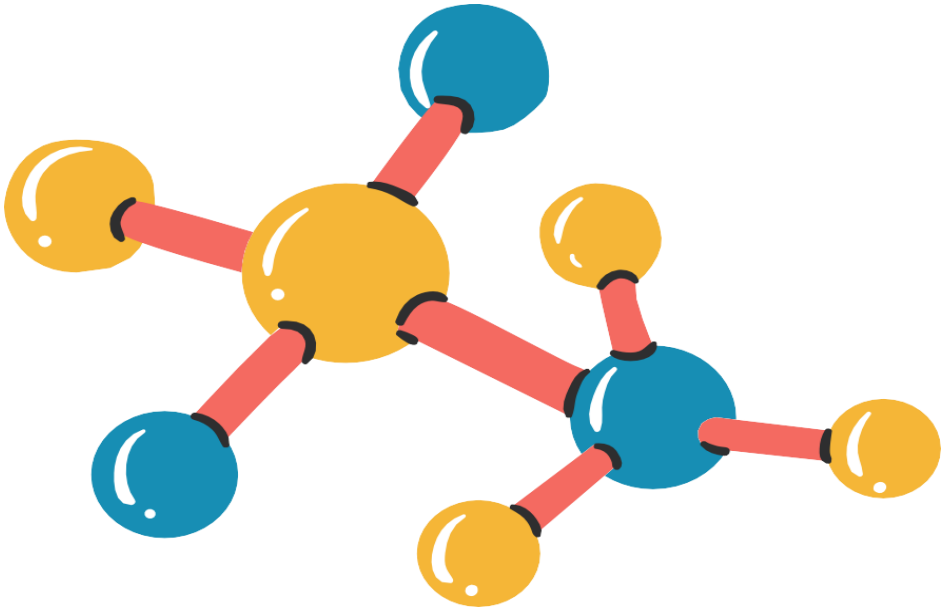
Sheet no.14

Biochemistry



Summer 2022

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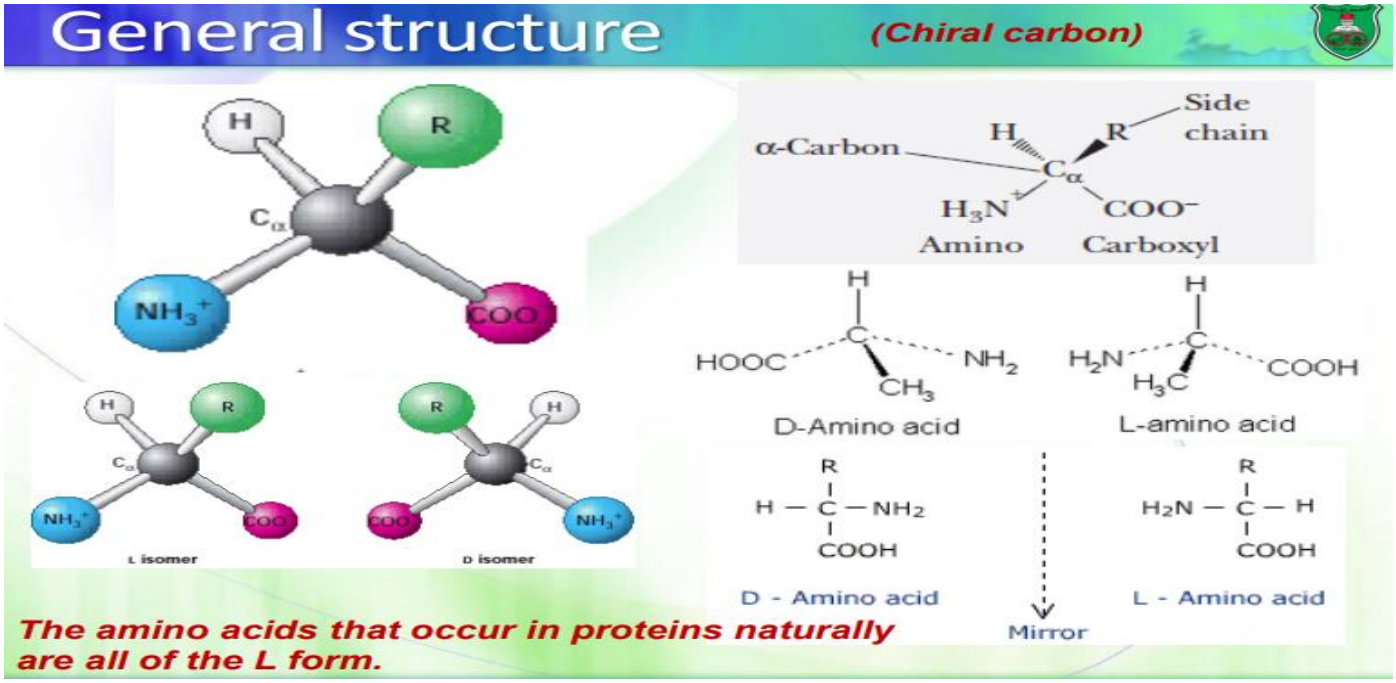
Amino acids

Introduction:

Amino acids

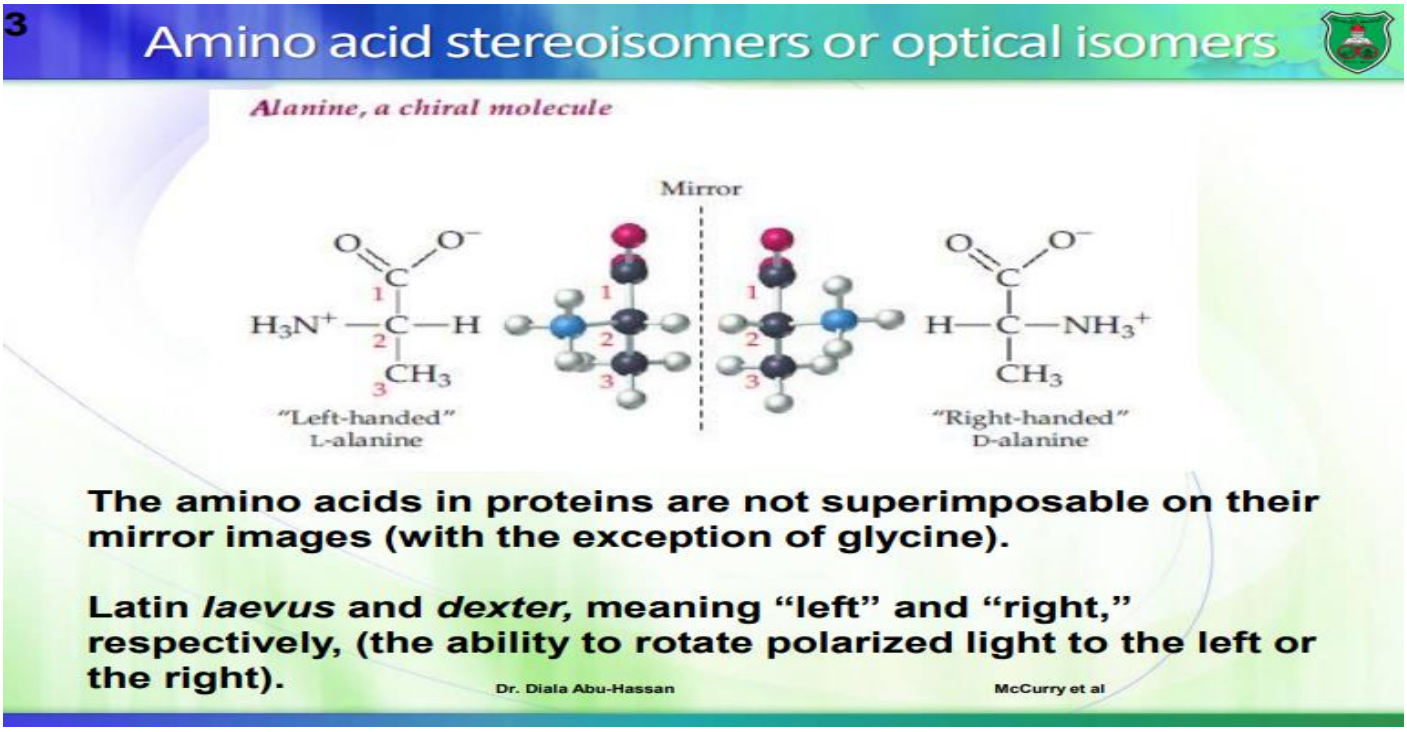
Amino —> amino group

Acids —> containing an acid group



Amino acids are carbon (organic) compounds with a central atom called the alpha carbon. Alpha carbon, like any carbon, will make four bonds, one of them is an amino group, the second is a carboxyl group, the third is R group, and the last is hydrogen. This is a basic structure of any amino acid (It is a central atom with four bonds). If the group (not a carboxyl, hydrogen, amine group), then the alpha carbon is going to chiral center. It is expected that I have D& L (enantiomers) .

The amino acids that we will study are about 20 amino acids found in the protein structure (there are many amino acids other than 20, but they do not enter into the structure of proteins (they do not make a polymer).



The amino acids contained in the protein are L configuration ,but the body has its own ways to deal with D configuration (If D- amino acid enters from other

sources, can deal with it). But it will not use it in the manufacture of protein.

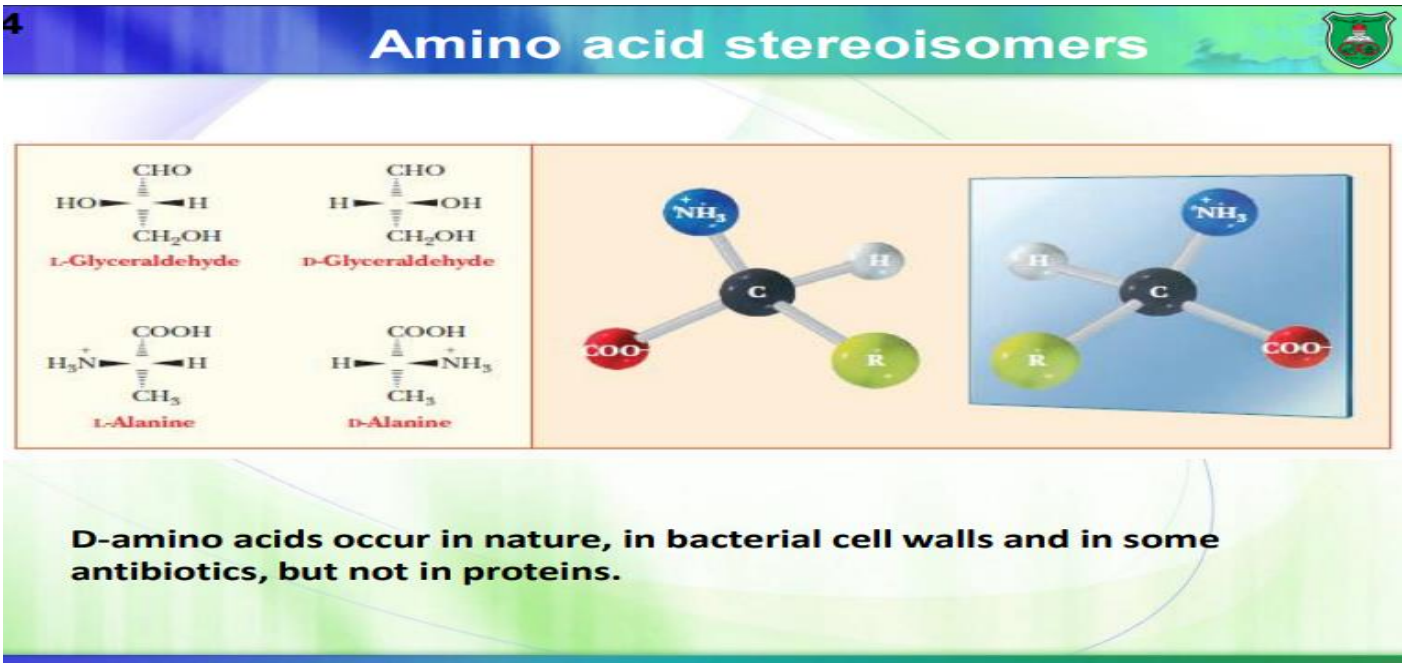
*An example of R group , It could be a **methyl group**, this is **Alanine amino acid** (4 different group —> Chiral —> D&L) .

