Protein metabolism:

The main role of amino acids is in the synthesis of structural and functional proteins. Unlike carbohydrates and fats, there is no storage form of proteins in the body. A 70 kg man has an average protein turnover rate of 400 g per day (same amount synthesized and same amount broken down. The non-essential amino acids are either derived from the diet or synthesized in the body. The essential amino acids are obtained from the diet. Even if one is deficient, protein synthesis cannot take place. The body amino acid pool is always in a dynamic steady state. In an adult, the rate of synthesis of proteins balances the rate of degradation, so that nitrogen balance is maintained.

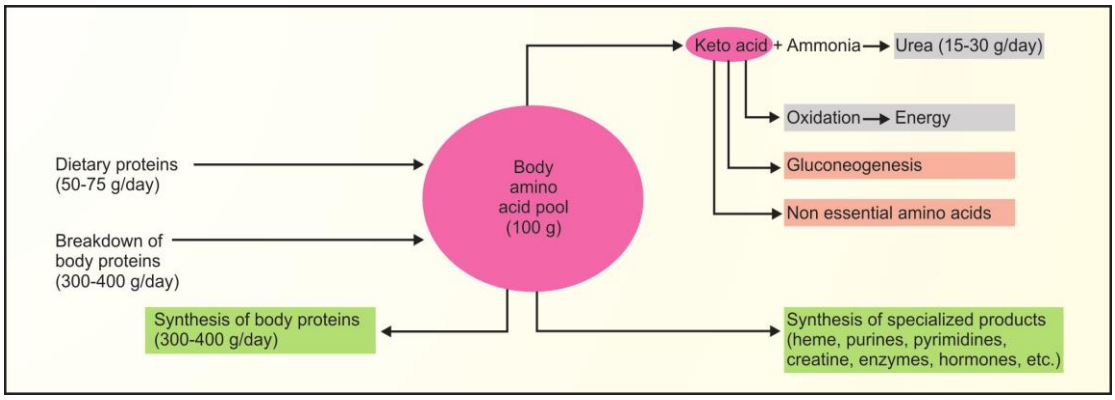
Clinical Applications

1. The allergy to certain food proteins (milk, fish) is believed to result from absorption of partially digested proteins.
2. Defects in the intestinal amino acid transport systems are seen in inborn errors of metabolism such as Hartnup's disease, Imino glycinuria, Cystinuria, etc.
3. Partial gastrectomy, pancreatitis, carcinoma of pancreas and cystic fibrosis may affect the digestion and absorption of proteins.

GENERAL METABOLISM OF AMINO ACIDS

These are summarized in Figure below:

1. The anabolic reactions are where proteins are synthesized.
2. Synthesis of specialized products such as heme, creatine, purines and pyrimidines.
3. The catabolic reactions where dietary proteins and body proteins are broken down to amino acids.
4. Transamination: amino group is removed to produce the carbon skeleton (keto acid). The amino group is excreted as urea.
5. The carbon skeleton is used for synthesis of non-essential amino acids.
6. It is also used for gluconeogenesis or for complete oxidation.

