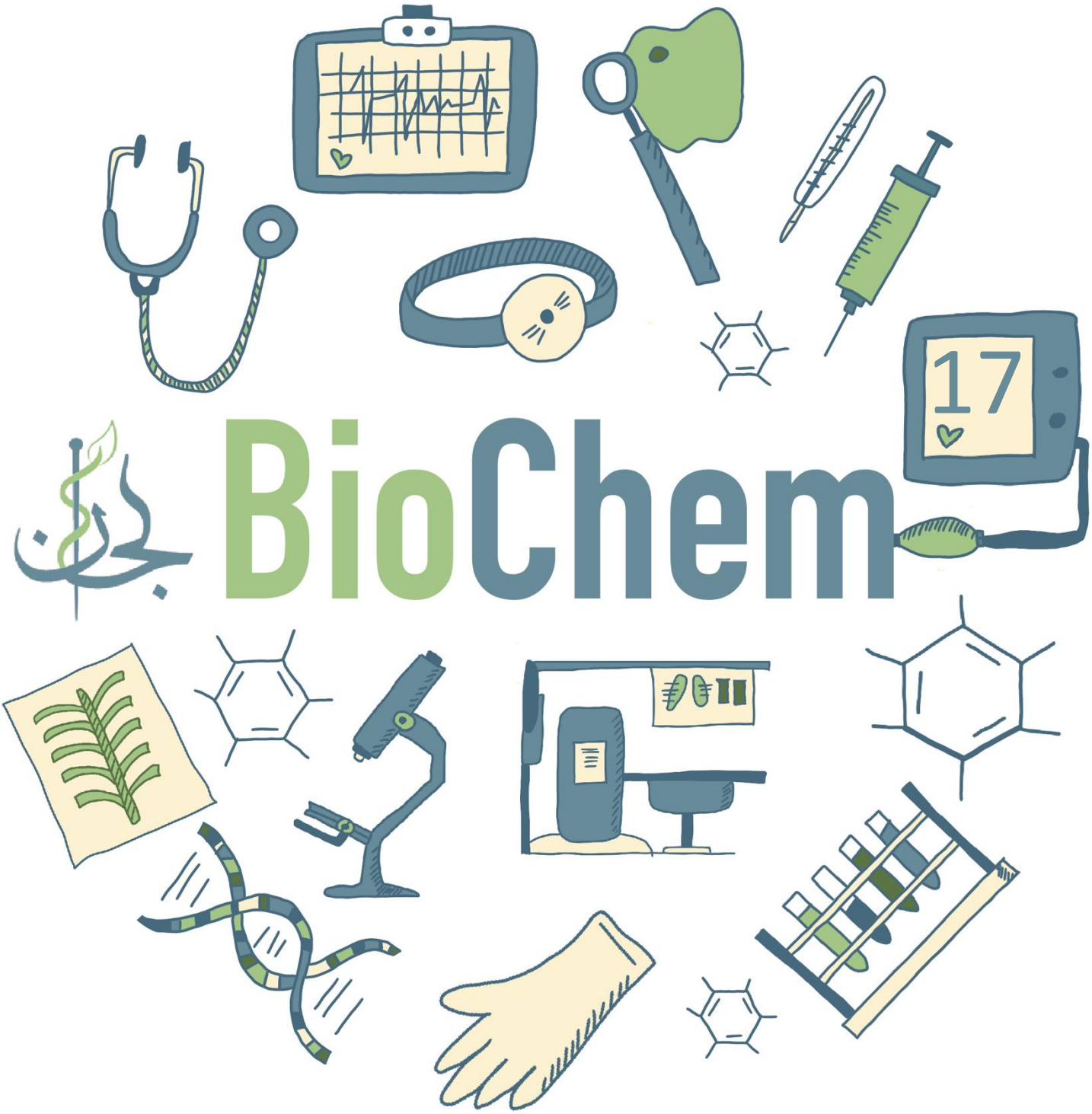

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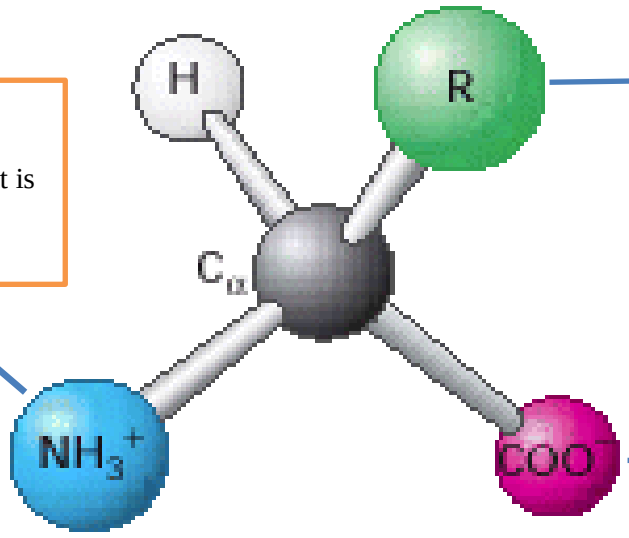
Amino Acids

- Amino acids as the name suggests are molecules that contain an amino group as well as an acidic group (carboxylic).
- They contain a carbon that is called an alpha carbon (α-carbon), which is a chiral carbon attached to four different groups; an **Amino group** (NH2), a **Carboxyl group** (COOH**),** a **Hydrogen**, and an **R group** (the variable part of an amino acid that specifies the type of the amino acid)

Amino group (NH2)

We will explain later why it is presented in the form of (NH3+)

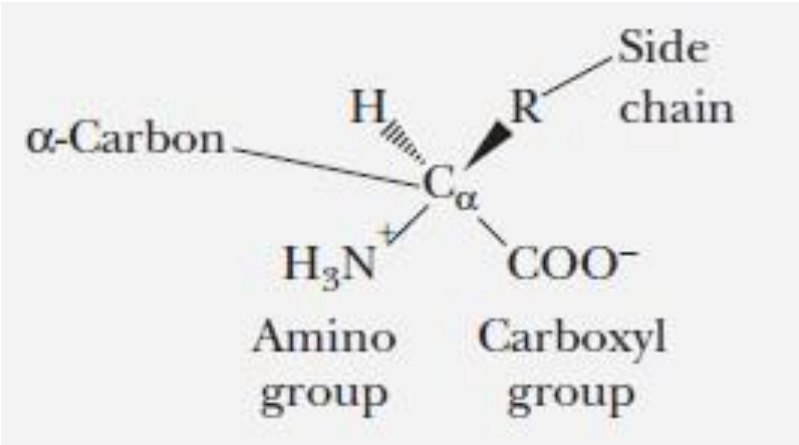


R group

Variable among different amino acids, each one contains a special R group.
R groups are the part of an amino acid that specifies its type

