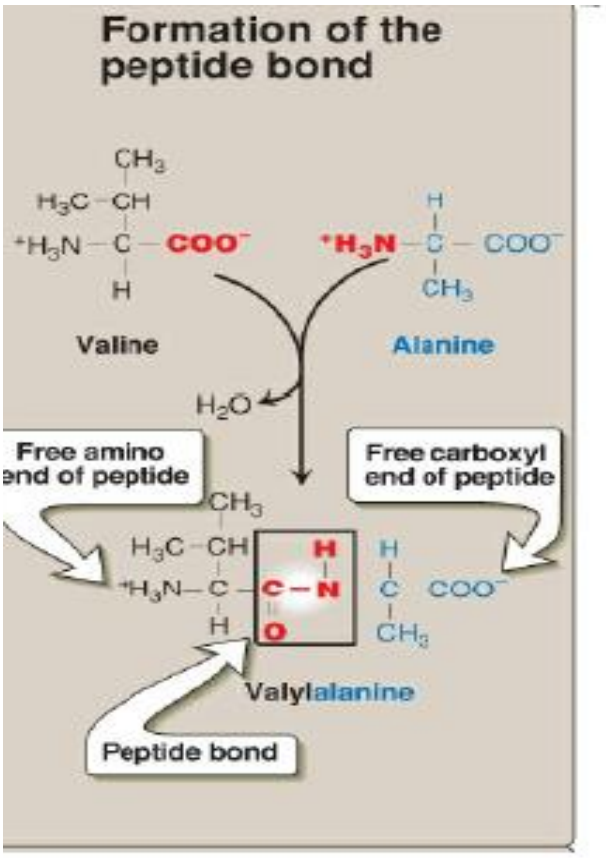
Proteins

Proteins are large and complex molecules that made up of 20 amino acids, which are linked together by peptide bond in a specific sequence to form a polypeptide chain.

- ✓ A peptide bond is a covalent chemical bond that forms between the amino group (NH_2) of one amino acid and the carboxyl group (COOH) of another amino acid during protein synthesis. This process is part of the larger biological process known as protein biosynthesis or protein translation.

Formation: peptide bonds are formed through a dehydration synthesis reaction; a molecule of water is eliminated as the amino and carboxyl groups combine to form a covalent bond.



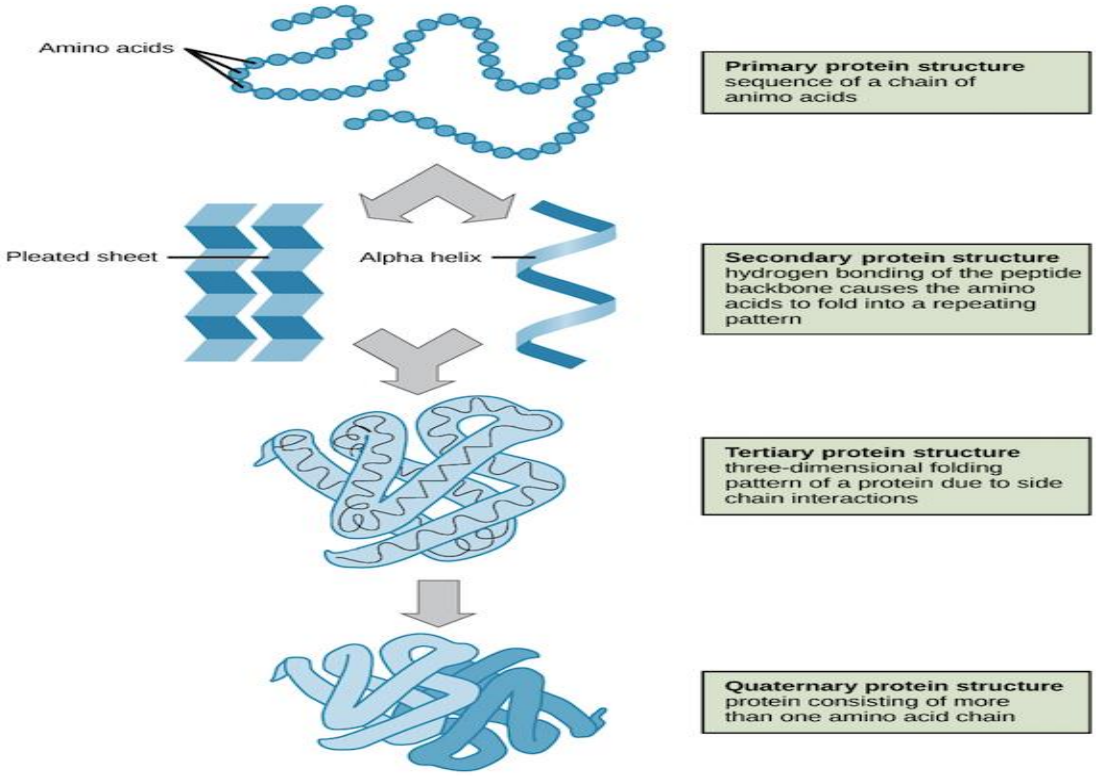
Structure of Proteins:

1. Primary Structure: is the linear sequence of amino acids, the order of amino acids is determined by the genetic code in DNA. Example: insulin

2. Secondary Structure: refers to local folded arrangements of the polypeptide chain. This structure has two common types are alpha helices and beta sheets, which are stabilized by hydrogen bonds between amino acid residues. Example is collagen folding, enable it in maintaining the integrity and structure of various tissues in the body.

3. Tertiary Structure: refers to the overall three-dimensional shape of a protein, it is influenced by interactions between amino acid side chains, including hydrogen bonds, disulfide bonds, hydrophobic interactions, and ionic interactions. Example: lysozyme (helps protect body against bacterial infections) the tertiary structure of this enzymes determine their active sites and catalytic capabilities.

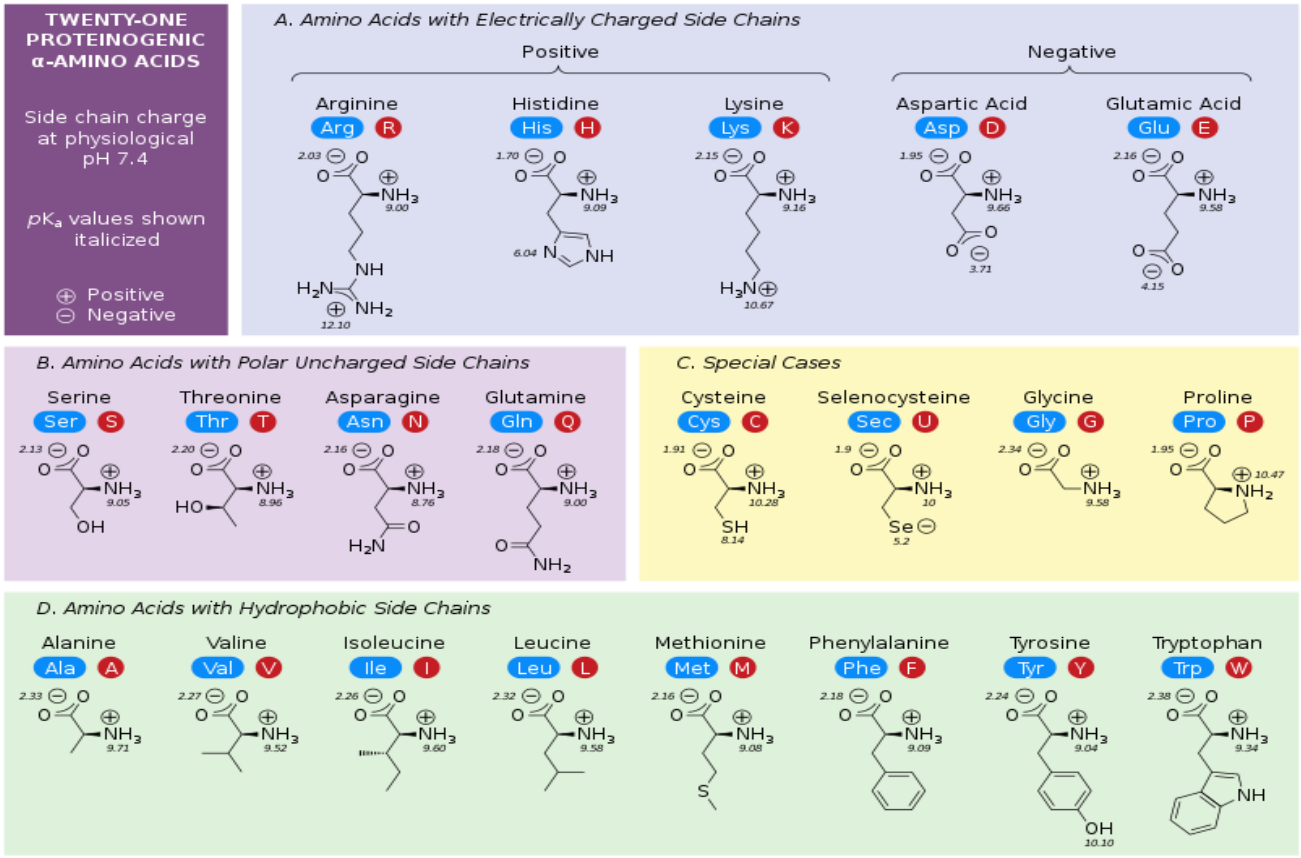
4. Quaternary Structure: refers to multiple polypeptide chains (subunits) that come together to form a functional protein. Example: Hemoglobin has a quaternary structure with four subunits.



Functions of Proteins:

1. Structural Support: They form the building blocks of various structures in the body, including muscles, bones, skin, and hair.
2. Enzymatic Functions: Proteins act as enzymes, which are biological catalysts that facilitate and speed up chemical reactions in the body. Enzymes play a vital role in metabolism, allowing biochemical processes to occur efficiently.
3. Transportation: Some proteins function as carriers and transport molecules, such as oxygen transport by hemoglobin in red blood cells, nutrients and ions throughout the body.
4. Immune System Function: Antibodies are proteins, play a crucial role in the immune system by recognizing and neutralizing harmful substances like bacteria and viruses.
5. Cell Signaling: Proteins are involved in cell signaling pathways, transmitting signals within and between cells.