How do I determine that it is D or L amino acid ?
Depending on the **amino group**

Left side —> L , Right side —> D

Amino group (NH_2), carboxyl group (COOH) in amino acids, amino group ($NH3^+$), carboxyl group (COO^-) why??

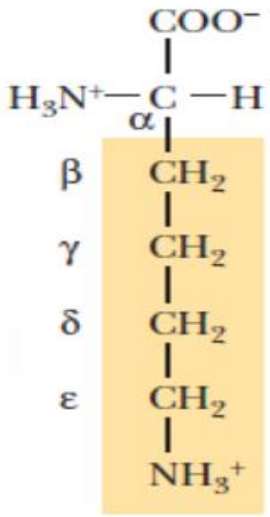
At physiological conditions, the pH surrounding them with respect to the carboxyl group will be **higher**, this leads to the loss of the proton, and the pH surrounding the amine group will be **lower** than it, and it will keep its proton. (The total charge = 0)



Stereoisomers (D&L) depending on amino group that determines left or right .

Designation of carbons

- Side-chain carbon atoms are designated with letters of the Greek alphabet, counting from the α-carbon. These carbon atoms are, in turn, the β-, γ-, δ-, and ε-carbons.
- If a carbon atom is terminal, it is referred to as the ω-carbon.



From alpha carbon towards R chain , atoms are named starting from (alpha , beta , gamma ,….) .Because all groups (carboxyl , amino , H , R) attached to alpha carbon , these groups are called alpha amino acids.

Types of amino acids

- There are twenty kinds of amino acids depending on the side chains varying in
  - Size
  - Shape
  - Charge → **(Polarity)**
  - Hydrogen-bonding capacity
  - Hydrophobic character
  - Chemical reactivity

***Different in what type of non covalent interaction they can form .**

***As a functional group—> what type of reactions they can form .**

R group is the different part actually of the structure of the amino group.

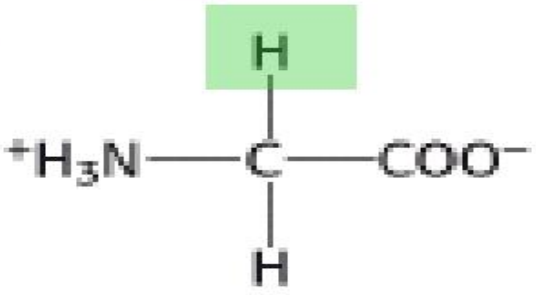
Classification (according to the polarity of R group)

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

Non polar amino acids:

Glycine

- Glycine is a derivative of acetic acid.
- It could be considered a derivative of ethylamine.



Glycine (Gly, G)

Is it chiral?

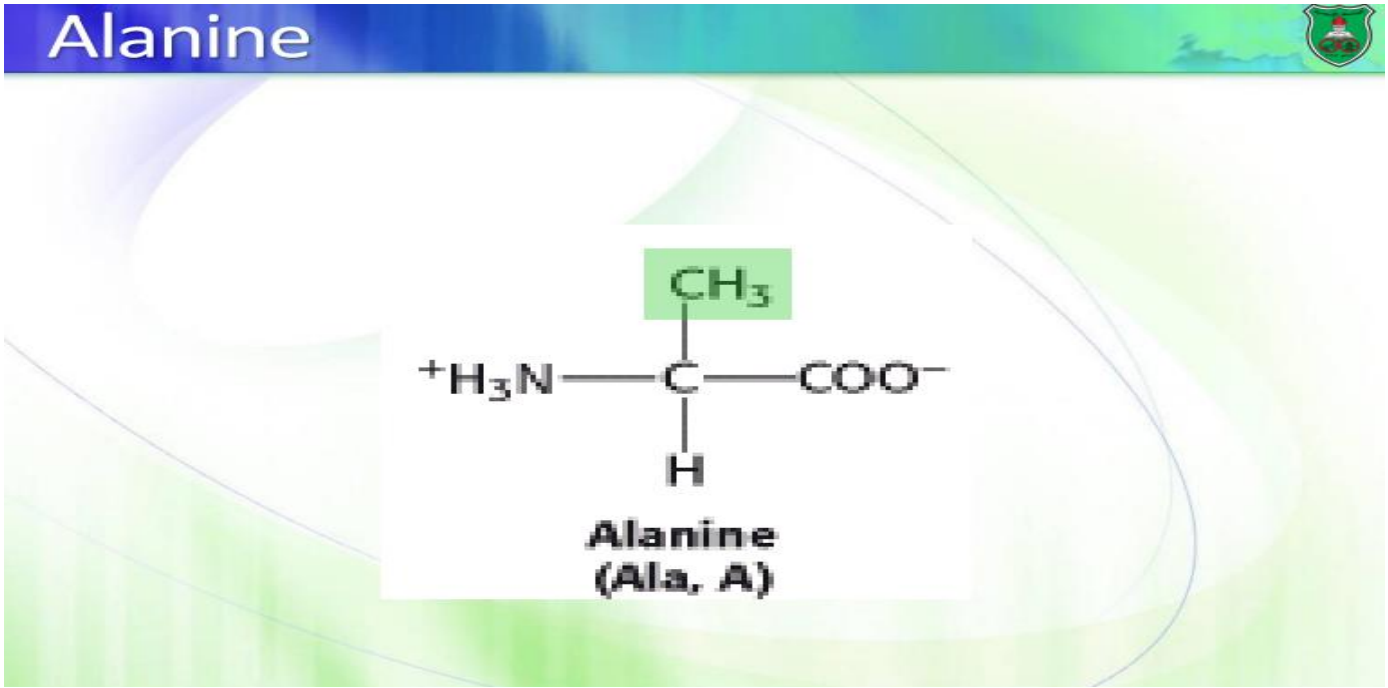
Glycine (simplest amino acids)

Abbreviation: Gly

R group: hydrogen (H)

*It has not carbon in R chain Because it has hydrogen in its side chain (it has 2 hydrogen on the alpha carbon) so , the carbon is a chiral (it doesn't have D& L enantiomers.

Aliphatic (There are no rings , benzine…)→ straight line.

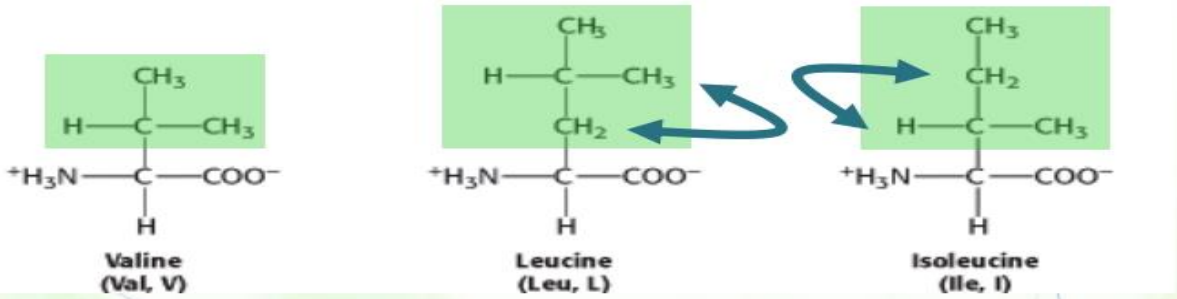


Alanine (very simple)

Abbreviation: Ala

R group : methyl group

Valine, leucine, and isoleucine



They are branched amino acids.
These are *essential amino acids in the sense that the body* cannot synthesize them.

Valine

Abbreviation: Val

R group : (3 carbon atoms + hydrogen)

***Carbon no.2 attached to alpha carbon**

Leucine

Abbreviation: Leu

R group :(4 carbon atoms + hydrogen)

Isoleucine (isomer of leucine) :

Abbreviation: Ile (I —ISO , le — leucine)

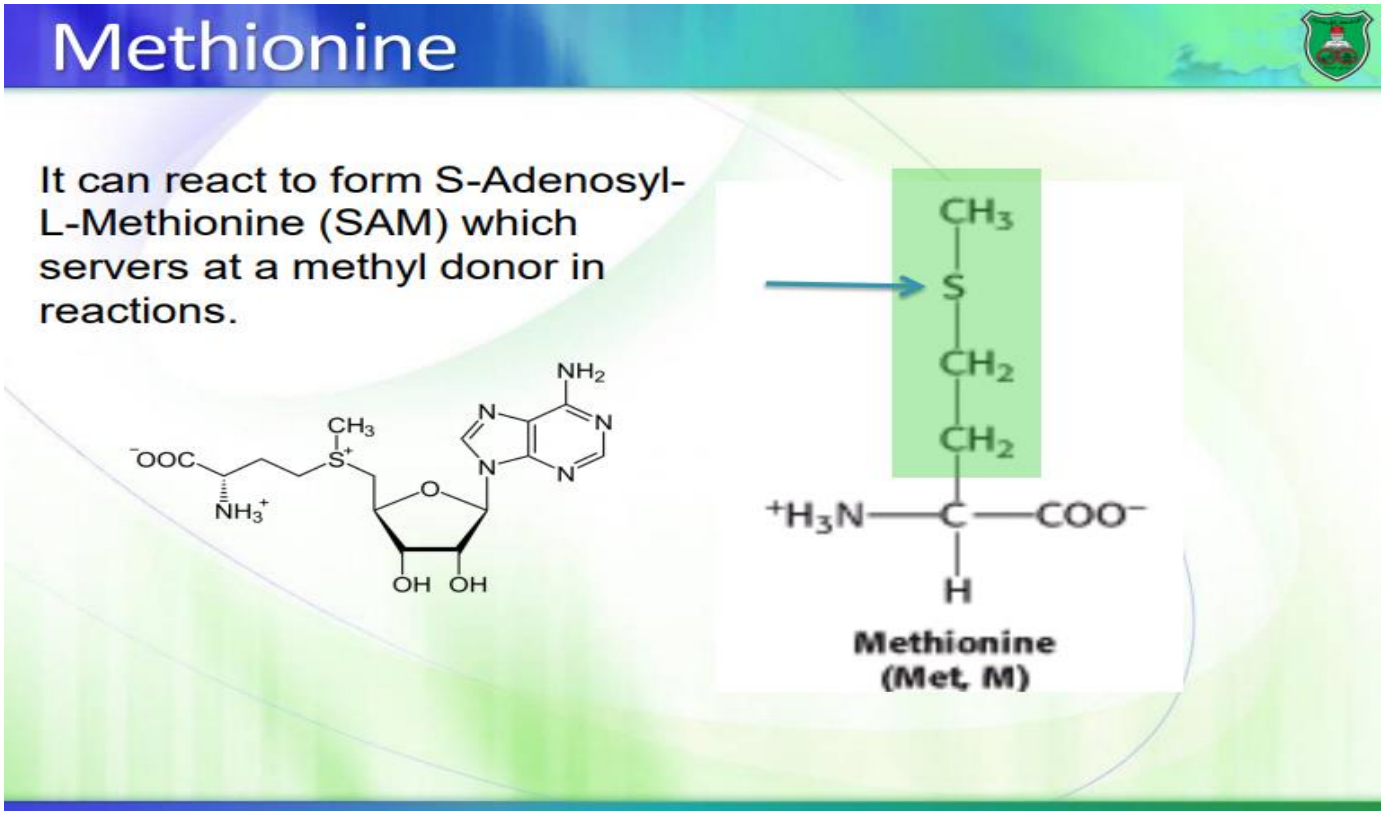
R group: (4 carbon (straight chain) + hydrogen)

*** Carbon no. 2 attached to alpha carbon**

****Leucine & Isoleucine—> isomers**

Val,leu ,Ile (branched chain amino acids)

*These are essential amino acids—> obtained from diet , we can't synthesis them in the cells.