Carboxyl group (COOH)

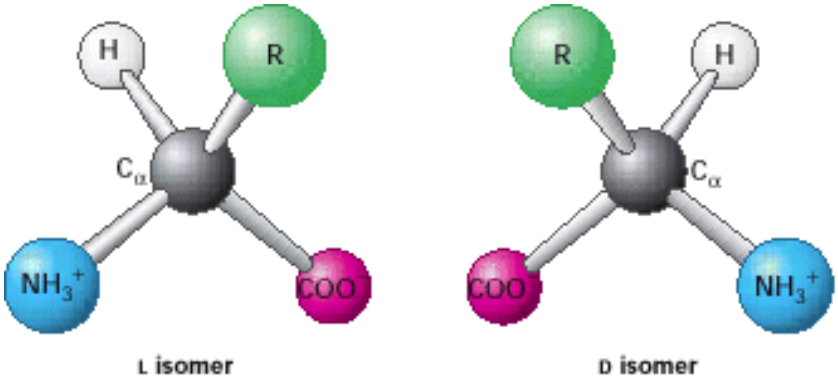
We will explain later why it is attached in the form of (COO-)



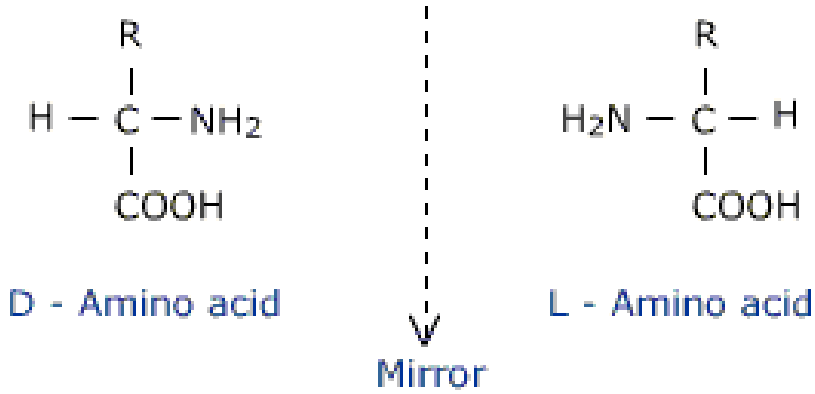
- Three of the four bonds around the (α-carbon) are similar, while the last one differs according to the type of R group, hence resulting in a large array of 20 different types of amino acids that constitute our proteins.

- There are other amino acids (other than the 20 that can be presented as just single molecules), performing different functions.

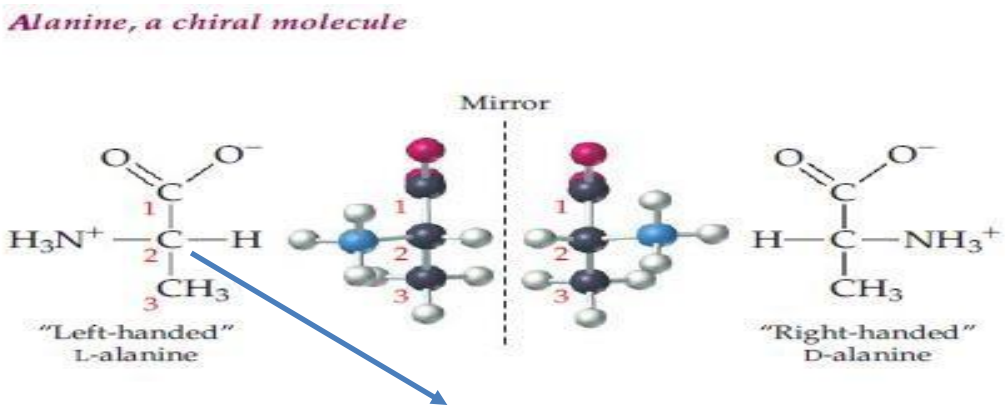
- Amino acids with their attached groups may be oriented in space in different ways around the (α-carbon).



- Here each molecule of these 2 is the mirror image of the other, and they are isomers (D-isomer and L-isomer)
- To determine which isomer is the D-isomer and which is the L-isomer, we look at the amino group:
  - If the amino group is on the right, then this amino acid is a **D-amino acid**
  - If the amino group is on the left, then this amino acid is an **L-amino acid**

