Doctor 022

Biochemistry

Sheet no. 12

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Amino acids

We can conclude from the name amino // acids that :

1) Amino acids contain an amino group (-NH2) , which can be positively charged.

2) Carboxyl (-COOH) group, which can be negatively charged.

General structure

Proteins are polymers of α-amino acids (or amino acids).

The basic structure of an amino acid contains :

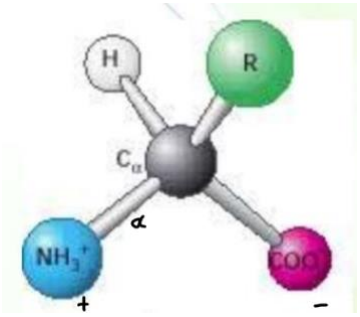
A central carbon atom , called α-carbon , linked to four groups:

1) An amino group (-NH2), NOTICE that it is positively charged (in its protonated form).

2) A carboxylic group (-COOH), NOTICE that it is negatively charged (in its deprotonated form).

3) A Hydrogen atom

4) A Specific R group (side chain), different among different amino acids..



L and D ISOMERS

The α-carbon atom is chiral (except for Glycine) and, thus, amino acids can be present in two forms that are mirror-images of each other (they are enantiomers).

Except in Glycine, all amino acids are chiral (when a central carbon is bonded to four different groups).

Therefore, there are L isomers and D stereoisomers.

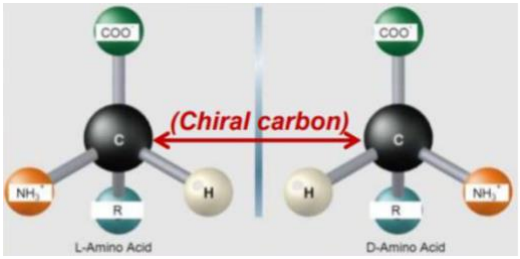
Only L amino acids naturally make up proteins.

*Now if we look to the amino acid structure:

Because carbon can be connected to four different groups, it is considered a chiral carbon, and the mirror image of the chiral carbon is different.

Amino Acids can be L or D based on the location of the amino(-NH2)group

REMEMBER: D = RIGHT SIDE L = LEFT SIDE



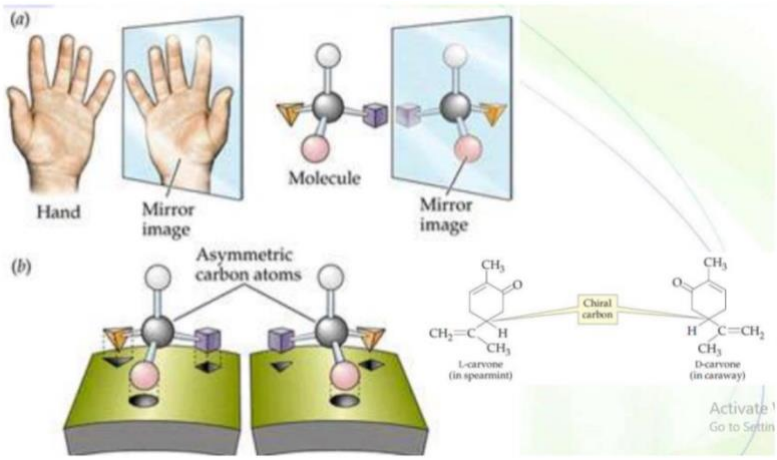
In our bodies SUGARS are in the D orientation, D isomers (the natural sugar form).

Dextrose is another name for D glucose (dextr = right, ose = sugar) In our bodies, most AMINO ACIDS exist as L-Amino acids.

(Although they are not synthesized as much as L-Amino acids), the body regulates the metabolism of D-Amino acids).

NOTICE the location of the amino group.

The amine group of L-amino acids occurs in the left side when drawn in the Fischer projection when keeping the carboxylic acid group on the bottom and the carbon chain on the top.



This figure is just to review where L,D isomers came from

الدكتور قال ما نركز عليها

Types of Amino acids

In our bodies, only 20 Amino Acids are mainly found in proteins (this does not mean only 20 amino acids are present in nature, more than 20 types are found in our bodies and in nature, but what is used in synthesizing proteins are mainly just 20 Amino Acids).

These 20 Amino acids can be classified according to different criteria:

- **Size**

They could be classified as SMALL Amino acids and LARGE Amino acids.

- **Shape**

Aliphatic (chain), ring, straight amino acids, branched.

- **Charge**

Uncharged or charged (positively or negatively).

- **Hydrogen bonding**

It could be said that this amino acid can form H-bonds while that can't.

- **Hydrophobic character**

Polar, non-polar, hydrophobic, not hydrophobic (hydrophilic).

- **Chemical reactivity**

When we have a reactive group = reactive amino acid

NOTE: Polar groups are chemically reactive groups.

Non-polar groups are "inactive" groups in terms of lacking chemically reactive groups like -OH, -COOH, or -NH2 , however, they do play a vital role in protein structure and function.

Classification (according to their R groups) MEMORIZE THEM مطلوبين منا

Non-polar	Polar	Charged (positive)	Charged (negative)
Alanine	Serine	Lysine	Glutamate
Valine	Threonine	Arginine	Aspartate
Leucine	Glutamine	Histidine	
Isoleucine	Asparagine		
Methionine	Cysteine		
Tryptophan	Tyrosine		
Phenylalanine			
Proline			
Glycine			

Now we are going to discuss each Amino acid one by one

الدكتور بحكي انها أهم محاضرة لحد آخر الفصل والأشياء الجاية بتعتمد على هذه الجزئية

According to their R groups we can say that amino acids can be classified as:

Non polar, Polar, Positively charged at physiological pH (Basic), or Negatively charged at physiological pH (acidic).

