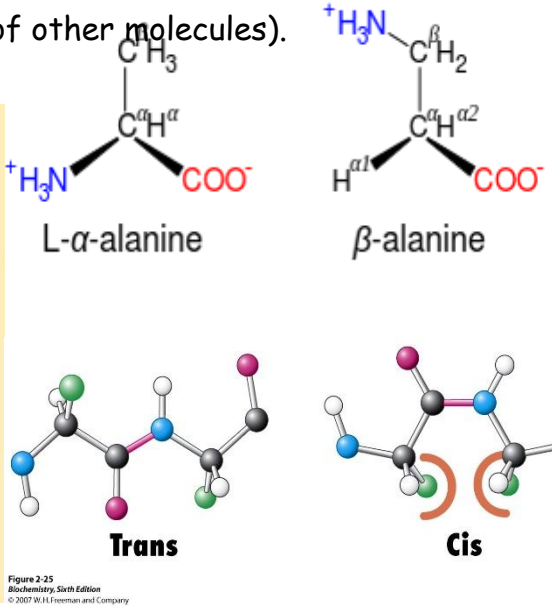
Some important peptides:

- **Carnosine** (beta-alanyl-L-histidine):
  - A di-peptide made of B-alanine and a histidine.
  - Highly concentrated in muscle and brain tissue

- It functions as **anti-oxidant**; which means that it gets oxidized in order to reduce another molecule
- Protects our cells from oxidation from:
  - Oxidizing molecules
  - Peroxides
  - Radical oxygen species

  Those three want electrons so they take electrons from any other molecule around them (they may attack [DNA, lipids of membrane, Protein] for example and damage them).
  So cells have these three anti-oxidants as a protection mechanism (they lose their own electrons to protect the electrons of other molecules).



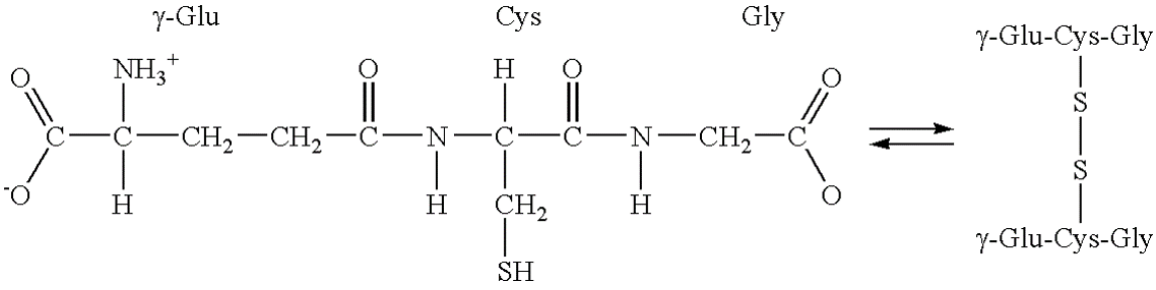


- Carnosine also functions in muscles construction.
  - What is special about carnosine? The alanine amino acid is not alpha, but its **beta**.
    What does that mean? The amino group is located on Beta-carbon not Alpha-carbon
    see the figure

- **Glutathione** (gamma-glutamyl-L-cysteinylglycine):
  - Tripeptide (gamma-glutamate, cysteine, glycine)
  - It is also an anti-oxidant
  - Glutamic acid is not normal; it is Gama-glutamic acid.
    Why is it Gamma? We expect the peptide bond to form with the carboxyl group that is attacked to the carboxyl group that is attached to the alpha carbon, but that does not happen, the peptide bond forms with the **carboxyl group linked to Gamma-carbon.**

    How does glutathione functions as anti-oxidant?
    Answer : It uses the cysteine as a Reducing group.

    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.



    When the two molecule link with each other via the (-SH) groups of Cysteine in order to form a disulfide bond. We get oxidized glutathione and other reduced molecule.

- **Eukephalines:**
  - Produced by the brain
  - Analgesics (pain relievers)
  - The two Eukephalines found in the brain are Penta peptides (5 amino acids),
    And they only differ in C-terminal amino acid:
    Methionine Eukephalines: Tyr-Gly-Gly-Phe-**Met**

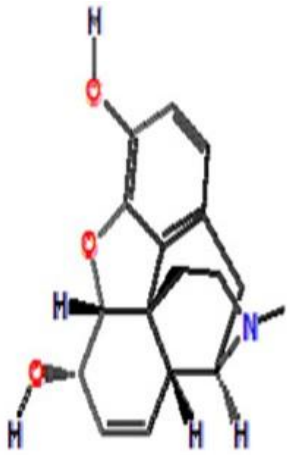
Leucine Eukephalines : Tyr-Gly-Gly-Phe-**leu**

The aromatic R-groups of [**tyrosine**] and [**phenylalanine**] play a role in their activities.