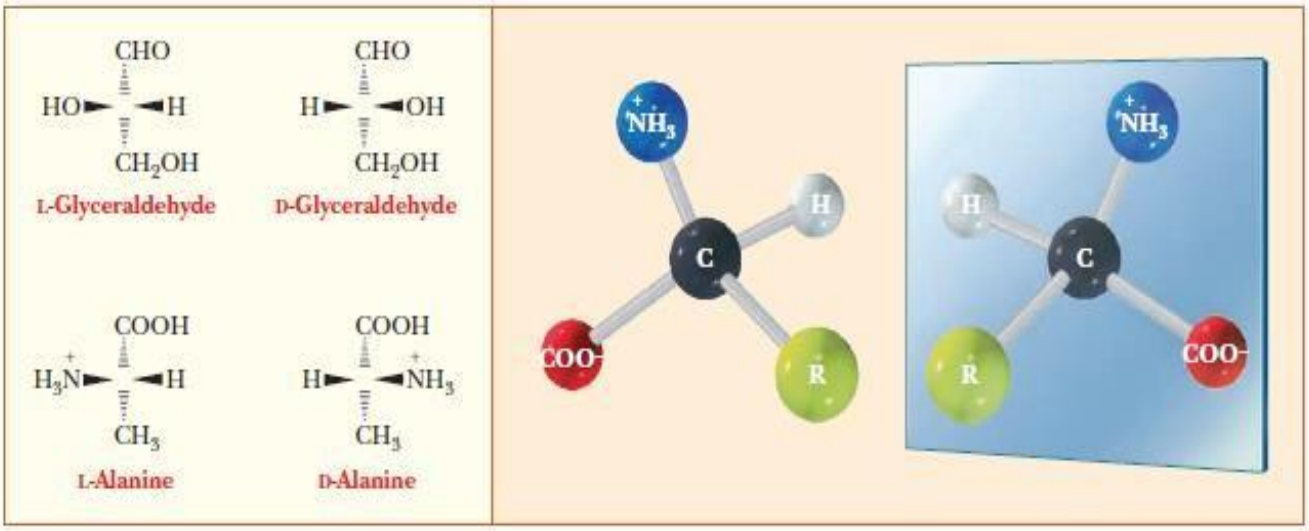


- ✓ In proteins that are presented naturally in our cells, the type of amino acids that are presented are **L-amino acids**, although this doesn't necessarily mean that we don't have D-amino acids (we have D-amino acids but they're not presented in the proteins that are synthesized In our cells).



- Having four different groups attached to the central carbon (α-carbon), gives us a chiral center, with D and L isomers. This can be achieved in all amino acids (meaning that they all have isomers) **except for glycine** because its R group is a hydrogen, therefore there would be 2 hydrogens, thus the (α-carbon) of glycine is achiral
- The amino acids in proteins are not superimposable on their mirror images (except for glycine).
- The Latin terms *laevus* and *dexter*, meaning "left" and "right", respectively, (the ability to rotate polarized light to the left or the right).

Amino acids stereoisomers

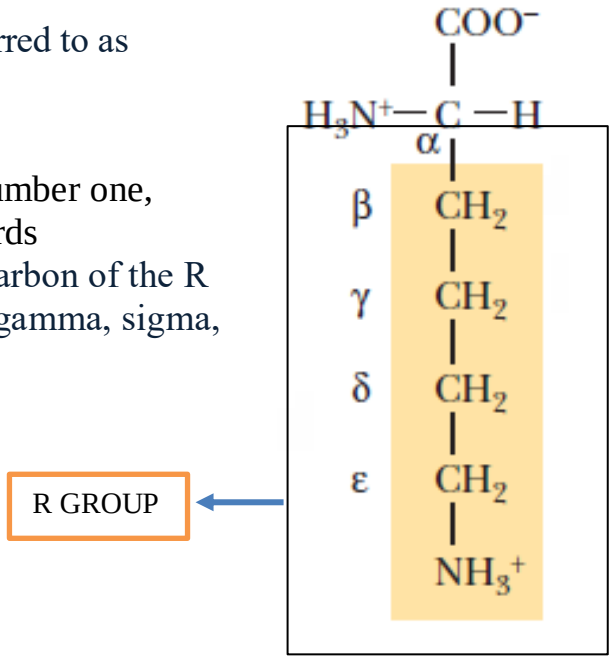


- It's the same idea here, all amino acids have stereoisomers; D and L (except for glycine), just like carbohydrates (they also have the concept of D and L isomers). But in sugars the D-isomer is mainly presented in our cell and body, while in amino acids the L-isomer is mainly the type presented in our proteins.

- **D-amino acids** occur in nature, in bacterial cell walls and in some antibiotics, but not in proteins.

Designation of carbons

- Side-chain carbon atoms are designated with letters of the Greek alphabet, starting from the α-carbon. These carbon atoms are, in turn, the β-, γ-, d-, and ε-carbons.
- If a carbon atom is terminal, it is referred to as the ω-carbon.
  - The α-carbon is like carbon number one, we start counting from it towards the R group, so then the first carbon of the R group is the beta carbon, then gamma, sigma, epsilon…etc.



Types of amino acids

- There are 20 kinds of amino acids, depending on their side chains varying in size, shape, charge, hydrogen-bonding capacity, hydrophobic character and chemical reactivity.

- The most effective classification of amino acids; is according to the polarity **of their R group** (because if you look at amino acids, they generally have polar groups, the amino group, the hydroxyl group whether the R group is polar or not):

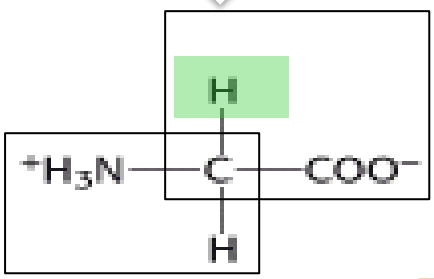
Non-polar	Polar (uncharged)	Charged (positive)	Charged (negative)
Alanine	Serine	Lysine	Glutamate

Valine	Threonine	Arginine	Aspartate
Leucine	Glutamine	Histidine	
Isoleucine	Asparagine		
Methionine	Cysteine		
Tryptophan	Tyrosine		
Phenylalanine			
Proline			
Glycine			

Non-polar amino acids

❖ Glycine

- The simplest amino acid
- Its R group is Hydrogen
- Is a derivative of acetic acid
- Could be considered as a derivative of ethylamine.



Acetic acid

Glycine (Gly, G)

You are required to know the three-letter abbreviation only **(GLY)**

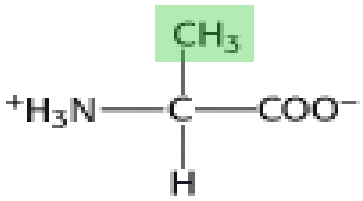
Ethylamine (ALMOST)

Non-polar (aliphatic amino acids)

Non-polar amino acids containing hydrocarbon chains without benzene rings.