We notice that Amino acids have two systems of abbreviation

- 3 letters abbreviation

- 1 letter abbreviation Single letter abbreviation isn't included.

The question in the exam won't directly ask about the abbreviations specifically, instead, the abbreviations will be written in the question while it is asking about something else, and we will have to know what they stand for in order to be able to answer.

Example: Which of the following is the classification of the amino acid Gly?

Therefore, in order to know the answer, we must know that Gly stands for Glycine and that it has a nonpolar side chain.

• Recall that all amino acids have the same backbone which contains an alpha-carbon attached to an amine group, to a carboxylic group and to a hydrogen atom.

• The alpha-carbon in the amino acid backbone is attached to an additional variable R group, we call it the side chain.

• Amino acids differ from each other by their side chains, as different amino acids have different side chains(R group). Contains an alpha-carbon attached to an amine group, to a carboxylic group and to a hydrogen atom.

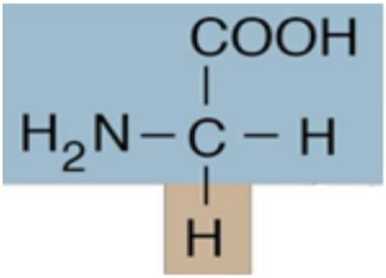
• Amino acids differ from each other by their side chains, as different amino acids have different side chains.

Now we will discuss each amino acid one by one, and what makes the the way they are.

- **The amino acids which are going to be discussed below are ordered according to their structural complexity.**

Glycine (Gly):

- The R group is only hydrogen.
- Glycine is the simplest and smallest amino acid, as it fits almost everywhere.
- The R group (the hydrogen atom) is nonpolar. But because the hydrogen atom is tiny with small molecular weight relative to the amino acid Glycine as a whole, the amino acid Glycine itself is a polar molecule overall.
- Glycine is a derivative of acetic acid; it could also be considered a derivative of amino ethane.
- Notice that the alpha-carbon is associated with 2 hydrogen atoms, which makes the amino acid Glycine achiral.
- Glycine is the only amino acid that is achiral.

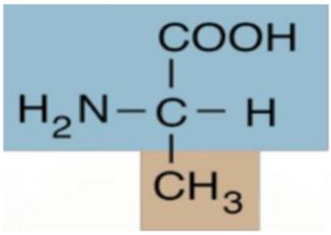


The blue box contains the backbone

The brownish box contains the R group (side chain)

*Non-polar, aliphatic (open chain) amino acids:

- Aliphatic means that the R group is an open chain.
- There are 8 non-polar amino acids which are involved in protein synthesis.
- Recall that Glycine has a non-polar R group but glycine itself is considered polar.



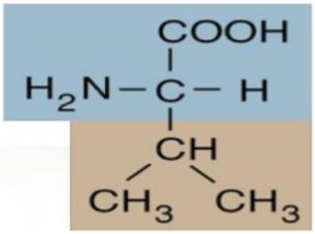
The blue box contains the backbone

The brownish box contains the R group (side chain)

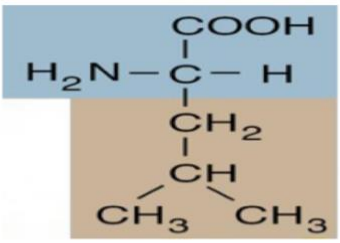
1) Alanine (Ala):

- In terms of complexity, the second simplest amino acid after Glycine is Alanine.
- The R group is a methyl group (-CH3).
- Alanine is a non-polar aliphatic amino acid.

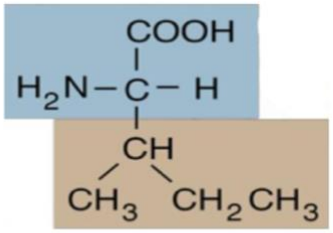
2) Valine (Val), Leucine (Leu), and Isoleucine (Ile):



Valine (Val)



Leucine (Leu)

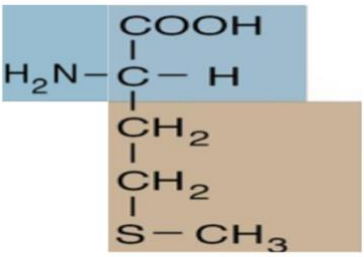


Isoleucine (Ile)

- **Leucine has an additional (-CH2 -) in its R group, when compared to that of Valine.**
- **Isoleucine has the branching occurring in its R group at beta-carbon, while branching occurs in the R group of leucine at the gamma-carbon.**
- **Valine, Leucine and Isoleucine are all aliphatic non-polar amino acids.**
- **They are all branched nonpolar amino acids.**
- **They are essential amino acids in a sense that our body cannot synthesize them, which means we have to get them from our diet.**

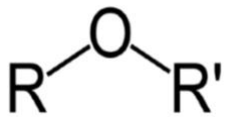
3) Methionine (Met):

- **Methionine**

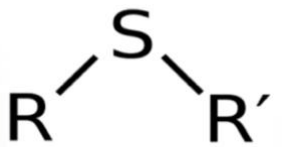


The blue box contains the backbone

The brownish box contains the R group (side chain)