Question: What are the functional groups in Eukephalines?

Answer: "Tyrosine and Phenylalanine "

There are similarities between the three-dimensional structures of opiates, such as morphine, and eukephalines.



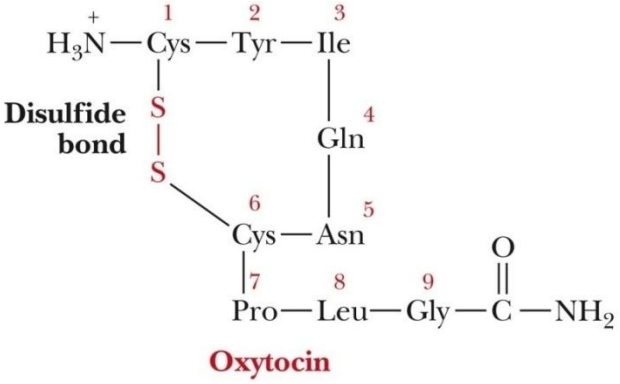
Morphine

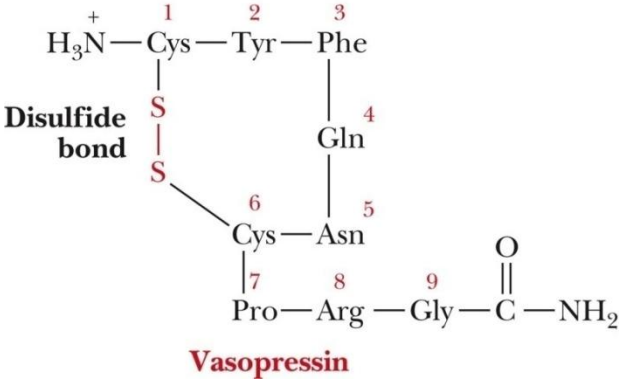
Enkephalins

- **Morphine:**
  - An addictive analgesic that functions like Eukephalines;
    Why?
    Because it has a similar structure.
    (Drugs don't usually have the same structures as a whole, but they have similar **functioning groups**).

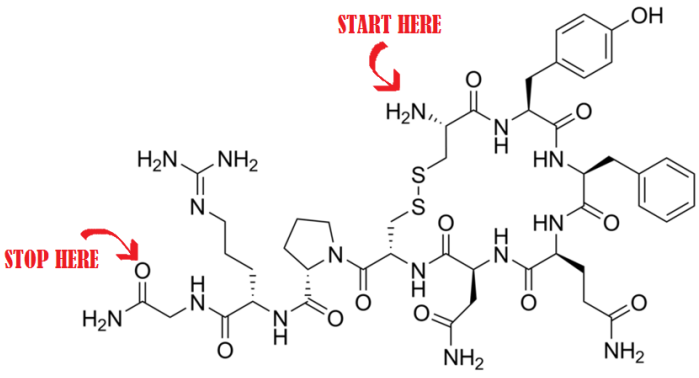
- **Oxytocin and Vasopressin:**
  - Hormones with cyclic structures due to S-S link between Cysteine.
  - Both have amide group at the C-terminus.
  - Both contain nine residues, but:

- The amino acid number 3 in Oxytocin is isoleucine and in Vasopressin is phenylalanine.
- The amino acid number 8 in Oxytocin is leucine and in Vasopressin is arginine.
- Oxytocin regulates contraction of uterine muscle (labor contraction) when delivering a baby.
- Vasopressin regulates contraction of smooth muscle, increases water retention, and increases blood pressure.



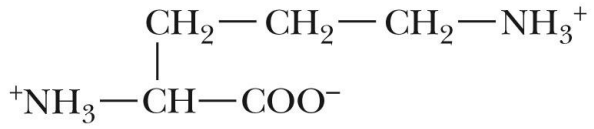


Practice: what is the primary structure (sequence of amino acids) for the following structure?

