Peptides

Summer 2023

Formation of a polypeptide

Definitions and concepts

A small molecule, but part of a larger system
Example: Glycogen consists of glucose residue

- A residue: each amino acid in a (poly)peptide
- Dipeptide, tripeptide, tetrapeptide, etc.
- Oligopeptide (peptide): a short chain of 20-30 amino acids
- Polypeptide: a longer peptide with no particular structure
- Protein: a polypeptide chains with an organized 3D structures

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3D structure

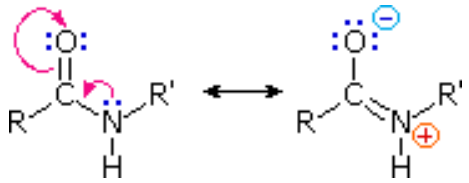
- The average molecular weight of an amino acid residue is about 110
  - The molecular weights of most proteins are between 5500 and 220,000 (calculate how many amino acids)
- We refer to the mass of a polypeptide in units of Daltons
  - A 10,000-MW protein has a mass of 10,000 Daltons (Da) or 10 kilodaltons (kDa)

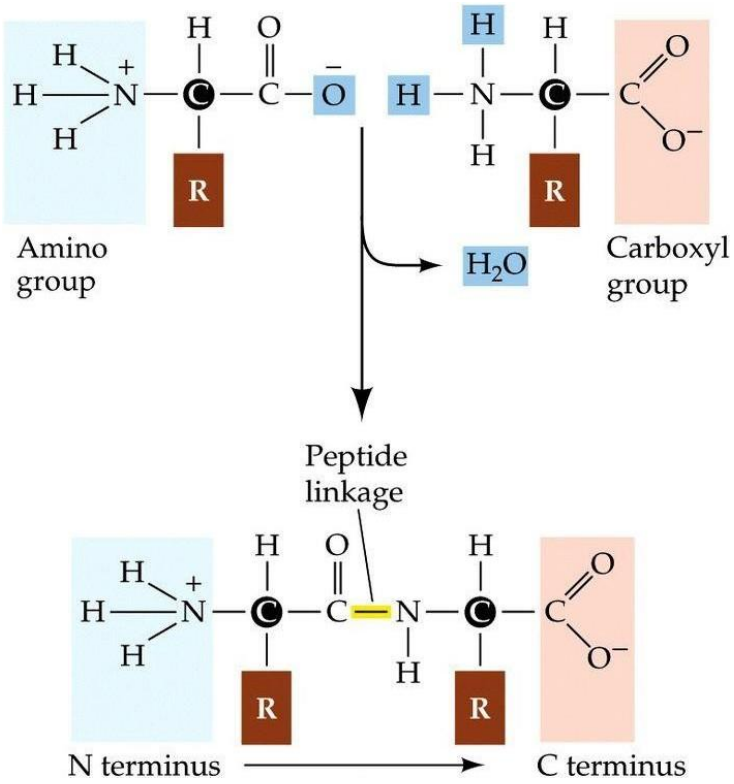
Dipeptide:**2** amino acids
tripeptide:**3** amino acids
Oligopeptide:**20-30** amino acids (short)
Polypeptide:**100-thousands** amino acids (long)

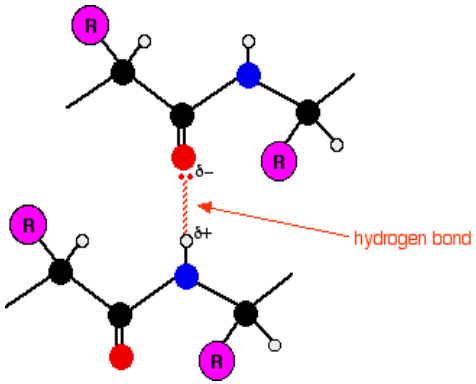
Peptide bond

Amide bond= peptide bond

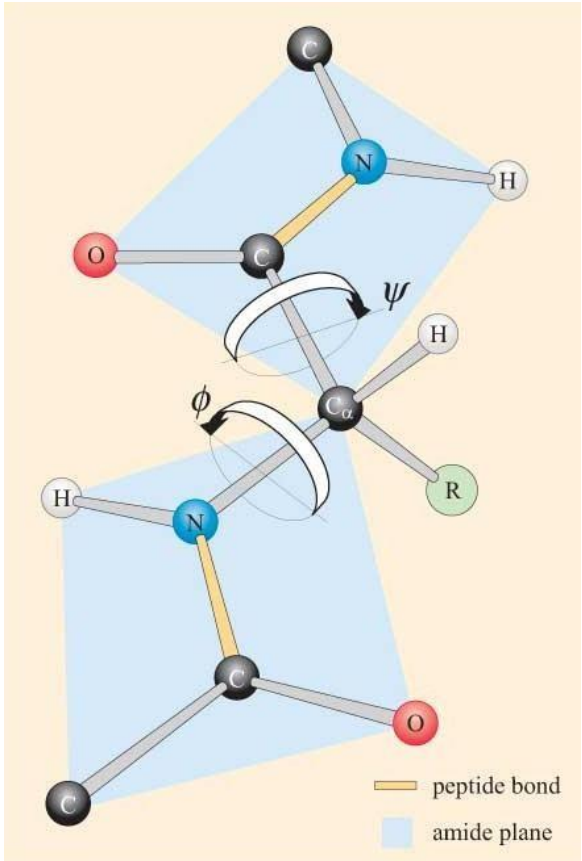
- It is called an amide bond formed via a condensation reaction.
- Features
  - It has a resonance structure
  - Zigzag structure
  - Double bond
    - Planar, charged, Rigid, Un-rotatable
  - Hydrogen bonding
    - Except proline

