Protein

3rd Stage
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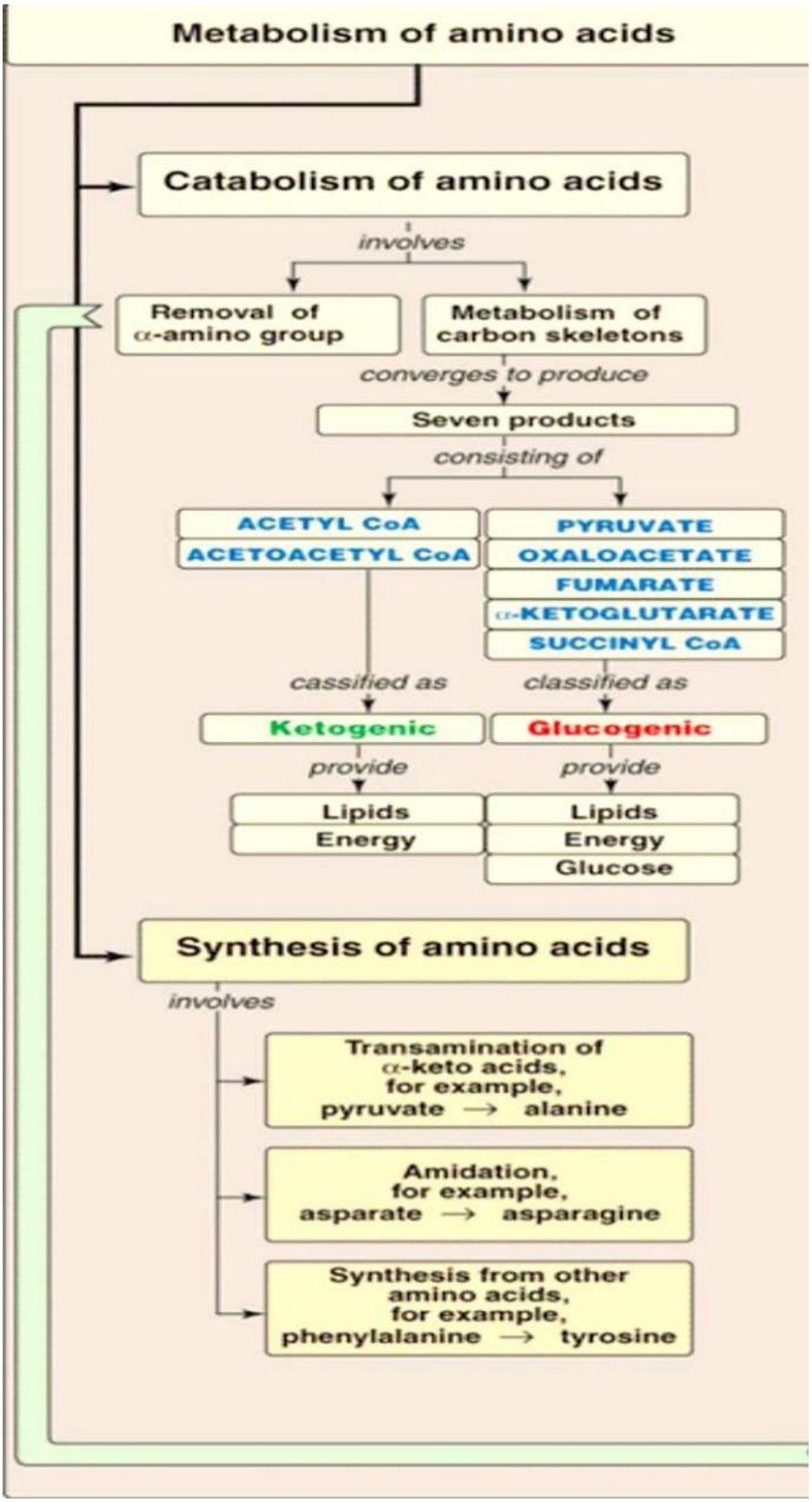
M.Sc. in Chemistry Sciences