Methionine

Abbreviation: Met

R group : (3 carbon atoms + sulfur) → (C-C -S-C)

*Sulfur(highly electronegativity)→ make polar bonds, but I consider it non-polar because the sulfur is not terminal(between 2 carbons) .

Methionine is important :

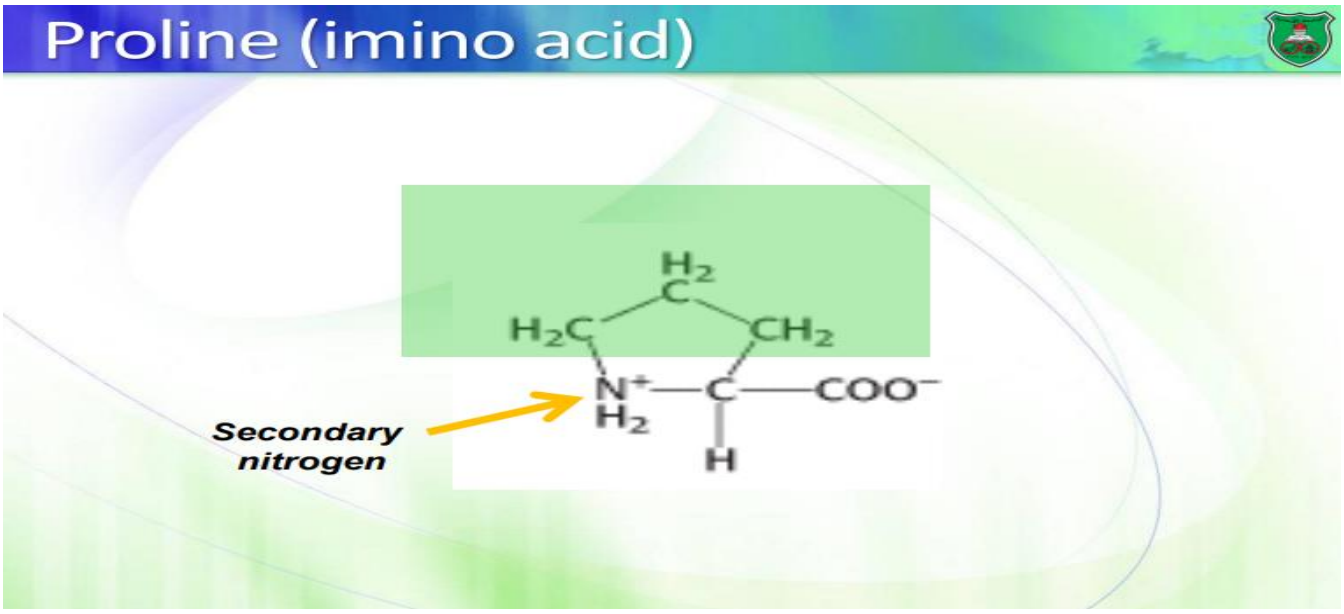
1*starting codon

2*during degradation of methionine, they will be generation of molecule called (SAM).

Adenosyl group is added to sulfur atom

nucleoside

Methyl donor: donating methyl group during methylation reaction



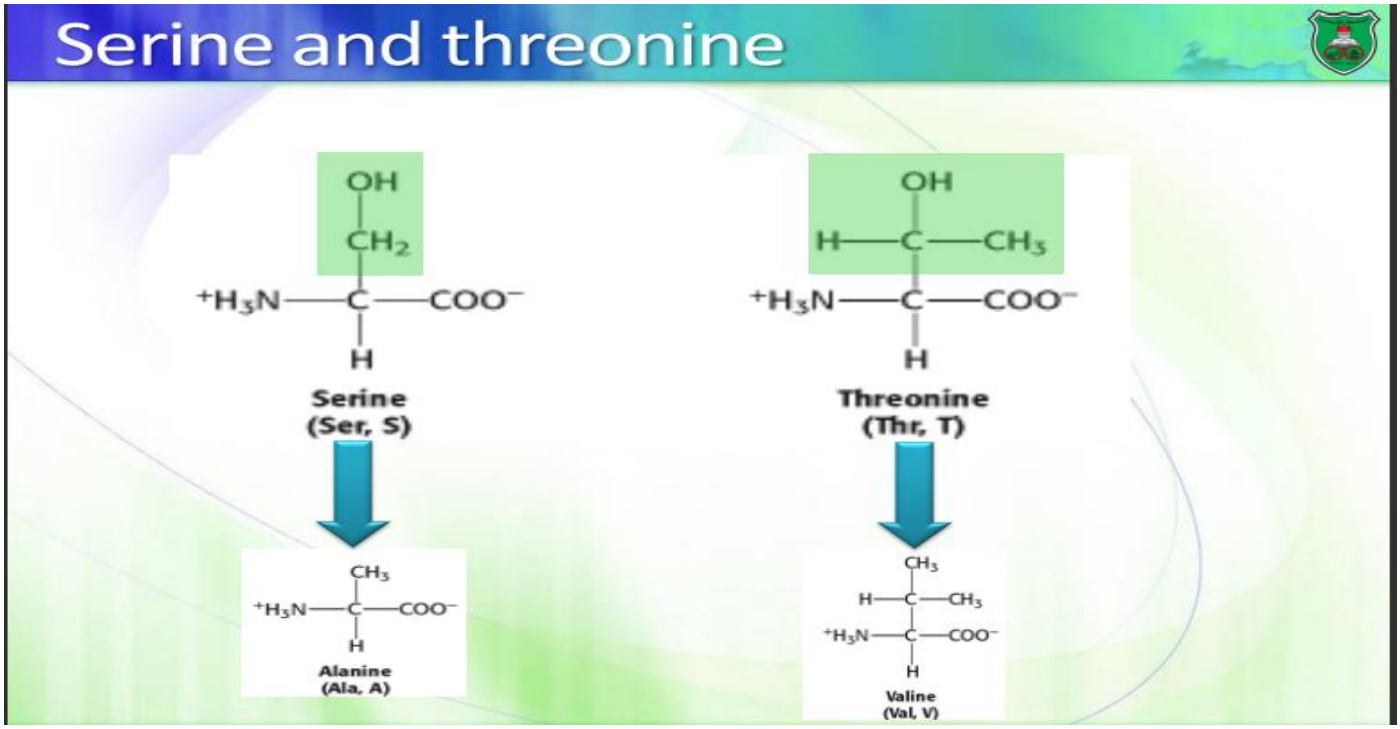
Proline

Abbreviation :Pro

R group : starting from alpha carbon (c-c-c) .Carbon no.3 connection with amino group with the backbone (the shared groups (amino group , carboxyl , hydrogen)) .As a result , 1*its name become imino acid

2* amine group make connection with carbon no.1 &2 , therefor consider it secondary amine.

Neutral :



Serine

Abbreviation: Ser

(like Alanine ,instead of methyl group → hydroxyl group)

R group : OH + one carbon

Threonine

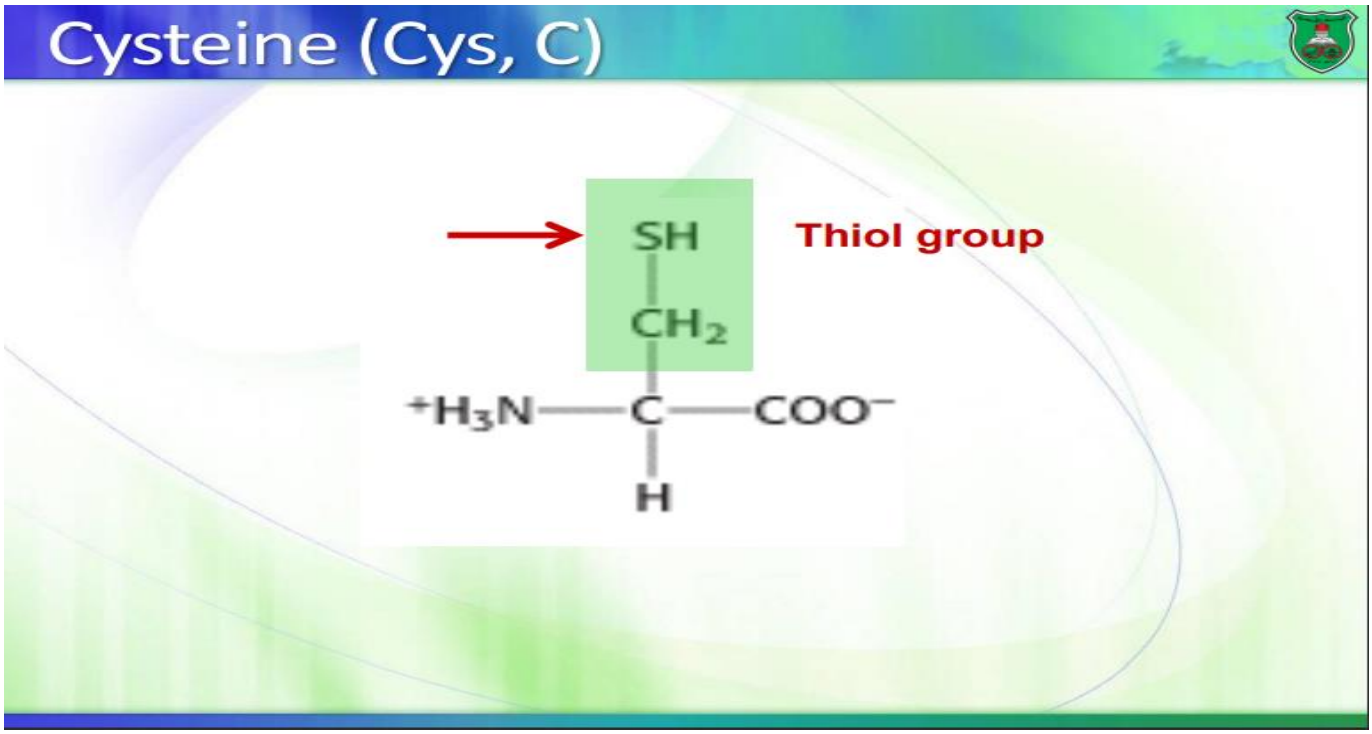
Abbreviation: Thr

R group : OH + two carbon +Hydrogen

(like Serine ,but it contains 2 carbons)