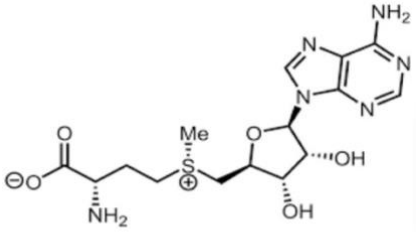


Ether group



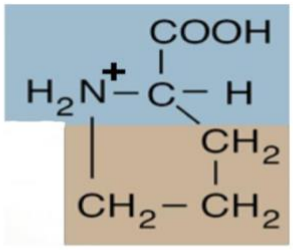
Thioether group

- **There are 2 sulfur-containing amino acids: Methionine & Cysteine.**
- **Methionine can react to form S-Adenosyl-L-Methionine (SAM), which serves as a methyl donor in reactions.**



S-adenosine-L-methionine (SAM)

4) Proline (Pro):



The blue box contains the backbone

The brownish box contains the R group (side chain)

• **Proline is the only cyclic amino acid (not that the R group is cyclic, but the whole amino acid is cyclic). By cyclic we do not mean that the R chain contains an aromatic ring (although there are few other amino acids out there with a benzene ring within their R group). By cyclic amino acid we actually mean that the R group is covalently linked with the backbone, specifically with the amino group.**

• **Notice that the nitrogen in the amino group within the backbone is a secondary nitrogen (not primary) as it is attached to two carbon atoms.**

• **Because the amino group is attached to the R group, it can be considered occupied, which makes it unable to accept protons.**

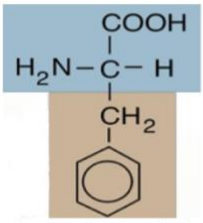
• **Because Proline is cyclic, it is considered a rigid molecule.**

It is significant to realize that proline is a rigid molecule as it influences the 3-dimensional structure of proteins and polypeptides.

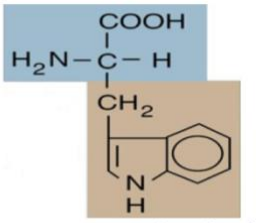
5) Phenylalanine (Phe) and Tryptophan (Trp):

• **They are both highly hydrophobic, and Tryptophan is even more hydrophobic.**

Tryptophan is the most hydrophobic amino acid residue.



Phenylalanine (Phe)

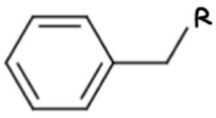


Tryptophan (Trp)

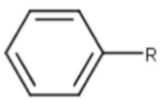
• **Their R groups contain ring structures.**

• **Phenylalanine contains a phenyl group.**

• **Phenylalanine is basically an alanine amino acid with its R group attached to a phenyl group (benzene ring).**



Benzyl group



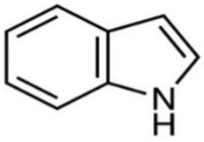
Phenyl group

*Note the difference between "phenyl" & "benzyl" groups

• **Tryptophan contains a double ring structure which contains nitrogen.**

• **The secondary amine group in the double ring structure within the R group of Tryptophan is polar, but the large R-group is hydrophobic overall.**

• **The double ring structure in the R group of Tryptophan is known as an <u>indole group</u>.**



Indole Ring/Group

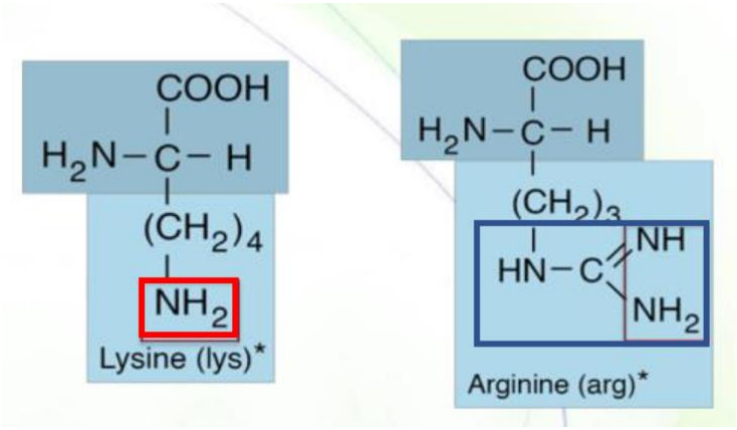
*Positively charged (Basic) amino acids

1) Lysine (Lys) and Arginine (Arg):

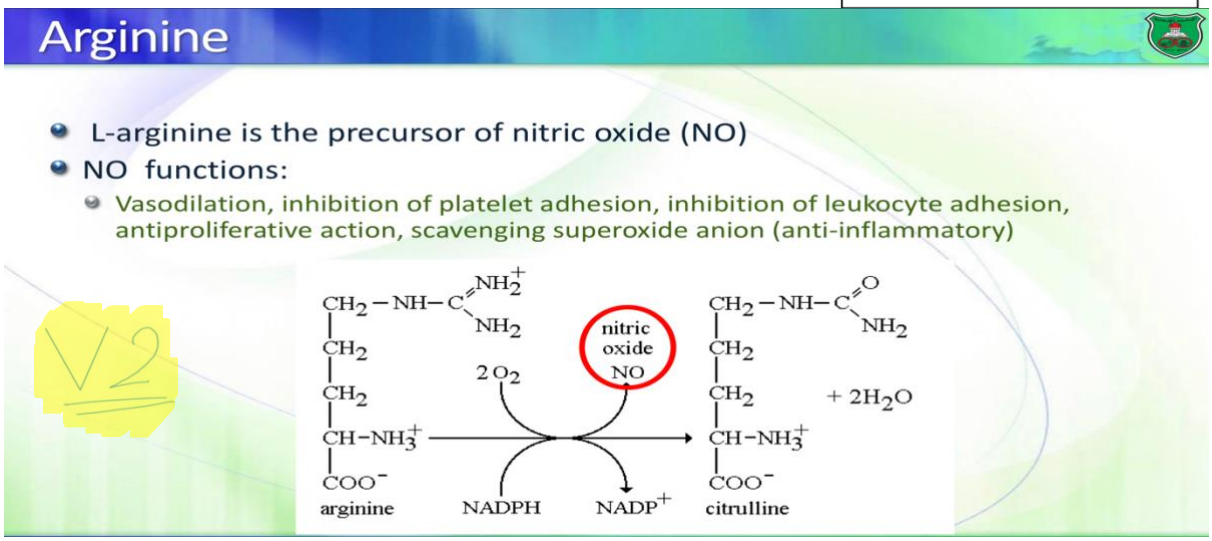
• **Lysine and arginine have relatively long side chains that terminate with groups that are positively charged at physiological pH.**