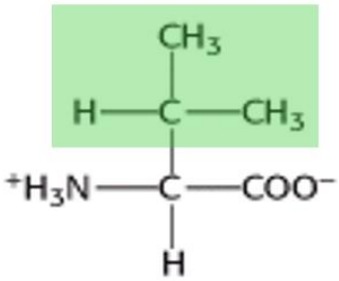
❖ Alanine

- The R group is a methyl group (CH3)



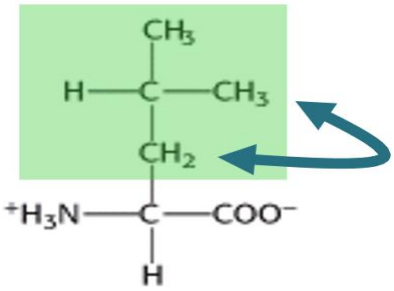
Alanine
(Ala, A)

❖ Valine



Valine
(Val, V)

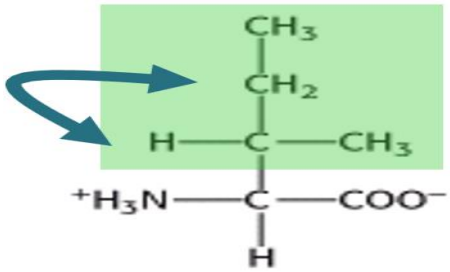
❖ Leucin



Leucine
(Leu, L)

They're isomers, we just change the position of the branch.

❖ Isoleucine

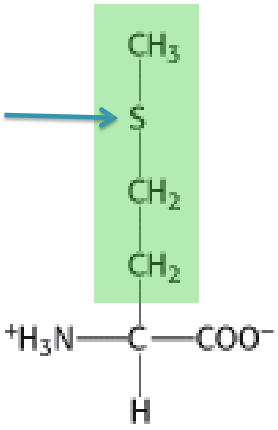


Isoleucine
(Ile, I)

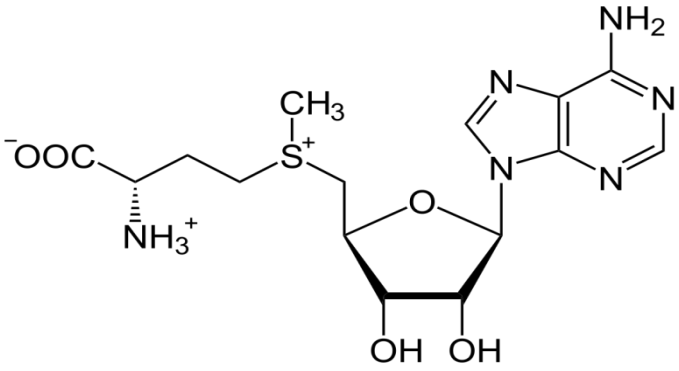
- Because isoleucine and valine start branching at the first carbon in the R chain, they are called **branched chain amino acids**. They are essential amino acids that cannot be synthesized in our cells and we obtain them from diet and nutrition.

❖ Methionine

- It has an R group of 3 carbons and sulfur in between.
- Even though sulfur is a highly electronegative atom that can attract electrons towards it, since it's located in between two carbons, the forces would be in the opposite direction with the same intensity, canceling each other, resulting in a non-polar amino acid.
- It can react to form S-Adenosyl-L-Methionine (SAM), which serves as a methyl donor in reactions.

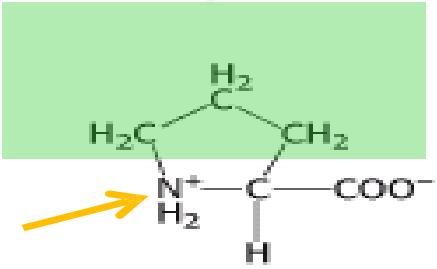


Methionine
(Met, M)



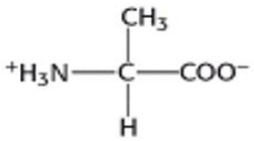
❖ Proline (imino acid)

- Exception of all amino acids because the amino group of the Backbone of the amino acid that is shared between all amino acids is attached to the R group, so it would form a ring structure between the R group and the amino group.
- The nitrogen of the amino group is a **secondary Nitrogen** because its attached to two carbons. While in the amino acids that we mentioned then nitrogen atom has just one connection and then it's a **primary nitrogen.**



Polar amino acids:

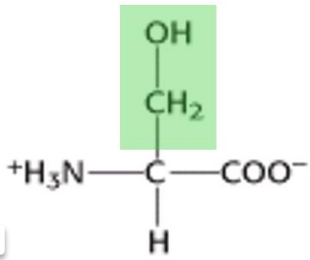
1 Polar uncharged



Alanine
(Ala, A)

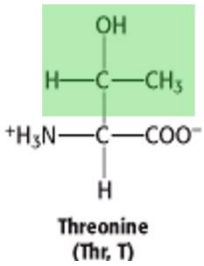
❖ Serine

It's just like alanine, except that there is a hydroxyl group attached to the first carbon.

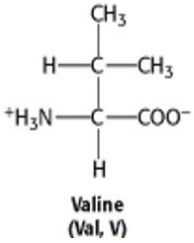


Serine
(Ser, S)

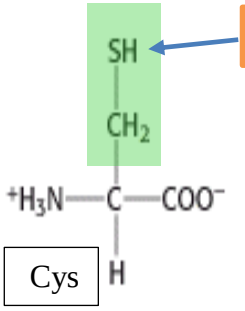
❖ Threonine



Threonine is just like valine except that it contains a hydroxyl group attached to the first carbon instead of a methyl group.



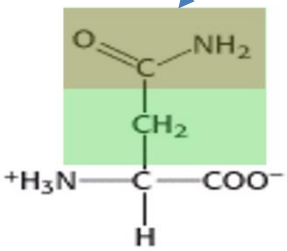
❖ Cystine

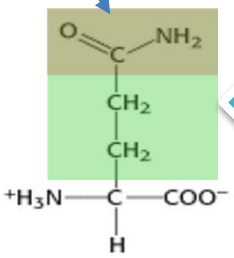


Thiol group

Amide group

❖ Asparagine





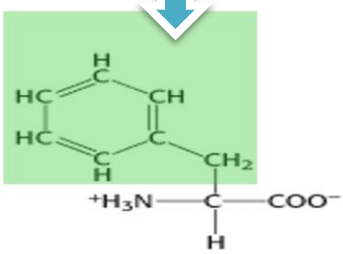
❖ glutamine

The difference between Asparagine and Glutamine, is one carbon.

