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Doctor 2022 - medicine - MU

biochemistry sheet

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Nutritional Classification depends on the individual's nutrition

Standard amino acids are divided into three types according to the classification based on nutrition and body requirement:

1-Essential amino acids

2-Non-essential amino acids

3-Conditionally essential amino acids

Essential Amino Acids

- **Cannot be produced by the body**
- **Must be supplied through diet**
- **8 amino acids: valine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine and tryptophan**

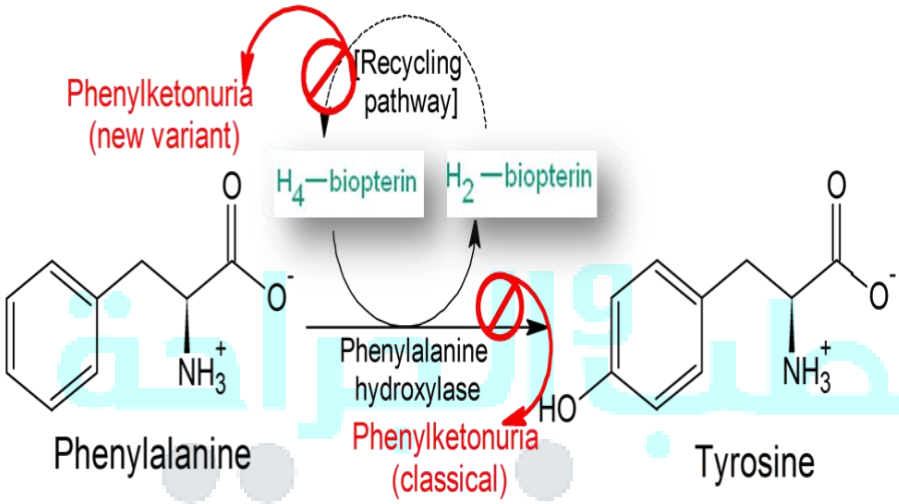
Non-essential Amino Acids

- **Can be synthesized by the body**
- **9 amino acids: Glycine, alanine, serine, cysteine, aspartic acid, glutamic acid, asparagine, glutamine and proline**

Conditionally Essential Amino Acids

- **Synthesized in the body in insufficient amounts so should be supplied in diet (requirements are higher than production rate)**
- **Essential only in certain cases: children, pregnant and lactating women**
- **3 amino acids : Histidine, arginine and tyrosine. For example, arginine and histidine are growth promoting factors and during growth are not synthesized in sufficient amounts so essential in growing children, pregnancy and lactation**
- **In normal adult tyrosine is non-essential because it gets made in the body but it can be deficient when someone has PKU**

- **When we eat something that has phenylalanine, an enzyme inside our body that is called phenylalanine hydroxylase adds a hydroxyl group to phenylalanine and turns this amino acid to tyrosine**
- **On the other hand, tyrosine is produced from phenylalanine (essential amino acid), so if the diet is deficient in phenylalanine or if an individual is congenitally deficient in an enzyme required to convert phenylalanine to tyrosine (the inherited/ inborn /congenital disease phenylketonuria PKU), tyrosine will be required as well.**



Phenylketonuria

The accumulated phenylalanine is toxic to brain and can lead to intellectual disability and mental disorders.

Newborn screening program

Amino Acid Derivatives

- **The non-standard/ non-proteinogenic amino acids are either not found in proteins (e.g. carnitine and GABA) or are not produced directly by standard cellular machinery (e.g. hydroxyproline)**
- **Most of them doesn't have protein role like GABA**
- **Some has protein role but in their own way like → post translation modification (to make the protein functional)**

- **When an amino acid gets a post translational modification and the name of the amino acid turns to non-protein genic /non standard**

  - Non-standard amino acids that are found in proteins are formed by post-translational modification. These modifications are often essential for the function or regulation of a protein:

1-The carboxylation of glutamate occurring in proteins involved in blood-clotting cascade allows for better binding of calcium cations

2-The hydroxylation of proline in collagen protein is critical for maintaining connective tissues

3-The phosphorylation of an OH group on serine, threonine or tyrosine introduces a large group with a negative charge that can alter the activity of a protein or enzyme

4-Glycosylation (addition of sugar moieties) stabilizes protein conformation and direct selected proteins to various intracellular organelles (targeting process)