6. Hormones: Many hormones are proteins or peptides that regulate physiological processes, including growth, development, metabolism, and reproduction.
7. Energy Source: body can use proteins for energy, especially during periods of starvation or intense physical activity.
8. Gene Expression: Proteins are essential for the regulation of gene expression. Transcription factors are proteins can control the process of turning genes on or off, influencing the synthesis of other proteins.
9. Repair and Maintenance: Proteins play a crucial role in the repair and maintenance of tissues. For example, collagen is a protein that provides structural support to connective tissues and is essential for wound healing.
10. Muscle Contraction: Proteins, such as actin and myosin, are integral to the contraction and relaxation of muscles. This is crucial for movement and various physiological functions.



Globular and fibrous proteins

Globular proteins and fibrous proteins are two major categories of proteins based on their structural characteristics and functions:

1.Globular Proteins:

Structure: Globular proteins have a compact, spherical shape. They are folded into intricate three-dimensional structures with numerous twists and loops. Because of possessing many hydrophilic amino acids on their outer surface, facing the aqueous environment to be water soluble, with presence more nonpolar amino acids in the interior of the protein providing hydrophobic interactions to further stabilize the globular structure during biochemical reactions within cells.

Function: These proteins are involved in biological processes, it serves as enzymes, hormones, signaling, transporters, and antibodies.

Examples: Enzymes like catalase and lysozyme, transport proteins like hemoglobin and myoglobin and immune proteins like antibodies.

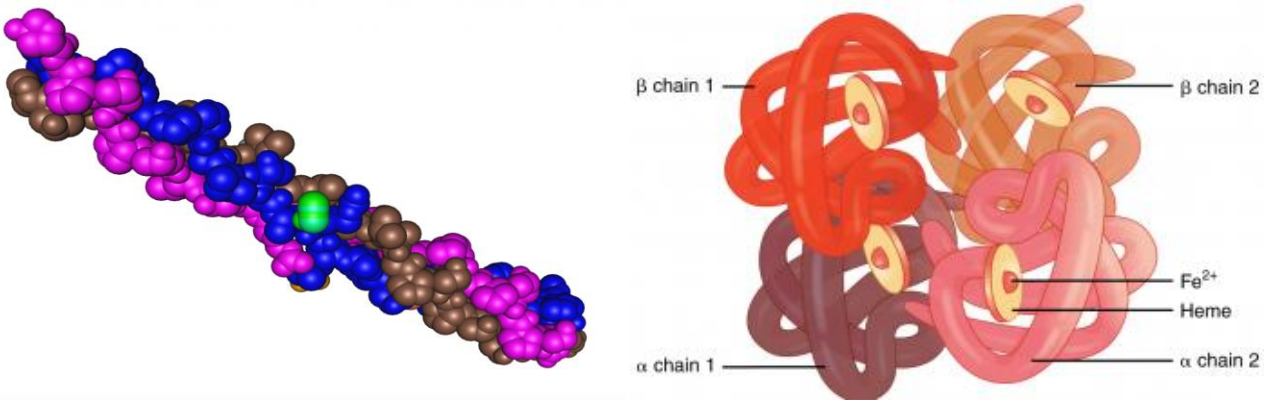
2. Fibrous Proteins:

Structure: Fibrous proteins are usually folded into either extended filaments or sheet-like structures, with repeated amino acid sequences.

Function: They are relatively insoluble and provide structural or protective function in our tissues, such as in connective tissues, tendons, bone, and muscle fibers. Collagen and elastin are examples of commonly occurring, well-characterized fibrous proteins of the extracellular matrix (ECM).

Examples: Collagen, keratin, elastin.

Q/ Differentiate between globular and fibrous proteins(Structure, Solubility, Function, Examples).



A. fibrous structure(collagen) B. globular structure(Hemoglobin)

1. Hemoglobin:

- ✓ Hemoglobin is a globular protein found in red blood cells (erythrocytes) and is responsible for transporting oxygen from the lungs to the tissues and organs of the body. Its primary function is to bind to oxygen in the lungs, where oxygen levels are high, and then release it in tissues with lower oxygen levels, where it is needed for cellular respiration.
- ✓ Hemoglobin is made up of four protein subunits, each containing a heme group. Each heme group contains an iron ion (Fe2+) that binds to an oxygen molecule.
- ✓ The binding of oxygen to hemoglobin is cooperative, meaning that once oxygen molecule binds to a subunit, it makes it easier for subsequent oxygen molecules to bind.
- ✓ Hemoglobin also plays a role in transporting carbon dioxide and hydrogen ions away from tissues to the lungs for exhalation.

Hemoglobinopathies

There are two main types of hemoglobinopathies:

1. Thalassemias: are characterized by reduced production of one or more types of globin chains that make up hemoglobin. The severity of thalassemia depends on the number of affected genes and the specific mutations involved. There are two main types of thalassemia:

a) Alpha thalassemia: occurs when there is a defect in the genes responsible for alpha globin production.

b) Beta thalassemia: occurs when there is a defect in the genes responsible for beta globin production.

2. Sickle cell disease (SCD): is caused by a specific mutation in the beta-globin gene (HBB) that leads to the production of abnormal hemoglobin known as hemoglobin S (HbS). HbS molecules can polymerize and cause red blood cells to become stiff and sickle-shaped. These sickled cells can lead to various complications such as vaso-occlusive crises, anemia, organ damage, and increased susceptibility to infections.

- ✓ Genetic counseling and prenatal testing are important for families at risk of having children with hemoglobinopathies.
- ✓ The prevalence of hemoglobinopathies varies among different populations, with higher rates in regions where malaria is or has been endemic, as the genetic mutations that cause hemoglobinopathies can confer some protection against malaria.
- ✓ The inheritance of two mutated alleles, one from each parent, results in the expression of the disorder.

2. Collagen

- ✓ Collagen is fibrous protein in the human body, making up a significant portion of our skin, bones, muscles, tendons, and ligaments.
- ✓ It provides structure and strength to various tissues and organs.

- ✓ Collagen is composed of amino acids, primarily glycine, proline, and hydroxyproline, and forms long chains that are woven together to create a strong framework.

There are 28 types of collagens found throughout the body, each with its specific function, for example:

a) Type I collagen: Found in bones, skin, tendons, and ligaments. It provides structure and support to these tissues.

b) Type II collagen: Found in cartilage, providing support in joints.

c) Type III collagen: Found in skin, blood vessels, and internal organs, supporting their structure and function.

- ❖ Collagen production naturally declines with age, which can lead to decreased skin elasticity, joint pain, and weaker bones. As a result, collagen supplements have importance to support skin health, joint function, these supplements come in the form of powders, capsules, or liquid, and they may contain collagen derived from animal or marine sources.

Enzymes *(lecture3)*

Objectives

- Definition of enzyme and its role in reactions
- Give idea about the history about discovery of enzymes
- List the molecules that related with enzymes
- Classes of enzymes
- Explain the major regulatory mechanisms that control enzyme activity
- Definition of isoenzyme with Ex.
- Discuss the inhibitors and its types.

Effects Of Enzymes On Chemical Reactions

What are enzymes?

- An efficient, specific protein molecules catalyze biochemical reactions
- Properties of enzymes including:
  - Act on one or few type of molecules, so they are specific.
  - Not be changed or consumed during the reactions
  - Increase the rate of the reaction by at least **10^6 fold**

How Enzymes Was Recognized?

- Studies first recognized on the digestion of meat by stomach secretions.
- Louis Pasteur concluded that fermentation of sugar into alcohol is catalyzed by “ferments” in living yeast cells.
- Eduard Buchner discovered that cell-free yeast extracts could ferment sugar to alcohol and continued to function when removed from cells.
- James Sumner found that urease crystals consisted of protein, and postulated that enzymes were proteins.

Enzyme Nomenclature

- Enzymes are named by the type of reaction they catalyse
- It needs the addition of the suffix **–ase** to the name of their substrate or reaction that they catalyse.
- Lactase hydrolyses lactose into glucose and galactose. DNA polymerase polymerises nucleotides to form DNA

Six major classes depend on the reaction catalyze

No.	Enzyme classes	Function
1	Oxidoreductase	Oxidation-reduction reactions
2	Transferase	Group transferase
3	Hydrolase	Hydrolysis reaction(transfer of functional group to water)
4	Lyase	Addition or removal of groups to form double bonds)
5	Isomerase	Isomerization
6	Ligase	Joining of two molecules

Chemical Components Related To Enzymes

- Coenzymes: organic molecules essential for action of some enzymes, eg, NADH, coenzyme A.
- Cofactors: inorganic ions such as Fe^{2+}, Mn^{2+} essential for structure or action of some enzymes.
- Prosthetic group: coenzyme or/and cofactor covalently bind the enzyme.
- apoenzyme or apoprotein : the protein part of such an enzyme .

Isoenzymes

- Isoenzymes: are variant forms of a particular enzyme that all catalyze the same reaction but have different physical properties because of genetically determined differences in amino acid sequence.
- Isoenzymes may contain different numbers of charged amino acids, which allows them to be separated from each other by electrophoresis (the movement of charged particles in an electric field).
- Examples: LDH is found in high concentration in most tissues; five isoenzyme forms of LDH exist, LD 1→5, with LD5 prevalent in liver and skeletal muscle, LD2 in red blood cells and LD1 in myocardial muscle. The plasma levels of isoenzyme forms of creatine kinase (CK) is CK-MB, CK-BB, CK-MM.

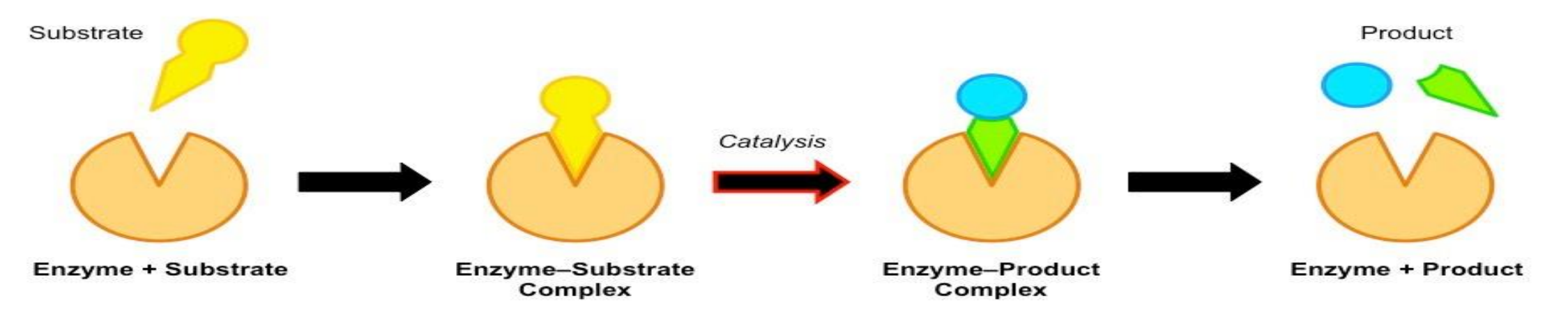
How do enzyme work?

