10.8: Stage II of Protein Catabolism

Learning Objectives

- To describe how excess amino acids are degraded.

The liver is the principal site of amino acid metabolism, but other tissues, such as the kidney, the small intestine, muscles, and adipose tissue, take part. Generally, the first step in the breakdown of amino acids is the separation of the amino group from the carbon skeleton, usually by a transamination reaction. The carbon skeletons resulting from the deaminated amino acids are used to form either glucose or fats, or they are converted to a metabolic intermediate that can be oxidized by the citric acid cycle. The latter alternative, amino acid catabolism, is more likely to occur when glucose levels are low—for example, when a person is fasting or starving.

Transamination

Transamination is an exchange of functional groups between any amino acid (except lysine, proline, and threonine) and an α-keto acid. The amino group is usually transferred to the keto carbon atom of pyruvate, oxaloacetate, or α-ketoglutarate, converting the α-keto acid to alanine, aspartate, or glutamate, respectively. Transamination reactions are catalyzed by specific transaminases (also called aminotransferases), which require pyridoxal phosphate as a coenzyme.

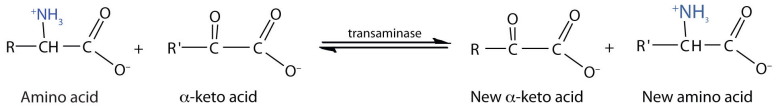


Figure 10.8.1): Transamination reaction.

> *In an α-keto acid, the carbonyl or keto group is located on the carbon atom adjacent to the carboxyl group of the acid.*

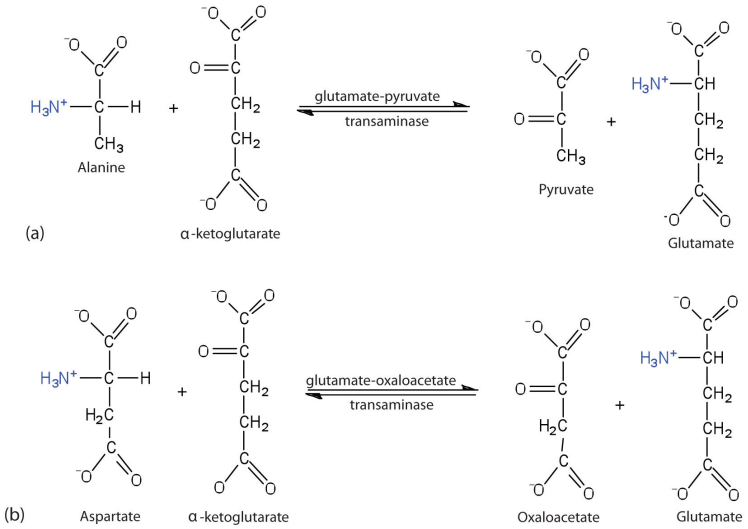
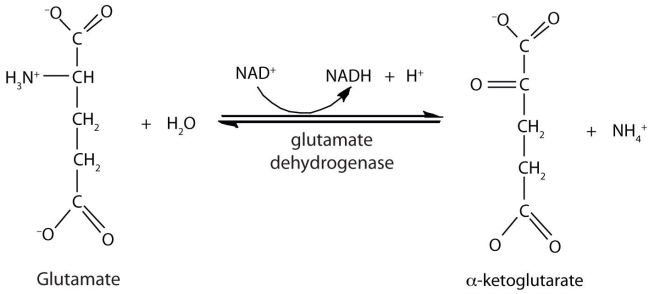


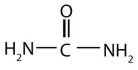
Figure 10.8.2: Two Transamination Reactions. In both reactions, the final acceptor of the amino group is α-ketoglutarate, and the final product is glutamate.

Oxidative Deamination

In the breakdown of amino acids for energy, the final acceptor of the α-amino group is α-ketoglutarate, forming glutamate. Glutamate can then undergo **oxidative deamination**, in which it loses its amino group as an ammonium (NH_4^+) ion and is oxidized back to α-ketoglutarate (ready to accept another amino group):



This reaction occurs primarily in liver mitochondria. Most of the NH_4^+ ion formed by oxidative deamination of glutamate is converted to urea and excreted in the urine in a series of reactions known as the **urea cycle**.