Non-protein Functions

- Some non-standard amino acids are not found in proteins. Examples include the neurotransmitter gamma-aminobutyric acid (GABA)
- Non-standard amino acids often occur as intermediates in the metabolic pathways for standard amino acids (e.g. ornithine and citrulline occur in the urea cycle which is part of amino acid catabolism)
- Many amino acids are used to synthesize other molecules called amino acid derivatives, for examples:

1-Tryptophan is a precursor of the neurotransmitter serotonin

2-Tyrosine is a precursor of the thyroxin (thyroid hormone) and the catecholamine neurotransmitters like dopamine, adrenaline and noradrenaline

3-The local mediator histamine which is released during allergy is derived from the decarboxylation of histidine

4--aminobutyric acid (GABA) is the major inhibitory NT in brain. It is nonstandard amino acid derived from glutamate.

Non-proteinogenic Non-standard

- **Nonproteinogenic nonstandard amino acids are derivatives of standard amino acids:**

1-As intermediates during metabolism

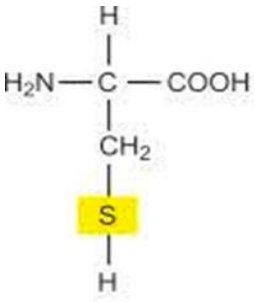
2-Post translational modification process

3-Other enzymatic reactions

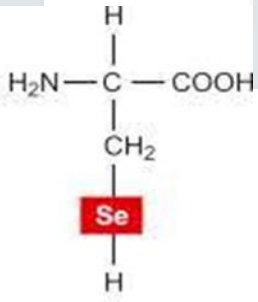
- **Nonproteinogenic nonstandard amino acids may have protein role or nonprotein role (they are active by themselves and have a function**

Proteinogenic Non-standard

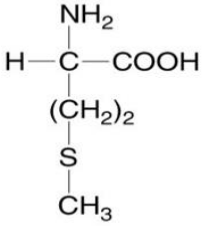
Proteinogenic nonstandard amino acids are also derivatives of standard amino acids



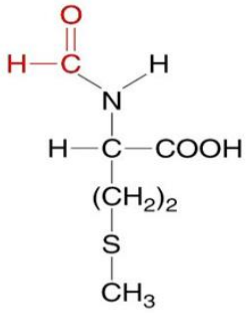
CYSTEINE



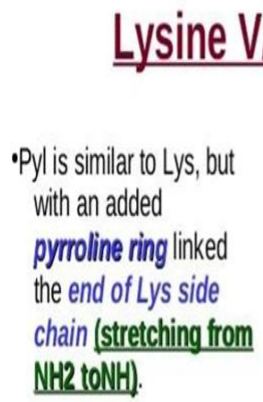
SELENOCYSTEINE



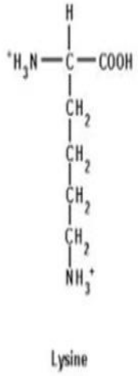
Methionine



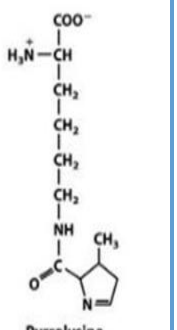
N-Formylmethionine



Has (-)(+)