- The distinguishing feature of an enzyme-catalyzed reaction is that it takes place within the confines of A pocket on the enzyme called the active site.
- The molecule that is bound in the active site and acted upon by the enzyme is called the substrate.
- The surface of the active site is lined with amino acid residues with functional groups that bind the substrate and catalyze its chemical transformation.

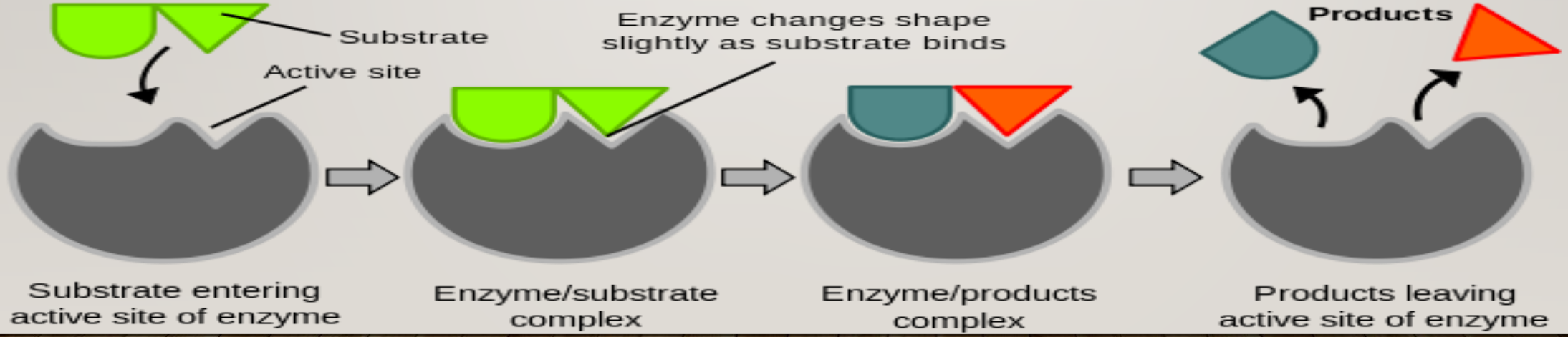
How Do Enzymes Accelerate Biochemical Reaction?

Enzymes accelerate biochemical reactions by lowering the activation energy that required for reaction. Activation energy is the energy barrier that must be overcome for a chemical reaction to proceed. Enzymes achieve this acceleration through several mechanisms:

1-lock And Key Model (Rigid Active Site)



2-induced Fit Model (Flexible Active Site)



How To Express The Enzyme?

- Enzymes are expressed in activity units rather than concentration.
- The unit of activity is the international unit (IU or U).
- One IU is the amount of enzyme that transforms 1.0 micromol of substrate per minute, under optimal conditions of measurement. **OR** that produce 1.0 micromole of product per minute, under optimal conditions of measurement.

Enzyme Inhibition

- What is the inhibition?
  - The ability of an enzyme to catalyze a reaction can be decreased by binding small molecules.
- Why study inhibition?
  - We use inhibition to understand the kinetics and properties of enzymes.
  - 60% of drugs are inhibitors of specific enzymes.

Types Of Enzyme Inhibition

- Irreversible inhibitors

➢ Inhibitors bind covalently to the enzyme molecule

➢ Destroy the enzyme function

➢ Aspirin is an example, it inhibits cyclooxygenase (COX) irreversibly by adding an acetyl group to the serine residue in the active site.

➢ Cyclooxygenase (COX) catalyses the production of prostaglandin from arachidonic acid.

Types Of Enzyme Inhibition

- Reversible inhibitors (activity returns)

➢ Competitive inhibitors

✓ Binds at the active site

✓ Increase Km but do not affect Vmax.

✓ Can be overcome by increasing the substrate concentration

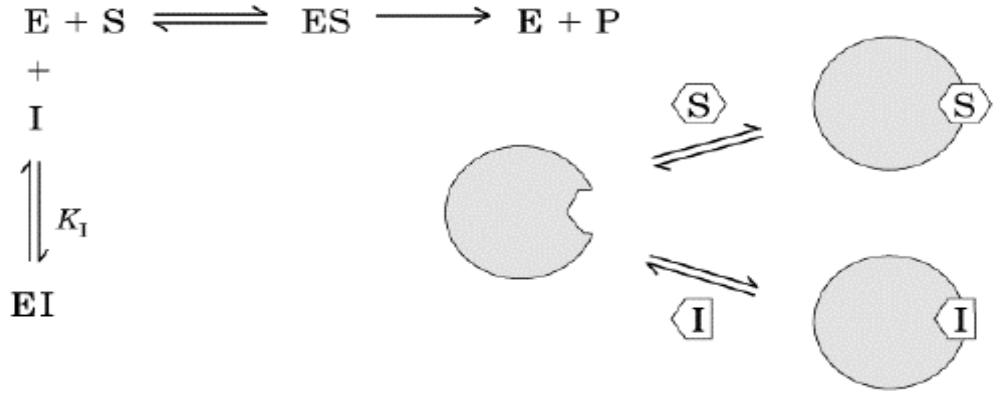
✓ Ibuprofen is competitive inhibitor for COX

Types Of Enzyme Inhibition:

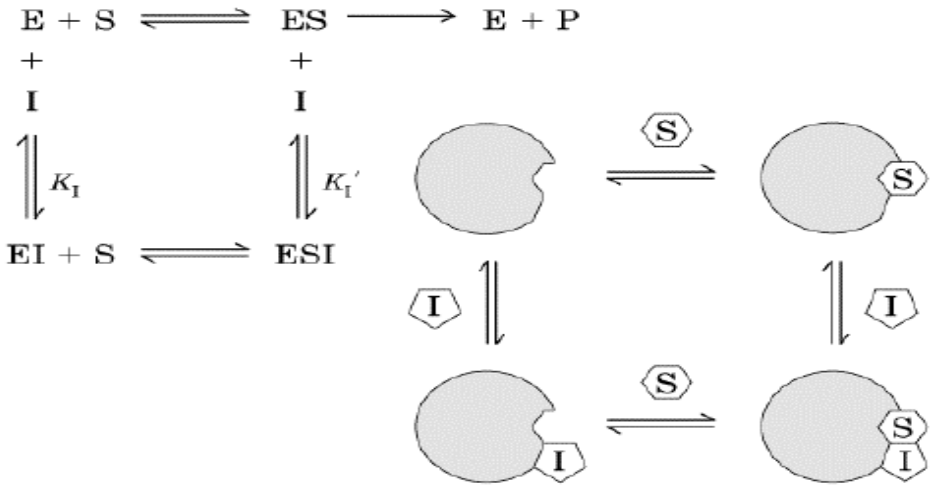
- Non-competitive inhibitors
  - ✓ binds at a site other than the active site
  - ✓ Decrease Vmax but do not affect Km.
  - ✓ Cannot be overcome by increasing the substrate concentration

Mechanism Of Inhibition

Competitive Inhibition



Noncompetitive Inhibition



THANK YOU FOR YOUR LISTING

Protein metabolism

Protein metabolism refers to the biochemical processes involved in the synthesis (anabolism) and breakdown (catabolism) of proteins in living organisms.

The key details of protein metabolism are:

1. Protein Synthesis (Anabolism):

a) Protein synthesis involves the assembly of amino acids into polypeptide chains according to the genetic information encoded in DNA.

b) The process begins with transcription, where the DNA sequence of a gene is copied into messenger RNA (mRNA) in the nucleus.

c) The mRNA then translated into a specific sequence of amino acids, forming a polypeptide chain.

d) Multiple polypeptide chains fold and interact to form functional proteins, which may undergo further modifications such as folding, cleavage, and addition of chemical groups.

2. Protein Degradation (Catabolism):

Protein catabolism involves the absorption dietary protein and breakdown of proteins into their constituent amino acids, which can be reused for protein synthesis or as a source of energy by converted into other molecules such as glucose (gluconeogenesis) or intermediates in the citric acid cycle.

3. Regulation of Protein Metabolism:

Protein metabolism is regulated by various factors, including:

1. Hormones such as insulin, glucagon, cortisol, and growth hormone play key roles in regulating protein synthesis and degradation.
2. Nutrient availability, particularly the intake of dietary protein and amino acids, influences the rates of protein synthesis and degradation.

3. Cellular signaling pathways, such as integrate signals from growth factors, nutrients, and energy status to modulate protein metabolism in response to changing conditions.

Dysregulation of protein metabolism can contribute to various health conditions, including muscle wasting (cachexia), metabolic disorders, and certain types of cancer. Adequate protein intake and proper regulation of protein metabolism are maintaining health and supporting physiological functions in the body.

How protein absorption is happens?

1. Digestion: Protein digestion begins in the stomach, which secretes gastric juice, a unique solution containing hydrochloric acid (HCl) and the proenzyme pepsinogen.

a) Hydrochloric acid: Stomach HCl is (pH 2 to 3) to hydrolyze proteins and kill some bacteria.

b) Pepsin: This is secreted by the cells of the stomach as an inactive zymogen or proenzyme pepsinogen. where the enzyme pepsin breaks down proteins into smaller peptides in presence of HCL.

c) Small intestine: Further breakdown occurs in the small intestine with help of enzymes such as trypsin, chymotrypsin, and peptidases, resulting in the production of free amino acids, dipeptides, and tripeptides.