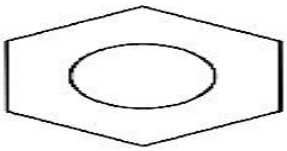
2 Polar uncharged (Aromatic amino acids):

- They have a benzene ring in their side chains. Different groups can be added to the benzene ring making the amino acid polar, or it just maintaining the benzene ring making it a non-polar amino acid.

❖ phenylalanine



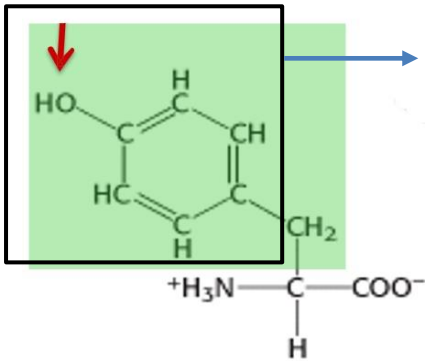
- Has R group of Benzene attached with Carbon atom so it's completely non-polar.



Benzene
C_6H_6

❖ Tyrosine

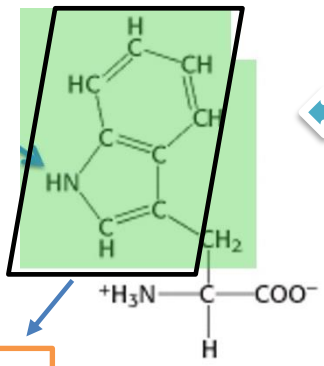
- Polar uncharged amino acid
- Has an R group of phenol attached to a carbon atom



Tyrosine
(Tyr, Y)

phenol

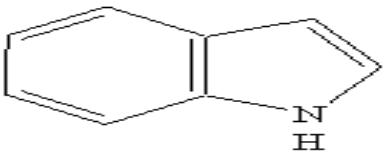
indole



Tryptophan
(Trp, W)

❖ tryptophan

- Has an R group of Indole attached to its carbon atom.
- It's considered as a hydrophobic, non-polar amino acid.



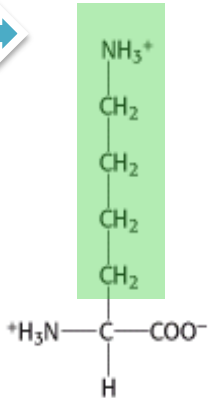
Indole

3 Positively charged amino acids (basic amino acids):

There are basic (positively charged amino acids):

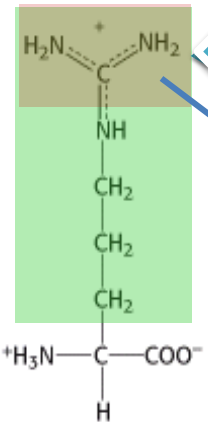
❖ Lysine

- contains an R group with alpha, gamma, beta, and epsilon carbons ending with an amino group.



Lysine
(Lys, K)

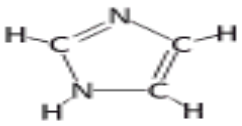
❖ Arginine



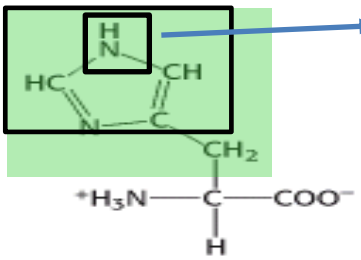
Guanidino group

Arginine
(Arg, R)

❖ His



Imidazole



Histidine
(His, H)

Nitrogen where it can accept a proton and become positively charged.

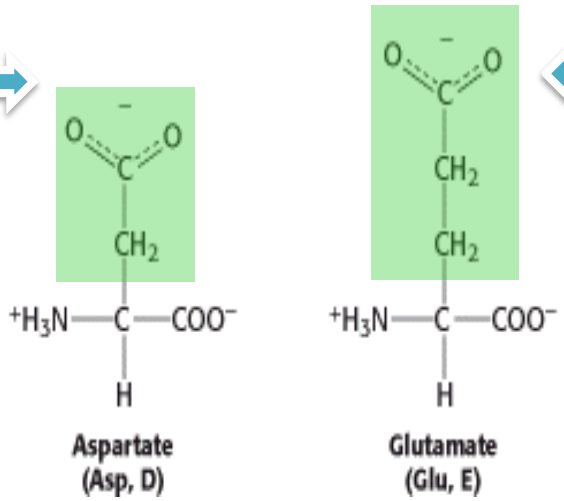
this amino acid with its nitrogen is the main factor that allows proteins to act as a buffer.

4 Negatively charged amino acids (Acidic amino acids).

- This includes 2 amino acids:

❖ Aspartate

❖ Glutamate



- They have a carboxyl group in their side chain, and like any acid they can donate their proton and become negatively charged.

Test yourself

1.Two amino acids are negatively charged _____ and _____

2.The following amino acid is achiral__

3.What is the amino acid that is a secondary amine?

4.Give examples on amino acids that contain an OH group in their side chains.

5.Name 2 amino acids that share a functional group in their side chain

ANSWERS: 1. Aspartate and Glutamate.

2. Glycine.

3.Proline. 4.Tyrosine and serine.

5.Aspragine and glutamine (Amide group),

Aspartate and glutamate (Carboxyl group).

Specialized and uncommon amino acids

→ There's an amino acid pool in our cells, which means that there's an input of amino acids into this pool and ways to consume them (depletion rounds).

The sources of the pool's amino acids:

1) Degradation of different body proteins (~400g/day)(a normal process).
2) Synthesis of different non-essential amino acids (essential amino acids can't be synthesized in our cells).
3) Digestion of amino acids.

Depletion rounds (consume these amino acids):

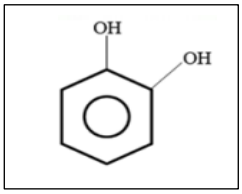
1) Use them to synthesize proteins and other types of molecules in our cells (glucose, glycogen, ketone bodies and fatty acids).
3) Brand them and get energy out of them under certain circumstances (with the presence of CO_2)
4) Use them to synthesize other natural containing compounds (such as: porphyrins, Creatine, Neurotransmitters, purines, pyrimidines and other nitrogen containing compounds).

(Biological significance of amino acids)

The α-nitrogen atom of amino acids is a primary source for many nitrogenous compounds such as: Hormones, Neurotransmitters and Biologically active peptides.