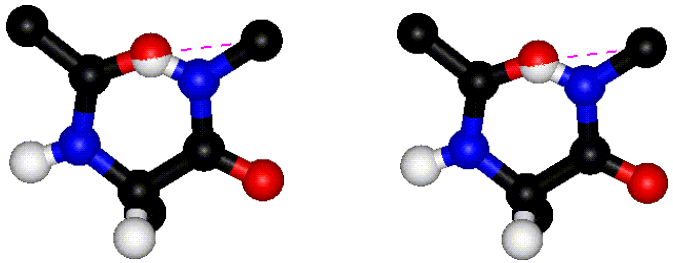






The flexibility of rotation occurs on the bonds within the amino acid itself not the peptide bond.





Further explanation regarding the previous slide:

- we can connect peptides via an **amide bond**
- **amide bond**: interaction between a carboxylic group and an amino group

We call the reaction **condensation** because it turns out a water molecule

In organic chemistry we call it **Amide Bond**, but in Biochemistry we call it **Peptide Bond**.

Features

1- It has a resonance structure(different shape)

2- Zigzag structure

3 Double bond:

Planar, charged, Rigid, Un-rotatable

The peptide bonds don't move, the ones that do move are the bonds around the alpha carbons within the amino acid

4 Hydrogen bonding (on the H atom of amine group)

Except proline

#The component ,the atoms, that make the peptide bond can participate in H bond except proline because it is the only cyclic , and because it is a secondary N, it has three bonds, one with the alpha carbon and the second from the R chain, and the third bond with H but when it forms a double peptide bond (due to the resonance) it loses the H and its ability to form hydrogen bonding.

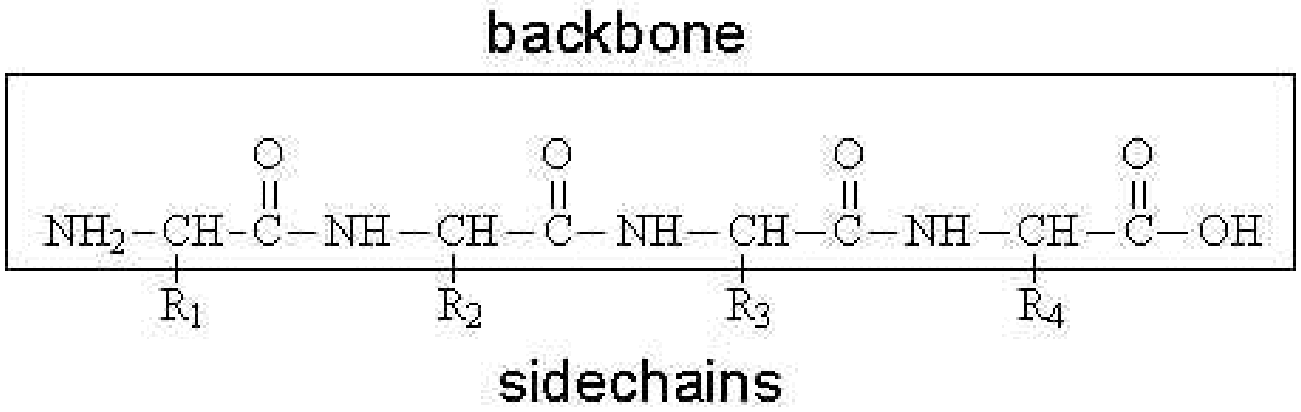
#It doesn't have to be a repulsion because it will destroy the protein and the amino acid needs to roll around