• **They differ in their terminal groups. In lysine, the terminal group is an amino group, while in Arginine; the terminal group is called a Guanidinium group (the conjugate acid of Guanidine).**

• **In the Guanidinium group, the positive charge could be on the nitrogen atom(s) of (NH) or (NH2) as indicated by its resonance structures.**

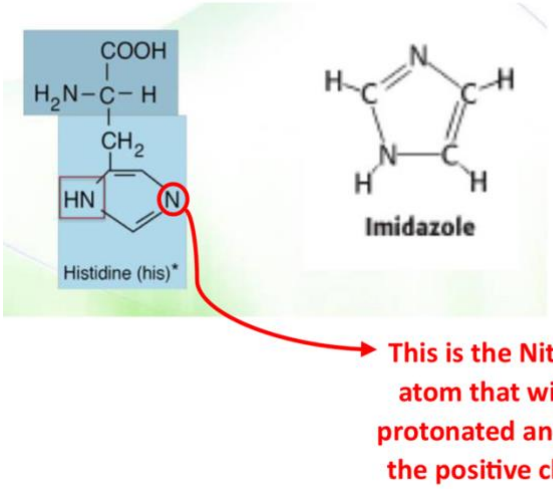


Notice the Red rectangle around the Amino group in the side chain of Lysine and the Blue rectangle around the Guanidine group in the side chain of Arginine



2)Histidine (His):

• It has a ring structure called imidazole which is an aromatic ring that can be charged (the positive charge



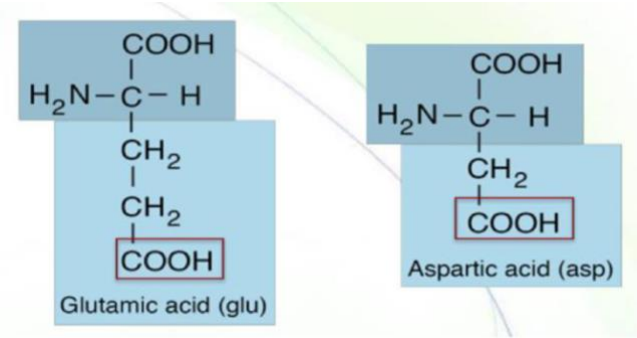
*Negatively charged (Acidic) amino acids

1)Aspartic Acid (Asp) and Glutamic acid (Glu):

• Two amino acids contain acidic side chains because they contain a carboxyl group. These amino acids are often called Aspartate and Glutamate when they are charged/ionized.

• Aspartate and Glutamate are the salts of Aspartic Acid and Glutamic Acid respectively, bearing a negative charge.

• Glutamic acid has a larger size because its terminal (R) group with a longer chain.

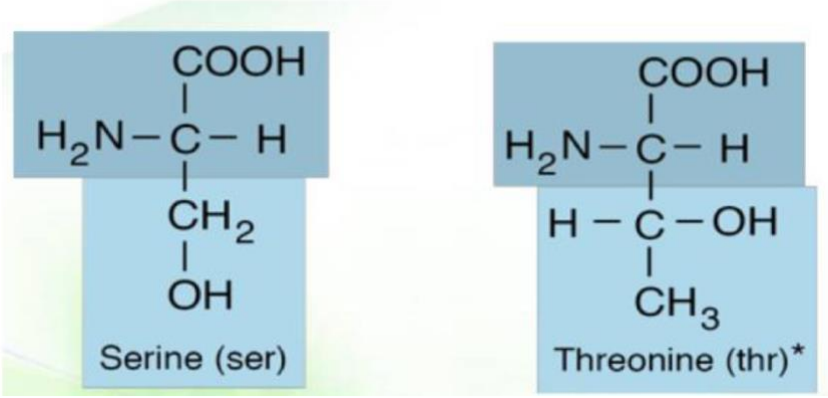


*Polar, hydrophilic, neutral amino acids

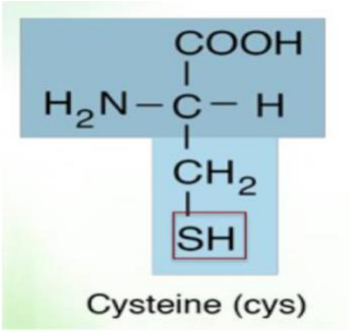
• These amino acids contain polar, hydrophilic groups which makes them reactive amino acids

1)Serine (Ser) and Threonine (Thr):

• Their R groups are hydroxyl groups (polar groups). These hydroxyl groups on Serine and Threonine makes them hydrophilic and reactive.