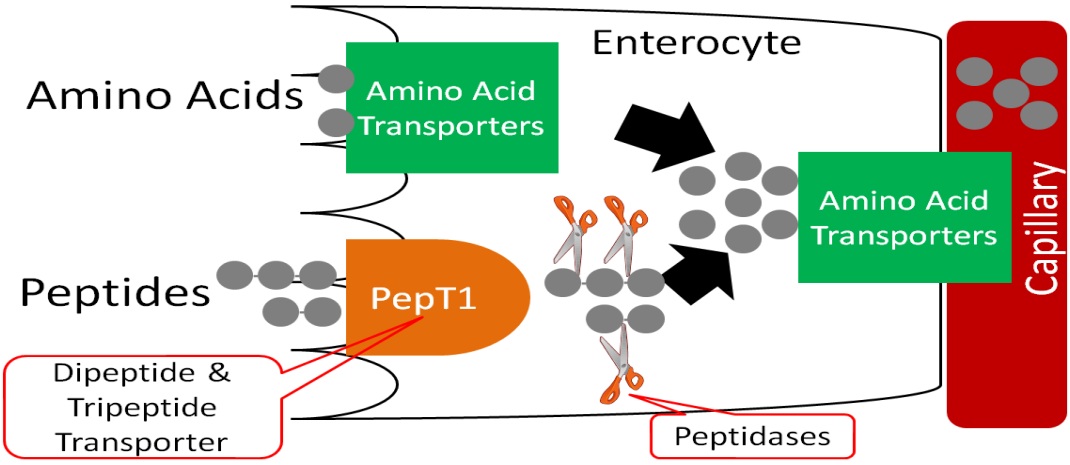


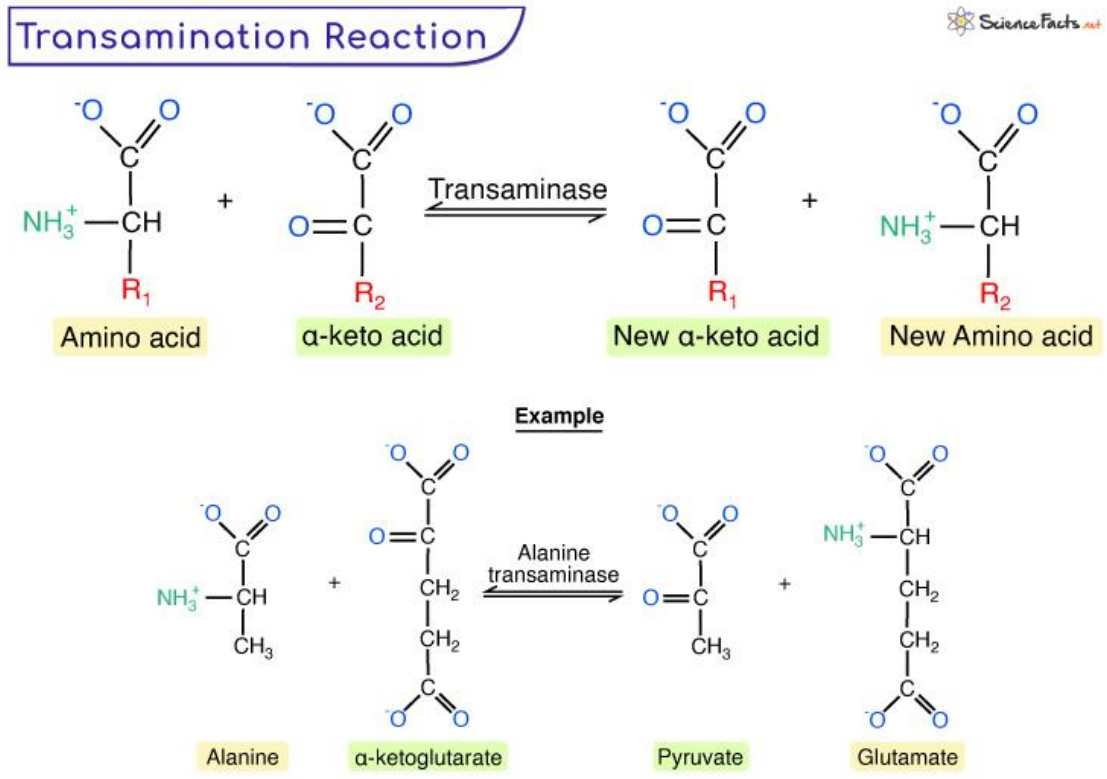
Figure: Small intestinal absorption (Transport amino acid in Bloodstream)

2. Nitrogen removal from amino acids

The presence of the α-amino group keeps amino acids safely locked away from oxidative breakdown, therefor removing the α-amino group is essential for catabolism of all amino acids.

A. Transamination: transfer amino groups to form glutamate

The catabolism of most amino acids is the transfer of their α-amino group to α-ketoglutarate, producing an α-keto acid and glutamate. α-ketoglutarate considers as citric acid cycle ketoacid intermediate. This transfer of amino groups from one carbon skeleton to another is catalyzed by a family of readily reversible enzymes called aminotransferases also called transaminases.



B. Oxidative deamination: amino group removal

Oxidative deamination reactions result in the liberation of the amino group as free ammonia. These reactions occur in the liver and kidney. They provide α-keto acids that can enter the central pathways of energy metabolism(TCA cycle) and ammonia, which is a source of nitrogen in hepatic urea synthesis.

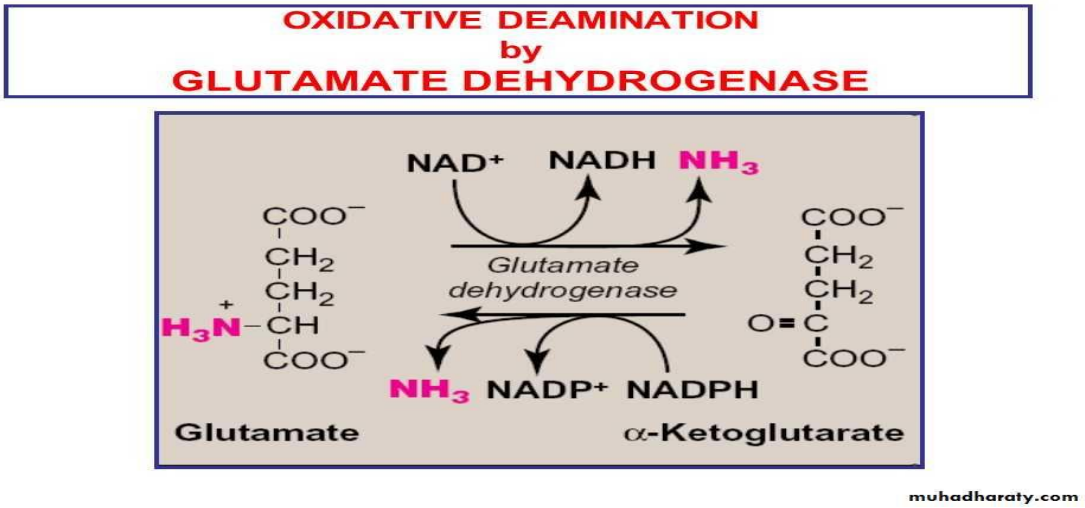


Figure: Formation of glutamine

C. Ammonia transport to the liver

Two mechanisms are available in humans for the transport of ammonia from peripheral tissues to the liver for conversion to urea. Both are important.

- The first mechanism uses glutamine synthetase to combine ammonia with glutamate to form glutamine, a nontoxic transport form of ammonia. The glutamine is transported in the blood to the liver where it is cleaved by glutaminase to glutamate and ammonia, then ammonia is converted to urea (last figure).
- The second mechanism involves the formation of alanine transported in the blood to the liver, where it is transaminated by ALT to pyruvate. The pyruvate is used to synthesize glucose, which can enter the blood and be used by muscle, a pathway called the glucose–alanine cycle.

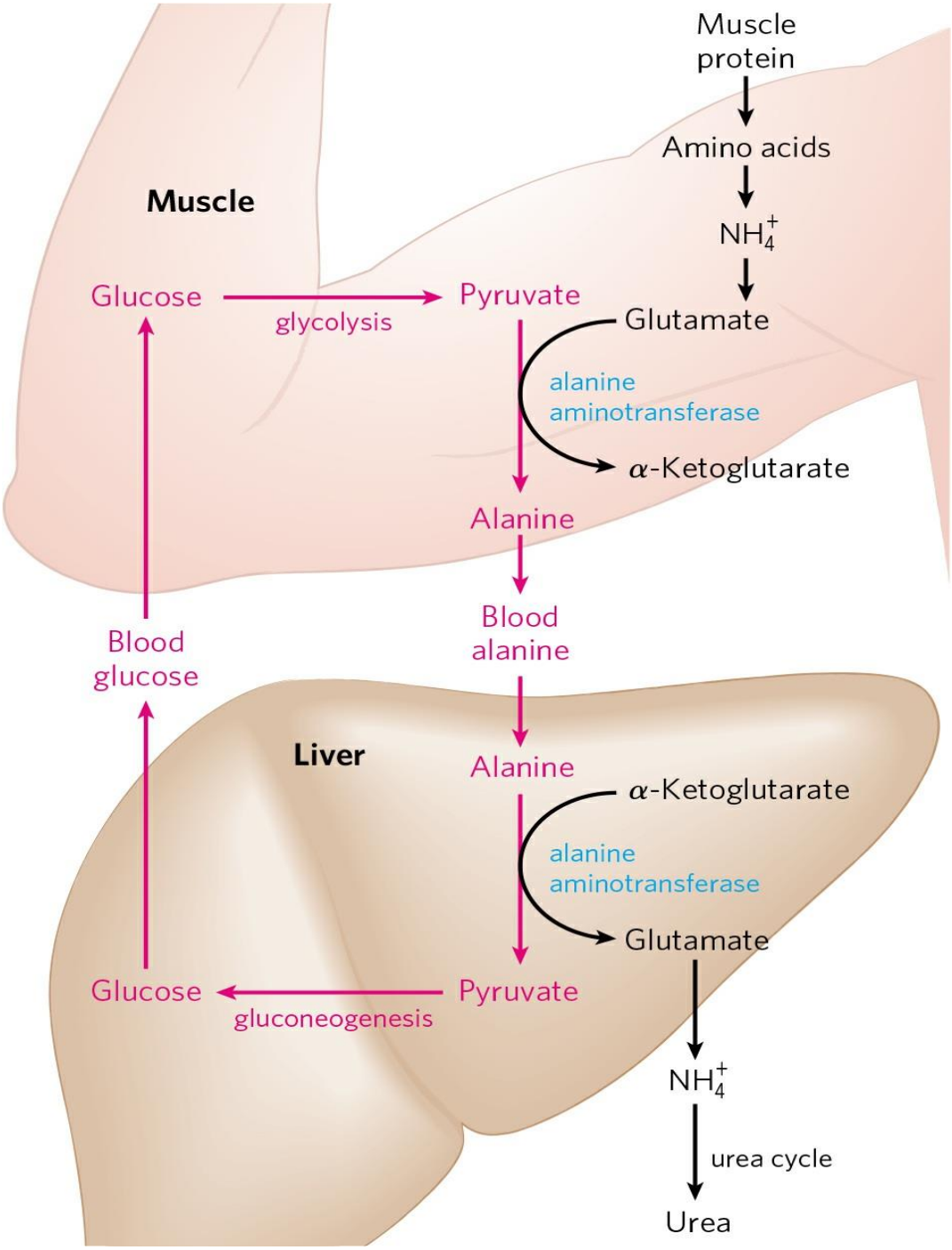

Muscle protein
Amino acids
NH_4^+
Muscle
Glucose
glycolysis
Pyruvate
Glutamate
alanine aminotransferase
α-Ketoglutarate
Alanine
Blood alanine
Blood glucose
Liver
Alanine
α-Ketoglutarate
alanine aminotransferase
Glutamate
Glucose
gluconeogenesis
Pyruvate
NH_4^+
urea cycle
Urea