(like Valine ,instead of methyl group → hydroxyl group)

This give us information how can we make non-essential amino acids from essential amino acid)



Cysteine :

Abbreviation :Cys

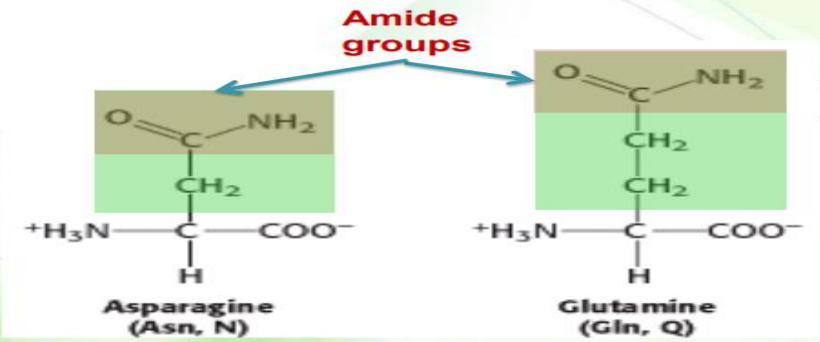
R group : one carbon + SH (Polar group)→ making amino acid active (specifically in oxidation –reduction reactions)

Thiol group is oxidized and it loss hydrogen and connect one cysteine to another cysteine by disulfide bridges .

(cysteine ----cysteine)→ cystine

Disulfide bridge

Asparagine and glutamine



Asparagine

Abbreviation : Asn→(amide group)

R group : one carbon+ amide group

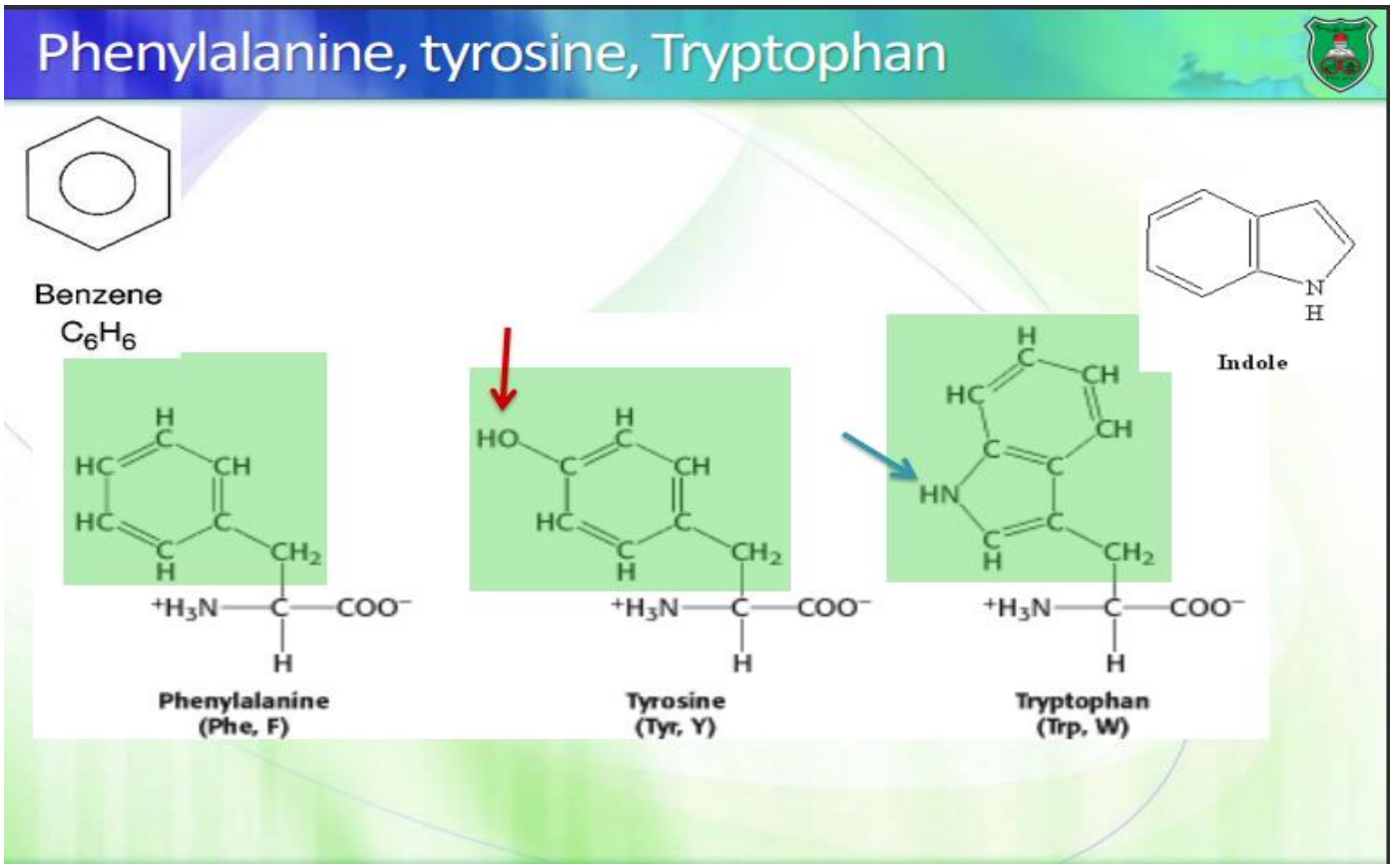
Glutamine

Abbreviation : Gln

R group : two carbon+ amide group

Aromatic amino acids

In some amino acids , they are distinguished by the benzene ring .



Phenylalanine (non-polar)

Abbreviation : Phe

R group : one carbon +benzene ring

Tyrosine (polar & charged)

Abbreviation : Tyr

R group : one carbon +benzene ring+OH

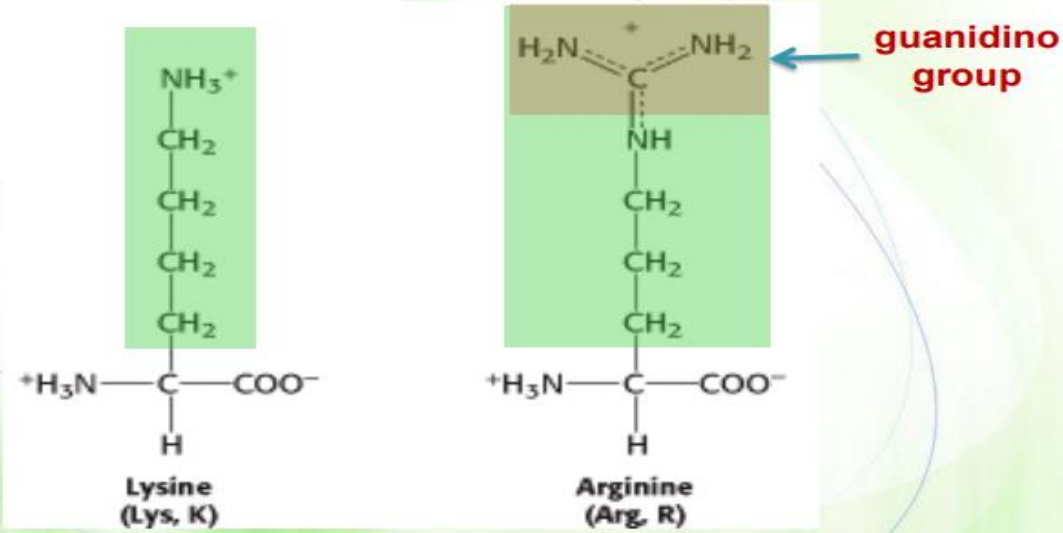
Tryptophan (bulky amino acid & non-polar)

Abbreviation : Trp

R group : one carbon +benzene ring fused with a five carbon ring (Indole)

Positively-charged amino acids (Basic amino acids)

Lysine and arginine



Lysine

Abbreviation: Lys

R group : (4 carbon + NH_3^+(amino group→ acceptor proton → positive charge))

Arginine

Abbreviation: Arg

R group : (3 carbon + NH (amino group)+guanidino group)

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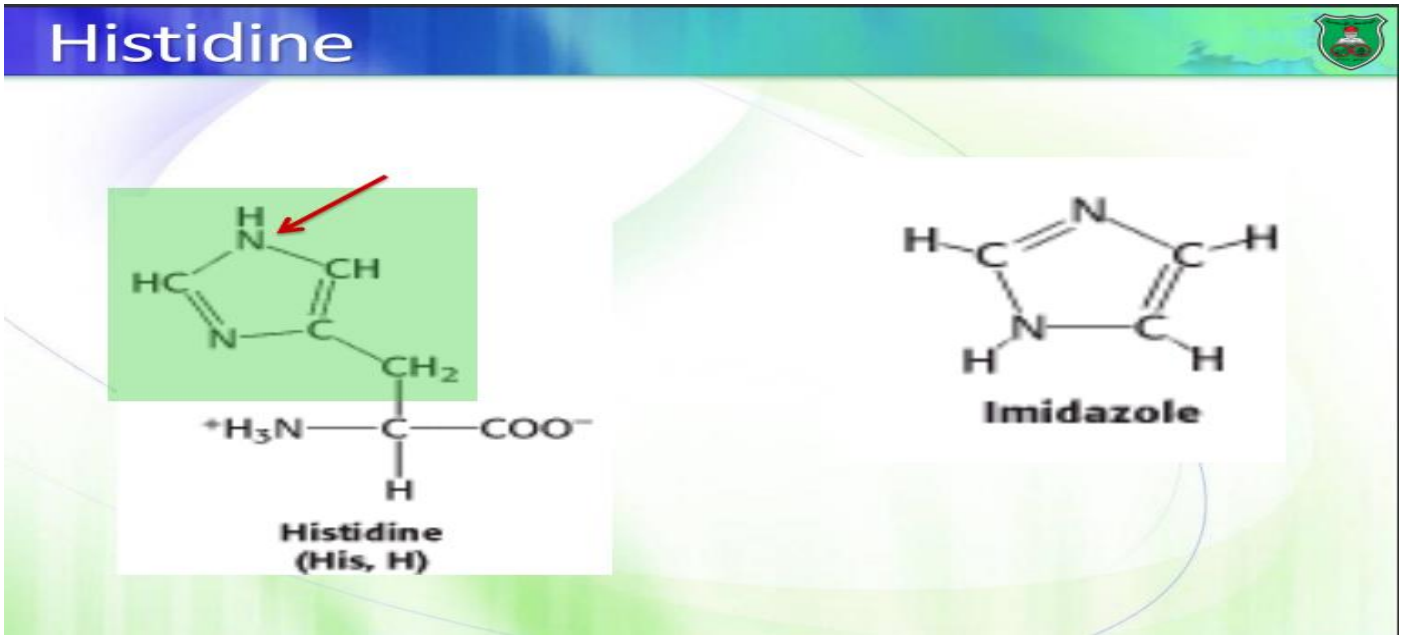
pKa of Lys & Arg is very higher .