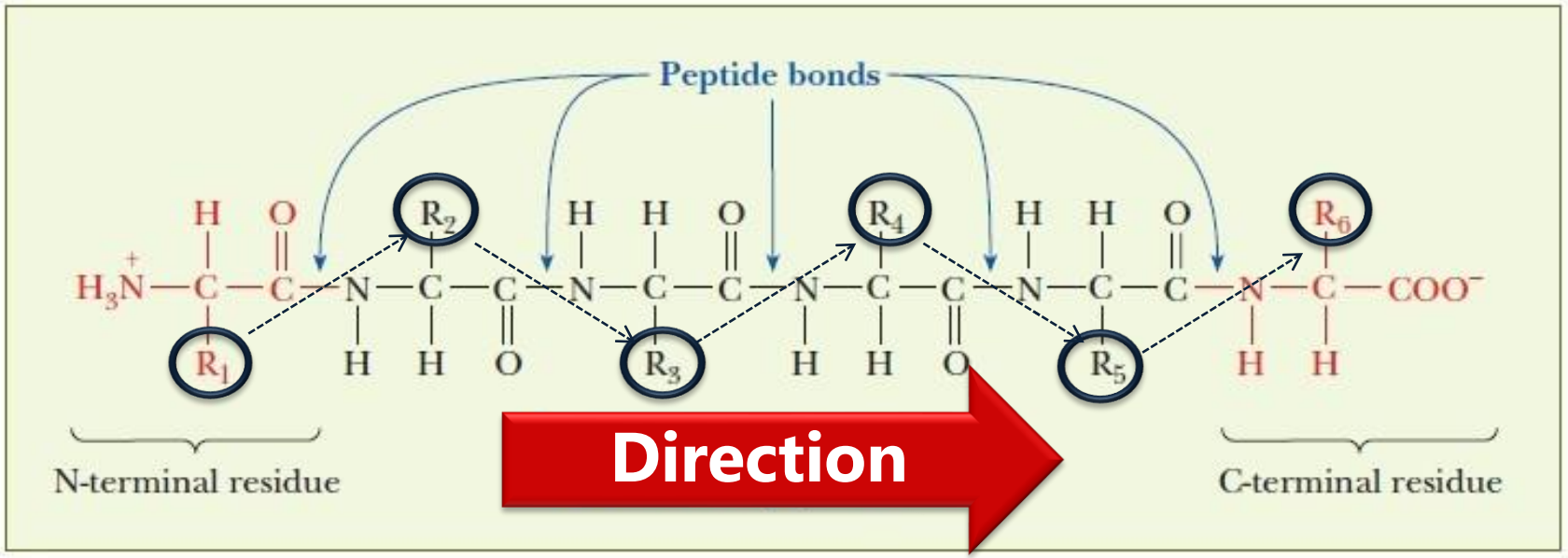
Carbonyl group—> H bond acceptor, NH group—> H bond donor

Adding amino acid to another will be on **C terminus**

Backbone, orientation and directionality

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





Further explanation regarding the previous slide:

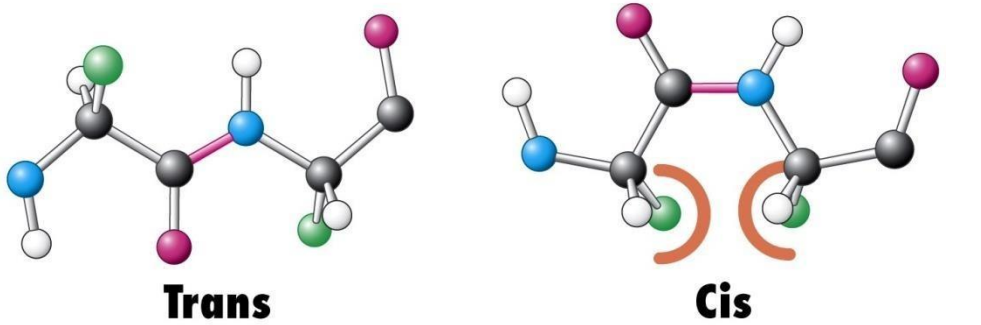
The multiple amino acid forms a peptide bond (the backbone is an amino group, an alpha carbon, a carbonyl group) N,C,C This is the main backbone that will carry the R group The R group is in Trans-Orientation, because if they are next to each other, there will be repulsion so one unit going up and the next one going down, and so on When reading the amino acid, it starts from the amino group (N terminus) and the last amino acid ends with a carboxylic group (C terminus).

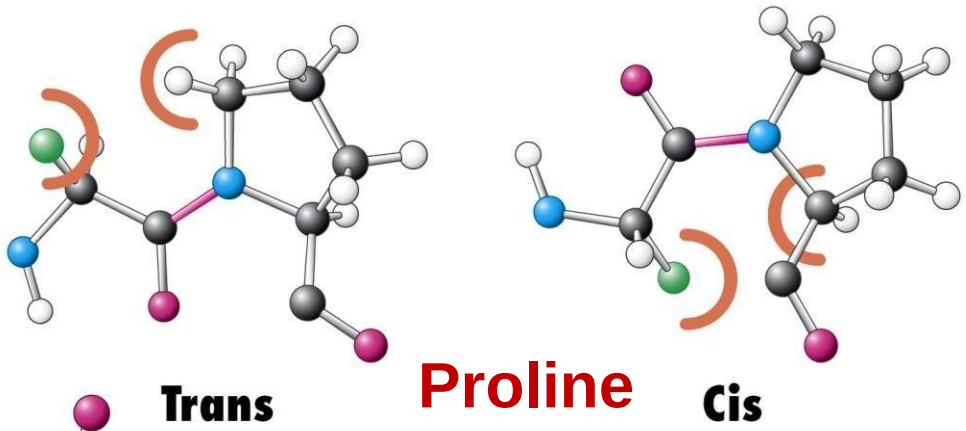
why is that?

Because the free end is the carboxylic group on which the new amino acid will be added. Another point to notice: the polypeptide chain has some source of polarity having the N terminus positively charge and the C terminus negatively charged.