Figure:
Combine glutamate with ammonia to form nontoxic glutamine

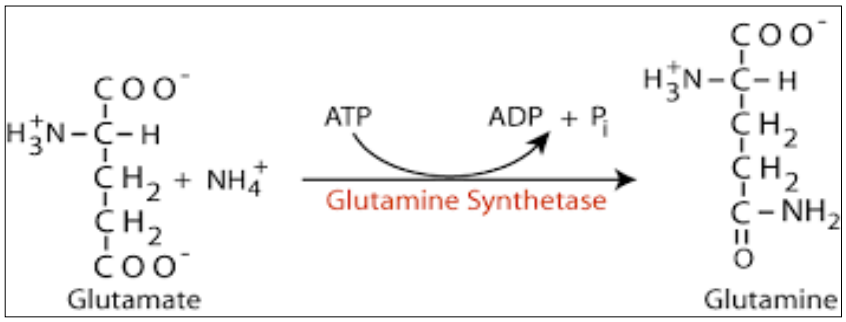
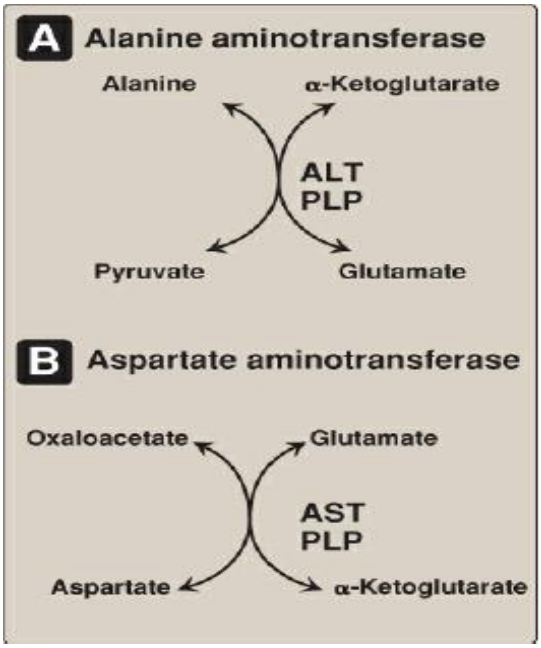


Figure :
Reactions catalyzed during amino acid catabolism. A: Alanine aminotransferase (ALT).
B: Aspartate aminotransferase (AST).
PLP = pyridoxal phosphate (active form of B6 vitamin)



Urea cycle

In humans and mammals, almost 80% of the nitrogen excreted is in the form of urea, which is produced through a series of reactions occurring in the cytosol and mitochondrial matrix of liver cells. These reactions are collectively called the urea cycle.

Urea cycle is pathway in which convert ammonia (a toxic product of nitrogen metabolism which should be removed from body) into urea in the mitochondria of liver cells, this urea forms, then enters the blood stream and filtered by the kidneys to ultimately excreted in the urine.

- The overall reaction for urea formation from ammonia is as follows:

1. Formation of Carbamoyl Phosphate:

The cycle begins in the mitochondria of liver cells, where the enzyme carbamoyl phosphate synthetase I (CPS I) catalyze the condensation of ammonia (NH3), which is derived from the breakdown of amino acids, with bicarbonate (HCO3-) and ATP. This reaction forms carbamoyl phosphate.

$$NH3 + HCO^{3-} + 2ATP \longrightarrow \text{Carbamoyl phosphate} + 2ADP + Pi$$

2. Formation of Citrulline:

Carbamoyl phosphate is then combined with ornithine, an amino acid, in a reaction catalyzed by the enzyme ornithine transcarbamylase (OTC) to form citrulline.

$$\text{Carbamoyl phosphate} + \text{Ornithine} \longrightarrow \text{Citrulline} + Pi$$

3. Formation of Argininosuccinate:

Citrulline is transported from the mitochondria to the cytosol. In the cytosol, citrulline reacts with aspartate, another amino acid, in a reaction catalyzed

by the enzyme argininosuccinate synthetase. This reaction forms argininosuccinate.

Citrulline + Aspartate + ATP ⟶Argininosuccinate + AMP + PPi

4. Formation of Arginine and Fumarate:

Argininosuccinate is then cleaved by the enzyme argininosuccinase into arginine and fumarate.

Argininosuccinate ⟶ Arginine + Fumarate

5. Formation of Urea:

Arginine is hydrolyzed by the enzyme arginase to form urea and ornithine.

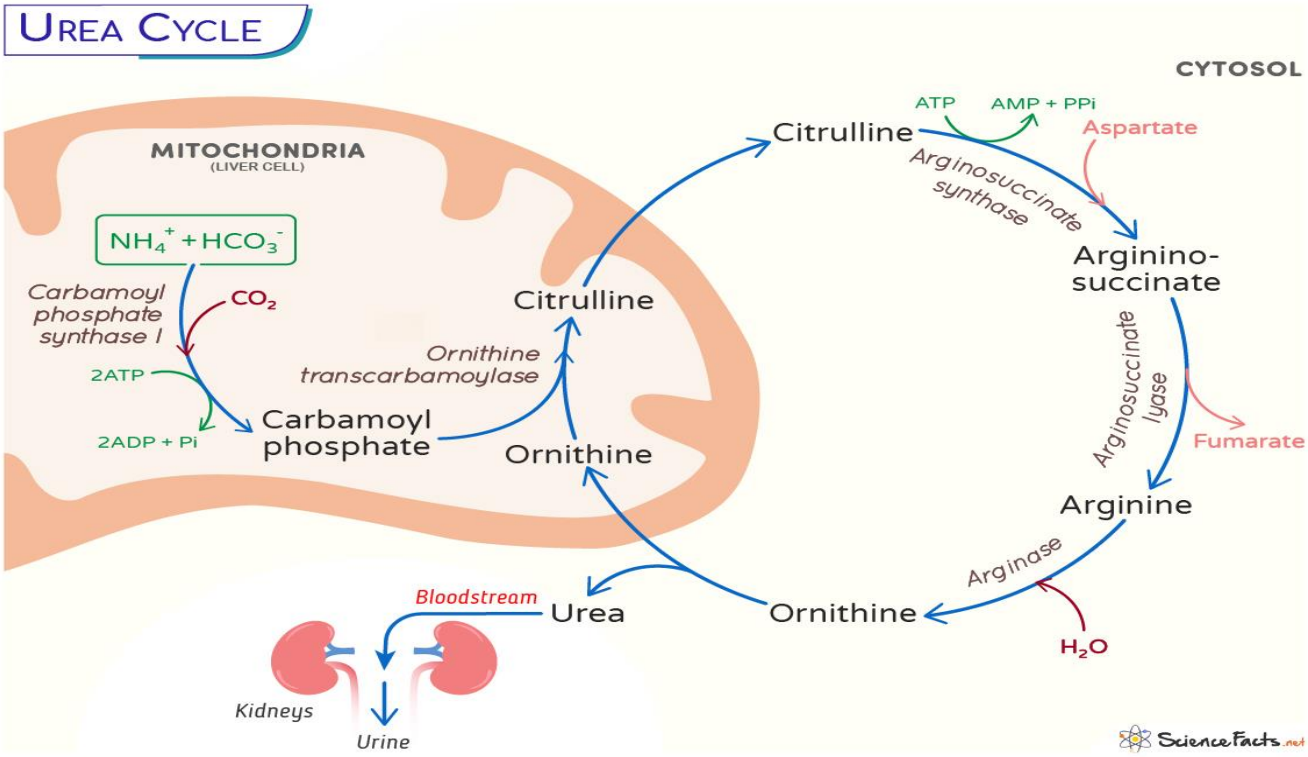
Arginine + H_2O ⟶Urea + Ornithine

6. Regeneration of Ornithine:

Ornithine produced in the urea cycle can re-enter the cycle to combine with carbamoyl phosphate for the synthesis of citrulline, completing the cycle.

Notes:

- The fumarate produced during the cycle enters the citric acid cycle and is converted back to oxaloacetate, which can then react with another molecule of aspartate to form more argininosuccinate.
- This cycle is vital for maintaining nitrogen balance in the body and preventing the accumulation of toxic ammonia.


UREA CYCLE
CYTOSOL
MITOCHONDRIA
(LIVER CELL)
$NH_4^+ + HCO_3^-$
Carbamoyl phosphate synthase I
CO_2
2ATP
2ADP + Pi
Carbamoyl phosphate
Ornithine transcarbamoylase
Citrulline
Ornithine
ATP
AMP + PPi
Aspartate
Citrulline
Argininosuccinate synthase
Arginino-succinate
Argininosuccinate lyase
Fumarate
Arginine
Arginase
H_2O
Ornithine
Urea
Bloodstream
Kidneys
Urine
ScienceFacts.net

vitamins

Vitamins are organic molecules that are essential for normal growth, metabolism, and overall health, they cannot be synthesized in adequate quantities by humans, therefore must be supplied by the diet.