The synthesis of glutamate occurs in animal cells by reversing the reaction catalyzed by glutamate dehydrogenase. For this reaction nicotinamide adenine dinucleotide phosphate (NADPH) acts as the reducing agent. The synthesis of glutamate is significant because it is one of the few reactions in animals that can incorporate inorganic nitrogen (NH_4^+) into an α-keto acid to form an amino acid. The amino group can then be passed on through transamination reactions, to produce other amino acids from the appropriate α-keto acids.

The Fate of the Carbon Skeleton

Any amino acid can be converted into an intermediate of the citric acid cycle. Once the amino group is removed, usually by transamination, the α-keto acid that remains is catabolized by a pathway unique to that acid and consisting of one or more reactions. For example, phenylalanine undergoes a series of six reactions before it splits into fumarate and acetoacetate. Fumarate is an intermediate in the citric acid cycle, while acetoacetate must be converted to acetoacetyl-coenzyme A (CoA) and then to acetyl-CoA before it enters the citric acid cycle.

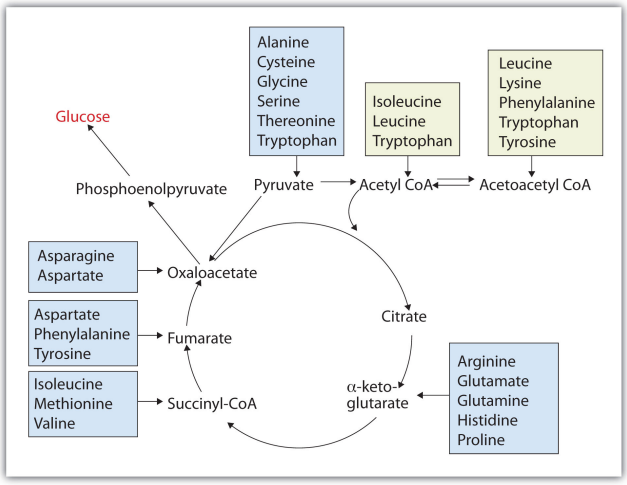


Figure 10.8.3: Fates of the Carbon Skeletons of Amino Acids

Those amino acids that can form any of the intermediates of carbohydrate metabolism can subsequently be converted to glucose via a metabolic pathway known as **gluconeogenesis**. These amino acids are called **glucogenic amino acids**. Amino acids that are converted to acetoacetyl-CoA or acetyl-CoA, which can be used for the synthesis of ketone bodies but not glucose, are called **ketogenic amino acids**. Some amino acids fall into both categories. Leucine and lysine are the only amino acids that are exclusively ketogenic. Figure 10.8.3 summarizes the ultimate fates of the carbon skeletons of the 20 amino acids.

Career Focus: Exercise Physiologist

An exercise physiologist works with individuals who have or wish to prevent developing a wide variety of chronic diseases, such as diabetes, in which exercise has been shown to be beneficial. Each individual must be referred by a licensed physician. An exercise physiologist works in a variety of settings, such as a hospital or in a wellness program at a commercial business, to design and monitor individual exercise plans. A registered clinical exercise physiologist must have an undergraduate degree in exercise physiology or a related degree. Some job opportunities require a master's degree in exercise physiology or a related degree.

Ergospirometry laboratory for the measurement of metabolic changes during a graded exercise test on a treadmill. from Wikipedia.

Example 10.8.1

Determine if each amino acid is glucogenic, ketogenic, or both.

a. asparagine
b. tyrosine
c. valine

Solution

a. glucogenic
b. both
c. glucogenic

Exercise 10.8.1

Determine if each amino acid is glucogenic, ketogenic, or both.

a. phenylalanine
b. leucine
c. serine

Summary

Generally the first step in the breakdown of amino acids is the removal of the amino group, usually through a reaction known as transamination. The carbon skeletons of the amino acids undergo further reactions to form compounds that can either be used for the synthesis of glucose or the synthesis of ketone bodies.