Metabolism of Amino Acids

Catabolism of amino acids

- **Removal of α-amino acid**
- **Metabolism of carbon skeletons**


Metabolism of amino acids
Catabolism of amino acids
involves
Removal of α-amino group
Metabolism of carbon skeletons
converges to produce
Seven products
consisting of
ACETYL CoA
ACETOACETYL CoA
PYRUVATE
OXALOACETATE
FUMARATE
α-KETOGLUTARATE
SUCCINYL CoA
cassified as
classified as
Ketogenic
Glucogenic
provide
provide
Lipids
Energy
Lipids
Energy
Glucose
Synthesis of amino acids
involves
Transamination of α-keto acids, for example, pyruvate → alanine
Amidation, for example, asparate → asparagine
Synthesis from other amino acids, for example, phenylalanine → tyrosine

Removal of Nitrogen from Amino Acids

Removing the α-amino group is essential for producing energy from any amino acid, and is an obligatory step in the catabolism of all amino acids. Once removed, this nitrogen can be incorporated into other compounds or excreted, with the carbon skeletons being metabolized.

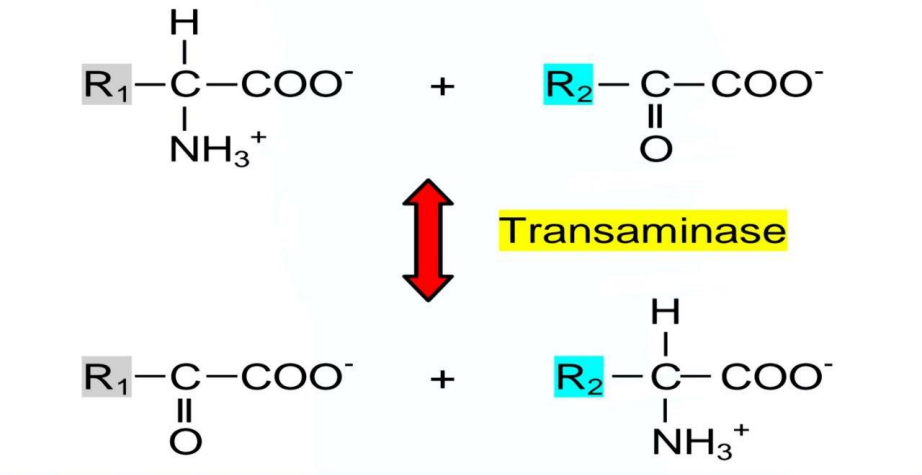
The first step in the catabolism of all amino acids achieved in three ways:

A. Transamination.

B. Deamination.

A. Transamination: It is the transfer of amino group from α-amino acid to α-ketoacid to form a new α-amino acid and a new α-ketoacid.

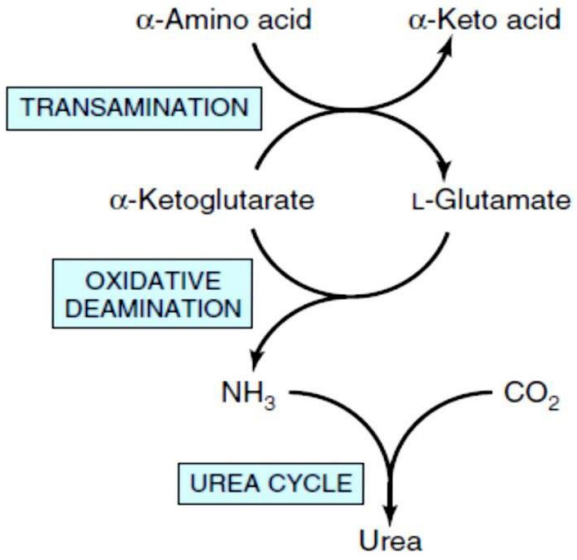
- Transamination reactions are carried out by Transaminases (Aminotransferases). (Figure 11)