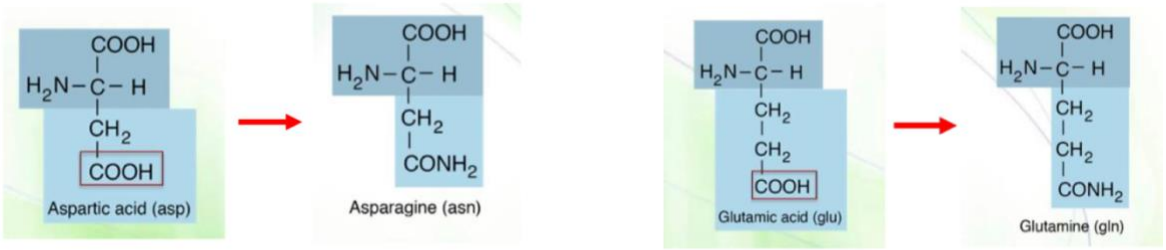
2)Cysteine (Cys):



- **The second Amino acid that contains sulfur (after Methionine).**
- **It contains a sulfhydryl (thiol because it is terminal) group which is also polar reactive group.**

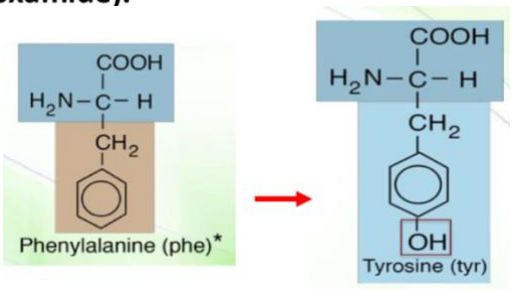
3) Glutamine (Gln) and Asparagine (Asn):

- **They are uncharged polar derivatives of Glutamate and Aspartate, which are negatively charged amino acids.**
- **Each contains a terminal Carboxamide group in place of a Carboxyl group.**



- **The -COOH group is converted to -CONH2 (Carboxamide).**

4)Tyrosine (Tyr):

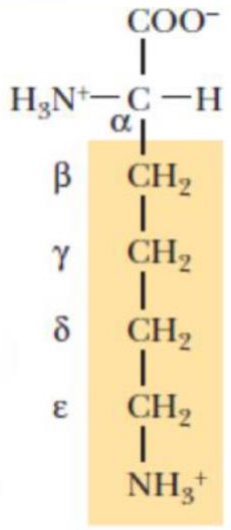


- **It is derived from phenylalanine, which is hydrophobic.**
- **It has a polar and reactive aromatic ring (with a hydroxyl group attached).**

Designation of carbons

Side-chain carbon atoms are designated with letters of the Greek alphabet, counting from the alpha α carbon. These carbon atoms are, in turn, the beta β, gamma γ, delta δ, and epsilon ε carbons.

If a carbon atom is terminal, it is referred to as the omega ω carbon.



Some Questions:

1- Name the only cyclic amino acid.

2- Name the only achiral amino acid.

3- Name the amino acid that contains a Guanidinium group.

4- Name the amino acid that contains an Indole ring.

5- Name the amino acid that contains an Imidazole ring.

6- Name the three amino acids that have a hydroxyl group in their side chains.

7- Name the two amino acids that are negatively charged.

8- Name the two amino acids that contain Sulfur.

9- Name the three amino acids that have branched side chains.

10) Name the three amino acids that contain a phenyl group in their structures.

11) Name the four amino acids that have aromatic side chains

12) An acidic amino acid is_____ charged at physiological conditions.

The Answers:

1- Proline.

2- Glycine.

3- Arginine.

4- Tryptophan.

5- Histidine.

6- Serine and Threonine and Tyr

7- Aspartate and Glutamate.

8- Methionine and Cysteine.

9- Valine, Leucine, and Isoleucine.

10) Phenylalanine, Tryptophan, and Tryosine.

11) Histidine, Phenylalanine, Tryptophan, and Tryosine.

12) Arg and glu

Specialized and uncommon amino acids:

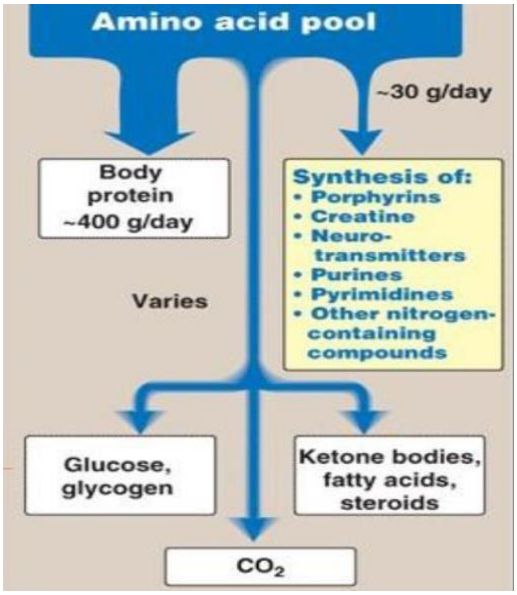
The α-nitrogen atom of amino acids is a primary source for many nitrogenous compounds:

-Hormones.

-Neurotransmitters.

-Biologically active peptides.

Amino acids are the building blocks of polypeptide chains, which then fold into specific shapes to form proteins that perform specific functions in the body. In fact, amino acids have many more functions, either by themselves or by converting into different molecules that perform important functions, such as sugars, specialized molecules (such as purines and pyrimidines), neurotransmitters, and being involved in the synthesis of DNA.