lysine

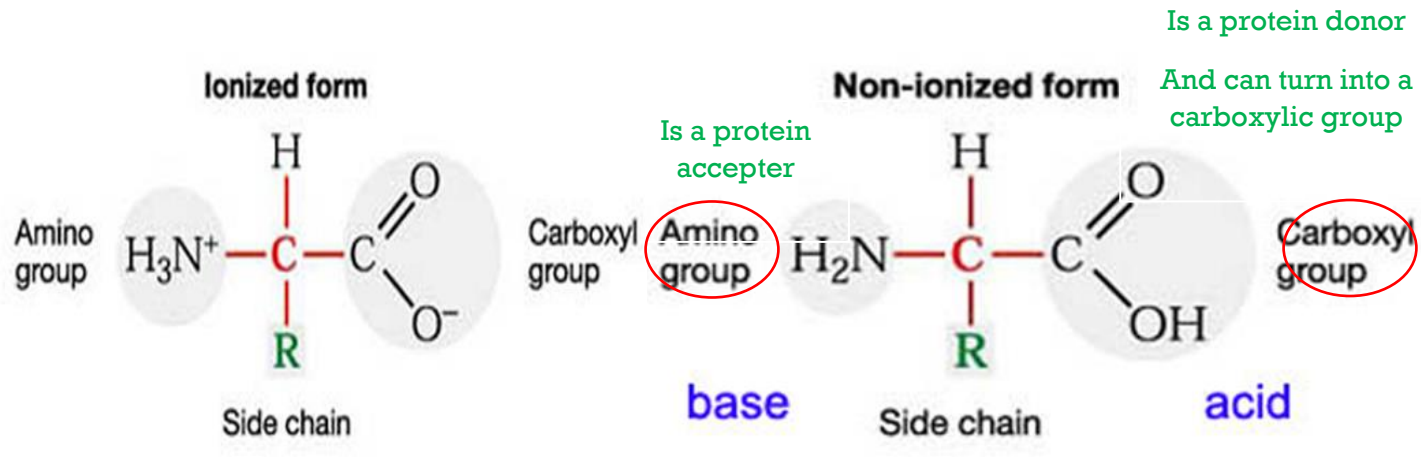


pyro lysine

Amphoteric property of Amino Acids

Amino acids are amphoteric molecules (ampholytes) having both acidic (-COOH) and basic (-NH2) groups

α-amino acids are ionized in aqueous solutions with the ionization state is dependent on the pH value



which group is ionized depends upon the pH

- **Ampholytes : group that has bases and acids (standard amino acid that have two functional groups)**
- **We call the amino acid amphoteric molecules**
- **It acts as both basic or acid depending on the PH**

Ionization of Amino Acids

At very low pH values, these groups are fully protonated and at very high pH values, these groups are deprotonated. At intermediate pH, both are ionized

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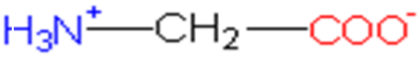
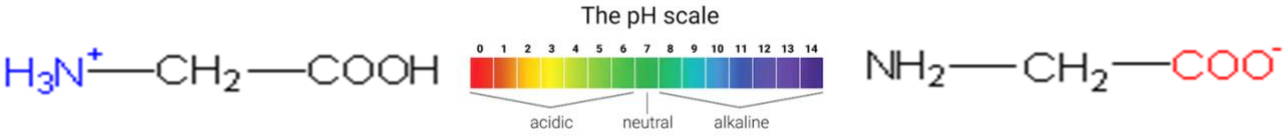
- Both groups are ionized
- NH3+ → protonated
- We increase the ph by adding a strong base



Intermediate pH

- net charge =zero (zwitterion)
- COO- is de protonated → H+ lowers

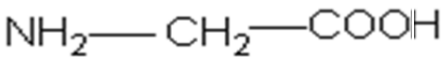


Low pH

- Net charge =+1 (cationic)
- Both functional groups are protonated

High pH

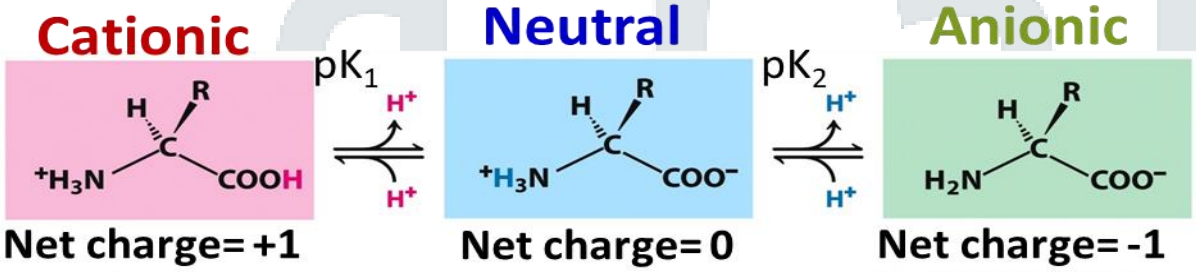
- Amino group loses (H+)
- Net charge = -1 (anionic)