Except for proline

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





The cis and trans configurations are found in equal amounts to one another in proline, but in comparison to other amino acids proline form the cis configuration more frequently.

Further explanation regarding the previous slide:

Every R group in amino acids take a trans orientation to prevent the repulsion except proline amino acid in both orientations (cis and trans) there is repulsion and that happens because the proline is a cyclic compaound.
If we look at any amino acid in any polypeptide we find that the distribution of trans side groups is about 90% and for cis side groups its about 10%, but the proline it's equally distribution (50:50).
All of amino acids is attached to each other by peptide bonds to produce a polypeptide.

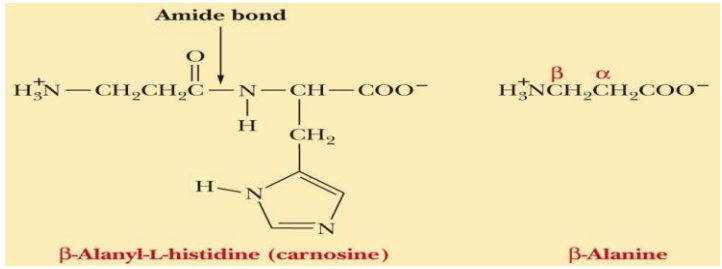
Examples of functional and exceptional peptides

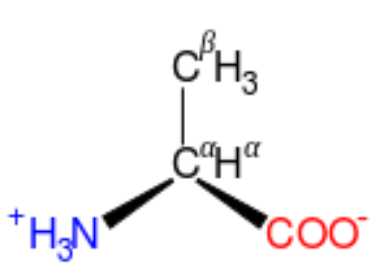
Carnosine (Beta-alanyl-L-histidine)

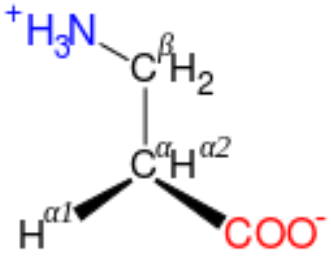
The major amino acid is histidine that's why we write it alanyl not alanine because we consider it as a branch.

- A dipeptide of β-alanine and histidine
- The amino group is bonded to the β -carbon of alanine It is highly
- concentrated in muscle and brain tissues
  - Protection of cells from ROS (radical oxygen species) and peroxides(antioxidant)
  - Contraction of muscle

ROS :can do oxidation-reduction reaction with any molecule to get an electron and they are dangerous when they react with DNA and fatty acids in membrane
and that will destroy the cell (vitamin C help to get the ROS out of the body).







لاكتذ روكا رنه ضيرور هۆ بينهم(الأسلم نحفظ للتركيب)

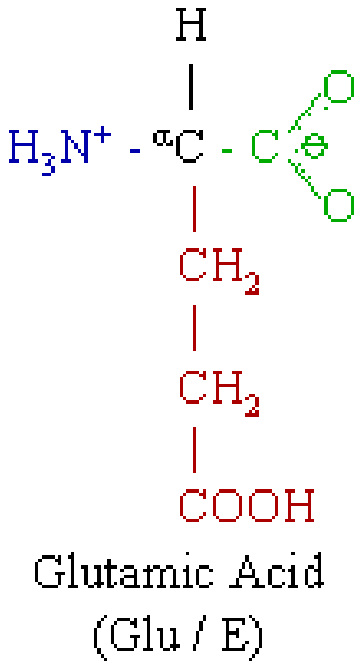
Peptide bond is between the carboxylic group of the first amino acid (alanine) and the amine group of the second amino acid (histidine).

Alpha alanine is the common amino acid in our bodies and beta alanine is exception of alanine.

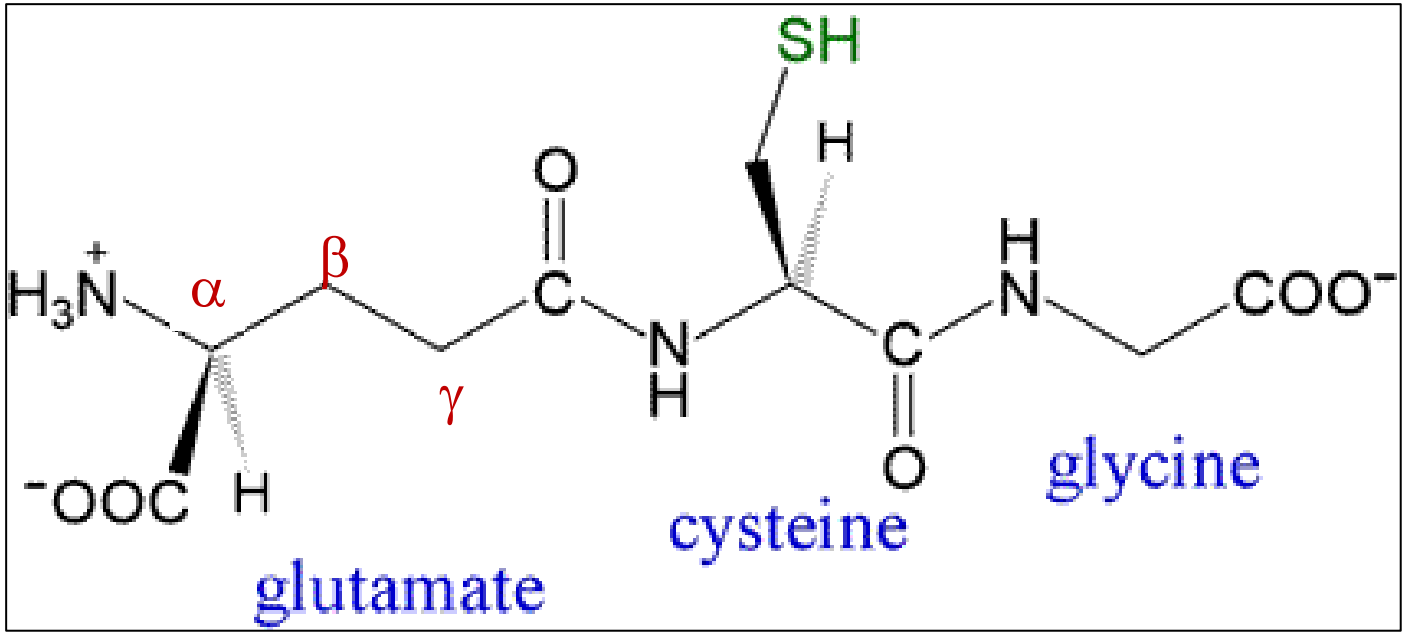
Glutathione (gama-glutamyl-L-cysteinylglycine)