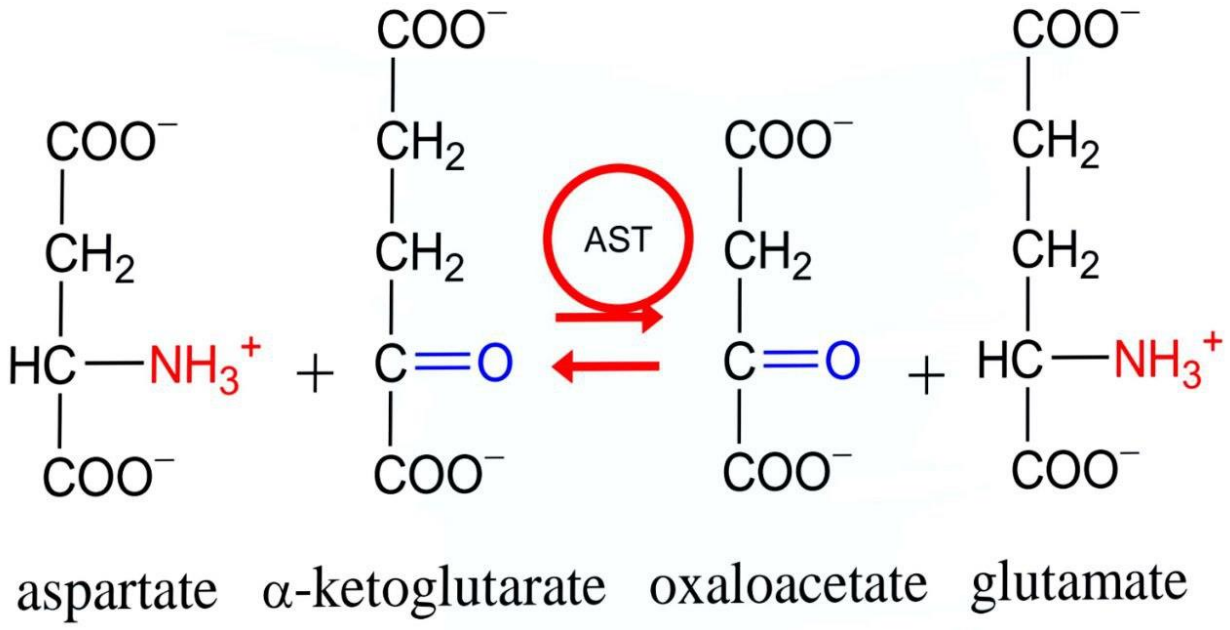
(Figure 11)

- Transaminases (aminotransferases) are present in cytoplasm and mitochondria of all tissues especially liver.
- Vitamin B6 (PLP) (pyridoxal phosphate) is essential for transamination reaction.
- For all amino acids except: (lysine, threonine, proline and hydroxyproline).

α-ketoglutaric acid can be accept amino group from all amino acids converting them to Glutamic acid, this is important because Glutamic acid is the only amino acid that undergoes oxidative deamination at an appreciable amount in liver by (L-glutamate dehydrogenase). (Figure 12)