→ We may have some modifications on amino acids that can produce different types of molecules that perform a wide range of functions.

<u>Tyrosine</u>: is a common amino acid, but how can we use it? and What types of products can we synthesize from it?



← Catechol

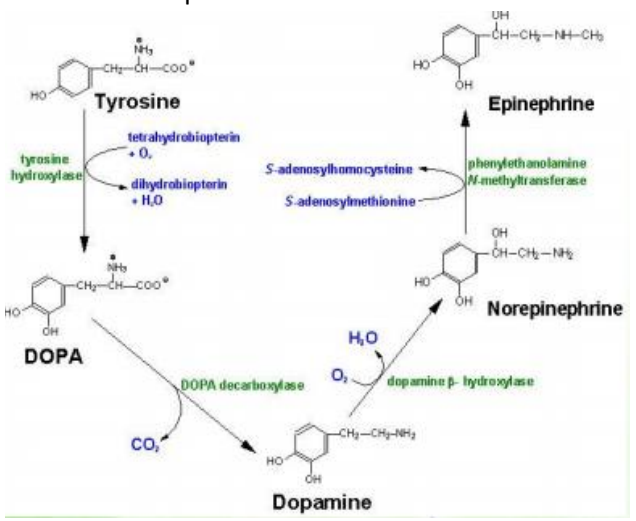
→It's converted into catecholamine neurotransmitters, such as:

1. Dopamine.
2. Norepinephrine.
3. Epinephrine. → flight or fight

→ Catechol: a benzene ring with two OH groups on adjacent positions.

→ We convert **tyrosine** into **catecholamine** by adding an OH group and removing a carboxyl group, resulting in having only the **amine** group as a functional group.

You are not required to know the details of reaction



→ Remember: Epinephrine and norepinephrine are hormones of the adrenal Medulla and norepinephrine is a neurotransmitter in the nervous system.

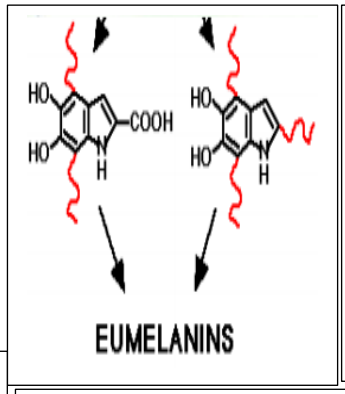
Tyrosine (2)

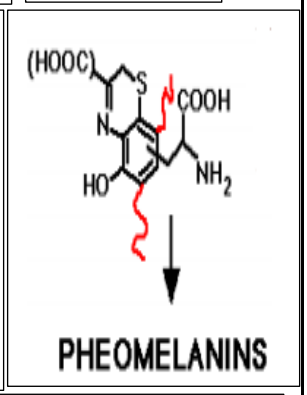
→ Tyrosine is converted into

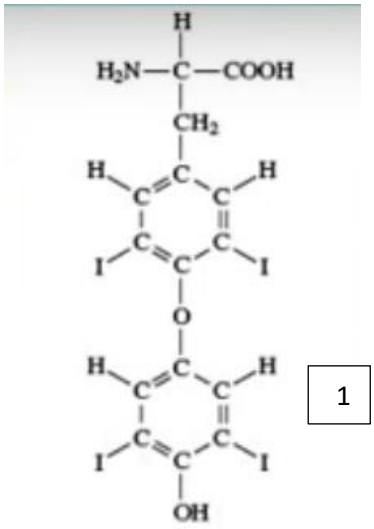
Pheomelanin: الميلانين الغير حقيقي

Eumelanin: الميلانين الحقيقي

a. Melanin pigment (skin color), it's two types:
1. Eumelanin (when present in large amounts it gives a dark color of hair, eyes and skin, while if present in little amounts it gives blonde hair, blue eyes and white skin).
2. Pheomelanin (gives a red hair color).

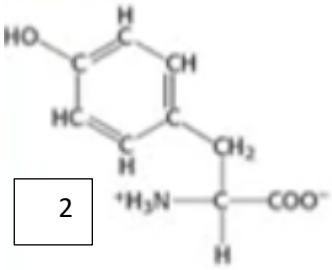






1

thyroxine (Thy)
occurs only in the hormone protein thyroglobulin: I=iodine



2

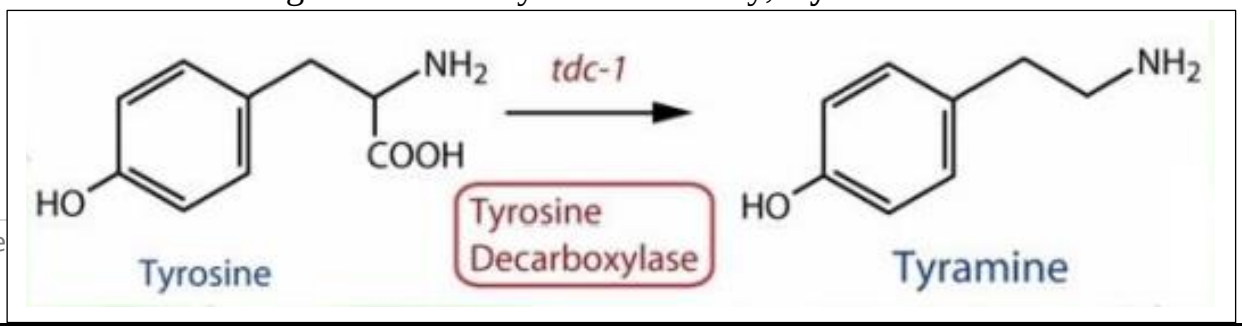
Tyrosine (Tyr, Y)

b. Thyroxine (hormone): secreted by the thyroid gland, it's responsible for regulating the metabolic processes that happen inside our cells in addition to the neuronal development of the fetus.

→ Thyroxine is derived from the tyrosine amino acid (consists mainly of phenol group).
→ Thyroxine is made of a tyrosine amino acid with a phenol group linked to it by an oxygen atom, plus the addition of iodine as shown in the picture.