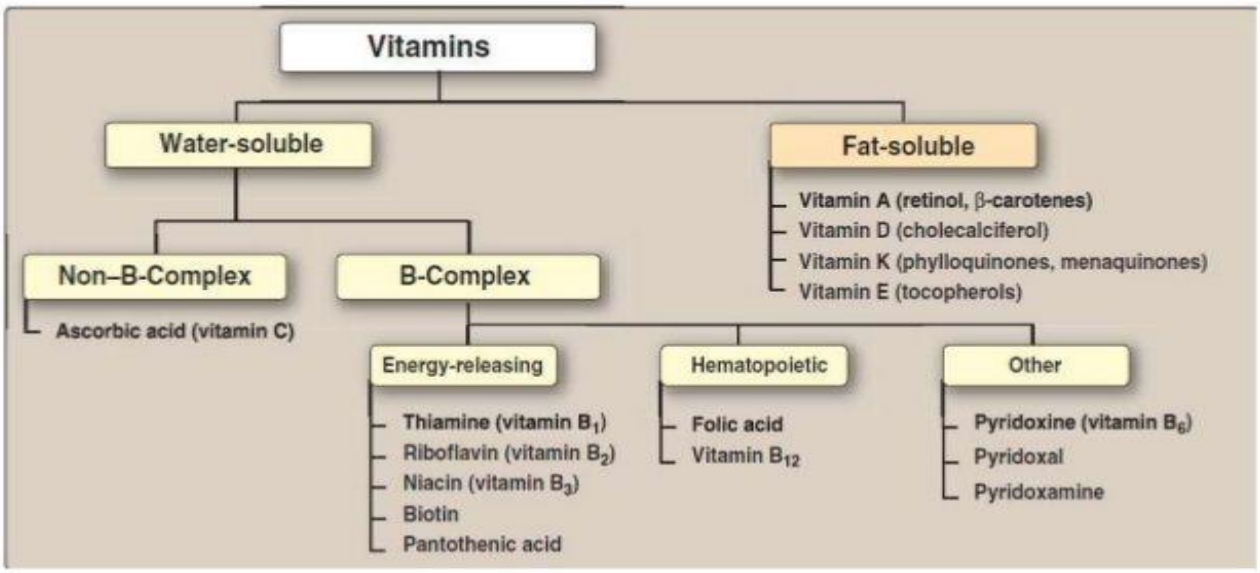
They are classified into two main categories based on their solubility:

1. Water soluble: These dissolve in water and excreted in the urine, toxicity is rare, they are including nine vitamins (folic acid, cobalamin, ascorbic acid, pyridoxine, thiamine, niacin, riboflavin, biotin, and pantothenic acid)

2. Fat soluble: These are soluble in fat and can be stored in the adipose tissue and liver, they are including four vitamins (A, E, D and K).

✓ Excess of vitamins A and D in Dietary Reference Intakes (DRI) can lead to accumulation of toxic quantities of these molecules.

Vitamins Classification Chart



- many of the water-soluble and one vitamin of fat-soluble (vitamin K) are precursors of coenzymes for enzymes of intermediary metabolism.

WATER SOLUBLE VITAMINS

1. FOLIC ACID (VITAMIN B9)

5-methyltetrahydrofolate (THF) is the active form of coenzyme folic acid (folate).

Function: THF receives one-carbon fragments from donors such as serine, glycine, and histidine and transfers them to intermediates, in the synthesis of

a) amino acids.
b) purine nucleotides.
c) thymidine monophosphate (TMP) a pyrimidine nucleotide incorporated into DNA.

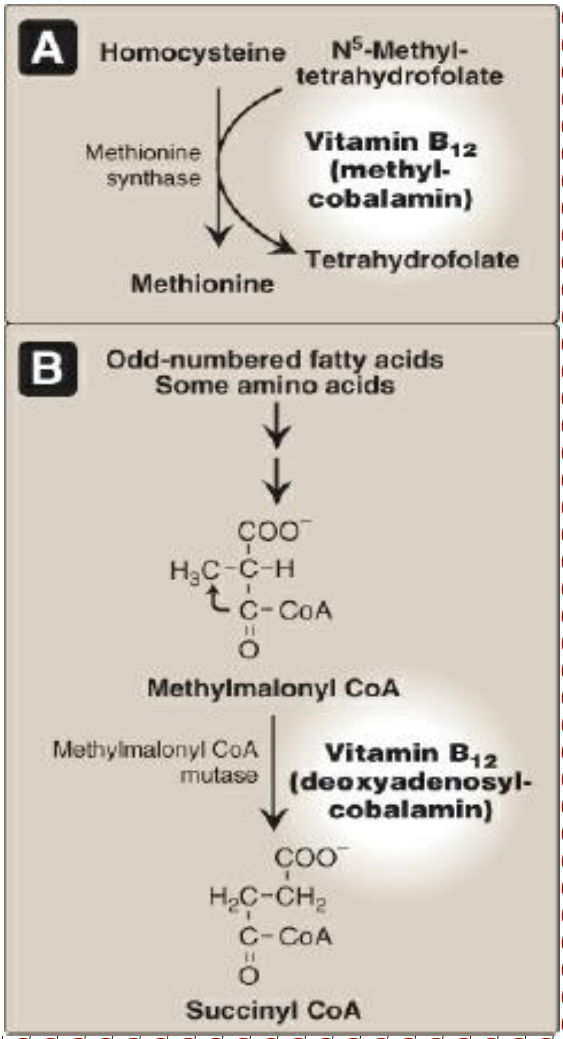
source: brussels sprouts, leafy green vegetables, such as cabbage, kale, spring greens and spinach, peas, chickpeas and kidney beans, liver (but avoid this during pregnancy) breakfast cereals fortified with folic acid

2. COBALAMIN (VITAMIN B12)

Vitamin B12 is required in humans for two essential enzymatic reactions:

a) The re-methylation of homocysteine to methionine.

b) The isomerization of methylmalonyl coenzyme A (CoA), which is produced during the degradation of some amino acids (isoleucine, valine, threonine, and methionine)



and fatty acids (FA) with odd numbers of carbon atoms.

- ✓ Vitamin B12 is synthesized only by bacteria in the gut microbiota in humans and other animals, and it is not present in plants.
- ✓ source: cobalamin is present in in liver, red meat, fish, eggs, dairy products, and fortified cereals.

3. ASCORBIC ACID (VITAMIN C)

The active form of vitamin C is ascorbic acid. Its

Functions:

a) reducing agent.
b) coenzyme in hydroxylation reactions
c) required for the maintenance of normal connective tissue
d) required for wound healing.
e) Vitamin C facilitates the absorption of dietary nonheme iron from the intestine by reduction of the ferric form (Fe+3) to the ferrous form (Fe+2).

- ✓ Vitamin C is one of a group of nutrients that includes vitamin E and β-carotene, which are known as antioxidants.
- ✓ Sources: citrus fruit, such as oranges and orange juice, peppers, strawberries, blackcurrants, broccoli, brussels sprouts, potatoes.

4. PYRIDOXINE (VITAMIN B6)

Vitamin B6 is a collective term for pyridoxine, pyridoxal, and pyridoxamine, all derivatives of pyridine. All three compounds can serve as precursors of the biologically active coenzyme, pyridoxal phosphate (PLP).

- ✓ Functions: as a coenzyme for enzymes that

a) catalyze reactions involving (Transamination, Deamination, Condensation, Decarboxylation) of amino acids example: in the transsulfuration of Homocysteine to cysteine.

b) in the synthesis of dopamine and serotonin.

- ✓ Source: chicken or turkey, some fish, peanuts, soybeans. wheat germ, oats, bananas.

5. THIAMINE (VITAMIN B1)

Thiamine pyrophosphate (TPP) is the biologically active form of the vitamin, formed by the transfer of a pyrophosphate group from ATP to thiamine.

- ✓ Function: TPP serves as a coenzyme in the formation or degradation of α-ketols by transketolase and in the oxidative decarboxylation of α-keto acids.
- ✓ Source: Fortified breakfast cereals, fish, beans, lentils, green peas, enriched cereals, breads, rice, sunflower seeds, yogurt.

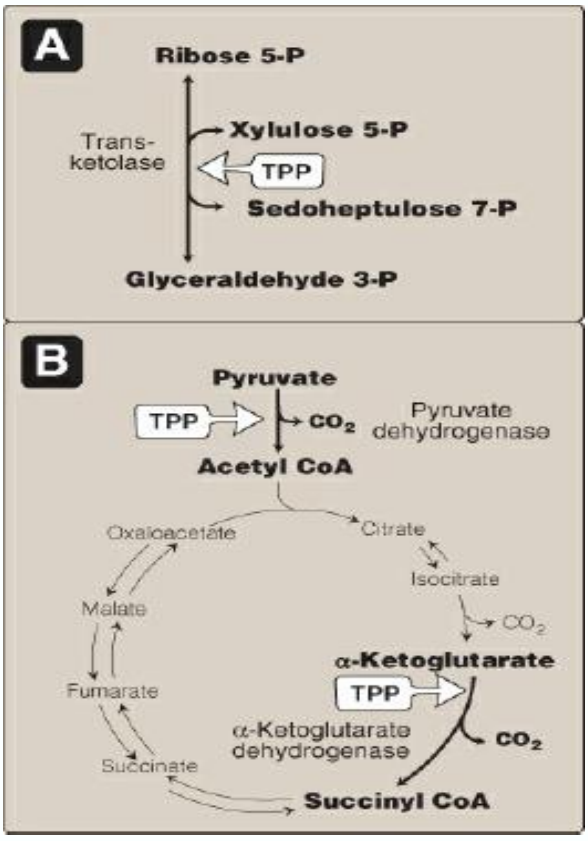


Figure: A & B the Action of Thiamine B1

6. NIACIN (VITAMIN B3)

or nicotinic acid, is a substituted pyridine derivative. The biologically active coenzyme forms are nicotinamide adenine dinucleotide (NAD+) and its phosphorylated derivative, nicotinamide adenine dinucleotide phosphate

(NADP+),

- ✓ Functions:

a) it serves as coenzymes in oxidation–reduction reactions in which the coenzyme undergoes reduction of the pyridine ring by accepting two electrons from a hydride ion.

b) Niacin is useful in the treatment of type IIb hyperlipoproteinemia, raises high-density lipoprotein and lowers Lp[A] levels.

- ✓ Source: Niacin is found in unrefined and enriched grains and cereal, milk, and lean meats (especially liver).

7. RIBOFLAVIN (VITAMIN B2)

The two biologically active forms of B2 are flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), formed by the transfer of an adenosine monophosphate moiety from ATP to FMN.