Tyrosine (1)

It is converted into catecholamine neurotransmitters such as:

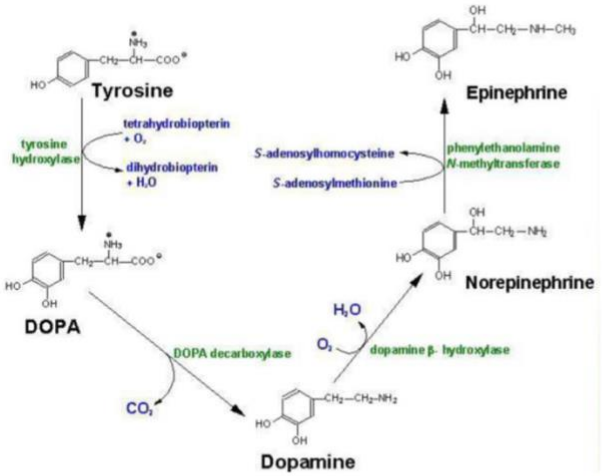
-Dopamine.

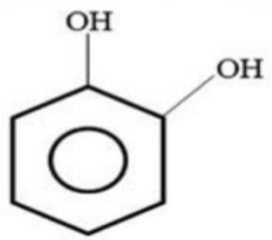
-Norepinephrine.

-Epinephrine.

Tyrosine is an amino acid that is converted into dopamine. Dopamine is further converted into norepinephrine, which is then converted into epinephrine. Each of them is a precursor to the next

neurotransmitter, and they are all considered as catecholamine neurotransmitters.
Catecholamine neurotransmitters are named so because they contain a "catechol" group, which is a benzene ring with two hydroxyl groups, and an amino group, which is a nitrogen-containing group.





catechol

The doctor said there is no need to know the details of the conversion process

Tyrosine(2)

Tyrosine can be converted into:

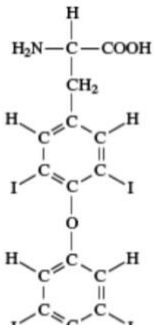
*Melanin:

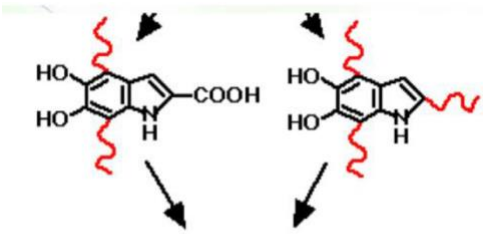
Melanin is a pigment that is responsible for the color of our skin, hair, and eyes. The more melanin a person has, the darker their skin color will be. Conversely, the less melanin a person has, the lighter their skin color will be.

We have two types of melanin: eumelanin, which is responsible for brownish color, and pheomelanin, which is responsible for red color.

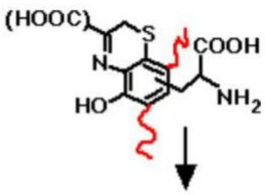
*Thyroxine (hormone)

Thyroxine is a hormone produced by the thyroid gland.





EUMELANINS



PHEOMELANINS

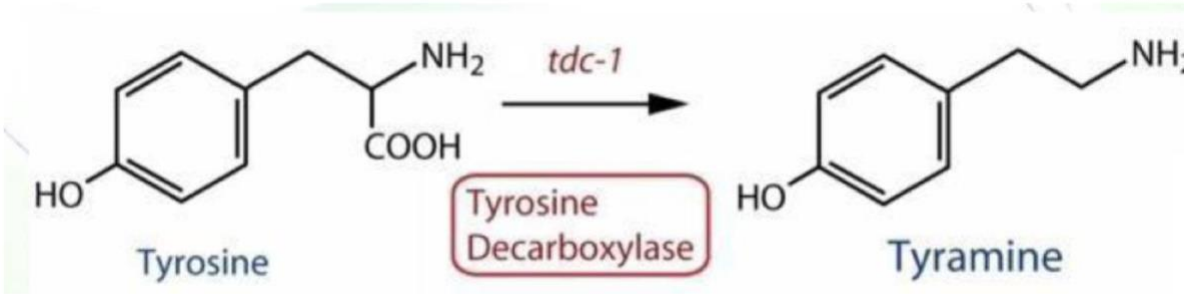
These structures have been provided to increase your understanding.
Do not memorize them.

Tyrosine and life

Cheese contains high amounts of tyramine, which mimics epinephrine; for many people a cheese omelet in the morning is a favourite way to start the day.

Somehow, Tyrosine gets converted into Tyramine , which "acts as" epinephrine.

Epinephrine is produced in response to stress and helps to provide the body with energy during fight-or-flight situations.



Tryptophan

Tryptophan serves as the precursor for the synthesis of a number of Neurotransmitters.

***Serotonin (neurotransmitter-sedative)**

Serotonin is a neurotransmitter that is associated with regulating mood, appetite and sleep. People who suffer from depression may be prescribed medications that increase the duration of serotonin at the synapse to help improve their mood.

***Interesting Fact (not included): new research and large-scale reviews found no convincing evidence that "lower levels of serotonin caused or were even associated with depression."**

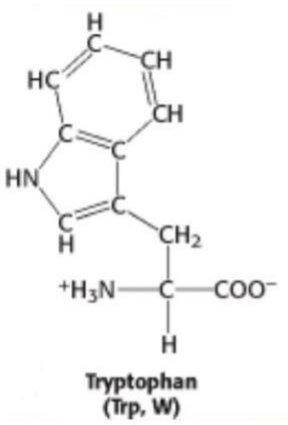
Source:

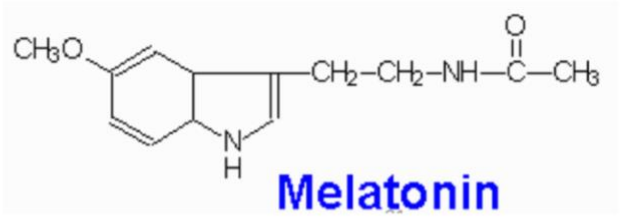
https://www.nature.com/articles/s41380-022-01661-0

Melatonin

Melatonin is a hormone that is secreted by the brain, it is associated with regulating the sleep-wake cycle. Melatonin levels tend to decrease as we age, so it is more commonly found in children than in the elderly.