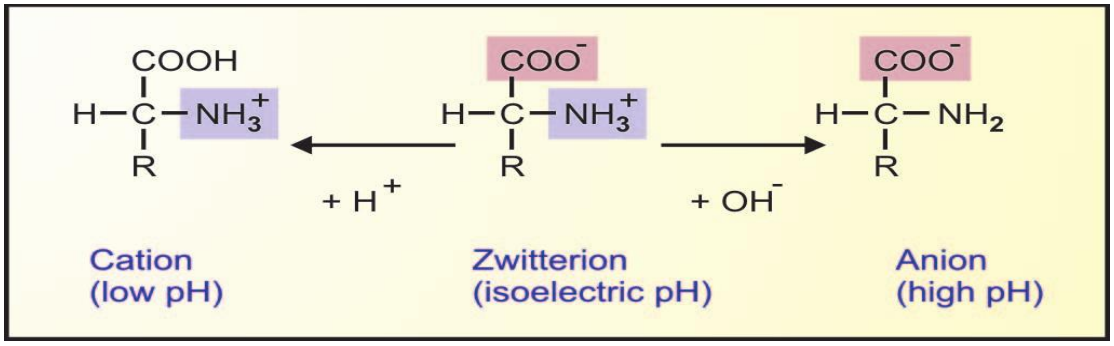


Overview of metabolism of amino acids

PROPERTIES OF AMINO ACIDS

1. Iso-electric Point

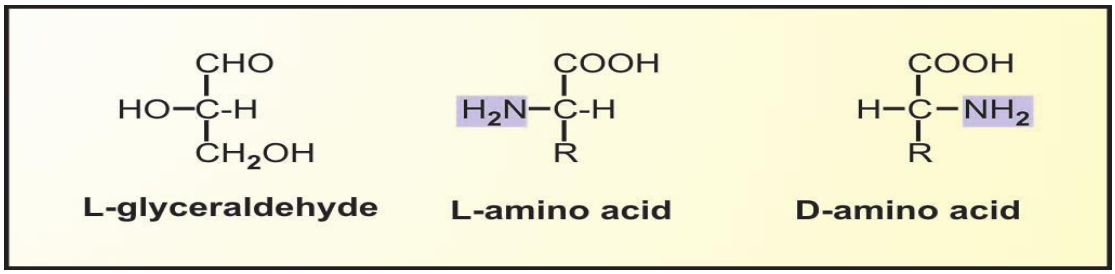
Amino acids can exist as ampholytes or zwitterions (German word "zwitter" = hybrid (in solution, depending on the pH of the medium. The pH at which the molecule carries no net charge is known as iso-electric point or iso-electric pH (pI). In acidic solution they are cationic in form and in alkaline solution they behave as anions



Ionic forms of amino acids

2. Optical Activity

Amino acids having an asymmetric carbon atom exhibit optical activity. Asymmetry arises when 4 different groups are attached to the same carbon atom.



D and L structure of amino acids

3. Reaction of amino acids

A. Decarboxylation reaction

The amino acids will undergo alpha decarboxylation to form the corresponding amine. Thus, some important amines are produced from amino acids. For example

i) Histidine ------→ Histamine + CO_2

ii) Tyrosine -------→ Tyramine + CO_2

iii) Tryptophan -----→ Tryptamine + CO_2

iv) Glutamic acid --→ Gamma amino butyric acid (GABA)+ CO_2

B. Transamination reaction

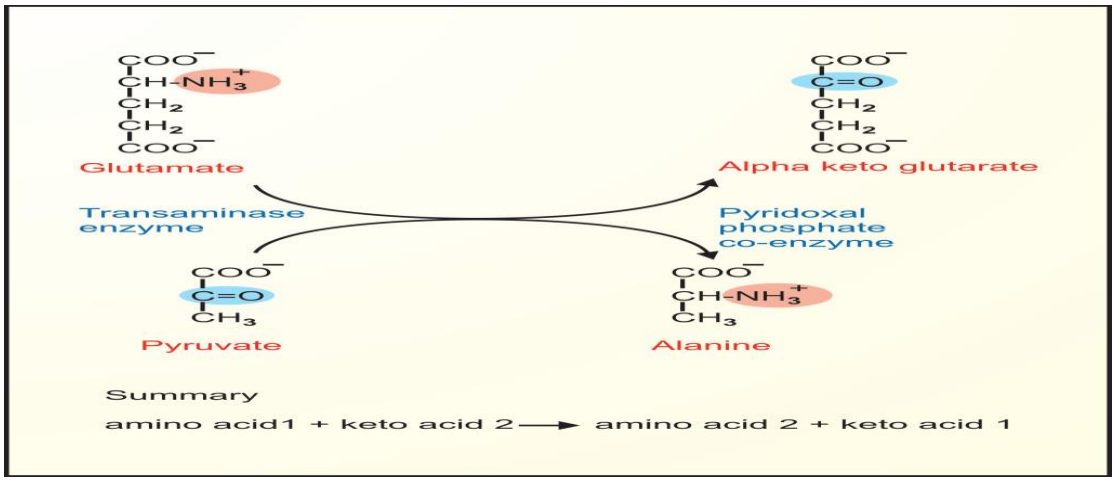
i. Transamination is the exchange of the alpha amino group between one alpha amino acid and another alpha keto acid، forming a new alpha amino acid.

amino acid 1 + keto acid 2 → a.acid 2 + keto acid 1

ii. As an example, amino group is interchanged between alanine and glutamic acid.

iii. In almost all cases, the amino group is accepted by alpha ketoglutaric acid so that glutamic acid is formed.

iv. The enzymes catalyzing the reaction as a group are known as transaminases (amino transferases). These enzymes have pyridoxal phosphate as prosthetic group. The reaction is readily reversible.