- ✓ Function: FMN and FAD are bound tightly, sometimes covalently, to flavoenzymes that catalyze the oxidation or reduction of a substrate.
- ✓ Source: Riboflavin is found mostly in meat and fortified foods but also in some nuts and green vegetables, Dairy milk, Yogurt, Cheese, Eggs, Organ meats (beef liver), Chicken breast.

8. BIOTIN (VITAMIN B7)

- ✓ Function: Biotin is a coenzyme in carboxylation reactions, in which it serves as a carrier of activated carbon dioxide (CO2) for the mechanism of biotin-dependent carboxylations. Biotin is covalently bound to the ε-amino group of lysine residues in biotin-dependent enzymes.
- ✓ Biotin deficiency does not occur naturally because the vitamin is widely distributed in food. Also, a large percentage of the biotin requirement in humans is supplied by intestinal bacteria.

- ✓ the addition of raw egg white to the diet as a source of protein can induce symptoms of biotin deficiency, raw egg white contains the glycoprotein avidin, which tightly binds biotin and prevents its absorption from the intestine.
- ✓ note: it has been estimated that 20 eggs/day would be required to induce a deficiency syndrome. besides that: Inclusion of raw eggs in the diet is not recommended because of the possibility of salmonellosis caused by infection with Salmonella enterica.)
- ✓ Sources of Biotin: Foods that contain the most biotin include organ meats, eggs, fish, meat, seeds, nuts, and certain vegetables (such as sweet potatoes)

9. PANTOTHENIC ACID (VITAMIN B5)

Pantothenic acid is a component of Coenzyme A.

- ✓ Function:

a) transfer of acyl groups (Examples of such structures are succinyl CoA, fatty acyl CoA, and acetyl CoA).

b) Pantothenic acid is also a component of the acyl carrier protein domain of fatty acid synthase

- ✓ Source: Beef, chicken, seafood. Eggs and milk. Vegetables such as mushrooms, avocados, potatoes, and broccoli. Whole grains, such as whole wheat, brown rice, and oats.

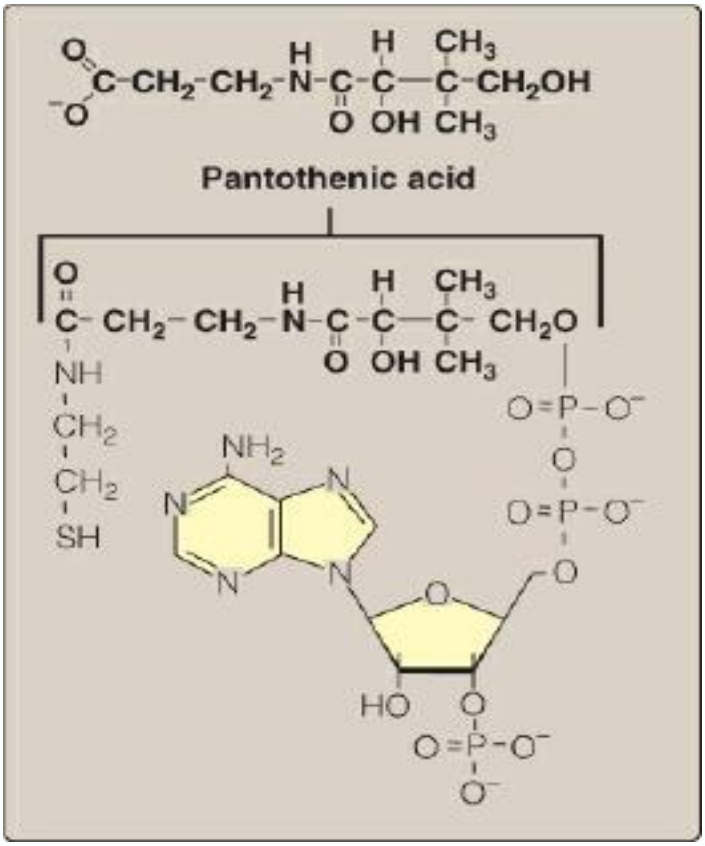


Figure:
Structure of Coenzyme A

vitamins

FAT SOLUBLE VITAMINS

1. VITAMIN A

Vitamin A is a fat-soluble vitamin that comes primarily from animal sources as retinol or a retinoid. The retinoids, a family of related molecules are essential for vision, reproduction, growth, and maintenance of epithelial tissues, also play a role in immune function.

Retinoic acid, derived from oxidation of retinol, mediates most of the actions of the retinoids, except for vision, which depends on retinal, the aldehyde derivative of retinol.

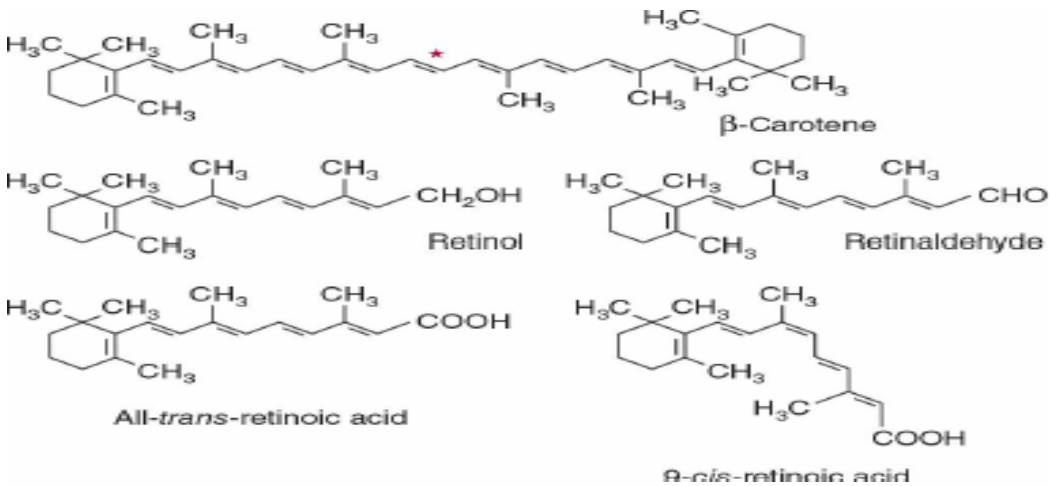
Structure:

1. Retinol: found in animal tissues as a retinyl ester with long-chain FA. It is the storage form of vitamin A.

2. Retinal: This is the aldehyde derived from the oxidation of retinol.

3. Retinoic acid: This acid derived from the oxidation of retinal.

4. β-Carotene: Plant foods contain β-carotene (provitamin A), which can be cleaved in the intestine to yield two molecules of retinal.



Functions:

1. Visual cycle: Vitamin A is a component of the visual pigments of rod and cone cells. Rhodopsin, the visual pigment of the rod cells in the retina, consists of 11-cis retinal bound to the protein opsin, G protein–coupled receptor, is exposed to light, a series of photochemical isomerization occurs triggering a nerve impulse that is transmitted by the optic nerve to the brain

2. Epithelial cell maintenance: Vitamin A is essential for normal differentiation of epithelial tissues and mucus secretion and supports the body's barrier defense against pathogens.

3. Reproduction: Retinol and retinal are essential for normal reproduction, supporting spermatogenesis in the male and preventing fetal resorption in the female. Retinoic acid is inactive in maintaining reproduction and in the visual cycle but promotes growth and differentiation of epithelial cells.

Transportation: Vit. A is transported according to the following:

1. From intestine to blood by chylomicrons, stored in liver as retinyl ester.

2. From liver tissue by retinol binding protein.

3. From cytosol to nucleus by retinoic acid binding protein.

Deficiency: night blindness, Xerophthalmia and Keratomalacia.

Excessive of Vitamin A: excessive intakes of vitamin A causes accumulation of intracellular binding proteins, cell membrane lysis and tissue damage.

Symptoms of toxicity:

1. Central nervous system (headache, nausea, ataxia, and anorexia, all associated with increased cerebrospinal fluid pressure)
2. Liver (hepatomegaly with histological changes and hyperlipidemia)

3. Skin (excessive dryness, desquamation, and alopecia).

2. VITAMIN D

The D vitamins are a group of sterols that have a hormone-like function. The active molecule 1,25-dihydroxycholecalciferol[1,25-diOH-D3] or called calcitriol, binds to intracellular receptor proteins. The [1,25-diOH-D3–receptor complex] interacts with response elements in the nuclear DNA of target cells and either stimulates or represses gene transcription.

Function: The most prominent actions of calcitriol are to regulate the serum levels of calcium and phosphorus. Calcitriol is maintaining adequate serum levels of Ca^{2+}. It performs this function by:

(1) increasing uptake of Ca^{2+} by the intestine.

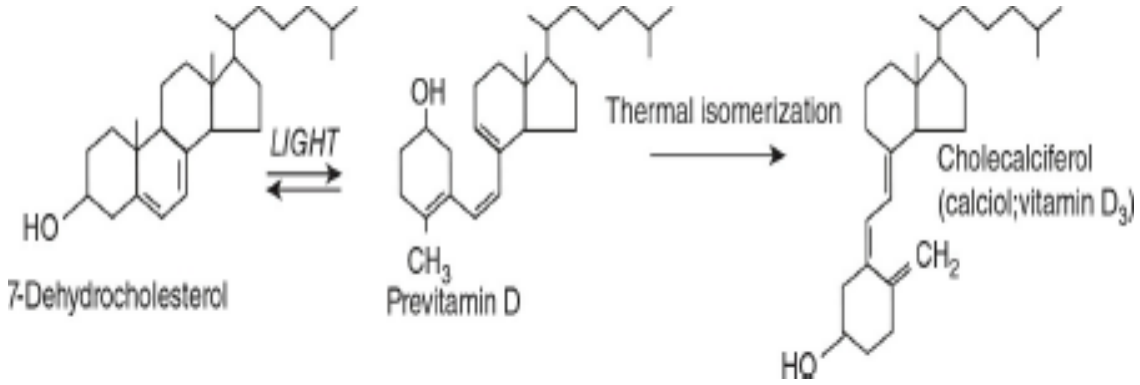
(2) minimizing loss of Ca^{2+} in kidney by increasing reabsorption.

(3) stimulating resorption (demineralization) of bone when blood Ca^{2+} is low.

Note: the mechanism of action of 1,25-diOHD3 is typical of steroid hormones.