Melatonin is regulated by the circadian rhythm, which is the body's internal clock that helps regulate sleep and other physiological processes. Melatonin levels increase in the evening and decrease in the morning, which helps to promote sleep at night and wakefulness during the day.

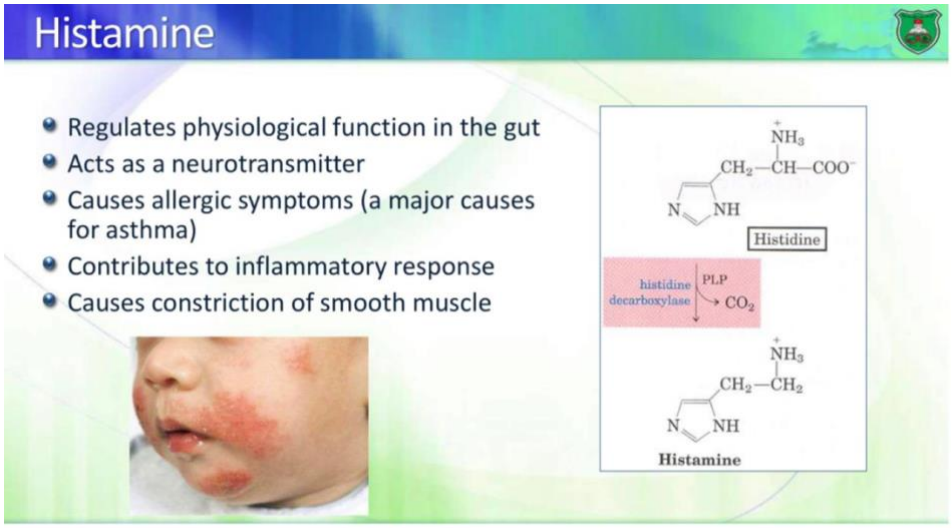




Histamine

Histamine is derived from an amino acid called *'Histidine'*. How do we classify 'Histidine' ?

1. **It is *positively* charged (at or near neutral pH), when having a protonated amino group and a protonated (N) atom in its ring.**
2. **It's abbreviation is *'His'* .**
3. **Contains a ring which is called *'imidazole'* .**
4. **It can exist in both protonated (charged) or unprotonated (uncharged) forms at physiologic pH (due to its low pKa value; relative to Lys/Arg).**



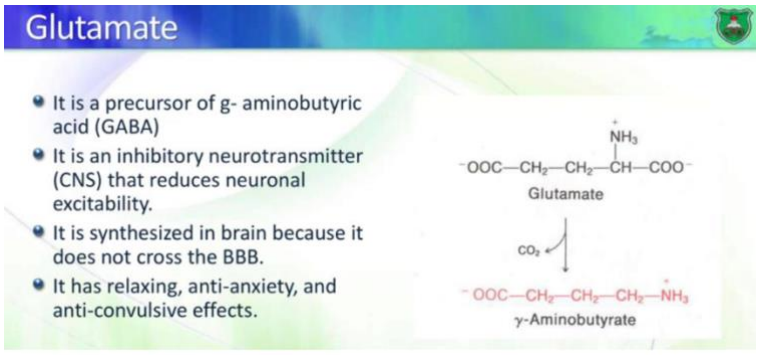
"YOU DON'T HAVE TO MEMORISE THESES FUNCTIONS ONE BE ONE, TRY TO UNDERSTAND!"

Anti-allergic medications are 'anti-histamines', since histamine causes allergic symptoms, these medications work by blocking specific histamine receptors or preventing Histamine's formation from Histidine (a typical antihistamines). Histamine causes constriction of smooth muscles that's why it plays a role in asthma development for asthmatic patients (acts directly to cause bronchoconstriction).

Glutamate 'Glu'

Glutamate can be converted to y-aminobutyric acid (GABA) as it is the precursor of it.

"YOU WON'T BE ASKED ABOUT THE FUNCTIONS, THEY MAY BE INCLUDED IN THE STEM OF THE QUESTION. FOR EXAMPLE, ONE OF THE FOLLOWING MOLECULES IS A DERIVATIVE OF GLUTAMATE AND HAS AN ANTIINFLAMMATORY FUNCTION"

