

METABOLISM OF AMINO ACIDS —GENERAL ASPECTS

The amino acids undergo certain common reactions like **transamination** followed by **deamination** for the liberation of **ammonia**. The amino group of the amino acids is utilized for the formation of **urea** which is an excretory **end product** of protein metabolism. The carbon skeleton of the amino acids is first converted to keto acids (by transamination) which meet one or more of the following fates.

1. Utilized to generate energy.
2. Used for the synthesis of glucose.
3. Diverted for the formation of fat or ketone bodies.
4. Involved in the production of non-essential amino acids.

A general picture of amino acid metabolism is depicted in following **Figure**.

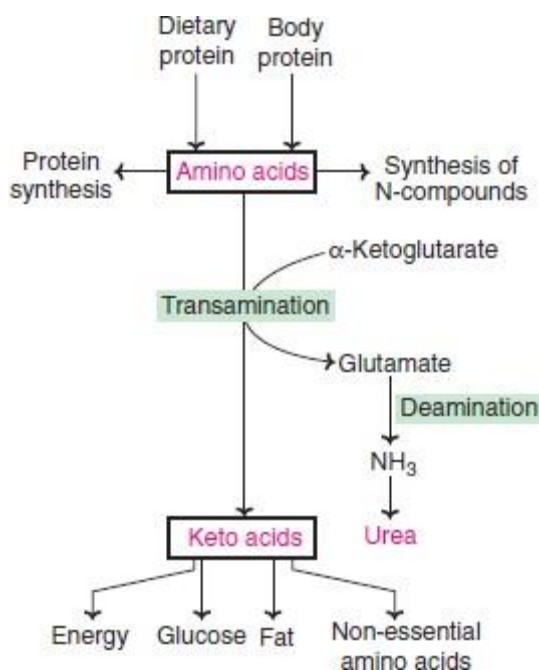


Figure1: An overview of amino acid metabolism

TRANSAMINATION

The **transfer of an amino (NH₂) group from an amino acid to a keto acid** is known as transamination. This process involves the interconversion of a pair of amino acids and a pair

of keto acids, catalysed by a group of enzymes called **transaminases** (recently, **aminotransferases**).

Salient features of transamination

1. All transaminases require **pyridoxal phosphate (PLP)**, a coenzyme derived from vitamin B6.
2. Specific transaminases exist for each pair of amino and keto acids. However, only two namely aspartate transaminase and alanine transaminase make a significant contribution for transamination.
3. There is no free NH_3 liberated, only the transfer of amino group occurs.
4. Transamination is **reversible**.

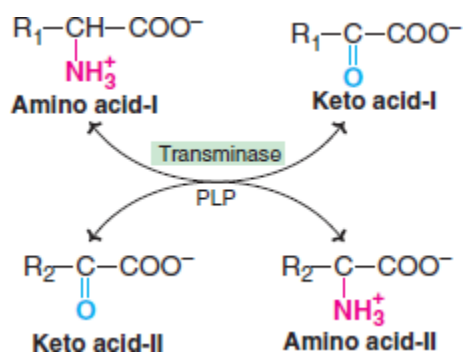


Figure2. Transamination reaction

5. Transamination is very important for the redistribution of amino groups and **production of non-essential amino acids**, as per the requirement of the cell. It involves both catabolism (degradation) and anabolism (synthesis) of amino acids.
6. Transamination diverts the excess amino acids towards **energy generation**.
7. The amino acids undergo transamination to finally concentrate nitrogen in glutamate. **Glutamate** is the only amino acid that undergoes oxidative deamination to a significant extent to liberate free NH_3 for urea synthesis.

8. All amino acids except lysine, threonine, proline and hydroxyproline participate in transamination.
9. Transamination is not restricted to α -amino groups only. For instance, δ -amino group of ornithine is transaminated.
10. Serum transaminases are important for diagnostic and prognostic purpose.

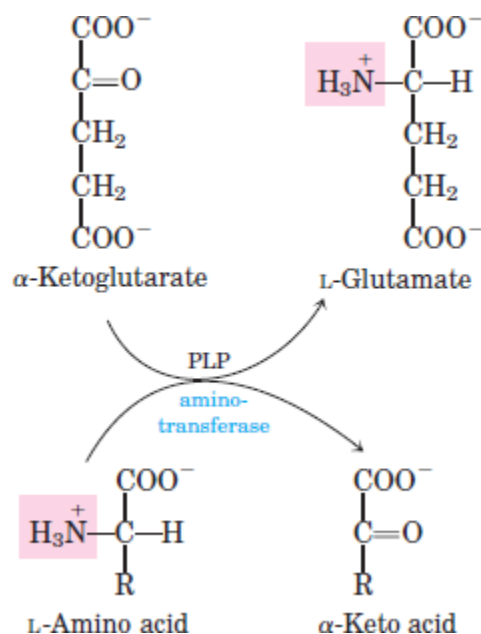


Figure 2: Enzyme-catalyzed transaminations. In many aminotransferase reactions, α -ketoglutarate is the amino group acceptor.