Synthesis of vit. D:

- **Endogenous vitamin precursor:** 7-Dehydrocholesterol, an intermediate in cholesterol synthesis, is converted to previtamin D and then to cholecalciferol in the dermis and epidermis of humans exposed to sunlight and transported to liver bound to vitamin D–binding protein (figure below)



- **Diet:** Ergocalciferol (vitamin D2), found in plants, and cholecalciferol (vitamin D3), found in animal tissues, are sources of preformed vitamin D activity. Vitamin D2 and vitamin D3 differ chemically only in the presence of an additional double-bond and methyl group in the plant sterol. Dietary vitamin D is packaged into chylomicrons. (Note:

  Preformed vitamin D is a dietary requirement only in individuals with limited exposure to sunlight.)

  Metabolism:

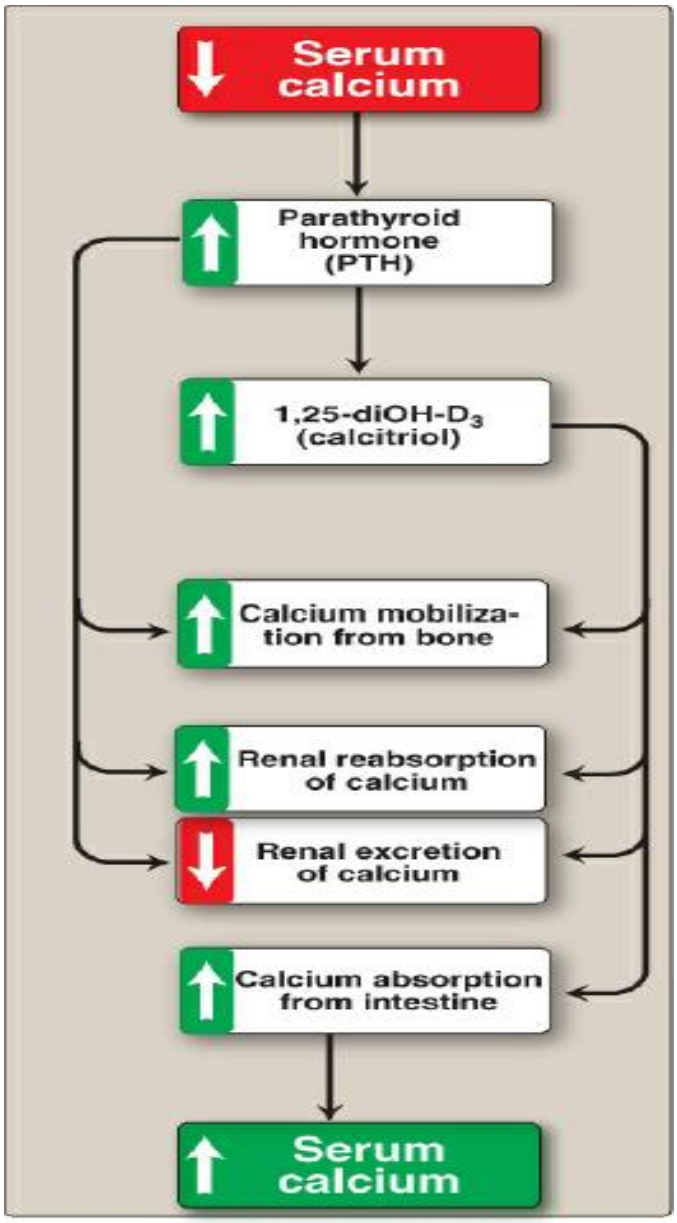
  1,25-Dihydroxycholecalciferol formation: Vitamins D2 and D3 are not biologically active but are converted in vivo to calcitriol, the active form of the D vitamin, by two sequential hydroxylation reactions:

✓ **The first hydroxylation** occurs at the 25 position and is catalyzed by a specific 25-hydroxylase in the liver. The product of the reaction, 25-hydroxycholecalciferol ([25-OH-D3], calcidiol), is the predominant form of vitamin D in the serum and the major storage form.

✓ **The second hydroxylation** at the 1 position by 25-hydroxycholecalciferol 1-hydroxylase found primarily in the kidney, resulting in the formation of 1,25-diOH-D3 (calcitriol).

Regulation: vitamin D is vitamin hormone like, metabolized to the Active Metabolite Calcitriol in Liver & Kidney. Its formation is tightly regulated by the level of serum phosphate ($PO4^{3-}$) and calcium ions (Ca^{2+}), 25-Hydroxycholecalciferol 1-hydroxylase activity is increased directly by low serum PO_4^{3-} or indirectly by low serum Ca^{2+}, which triggers the secretion of parathyroid hormone (PTH) from parathyroid gland. PTH upregulates the 1-hydroxylase. Thus, hypocalcemia caused by insufficient dietary Ca^{2+} results in elevated levels of serum 1,25-diOH-D3. (Note: 1,25-diOH-D3 inhibits

expression of PTH, forming a negative-feedback loop. It also inhibits activity of the 1-hydroxylase.)



Deficiency: vitamin D deficiency disease rickets, Osteomalacia.

Excessive: vitamin D elevation resulting in an elevated plasma concentration of calcium. This can

lead to contraction of blood vessels, high blood pressure, and calcinosis (the calcification of soft tissues).

excessive exposure to sunlight does not lead to vitamin D poisoning, because there is a limited capacity to form the precursor (7-dehydrocholesterol)

3. VITAMIN E

fat-soluble vitamin also called tocopherols the active form is α- tocopherols, it has several important functions:

1. Antioxidant Activity: Vitamin E acts as an antioxidant, helping to protect cells from damage caused by free radicals.

Free radicals are molecules that can cause oxidative stress, which is linked to various chronic diseases and aging.

3. Skin Health: It contributes to maintaining healthy skin by protecting it from UV radiation, pollution, and other environmental factors. It's often used in skincare products for its antioxidant properties.

4. Vision: Vitamin E may also play a role in maintaining eye health, particularly as an antioxidant protecting the cells of the eyes from damage.

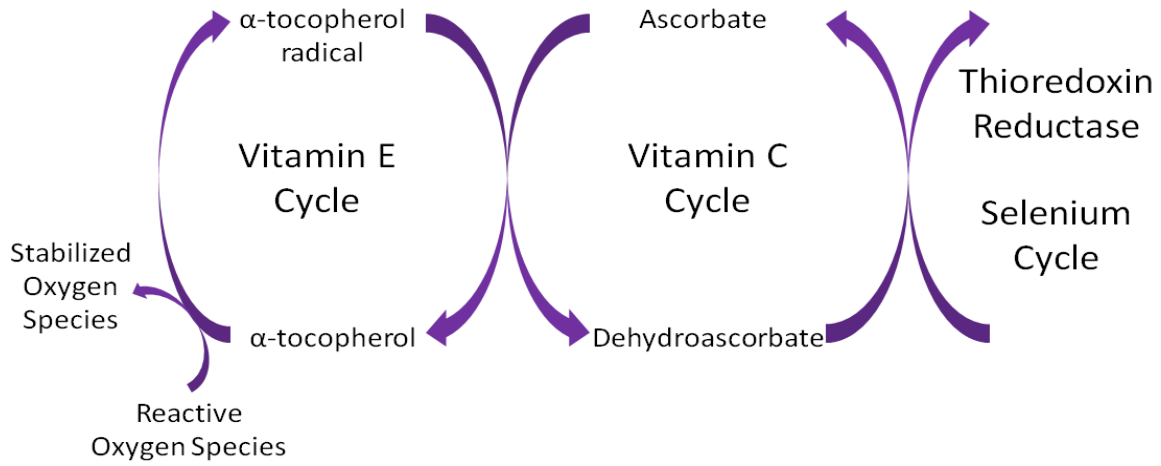
5. Cardiovascular Health: Some research suggests that vitamin E may help prevent or delay the onset of heart disease by preventing the oxidation of LDL cholesterol, which can lead to plaque buildup in arteries.

Deficiency in vitamin E is relatively rare but can lead to health problems over time. Symptoms of deficiency may include:

Muscle weakness, Vision problems, weakened immune function, Nerve damage, Anemia in severe cases, the erythrocyte membranes are abnormally fragile as a result of lipid peroxidation, leading to hemolytic anemia.

Excessive intake of vitamin E is uncommon, primarily because it's not typically obtained in excessive amounts from food alone. Excessive supplementation can lead to adverse effects, including:

- Increased risk of bleeding: High doses of vitamin E can interfere with blood clotting, leading to an increased risk of bleeding. Nausea, Diarrhea, Headaches, Fatigue, Weakened immune function.



4. VITAMIN K

Vitamin K is a fat-soluble vitamin that plays a critical role in blood clotting (coagulation), bone metabolism and posttranslational modification of a number of proteins (most of which are involved with blood clotting), in which it serves as a coenzyme in the carboxylation of certain glutamic acid residues in these proteins. Vitamin K exists in several active forms, for example, in plants as phylloquinone (or vitamin K1), and in intestinal bacteria as menaquinone (or vitamin K2). A synthetic form of vitamin K, menadione, is able to be converted to K2.

Functions:

1. Blood Clotting: Vitamin K is essential for the synthesis of several proteins involved in blood clotting, particularly prothrombin, which is converted to thrombin during the

clotting process. Thrombin then converts fibrinogen into fibrin, forming blood clots to stop bleeding when blood vessels are injured.

2. Bone Health: Vitamin K is also involved in bone metabolism. It considers as coenzyme in activate osteocalcin; a protein necessary for bone and teeth mineralization, adequate vitamin K levels contribute to maintaining bone density and reducing the risk of fractures.

Deficiency:

Vitamin K deficiency is rare but can occur in certain situations:

1. Newborns: Babies are born with low levels of vitamin K and may be at risk of bleeding disorders, particularly if they are exclusively breastfed.

2. Malabsorption Disorders: Conditions affecting fat absorption, such as celiac disease, cystic fibrosis, and certain liver diseases, can lead to vitamin K deficiency.

3. Prolonged Antibiotic Use: Some antibiotics can interfere with vitamin K-producing bacteria in the gut, leading to vitamin K deficiency.

Symptoms of vitamin K deficiency may include easy bruising, excessive bleeding from wounds or mucous membranes, and, in severe cases, hemorrhage.

Excessive Intake:

Prolonged administration of large doses of vitamin K can produce hemolytic anemia and jaundice in the infant, because of toxic effects on the RBC membrane.