Transamination reaction. In this example، enzyme is Alanine amino transferase (ALT) and pyridoxal phosphate is the co-enzyme. The reaction is readily reversible

C. Amide Formation

The -COOH group of dicarboxylic amino acids other than alpha carboxyl) can combine with ammonia to form the corresponding amide For example:

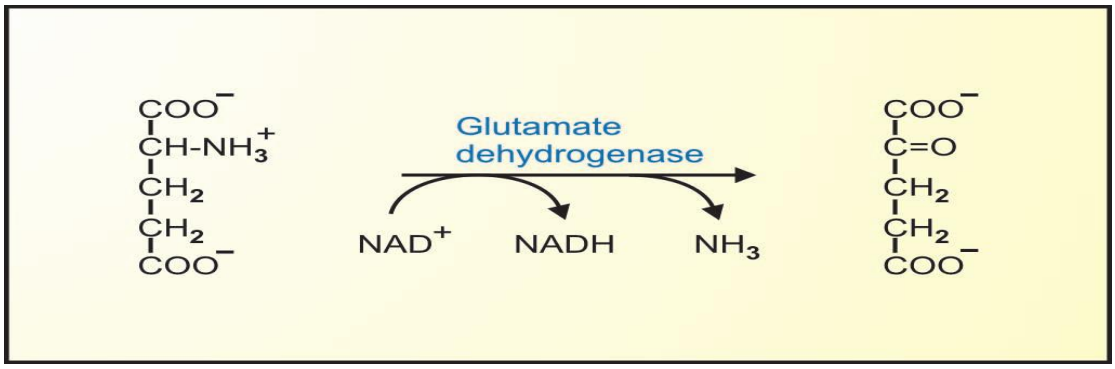
Aspartic acid +NH3 ----→ Asparagine

Glutamic acid+NH3 -----→Glutamine

These amides are also components of protein structure. The amide group of glutamine serves as the source of nitrogen for nucleic acid synthesis.

D. Oxidative Deamination

The alpha amino group is removed from the amino acid to form the corresponding keto acid and ammonia. In the body, Glutamic acid is the most common amino acid to undergo oxidative deamination.



Oxidative deamination

E. Reactions due to Side Chains

A. Ester Formation by OH Group

The hydroxy amino acids can form esters with phosphoric acid. In this manner the Serine and Threonine residues of proteins are involved in the formation of phosphoproteins. Similarly these hydroxyl groups can form O-glycosidic bonds with carbohydrate residues to form glycoproteins.

B. Reaction of the Amide Group

The amide groups of Glutamine and Asparagine can form N-glycosidic bonds with carbohydrate residues to form glycoproteins.

Classification of amino acids Based on Side Chain

A. Amino acids having nonpolar side chains: These include Alanine, Valine, Leucine, Isoleucine، Methionine, Proline, Phenylalanine and Tryptophan. These groups are hydrophobic (water repellant) and lipophilic

B. Amino acids having uncharged or non-ionic polar side chains: Glycine, Serine, Threonine, Cysteine, Tyrosine، Glutamine and Asparagine belong to this group. These amino acids are hydrophilic in nature.

C. Amino acids having charged or ionic polar side chains:

They are hydrophilic in nature.

C-a. Acidic amino acids: They have a negative charge on the R group: Aspartic acid and Glutamic acid (Tyrosine is mildly acidic).

C-b. Basic amino acids: They have a positive charge on the R group: Lysine, Arginine and Histidine.

Classification of amino acids Based on Nutritional Requirement:

Essential or Indispensable:

The amino acids may further be classified according to their essentiality for growth. Thus Isoleucine, Leucine, Threonine, Lysine, Methionine, Phenylalanine, Tryptophan, and Valine are essential amino acids. Their carbon skeleton cannot be synthesized by human beings and so preformed amino acids are to be taken in food for normal growth.