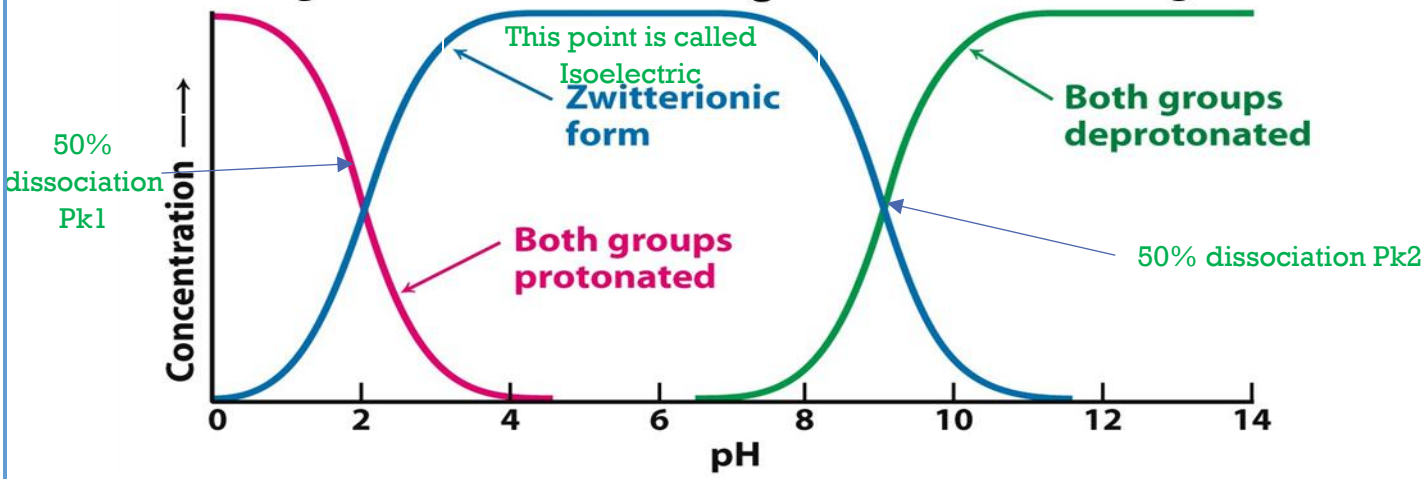


State of glycine ionization in an acidic and an alkaline solution

Amino Acids as Zwitterions

Zwitterions (dipolar molecules) have charged —NH3+ and COO- groups (both groups are ionized). Zwitterion is neutral as it carries + and - charges





Isoelectric Point (pI)

Isoelectric point is the pH at which a particular molecule carries no net electrical charge (overall charge = zero) so no need for electrical charge

At pI, zwitterion is the dominant form of the amino acids

pI = average of pK's = ½ (pK1 + pK2)

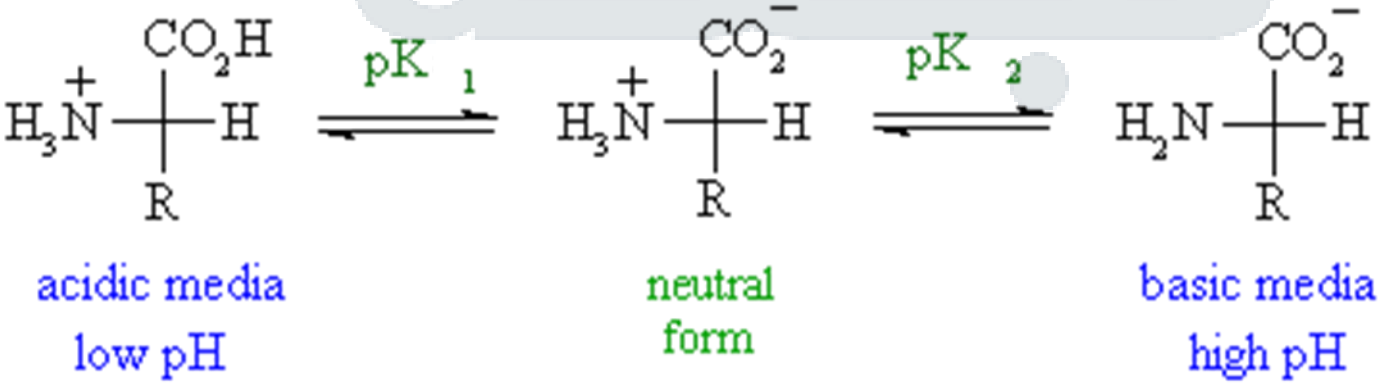
Note: pK = -log [K] where K is the dissociation constant of a weak acid or base

For example, the simplest amino acid glycine has pK1 = 2.34 and pK2 = 9.6

pI = ½ (pK1 + pK2)

= ½ (2.34 + 9.6)