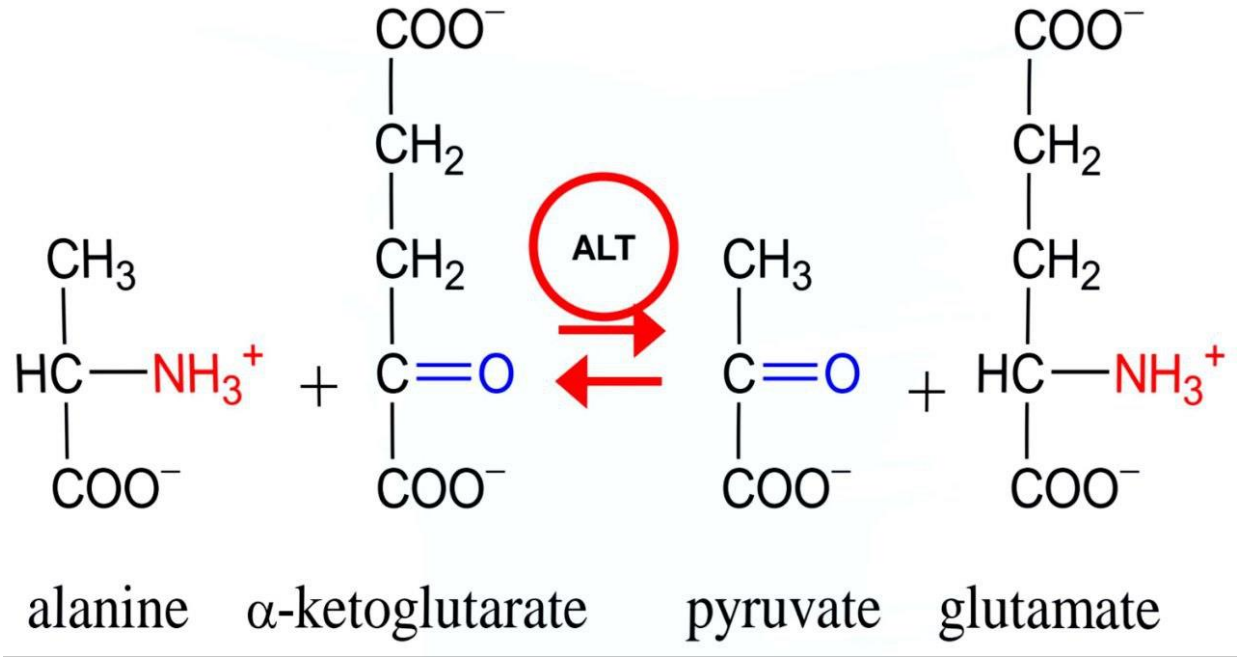


(Figure 12)



(Figure 13)

AST (Aspartate Amino Transferase)



(Figure 14)

ALT (Alanine Amino Transferase)

B. Deamination: It is the removal of amino group from amino acids in the form of ammonia (NH3).

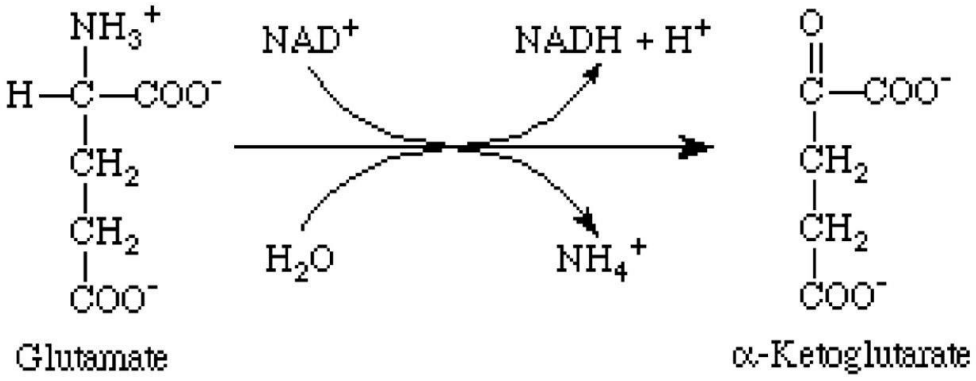
1) Oxidative deamination:

- **L-Glutamic dehydrogenase:**

- Site: mitochondria of liver, heart, kidney and muscle

-It needs NAD as coenzymes

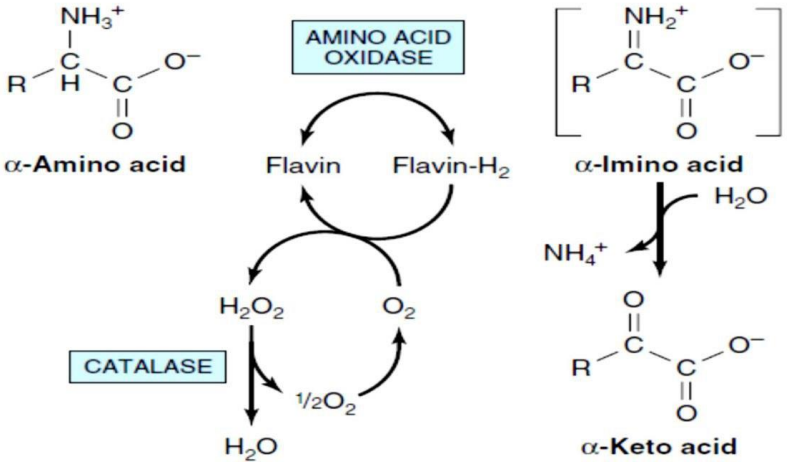
-It catalyzes the reversible oxidative deamination of Glutamic acid into α-ketoglutaric acid.