Partially essential or Semi-essential:

Histidine and Arginine are semi-indispensable amino acids. Growing children require them in food. But they are not essential for the adult individual.

Non-essential or dispensable:

The remaining 10 amino acids are non-essential. However they are also required for the normal protein synthesis. All body proteins do contain all the non-essential amino acids. But their carbon skeleton can be synthesised by metabolic pathways and therefore their absence in the food will not adversely affect the growth.

Classificcation

Proteins may be classified into different groups acording to functions (immunoglobulines, clotting factors, or enzemes), composition (glycoprotiens, mucoproteins, lipoproteins)relative migration distance in an electrical field, or sedimentation rate when subjected to a centerfugal force.

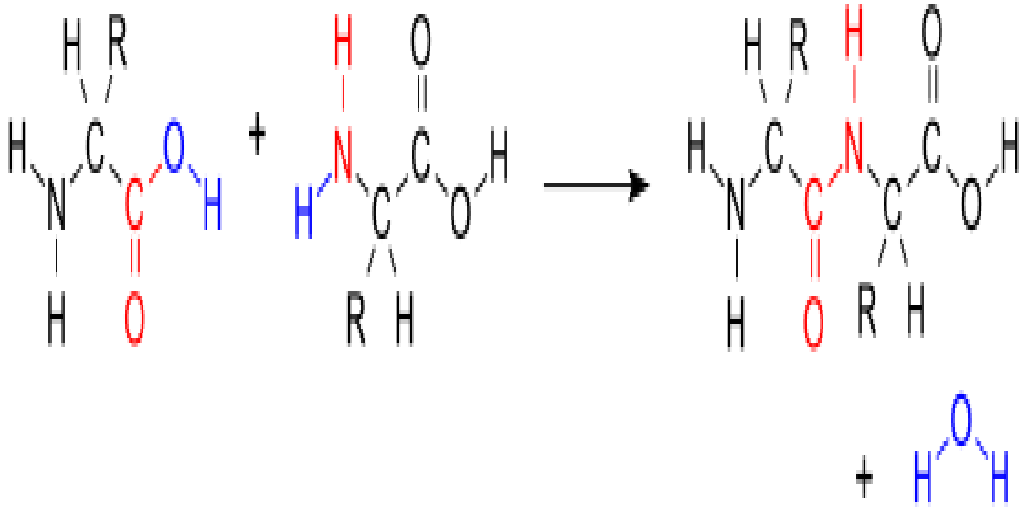
CLASSIFICATION OF PROTEINS

Classification based on Functions

i) Catalytic proteins, e.g. enzymes.
ii) Structural proteins, e.g. collagen, elastin، keratin.
iii) Contractile proteins, e.g. myosin, actin.
iv) Transport proteins, e.g. hemoglobin، myoglobin, albumin, transferrin.
v) Regulatory proteins or hormones, e.g. ACTH، insulin, growth hormone.
vi) Genetic proteins, e.g. histones.
vii) Protective proteins, e.g. immunoglobulins, clotting factors.

Peptide bond formation :

When two amino acids form a *dipeptide* through a *peptide bond* it is called condensation. In condensation, two amino acids approach each other, with the acid moiety of one coming near the amino moiety of the other. One loses a hydrogen and oxygen from its carboxyl group (COOH) and the other loses a hydrogen from its amino group (NH_2). This reaction produces a molecule of water (H_2O) and two amino acids joined by a peptide bond (-CO-NH-). The two joined amino acids are called a dipeptide.