Glycine is the base and it hold cysteine and the cysteine hold glutamate.

مبغى ا هنالغلايسيا و هـ ن لحما ض لأميني ا لأساسي ثم للسيستين ثم للغلوتاميت.



Glutamic Acid
(Glu / E)

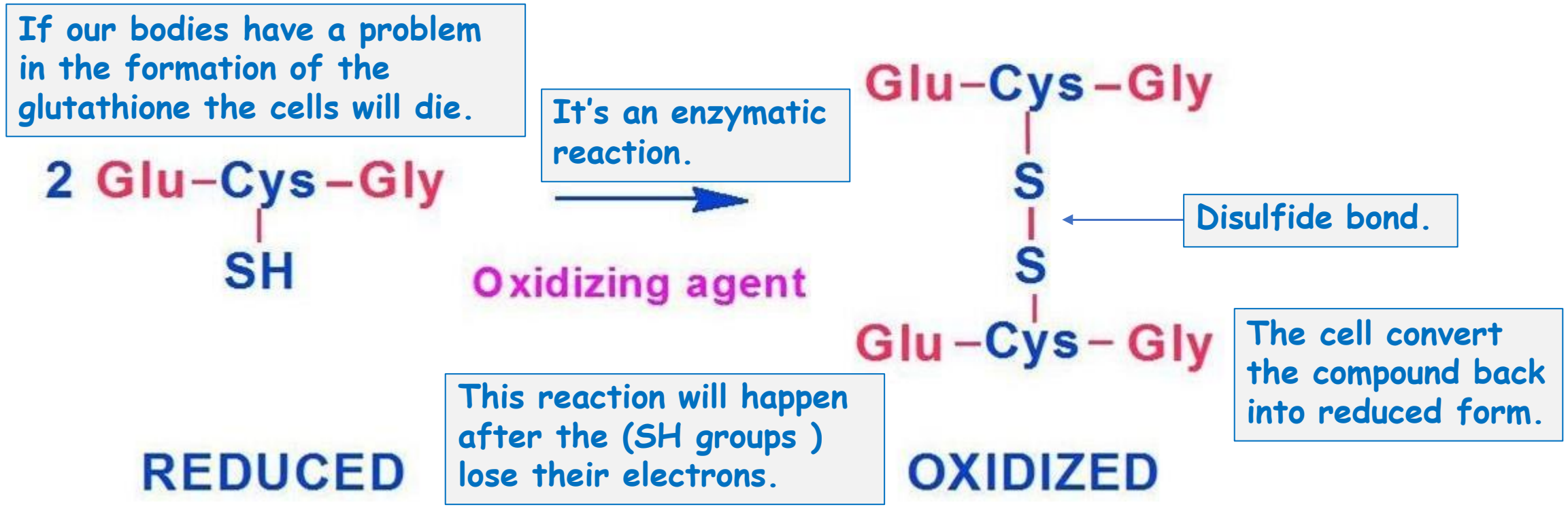


The peptide bond between the R group of glutamate(gama carbon) and the amine group of cystine and that is the reason of put Gama in the compound name.

Note:we have to know the sequence of the glutathione.

Function of glutathione

- 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.



It is a tripeptide that consists of 3 amino acids: Glutamate, Cysteine & Glycine. It functions as an antioxidant. The high functioning of this tripeptide as an antioxidant is mainly due to the presence of cysteine residue; when it performs its antioxidizing function its oxidized form is generated from its reduced form BY forming disulfide bridges with another molecule of Glutathione. It can be recycled by our cells by reducing it back to its original form and then it can be reused.