→ In a protein produced by the thyroid gland called thyroglobulin there are amino acids of different types, one of them is tyrosine acid, different tyrosine amino acids within a thyroglobulin protein become modified (picture 1) by adding another phenol group with 4 iodides, producing a thyroxine hormone.
→Thyroxine is cleaved from the thyroglobulin (it loses an iodide atom) and released to become active and perform its function (active form: T3)(Non active form:T4).

→ Cheese contains high amounts of tyramine, which mimics epinephrine; for many people cheese in the morning is the best way to start the day, **Tyramine is the amine of tyrosine**



Melatonin : هرمون النّوم

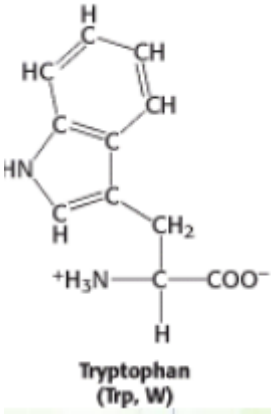
Serotonin :هرمون السّعادة

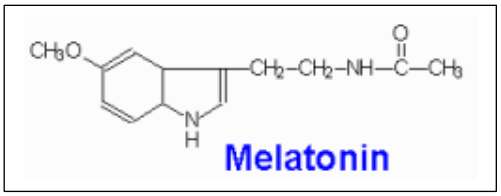
Tryptophan

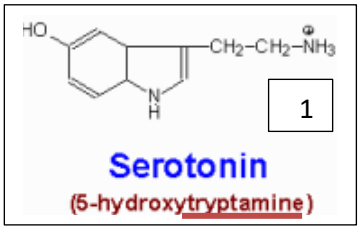
→**Tryptophan** serves as the precursor for the synthesis of Neurotransmitters.

1.Serotonin (neurotransmitter sedative): formed when tryptophan is hydroxylated on the fifth carbon, decarboxylation makes tryptamine (see the underlined word in the picture 1), thus serotonin is formed.

2.Melatonin: it's released by the pineal gland and responsible for the regulating of the day night cycle, it's very similar to the structure of serotonin except with a few changes as shown in the pictures, it's released at night causing sleepiness and reduced during day time so you feel active, it's regulated daily. If you travel to a country with a different time zone, you need time to adjust your melatonin levels (2-3 weeks), or you can use melatonin hormone supplements until your sleep is regulated.

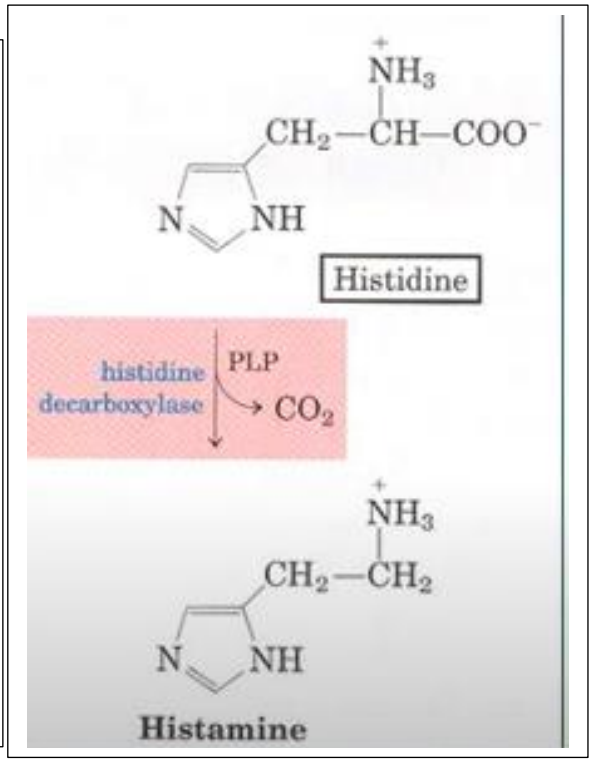






Histamine

- Regulates physiological function in the gut.
- Acts as a neurotransmitter.
- Causes allergic symptoms (a major causes for asthma).
- Contributes to inflammatory response.
- Causes constriction of smooth muscle.
- Comes from different cells such as: mast cells during allergic reactions acting as a vasodilator inducing more leakage of fluid causing edema and swelling of the site of allergy, thus gaining symptoms like a runny nose in the example of a respiratory allergy like fever during spring time.
- We treat allergy with **anti-histamines**.



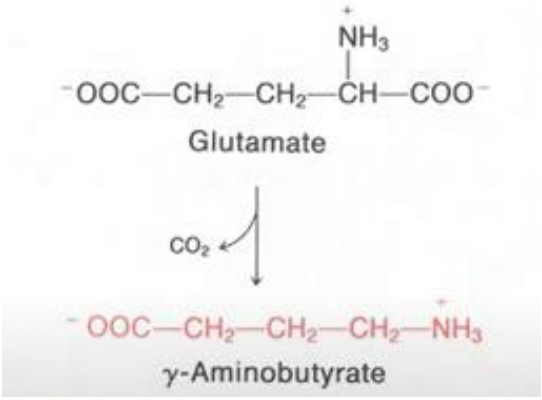
Glutamate

→Is a precursor of γ- aminobutyric acid (GABA), GABA comes from decarboxylation of glutamate (removal of carboxyl group of the backbone that is shared between all amino acids and connected to the α carbon).

→ GABA (acts only in CNS) is an Inhibitory neurotransmitter that reduces neuronal excitability and isn't able to cross the blood brain barrier. Because it's inhibitory, it causes relaxation instead of excitation.

→ GABA is synthesized in the brain because it doesn't cross the BBB.

→GABA has relaxing, anti-anxiety, and anti-convulsive effects.



anti-convulsive :مضاد تشنّجات

anti-anxiety :مضاد توتّر

γ- carboxyglutamate (Gla)

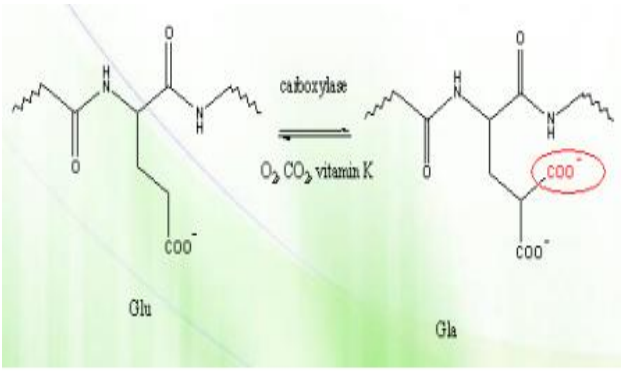
→The glutamate residues of some clotting factors are carboxylated to form γ-carboxyglutamate (Gla) residues.