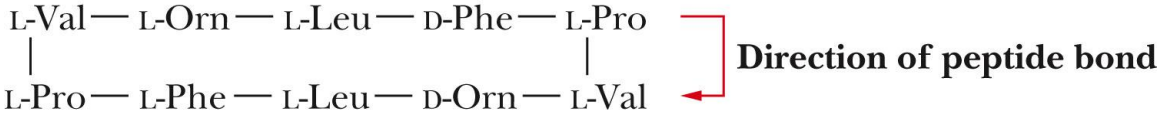


*In this sort of questions, we depend on the R-groups (side chains) in order to find the sequence. *

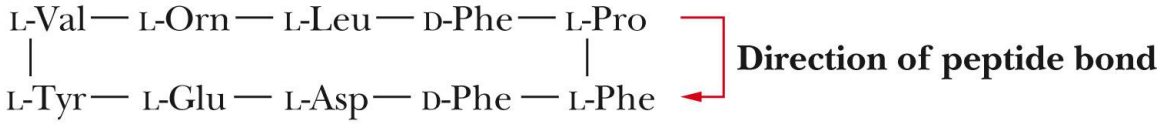
- **Gramicidin S and Tyrocidine A:**
  - Antibodies (produced by bacteria to kill other bacteria)
  - What is special about them?
    - They contain both (L) and (D) amino acids.
      *the amino acid that exist in our bodies is normally (L), but here we can find **(D) amino acids** as well.
    - Both contain the amino acid **ornithine (Orn)**, which does not occur in proteins, but we can find it in these two peptides.
    - They are cyclic Decapeptides (ten amino acids) not because of a disulfite bond but because of a peptide bond
    - They are produced by the bacterium Bacillus brevis and act as antibiotics.



Ornithine (Orn)



Gramicidin S



Tyrocidine A

What is the reason of cycle formation in?

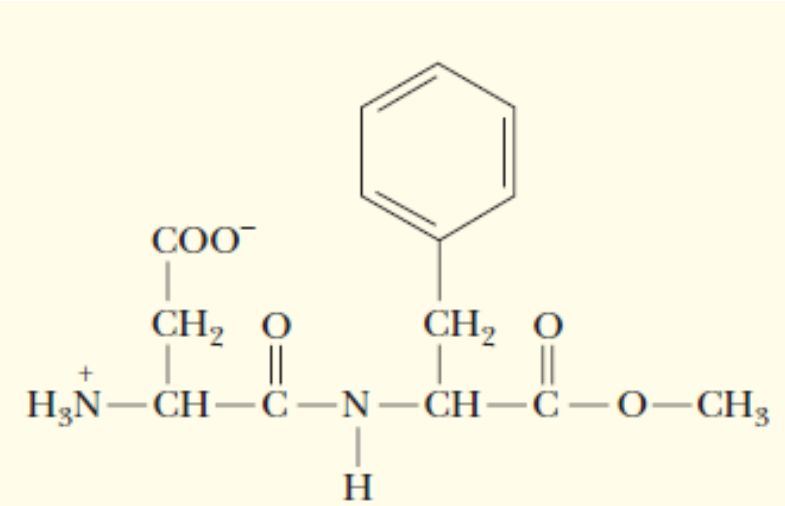
1- Oxytocin 2- vasopressin 3- Gramicidin S 4- Tyrocidine A

Answers: 1 and 2 ---> disulfide bond
3 and 4 ---> peptide bond

Dr Mamoun Lecture 16

Minutes: 6-14

- **Aspartame (L-Aspartyl-L-phenylalanine (methyl ester):**
  - it is a sweetener
  - a dipeptide of (Asp and Phe)
  - we have methyl group at the C-terminus and we call it (methyl ester)
  - This dipeptide is about 200 times sweeter than sugar.
  - If a D-amino acid is substituted for either amino acid or for both of them, the resulting derivative is bitter rather than sweet.



L-Aspartyl-L-phenylalanine (methyl ester)

- **Phenylketonuria (PKU)**
  - PKU is a hereditary "inborn error of metabolism" caused by defective enzyme, phenylalanine hydroxylase.
  - people with this disease shouldn't use aspartame.
  - it is a defect in the metabolism of (phe)
  - (phe) is normally metabolized in our body to produce tyrosine, but because that the enzyme phenylalanine hydroxylase is defected; the (phe) will go in another pathway

where the enzyme (trans-aminase) convert it to phenylpyrovic acid.

- the accumulation of phenylpyrovic acid in the body affects CNS and cause mental retardation.
- newborns are always test in order to detect PKU.
- Sources of phenylalanine such as aspartame must be limited.
- A substitute for aspartame, known as alatame, contains alanine rather than phenylalanine.