-Some oxidizing agents are harmful and play a role in the development of cancer
-Oxidized form is generated by the interaction of two reduced molecules by forming a disulfide bond between the —SH groups of the two cysteine residues

Enkephalins

- Two pentapeptides found in the brain known as enkephalins, and function as analgesics(كنات لها) (pain relievers).
  - 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.
- There are similarities between the three-dimensional structures of opiates, such as morphine , and enkephalins.

They have the same sequence of amino acids except the last on ,met-enkephalin because the last amino acid is methionine ,and leu-enkephalin because the last amino acid is leucine.

Morphine

Enkephalins

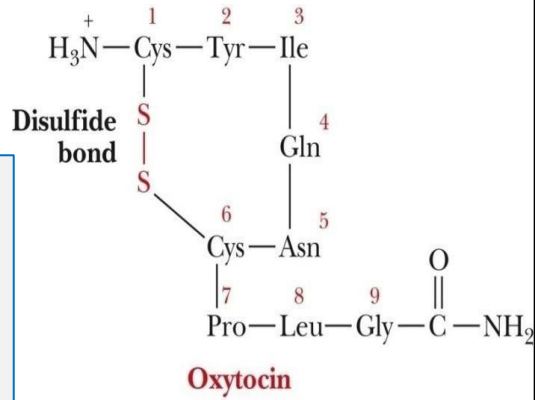
Enkephalins and morphine have the same function as a pain relievers ,the patients get doses of morphine after surgery to decrease the pain feeling,they have similar structures.

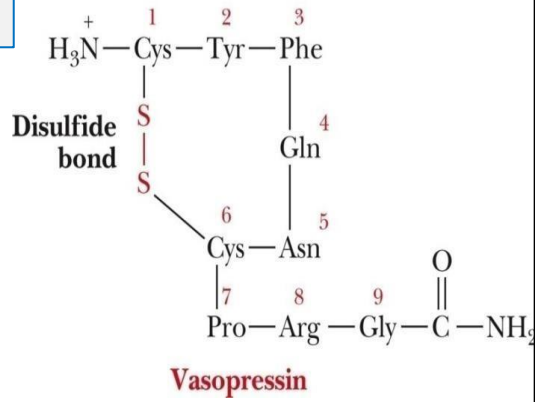
Kepha = related to the brain. Enkephalins are pentapeptides that are produced in the brain and have their own receptors. The binding of an Enkephalin to its receptor causes a "pain killing/relieving" response (they function as internal natural .(يعية كنات لها /analgesics

Oxytocin and vasopressin

- Hormones with cyclic structures due to S-S link between Cys.
- Both have amide group at the C-terminus.
- Both contain nine residues, but:
  - Oxytocin has isoleucine and leucine.
  - Vasopressin has phenylalanine and arginine .
- Oxytocin regulates contraction of uterine muscle (labor contraction).
- Vasopressin regulates contraction of smooth muscle, increases water retention, and increases blood pressure.

The difference between oxytocin and vasopressin is the sequence of two amino acids (doctor didn't mention them).