(Figure 15)

- **L- amino acid oxidases:**

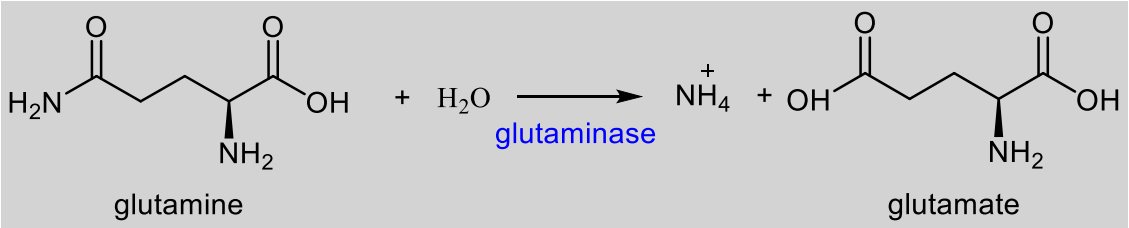
- They are flavoprotein dependent enzymes.



(Figure 16)

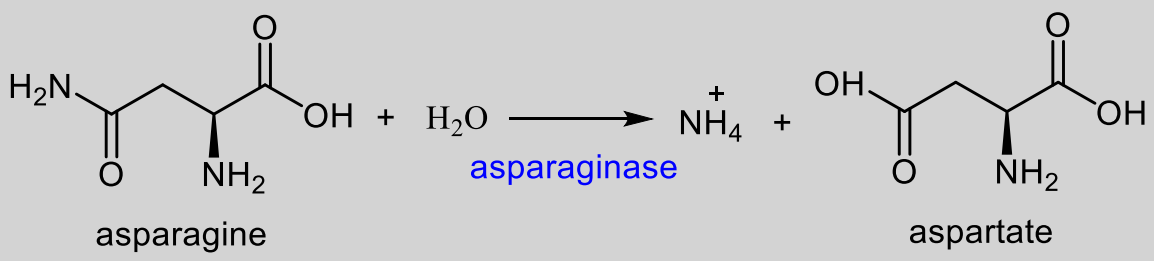
2) Non-Oxidative deamination (Hydrolytic deamination):

- **Glutaminase.**



(Figure 17)

- **Asparaginase.**



(Figure 18)

Ammonia is a toxic substance especially to the central nervous system, any ammonia formed in the peripheral tissue must be moved to the liver to be converted into urea.

Urea Formation

1. The first two reactions occur in mitochondria where other reactions occur in cytosol.
2. Six amino acids share in urea cycle: ornithine, citrulline, arginosuccinate, Aspartate. And Arginine.

STEPS

1. Formation of Carbamoyl phosphate:

a) This reaction occurs in mitochondria.

b) It needs CO_2 (a product of citric acid cycle), ammonia (a product of deamination of glutamate) and phosphate (from ATP).

c) This reaction is catalyzed by Carbamoyl phosphate synthase I. It needs magnesium (Mg) ions, manganese (Mn^{++}) and N-acetyl glutamate as activators.

d) 2 ATP molecules are used in this reaction, one to provide phosphate and the other to supply energy.

2. Formation of citrulline:

a) This reaction also occurs in mitochondria.

b) Carbamoyl phosphate reacts with ornithine, in the presence of ornithine transcarbamoylase enzyme producing citrulline.

c) Citrulline then passes to cytosol.

d) Ornithine is regenerated with each turn of urea cycle.