= 5.97

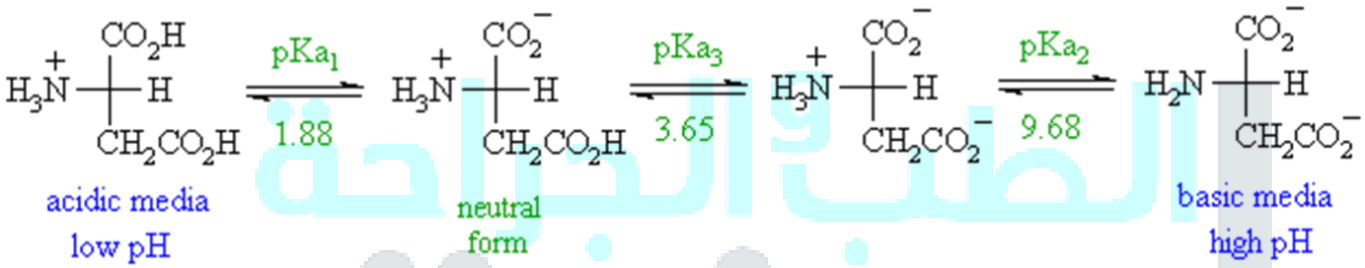


pI of Acidic and Basic Amino Acids

For the acidic and basic amino acids which contain an ionizable "R" group in their side chains, pI calculation is different from those with neutral side chains

1-Acidic side chain: zwitterion exists at more acidic conditions when the extra –ve has been neutralized

pI = ½ (pK1 + pK3)



For example, the aspartic acid which has pK1= 1.88, pK3 = 3.65 and pK2= 9.68

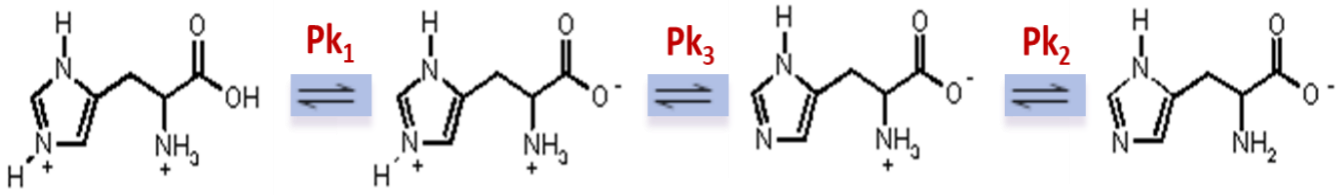
pI = ½ (pK1 + pK3)

= ½ (1.88 + 3.65)

= 2.77

2-Basic side chain: zwitterion exists at more basic conditions when the extra +ve has been neutralized

pI = ½ (pK2 + pK3)



For example, histidine which has pK2= 6.00, pK3 = 9.17

pI = ½ (pK2 + pK3)

= ½ (6.00 + 9.17)

= 7.59

pKa values of Amino Acids

The pK values for the α-carboxyl, α-amino groups and side chains

Amino acid	pK_1	pK_2	pK_R
Alanine	2.4	9.9	-
Arginine	1.8	9.0	12.5
Asparagine	2.1	8.7	-
Aspartate	2.0	9.9	3.9
Cysteine	1.9	10.7	8.4
Glutamate	2.1	9.5	4.1
Glutamine	2.2	9.1	-
Glycine	2.4	9.8	-
Histidine	1.8	9.3	6.0
Isoleucine	2.3	9.8	-

Amino acid	pK_1	pK_2	pK_R
Leucine	2.3	9.7	-
Lysine	2.2	9.1	10.5
Methionine	2.1	9.3	-
Phenylalanine	2.2	9.3	-
Proline	2.0	10.6	-
Serine	2.2	9.2	-
Threonine	2.1	9.1	-
Tyrosine	2.2	9.2	10.5
Tryptophan	2.5	9.4	-
Valine	2.3	9.7	-

يَا ولدِي، للَّيالي الثقيلةِ ربٌّ يُهيمن علىٰ المُعاناة، وللفرصِ المُقفلة ربٌّ بيدِهِ مَفاتيح الفرَج، وللأوقاتِ المرَّة دعاءٌ يهزُّ جذعَ المُستحيلات!
فقُل: إلهي، أعنَّا واسكُب الفضلَ علىٰ أفئدةٍ ضاقَت عليهَا المخارِج.
قُل: إلهي، إني فِي انتظارِ وعدِك ﴿وَنَجَّيْنَاهُ مِنَ الْغَمِّ﴾.
أنتَ المُهيمن علىٰ الزمَان والمَكان والأسبَاب، إليكَ سلَّمنا الأمرَ كلَّه.🕊️
- د. كِفاح أبُو هنُّود.