Histidine

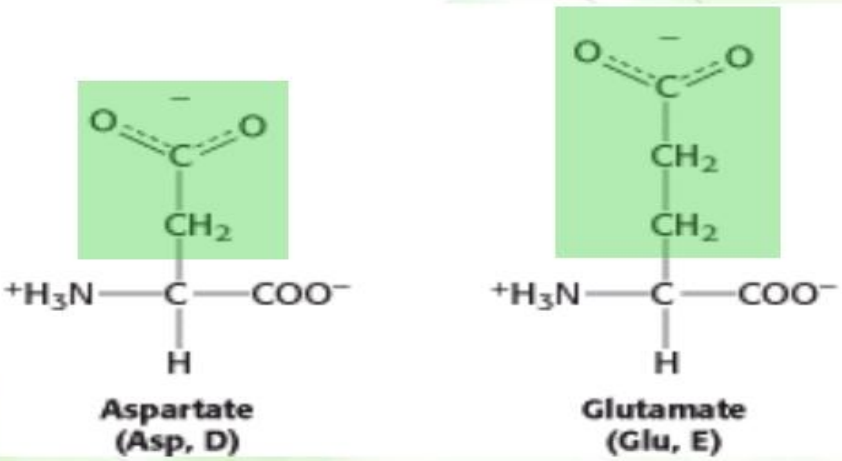
Abbreviation: His

R group : (one carbon+ imidazole ring (containing 2N)

pKa of Histidine is lower , close to physiological pH (between two cases ; protonation & deprotonating)

Negatively-charged amino acids (Acidic amino acids)

Aspartic acid and glutamic acid



Aspartate (loss proton)

Abbreviation: Asp

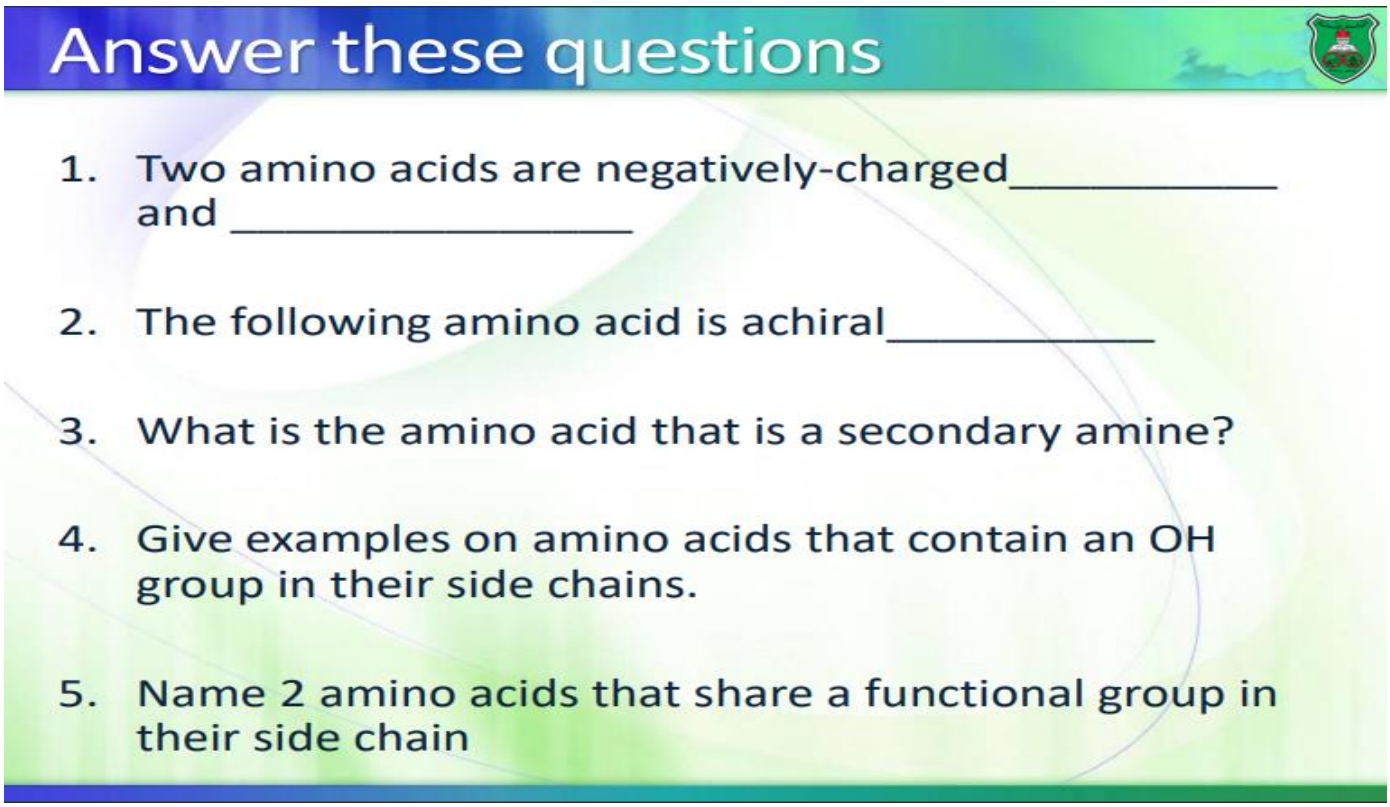
R group : (one carbon + carboxyl group)

Glutamate (loss proton)

Abbreviation: Glu

R group : (two carbons + carboxyl group)

pKa of Glu & Asp is very lower (about 3). As a result , they will always be negatively charged .



1*Asp & Glu

Positively charged (Lys & Arg)

2*Gly 3*Pro

Q:

***Give examples on amino acids that share the same functional group ??**

OH →Ser, Thr , Tyr

Aromatic → Phe, Tyr , Trp

Carboxyl → Glu, Asp

Amide → Asn , Glu

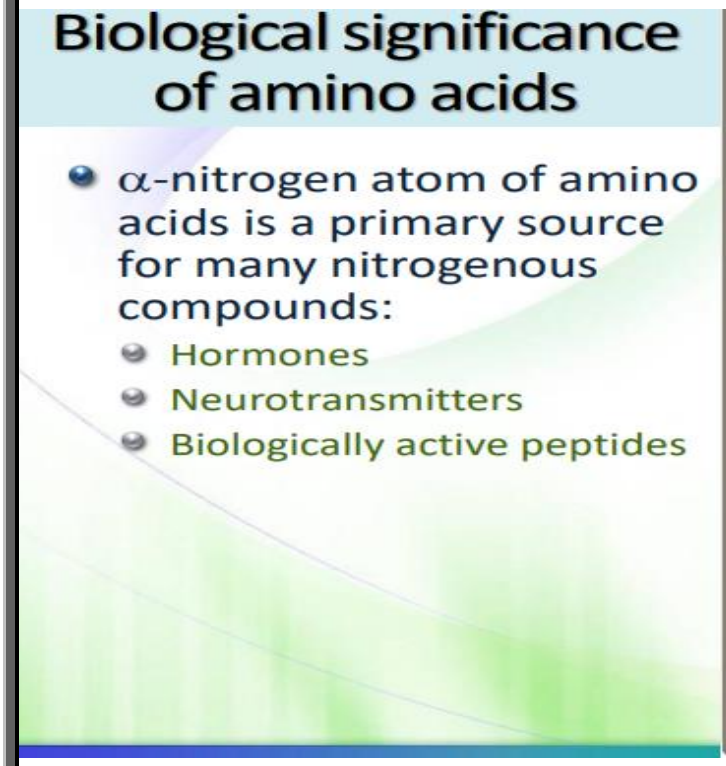
Sulfur →Cys, Met

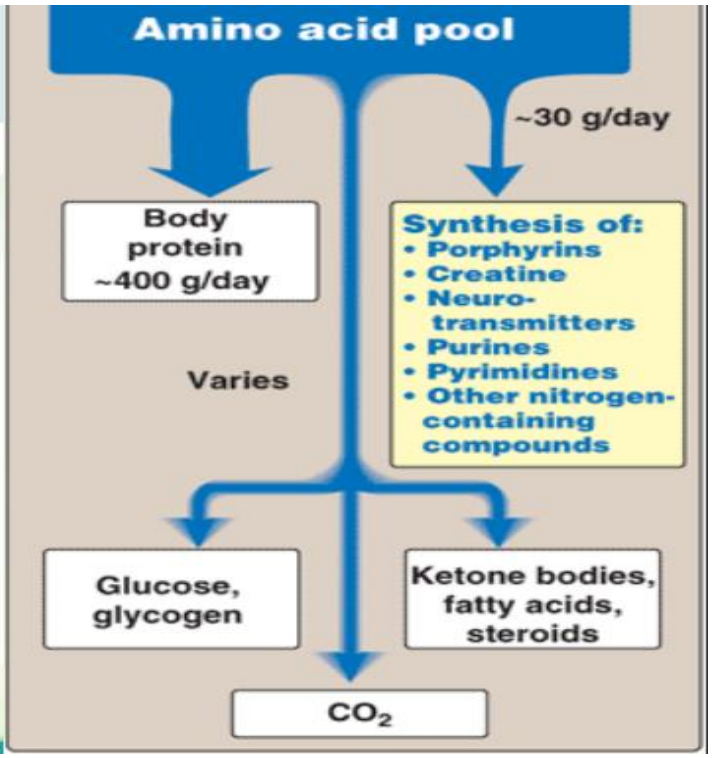
Amino group → Gly ,Arg, His

* the bulkiest amino acid→ Trp

Amino group is acting in nitrogenous balance in our bodies , can obtained from it many molecules as : ammonia which is very toxic so we should convert it into other compounds that are less toxic.

Amino acid could be directly used in forming other molecules , or firstly degraded (releasing ammonia) .





1. enter in the structure of:

a) Body peptides and proteins: e.g. plasma proteins, tissue proteins, enzymes, etc.