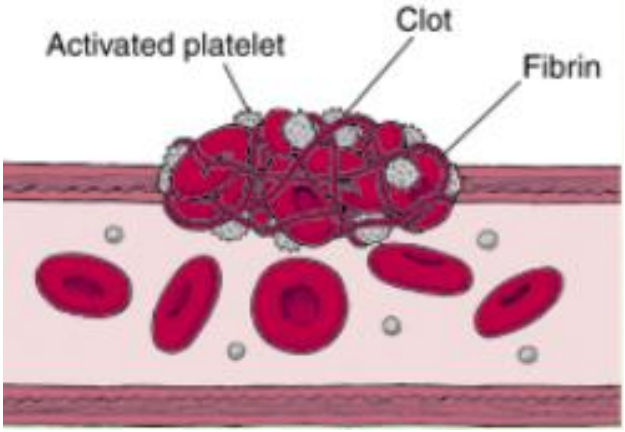
Vitamin K is essential for the process (loss of it will cause problems in coagulation).

This carboxylation is essential for the function of the clotting factors.

→In the presence of proper enzymes and vitamin k there would be modification and carboxylation of glutamate as shown in the picture.

→Once we have two carboxyl groups (in Gla) we would have additional negative charge, so there would be more attraction to Calcium ions, Calcium is a very important mediator that acts in clotting, thus increasing the activation of coagulation.



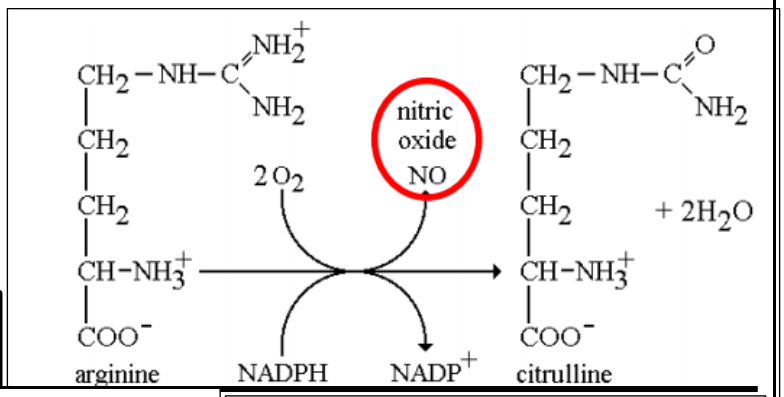


Arginine

L-arginine is the precursor of nitric oxide (NO).

• (NO) is a signaling gas molecule that has a variety of functions: vasodilation, inhibition of platelet adhesion (the initial step of stopping bleeding and clotting), inhibition of leukocyte adhesion of the site of injury, antiproliferative action (inhibiting cell division), scavenging (searching) superoxide anion (anti-inflammatory).

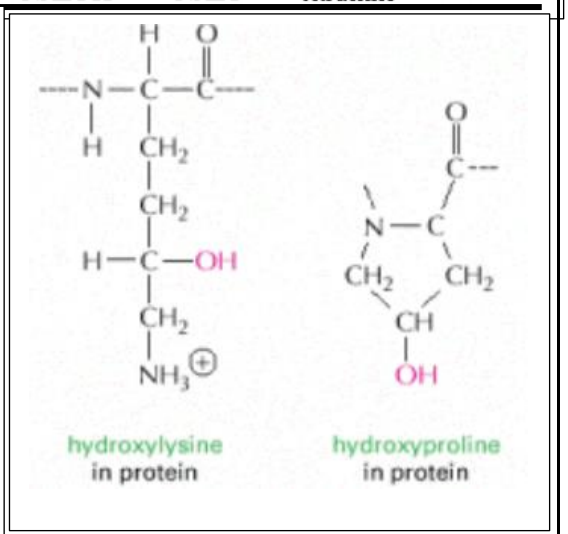
→ This reaction happens during the metabolism of amino acids.
→in the reaction, we just get rid of one of the nitrogen atoms and replace it with an oxygen atom.

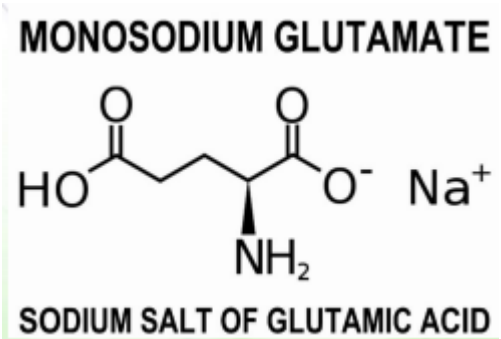


Lysine and Proline

Both are hydroxylated and are part of the structure of collagen. (collagen: a structural protein that is present in connective tissue, analogous to bone and cartilage, collagen is very strong as it's made of 3 helices to form it's mechanical properties).
Derived from the common amino acids by hydroxylation, the extra hydroxyl groups are going to have more hydrogen bond donors and hydrogen bond acceptors so that makes the collagen stronger, and this is a post-translational modification that happens to the lysine and proline amino acids, they're not synthesized in this format. There's no amino acid that is called hydroxylysine, it's a lysine amino acid that's modified after translation by hydroxylation, and similarly there's no amino acid that's called hydroxyproline.

These are produced by modification of the parent amino acid after protein synthesis (posttranslational modification).





Biochemical applications: Monosodium glutamate (MSG), it looks like salt.
→It's a glutamic acid derivative, as it comes from the reaction of the negative hydroxyl group in glutamic acid with sodium.
→Used as a Flavor enhancer, mainly in Asian food.
→MSG causes a physiological reaction in some people (chills, headaches, and dizziness).
→This physiological reaction is called Chinese restaurant syndrome, due to Asian food that containing MSG.