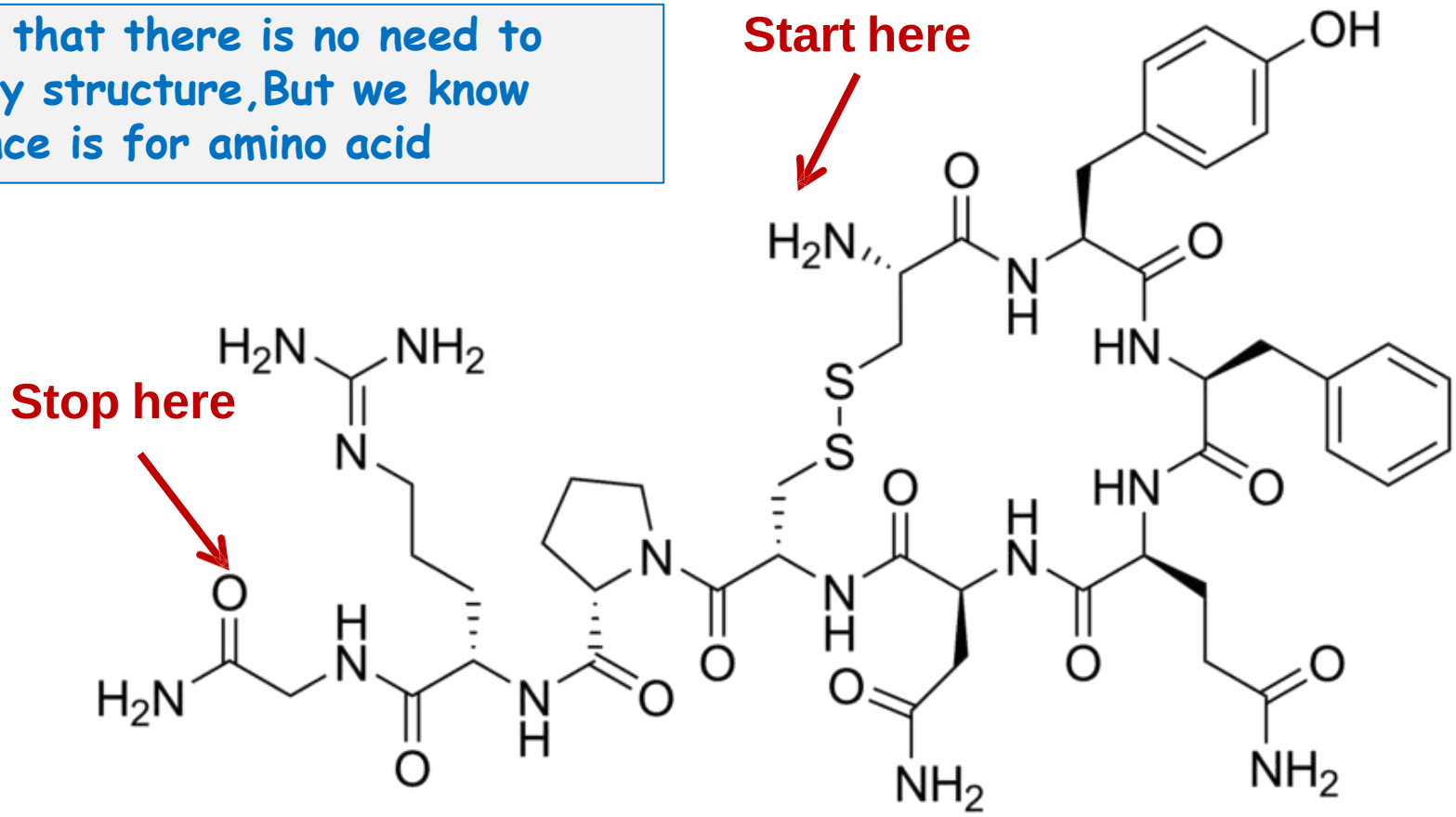


Notice that the structure of two hormones start and end with amino group, the amino group at the end added on carboxyl group(amide) probably to increase the stability of the peptides.

Vasopressin

Practice: what is the primary structure?

The doctor said that there is no need to know the primary structure,But we know what the sequence is for amino acid

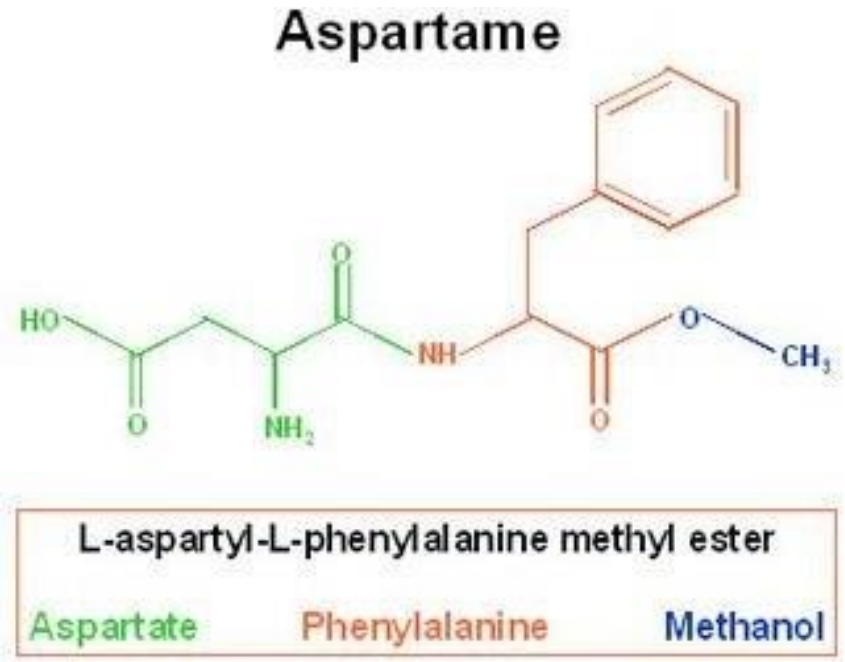


Note: the structure ends with NH2

Aspartame

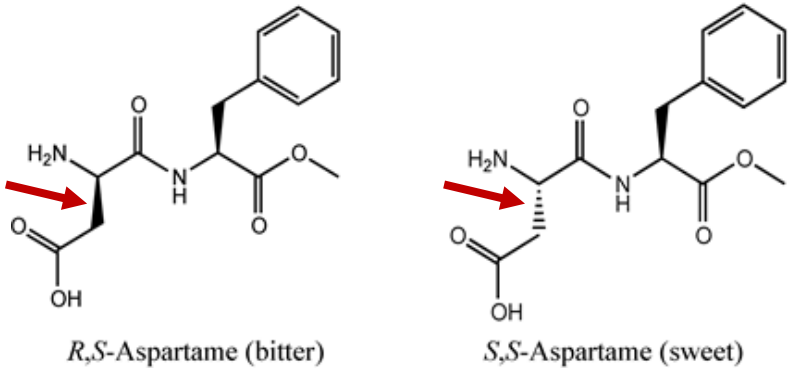
L-Aspartyl-L-phenylalanine(methyl ester)

- A dipeptide that is 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.