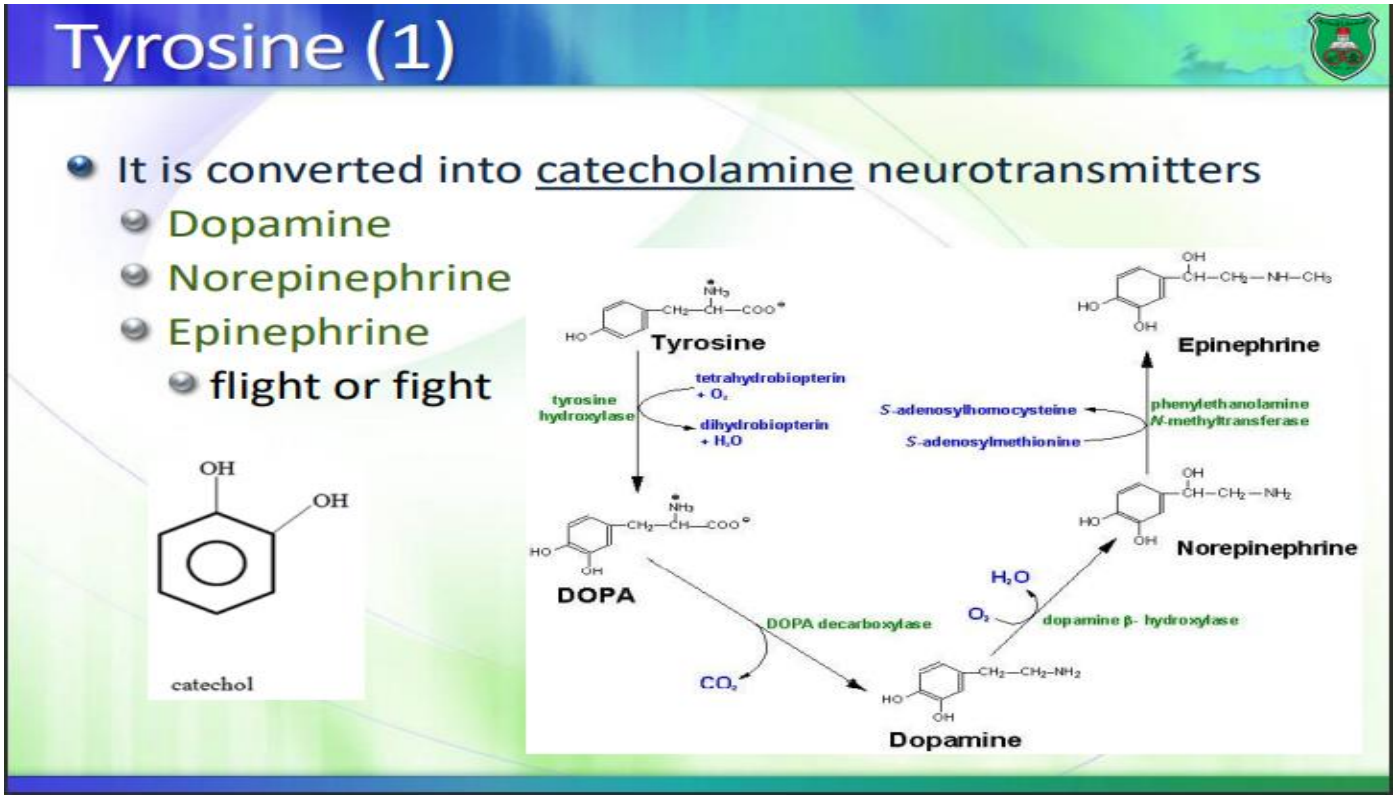
b) Hormone: some hormones are amino acid derivatives e.g. thyroxin.

c) Amines: Some amino acid gives corresponding amines by decarboxylation e.g. histidine gives histamine which is vasodilator

2. Neurotransmitters: Some amino acids as glycine and glutamate act as N.T

3. Detoxication: Some amino acids are used in detoxication reactions

We will take some examples of these modified amino acid:



Tyrosine

It is converted into catecholamine (catechol : benzene with 2 OH on the adjacent carbon) neurotransmitters:

-Dopamine

-Norepinephrine(neurotransmitter & hormone)

-Epinephrine(hormone)

} **are secreted from adrenal glands**

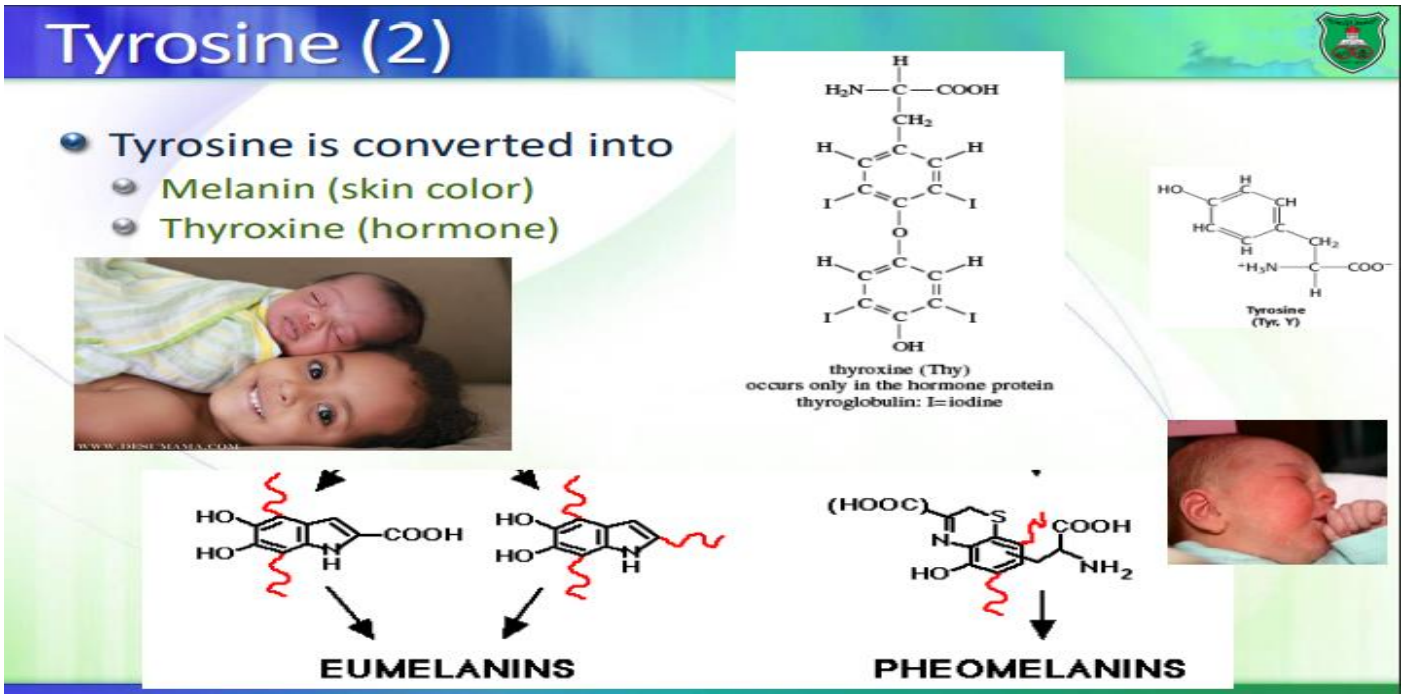
***Tyrosine* get hydroxylation (add OH group)**

into *DOPA* , it get decarboxylation (loss of carboxyl group) we get *Dopamine* .

Dopamine also get hydroxylation (add OH group)

then we have *Norepinephrine* >>>>> *Epinephrine*

by methylation reaction.



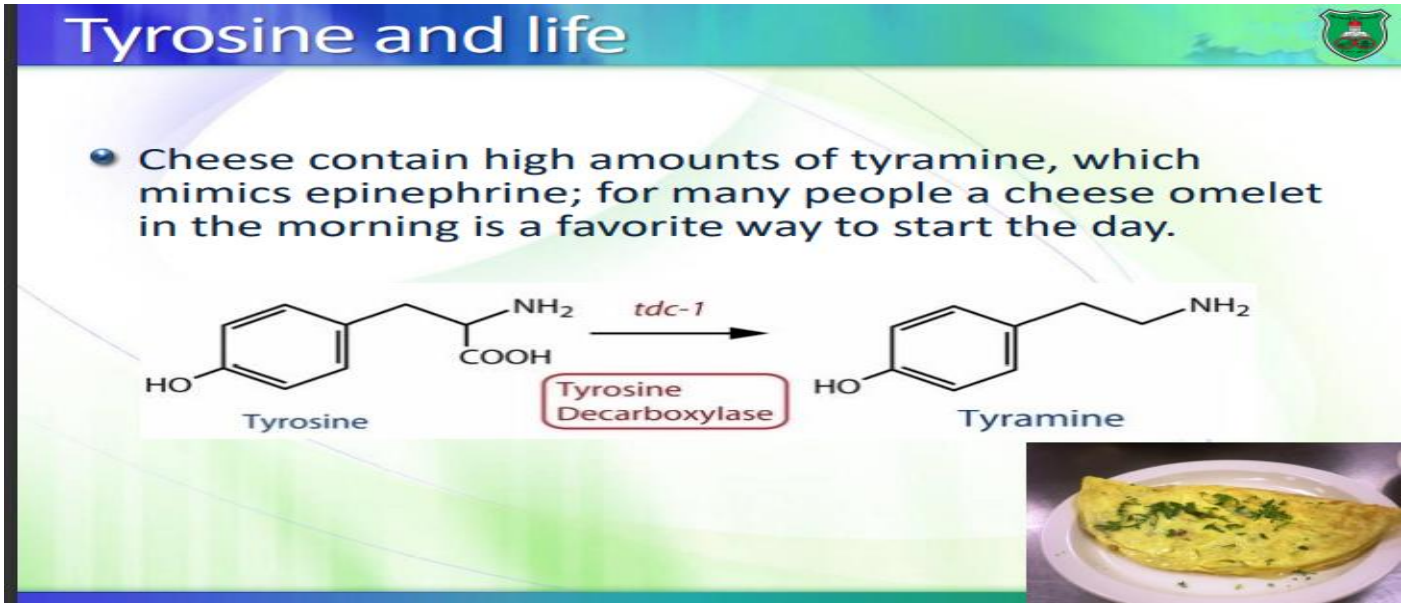
Tyrosine also converted into :

***Melanin (skin colour) .**

There are two types of Melanin : EU which is present in the majority of us by relative different concentration. And PHEO that we find it in " red head " people.