DEAMINATION

The **removal of amino group** from the amino acids as NH_3 is deamination. Transamination (discussed above) involves only the shuffling of amino groups among the amino acids. On the other hand, deamination results in the liberation of ammonia for urea synthesis. Simultaneously, the carbon skeleton of amino acids is converted to keto acids. Deamination may be either oxidative or non-oxidative. Although transamination and deamination are separately discussed, they occur simultaneously, often involving glutamate as the central molecule

I. Oxidative deamination

Oxidative deamination is the **liberation of free ammonia** from the amino group of amino acids **coupled with oxidation**. This takes place mostly in liver and kidney. The purpose of oxidative deamination is to provide NH_3 for urea synthesis and α -keto acids for a variety of reactions, including energy generation.

Role of glutamate dehydrogenase : In the process of transamination, the amino groups of most amino acids are transferred to α -ketoglutarate to produce glutamate. Thus, **glutamate** serves as a **'collection centre' for amino groups** in the biological system. Glutamate rapidly undergoes oxidative deamination, catalysed by glutamate dehydrogenase (GDH) to liberate ammonia. This enzyme is unique in that it can utilize either NAD^+ or NADP^+ as a coenzyme. Conversion of glutamate to α -ketoglutarate occurs through the formation of an intermediate, α -iminoglutarate (**Figure 3**). Glutamate dehydrogenase catalysed reaction is important as it reversibly links up glutamate metabolism with TCA cycle through α -ketoglutarate. GDH is involved in both catabolic and anabolic reactions.

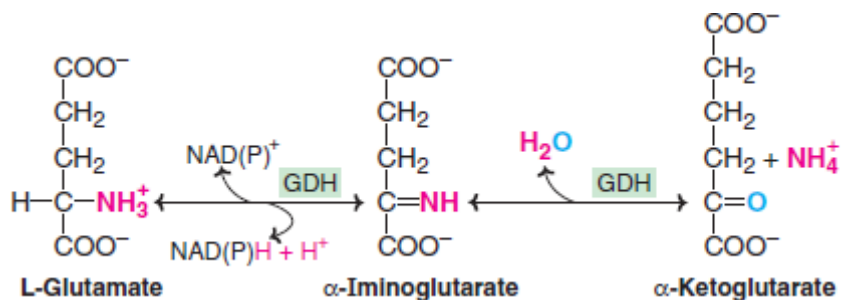


Figure 3: Oxidation of glutamate by glutamate dehydrogenase (GDH).

GDH is controlled by allosteric regulation. **GTP** and **ATP inhibit**—whereas **GDP** and **ADP activate**—glutamate dehydrogenase. Steroid and thyroid hormones inhibit GDH.

After ingestion of a protein-rich meal, liver glutamate level is elevated. It is converted to α -ketoglutarate with liberation of NH_3 . Further, when the cellular energy levels are low, the degradation of glutamate is increased to provide α -ketoglutarate which enters TCA cycle to liberate energy.

Oxidative deamination by amino acid oxidases

L-Amino acid oxidase and D-amino acid oxidase are flavoproteins, possessing FMN and FAD, respectively. They act on the corresponding amino acids (L or D) to produce

α -keto acids and NH_3 . In this reaction, oxygen is reduced to H_2O_2 , which is later decomposed by catalase (Figure 4).

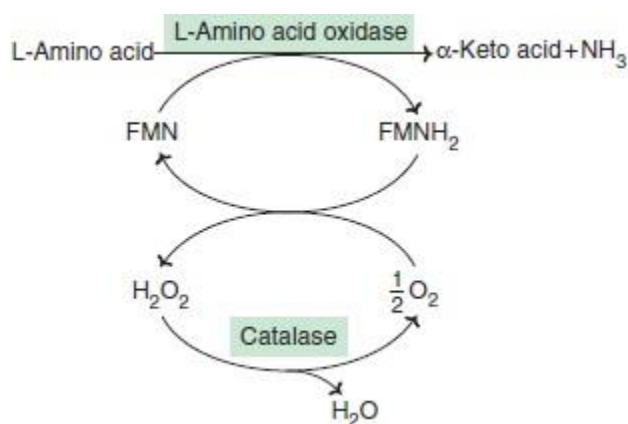


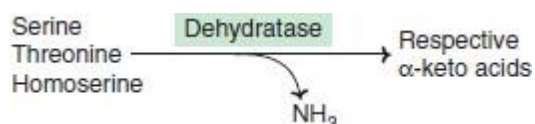
Figure 4: Oxidative deamination of amino acids

II. Non-oxidative deamination

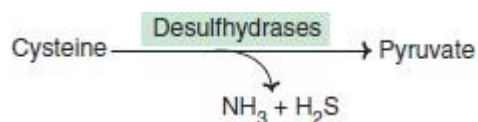
Some of the amino acids can be deaminated to liberate NH_3 without undergoing oxidation

(a) **Amino acid dehydrases** : Serine, threonine

and homoserine are the hydroxy amino acids. They undergo non-oxidative deamination catalysed by PLP-dependent dehydrases (dehydratases).



(b) **Amino acid desulfhydrases** : The sulfur amino acids, namely cysteine and homocysteine, undergo deamination coupled with desulfhydration to give keto acids.



(c) **Deamination of histidine**: The enzyme histidase acts on histidine to liberate NH_3 by non-oxidative deamination process.