Metabolism of amino acids

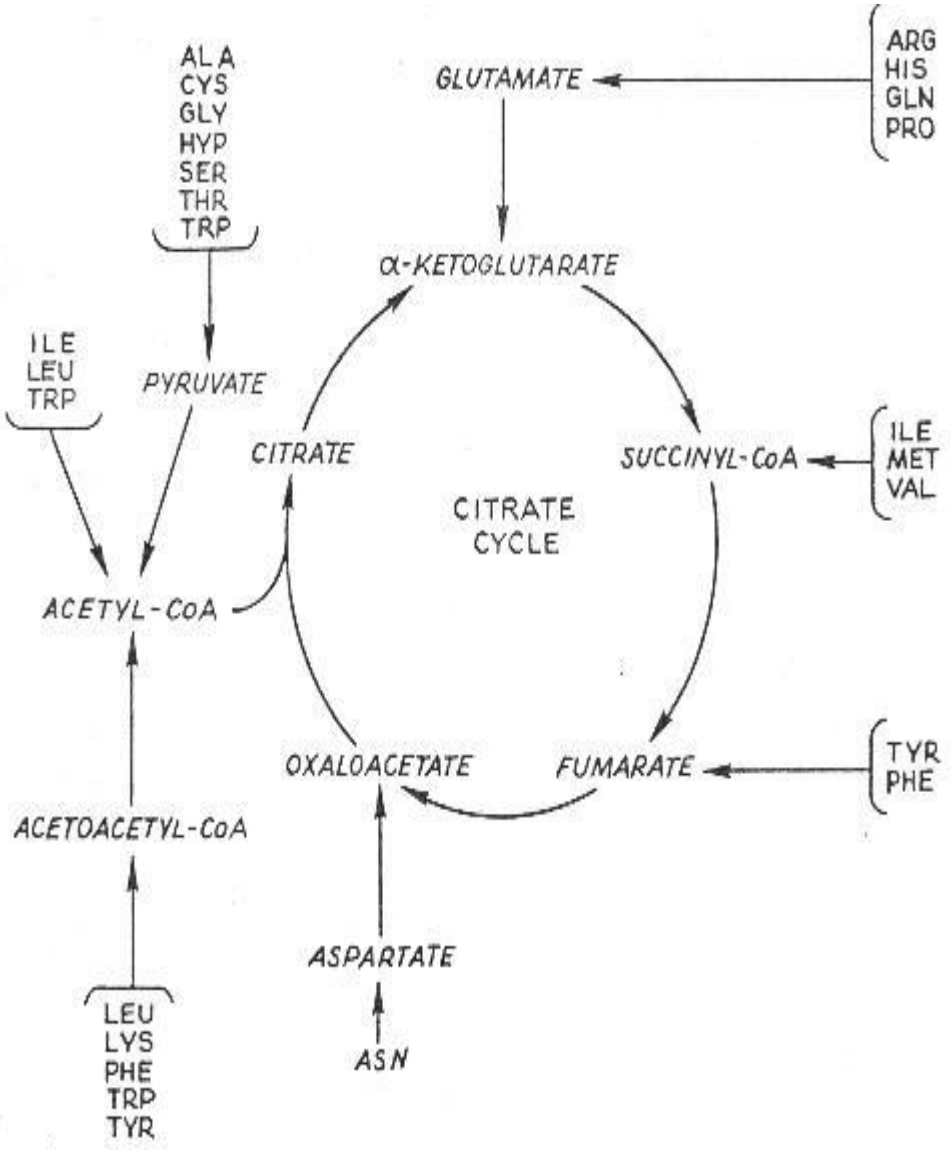


Figure Amphibiolic intermediates formed from the carbon skeleton of amino acids.

Electrophoresis

The technique for seperation proteins by mean of an electrical current is called electrophoresis. At pH 8.6 , all the serum proteins carry anegative charge to a greater or leaser extent. if a small serum sample is placed upon a wet (pH 8.6 buffer) support medium, such as cellulose acetate or agarose gel interposed between two electrodes immersed in pH 8.6, and subjected to an elctrecal chrage of several hindered volts, the proteins move toward the positive pole (anode). The imgration distance varies directly with the charge carried by the protein, but is modified to a slight extent by buffer flow.

The buffer flow (electro-osmotic or endosmotic flow) is caused by the negative chrage of the support medium when the capillaries or pores become wet, therby leaving the liquid medium (buffer) with small positive charge. When the current is turned on, a flow or movement of buffer occurs toward the negative electrode (cathode), and this movement passively carries with it, to a small extent, the proteins that tend to migrate toward the anode becouse of their negaative charge. After seperation on cellulose acetate or agarose gel by elctrophoresis, protein band are visualized by staining with a coomassie blue type of stain.