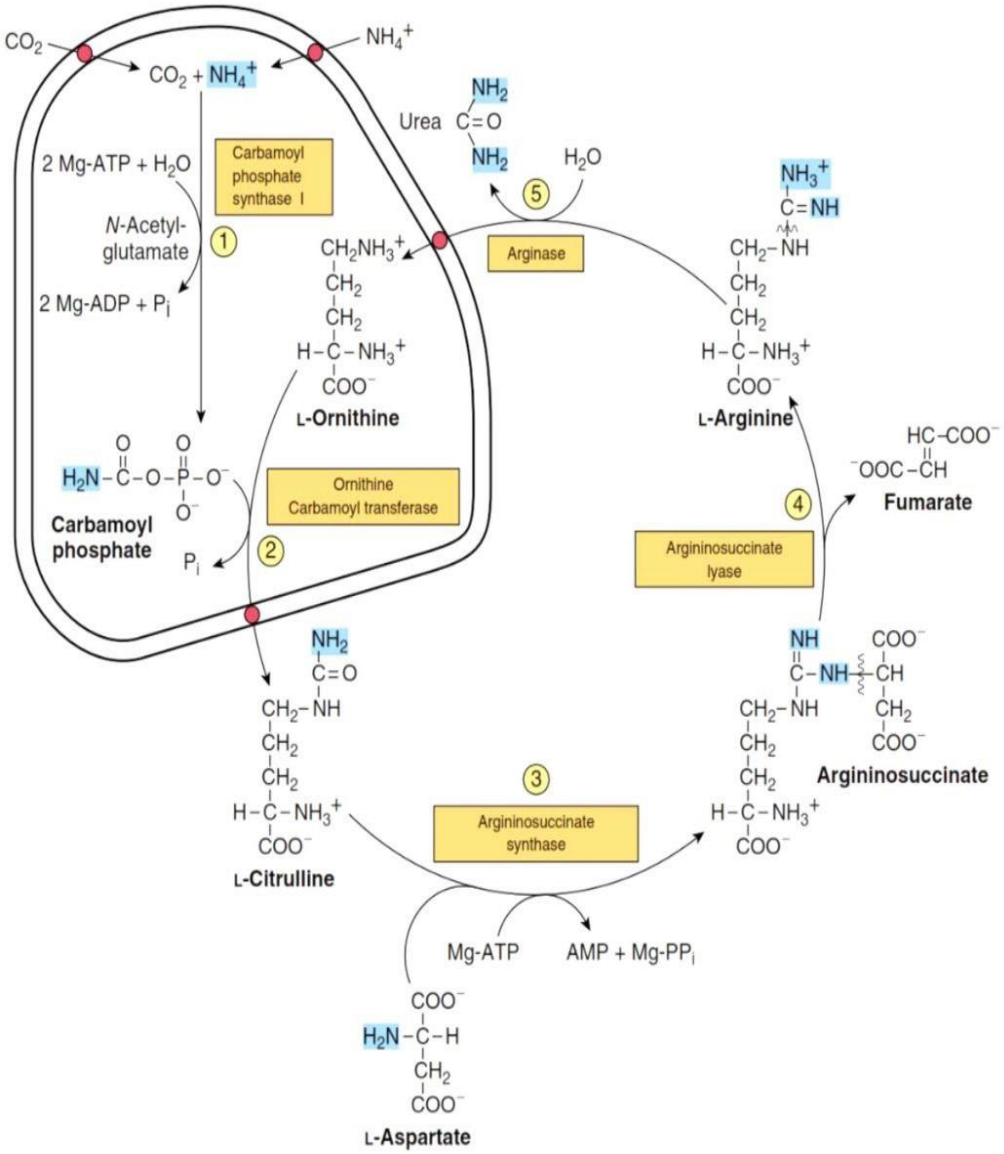
3. Formation of arginosuccinate: Citrulline reacts with Aspartate in the cytosol to form arginosuccinate.

4. Cleavage of arginosuccinate: It is cleaved into Arginine and Fumarate.

5. Cleavage of Arginine into ornithine and urea:

a) Ornithine then passes to the mitochondria to start a new cycle.

b) Urea passes to the blood to be excreted by the kidney in urine. **(Figure 19)**



(Figure 19)

Three ATP molecules and four high-energy phosphate bonds are utilized in the reactions.