***Thyroxin hormone(2 benzene rings + OH +2I on each ring)**

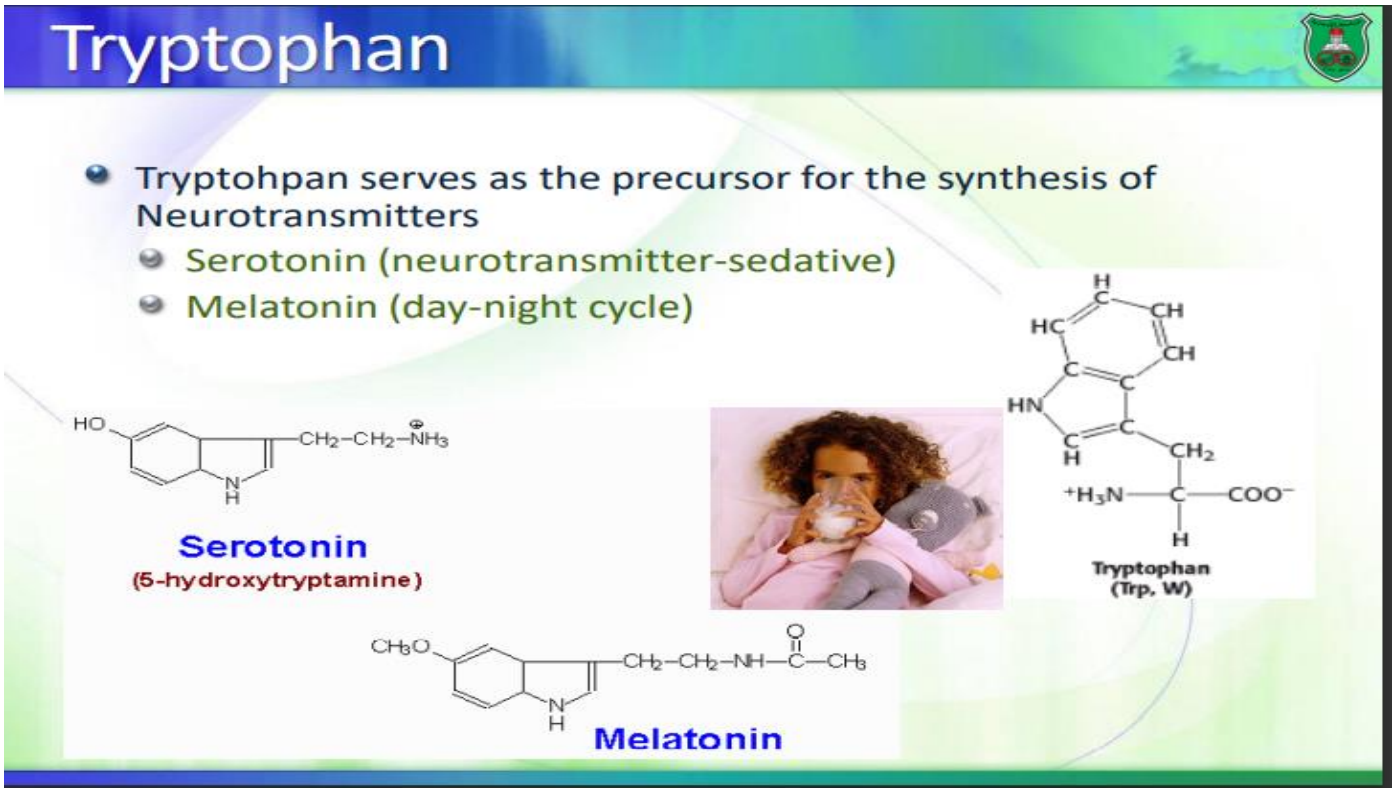
Function : regulates metabolism



Tyrosine→ (2carboxyl groups + amino group)

Tyrosine – carboxyl group → Tyramine (found in the cheese

*Function : stimulation like epinephrine



Tryptophan(bulkiest structure)

Tryptophan serves as the precursor for the synthesis of Neurotransmitters:

The molecules can we obtained from modifying Try:

*Serotonin(neurotransmitter-sedative)

By its name(5-hydroxytryptamine), we can see the changes that happens to Try.

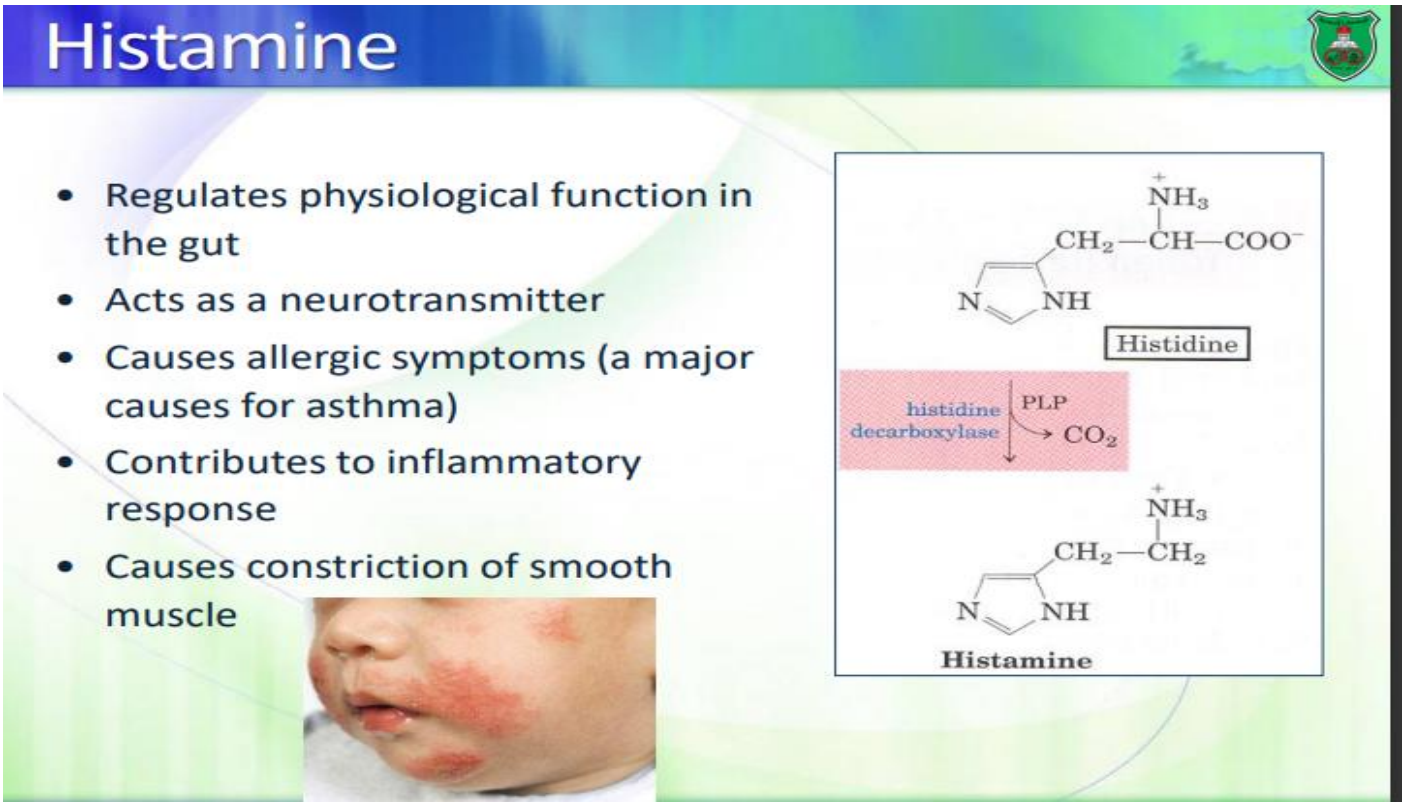
By modifying, we loss a carboxyl group (convert it to amine) and we add a hydroxyl group to the ring.

*Melatonin (day-night cycle)

It is secreted from pineal gland to regulate the sleeping process, it gives the body feeling of darkness so it should go to sleep.

It may distribute when travel to other places with huge different time , either you take a drug to moderate the concentration of it or you take a few weeks to adapt the new method of life.

*Serotonin → melatonin (CH_3O instead OH , adding carboxyl group)



Histamine is secreted from blood vessel cells (Histidine loss carboxyl group)→ allergic mediator .

Histamine as neurotransmitter that mediates allergic symptoms that happens in the body .

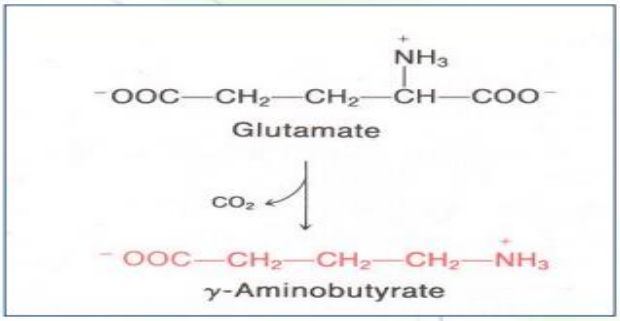
Function :construction of the smooth muscles (vasodilation →edema)

Glutamate

- Is a precursor of γ-aminobutyric acid (GABA)
- **Inhibitory neurotransmitter (CNS) that reduces neuronal excitability.**

GABA is synthesized in brain because it does not cross the BBB.

GABA have relaxing, anti-anxiety, and anti-convulsive effects.



Glutamate(acidic amino acid)→ anti-anxiety and anti-convulsive

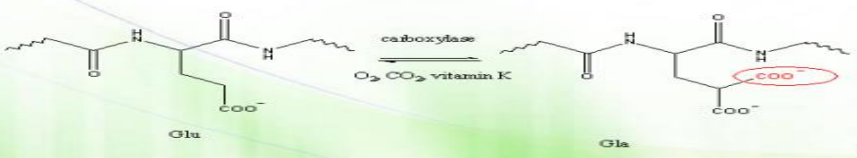
It is a precursor of *γ-amino butyric acid* (GABA)

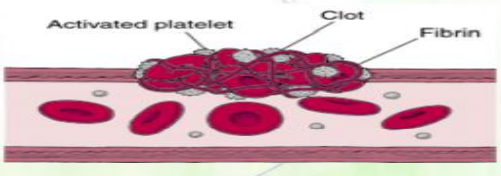
which is an inhibitory neurotransmitters(relaxation) of CNS, where is synthesized in brain because it does not cross the BBB (blood brain barrier),and use it there.

***In modifying process*, the carboxyl group from the backbone is removed so we get the amine form.**

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

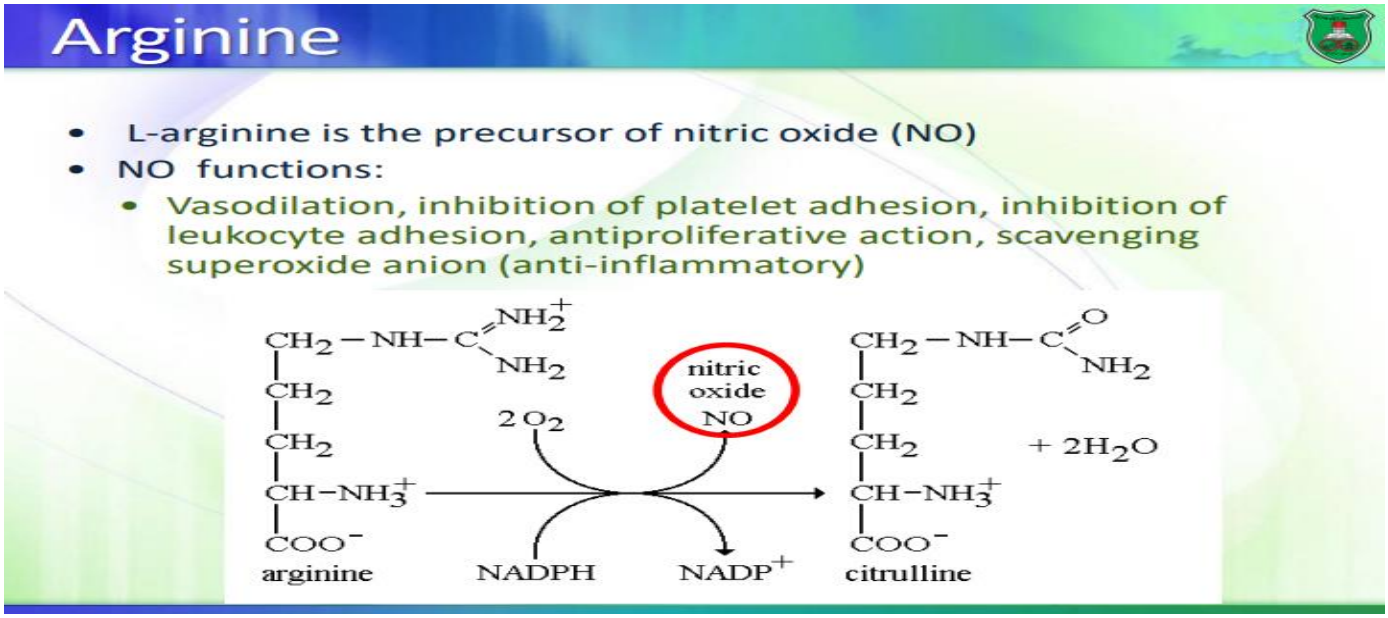




Production of γ-carboxyglutamate (Gal)

The glutamate residues of some clotting factors are carboxylation (adding a COO^-) to form γ-carboxyglutamate (Gla) residues that have high affinity sites for calcium.