Aspartame: It is a sweetener, not sugar, it is a dipeptide, but it works like sugar.
 # is very sweet, 200 times sweeter than regular sugar.

Structure: Aspartate & phenylalanine
 # The carboxylic group followed the last amino acid with a methyl group in order to increase the stability of the molecule



R,S-Aspartame (bitter) *S,S*-Aspartame (sweet)

It may caused cancer

Aspartame and cancer

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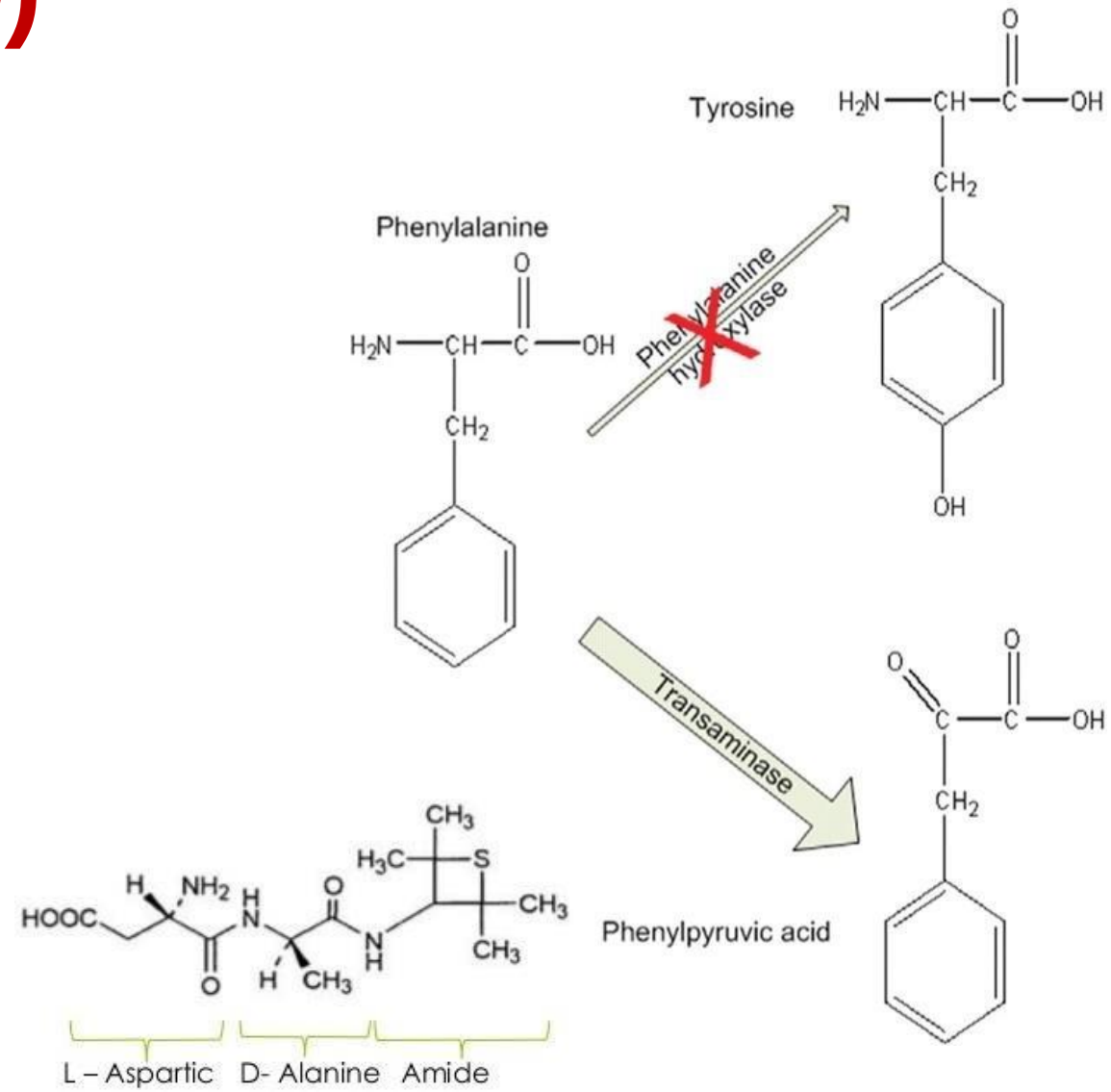
Exclusive: WHO's cancer research agency to say aspartame sweetener a possible carcinogen -sources

By **Jennifer Rigby** and **Richa Naidu**

June 29, 2023 10:17 PM GMT+3 · Updated 7 days ago

Phenylketonuria (PKU)

- PKU is a hereditary “inborn error of metabolism” caused by defective enzyme, phenylalanine hydroxylase.
- It causes accumulation of phenylpruvate, which causes causes mental retardation.
- Sources of phenylalanine such as aspartame must be limited.
- A substitute for aspartame, known as alitame, contains alanine rather than phenylalanine.



Phenylketonuria cannot metabolize phenylalanine, Phenylalanine must be hydroxylated to convert to tyrosine phenylalanine hydroxylase is not present It turns into phenylpruvate and accumulates inside children in the central nervous system and leads to mental retardation.