Metabolism of carbon skeletons

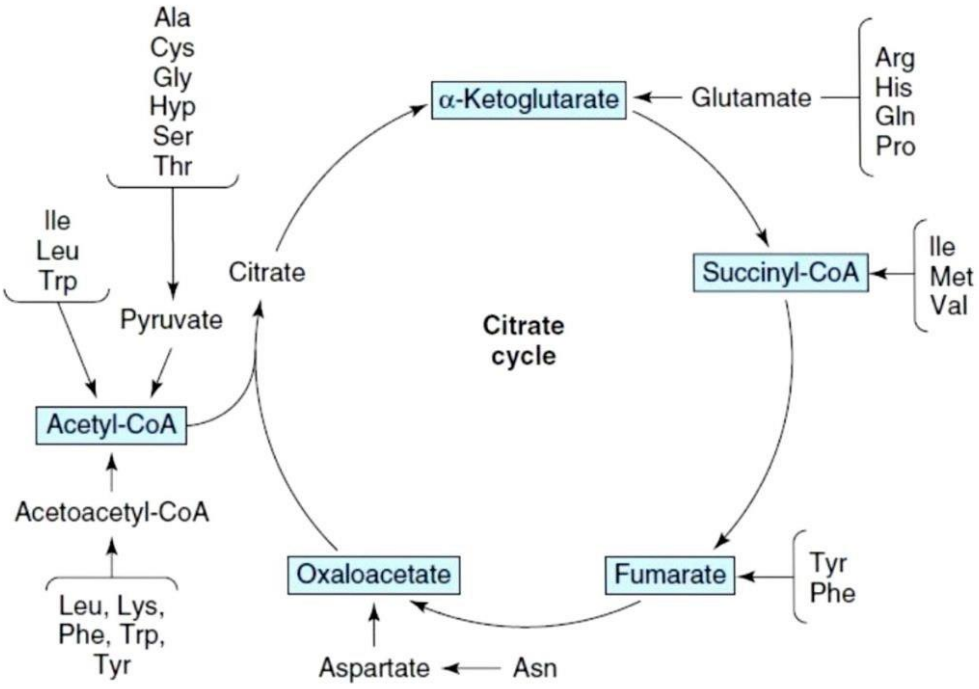
The α-ketoacid (the carbon skeleton) remaining after the removal of the amino group (NH_2) by transamination and deamination of amino acids may undergo:

A. **Reamination:** by ammonia (NH_3) to form again the corresponding amino acid (by glutamate dehydrogenase).

B. **Catabolized to form seven products:** pyruvate, acetyl CoA, acetoacetyl CoA, Fumarate, oxaloacetate, α-Ketoglutarate and Succinyl CoA. C.

These products enter different pathways which lead to:

1. Synthesis of glycogen or glucose.
2. Synthesis of lipids.
3. Complete oxidation into CO_2 and H_2O.



(Figure 20)

Metabolic Classification of Amino Acids

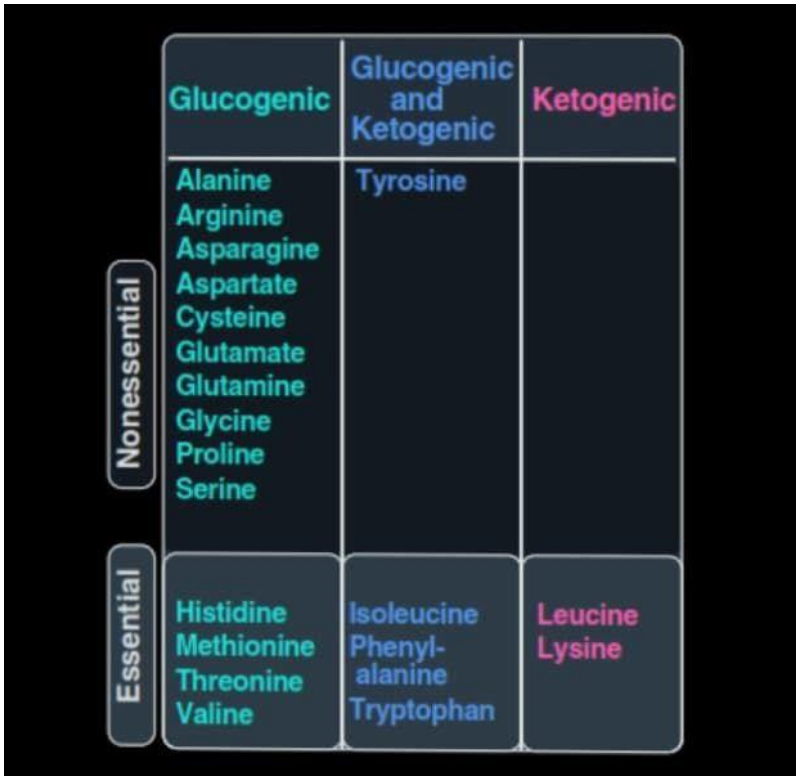
Amino acid can be classified in to three kinds based on their metabolic pathways for energy production in the body:

1.Glucogenic Amino Acids: can be converted into glucose through gluconeogenesis in the liver.

2.Ketogenic Amino Acids: are converted into acetoacetate and acetyl- CoA, which can be used as an energy source especially during fasting or low-carbohydrate diet.

This amino acid cannot be used to produce glucose directly.

3.Both Glucogenic and Ketogenic Amino Acids: some amino acids can follow both pathways.



(Figure 21)