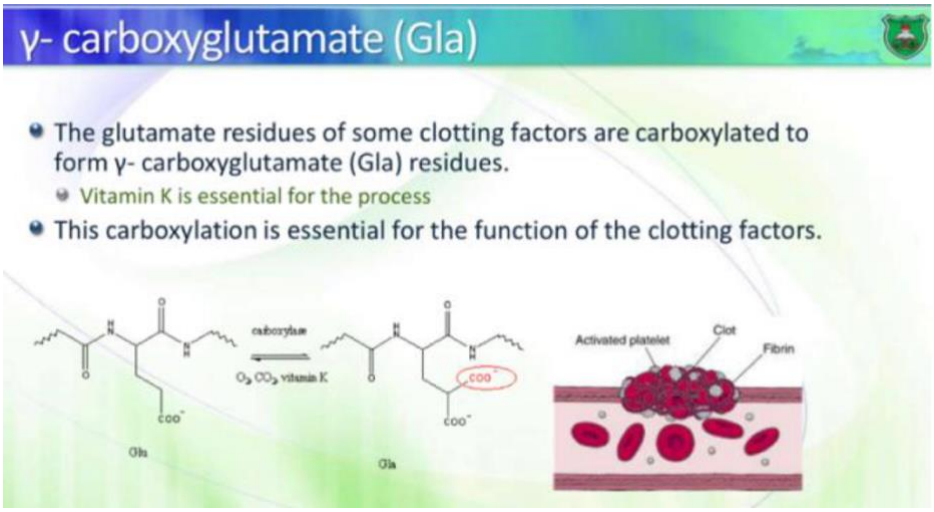


***BBB = Blood Brain Barrier.**

γ-Carboxyglutamate (Gla)

Glutamate can be modified to produce 'carboxyglutamate'. This modification is the carboxylation of specific 'Glu' residues and that process gives a "fork-like" shape.

Vitamin 'K' is important for the addition of a carboxyl group to Glutamate, and 'Gla' is essential for the function of clotting factors, that is why Vitamin 'K' is a coagulant (important in blood-clotting).



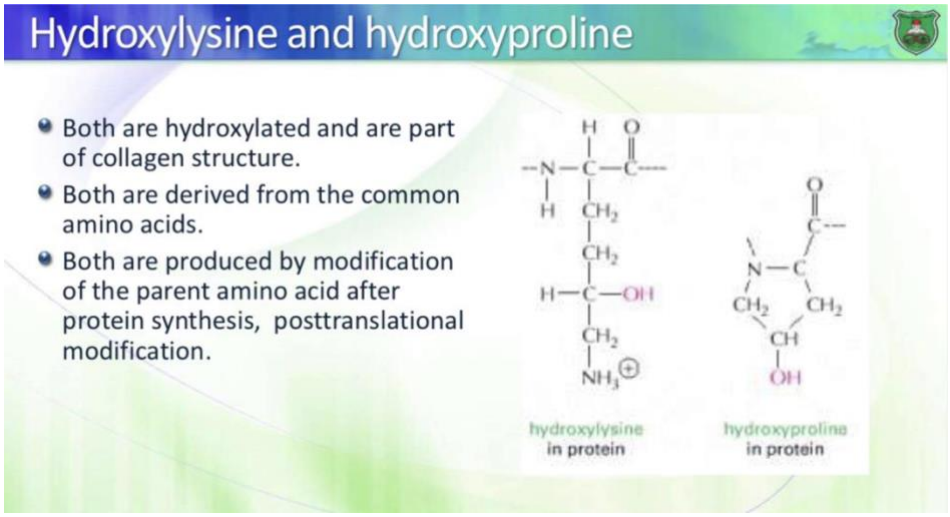
Arginine 'Arg'

Classification: positively charged amino acid, has 'Guanidinium' group .

Nitric oxide (NO) gas can be released (synthesized) from Arginine, which is important and produced by endothelial cells. (NO) causes vasodilation, so it is important for coagulation and inflammatory responses. Also, it has some protective roles against radicals.

Hydroxylysine and Hydroxyprolin

Lysine (Lys) is a positively charged amino acid due to having protonated amino group (at pH < pK; near or at neutral pH). We can add a hydroxyl group to its structure in order to convert it into hydroxylysine. Also, a hydroxyl group can be added to Proline (Pro) which is a cyclic rigid molecule and it will be converted to hydroxyproline. Hydroxylysine and Hydroxyprolin



Both molecules (hydroxylysine and hydroxyproline) are present in collagen, which is a fibrous protein, and these hydroxyl groups are important for the function of collagen.

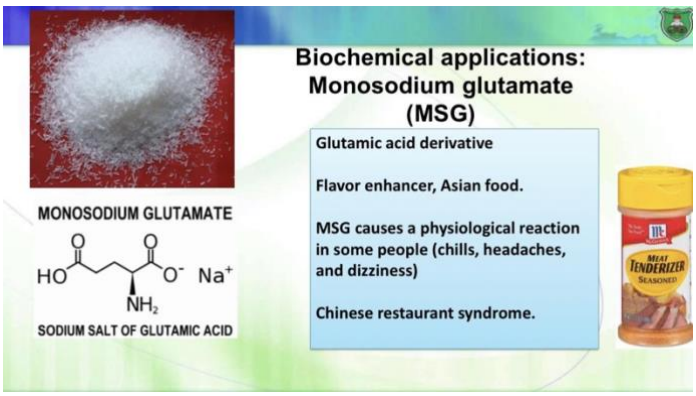
Biochemical applications: MonosodiumGlutamate (MSG)

We can make MSG from glutamate.

"لمّا تروحوا لمطاعم المشاوي ممكن تلاقوا الشُّقف قاسية بمطاعم وهشّة زي ال tender بمطاعم ثانية، ليش؟ المطاعم الي بكون عندها الشقف هشة بتكون بتضيف عليهم مادة ال (MSG) بتخلي اللحمة تصير زي الtenders

Chinese people use it a lot in their food, so in Chinese restaurants in America, Americans have noticed that whenever they eat from a Chinese restaurant they consequently have a shiver .

Further studies have shown that MSG can cause some lesions on the brain, so they called it "CHINESE RESTAURANT SYNDROME".



وَتَعظُمُ في عَينِ الصَغيرِ صِغارُها وَتَصغُرُ في عَينِ العَظيمِ العَظائِمُ

V2

We just added the slide which is in doctor's slides (page 9)