When the glutamate get carboxylation , more negative charge it will have .So the reaction with Ca^{+2} would be more stable and stronger which is very important in clotting.



Arginine

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

Although Nitric oxide is a small , gaseous molecule that functions in chemical signalling , it has toxicity in the body.

Since it's small and gas, it can diffuse through the membrane not like other neurotransmitters.

Function:(as signalling molecule)

1-Vasodilation

2-Inhibition of platelet adhesion

3-inhibition of leukocyte adhesion

4-anti-proliferative action (inhibit cell growth)

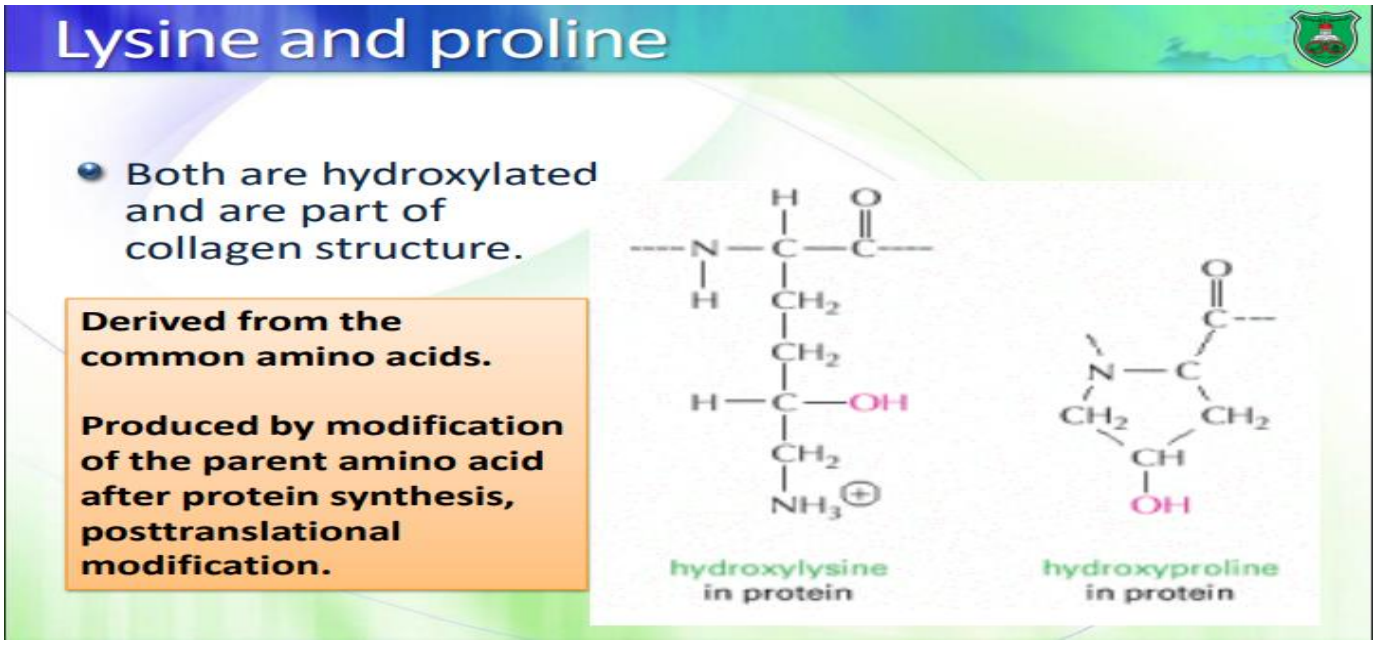
5- scavenging superoxide anion(anti-inflammatory)

*Superoxide is produced by immune system to kill microorganisms, NO is superoxide scavenger this protect the normal cell from damage.

*scavenging of superoxide ions→reacting with them →forming reactive oxygen-nitrogen species

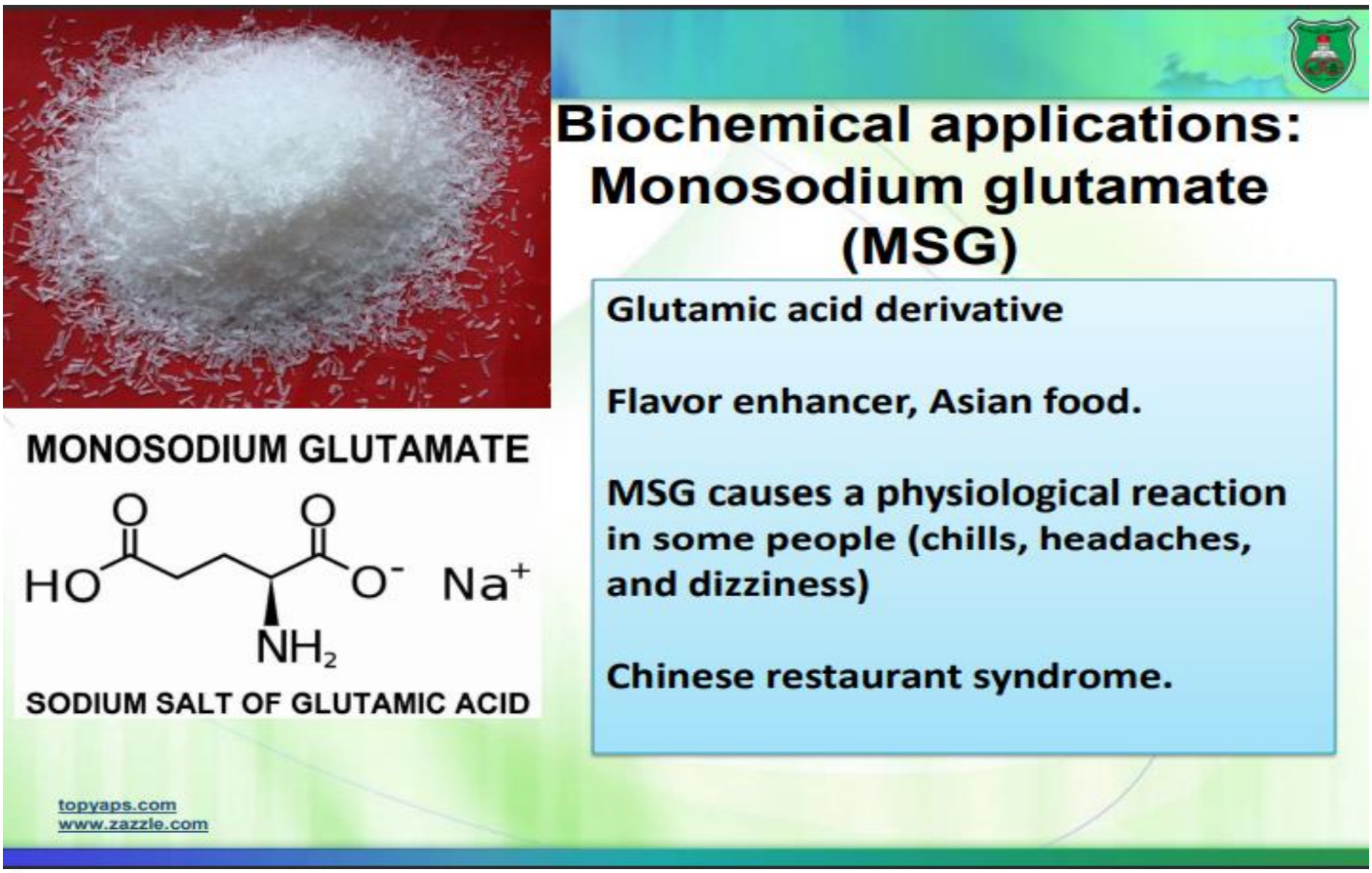
Bad effect: reduce the killing of microorganisms.

*Arginine reacts with oxygen and nitrogen → NO (exited molecule)



Lysine and proline(modified amino acids)

Adding OH group to *Pro, Lys* as one of modifying methods to it.Both are **hydroxylation** and are part of collagen structure (very strong .To increase its strength , we make cross linking by using molecules ability to make many hydrogen bonds) ,produced by modification of the parent amino acid after protein synthesis posttranslational modification.



Biochemical applications:

We have many applications of modifying amino acids as Heme group where we find it in hemoglobin and myoglobin.

Mono sodium glutamate **(MSG)**

Amino acid: **glutamate**

Modification: reacts the carboxyl group (salt of the a.a) of the backbone with Na .

Effect: Flavour enhancer

* Usually used in Asian food.

Symptoms: chills, Headaches, and dizziness

Dr.said that these symptoms may appear in different strength from one to another.

Disease : Chinese restaurant syndrome.

*MSG has non-healthy effect whether you feel it or not , so take care.

Q:

1*One of the amino acids listed below is not basic:

a-Arginine b- Histidine (c-) Glutamine d- Lysine

2*All the following amino acids are neutral, EXCEPT:

(a-) Aspartic acid b- Tyrosine c- Glycine d- Threonine

3.Guanido group is present in:

(a-) Arginine b- Tryptophan c- Histidine d- Proline

4.Indole ring is present in:

a- Arginine (b-) Tryptophan c- Histidine d – Proline

5. All the following are branched chain amino acids, EXCEPT:

a- Valine b- Leucine c- Isoleucine (d-) Threonine

6.The following amino acids have hydrophobic side chains, EXCEPT:

a- Tyrosine b- Alanine c- Leucine d- Valine

7.Imidazole ring is present in:

a- Arginine b- Tryptophan c- Histidine d- Proline

8. Which of the following amino acids has a non-polar side chain?

a- Serine b-Valine c- Asparagine d- Threonine

9.The following are aliphatic amino acids:

a- Alanine, valine, and leucine.

b-Glycine, leucine, and serine.

c- Threonine, serine, and glutamic acid.

d. Phenylalanine, tryptophan, and histidine.

10. All the following are heterocyclic amino acids, EXCEPT:

a- Histidine b- Phenylalanine

c- Tryptophan d- Proline.

11. The following are basic amino acids:

a- Tryptophan and phenylalanine .

b-Alanine and glycine.

c- Histidine, lysine, arginine.

d- Valine, leucine, and isoleucine

NO :FREE RADICALS are unstable substances produced during cell metabolism

Scavenging means that superoxide protects the cell from the damage caused by free radicals

-Superoxide is produced by immune system to kill microorganisms. It is produced in large amounts in phagocytes by NADPH Oxidase enzyme

NO reduce releasing of superoxide anion.

*So it has bad effect >>> reduce killing microorganism (anti – inflammatory)

Good effect >>> reduce killing the normal cells.

Histamine is allergic , it involves in smooth muscles contraction of bronchi in allergic reactions resulting emergency case called *anaphylactic shock* that cause death in less than a minute without medical intervention .how ?

→Histamine cause dilation of small blood vessels (venues, arteriole , capillaries) this make these vessels filled with blood and decrease blood in the large vessels especially the important (aorta) causing shock.

it also increases blood vessel permeability causing edema , it decrease amount of blood inside blood vessels and decrease blood pressure.