Biochemistry

Sem-II

Important Questions & Solutions

UNIT - III

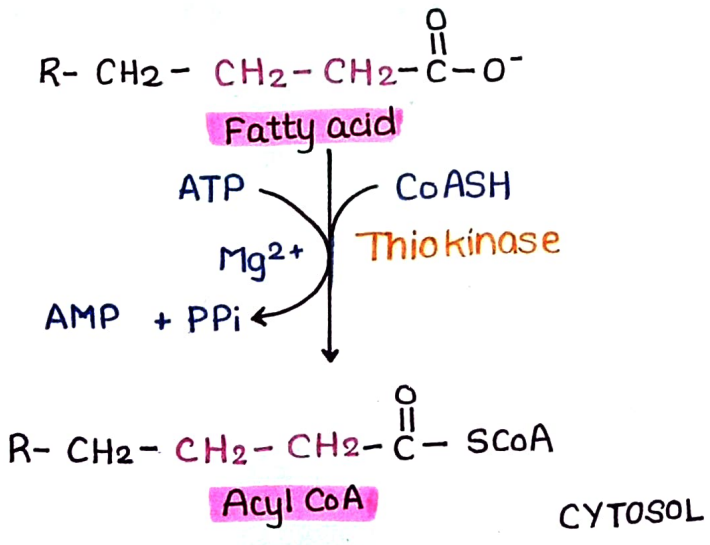
10/15 Marks Question

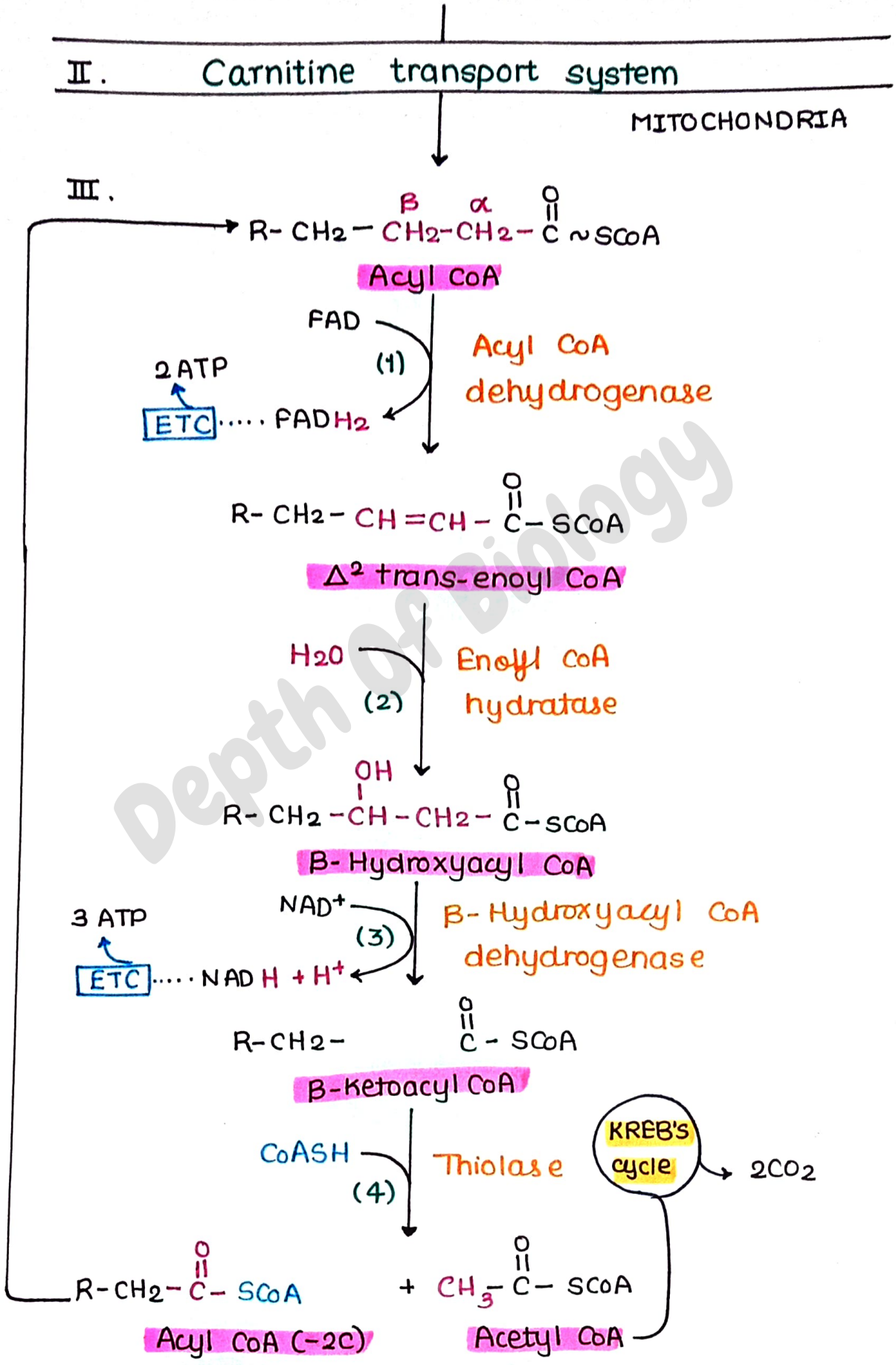
Q.1. Explain oxidation of saturated fatty acid (Palmitic acid)

ANSWER : Introduction :

- Oxidation of fatty acids is the major pathway for the breakdown of fats to produce energy.
- It occurs mainly in the mitochondria of liver, heart and skeletal muscle.
- Among the saturated fatty acids, palmitic acid is the most common, having 16 carbon atoms.
- It undergoes complete oxidation through a cyclic process known as β-oxidation.
- **Oxidation of Saturated fatty acid**

I.





Steps in the Oxidation of Palmitic Acid :

1. Activation of Palmitic Acid :

- Site : Cytosol (outer mitochondrial membrane).
- Before oxidation, free palmitic acid is activated to palmitoyl-CoA.
- Energy cost : 2 high-energy phosphate bonds (equivalent to 2 ATP).

2. Transport into Mitochondria [Carnitine Shuttle]

- Long chain fatty acyl-CoA cannot directly enter the mitochondria so a carnitine shuttle system is used.
- Steps of Carnitine Shuttle :

1). Palmitoyl-CoA + Carnitine ⟶ Palmitoyl-carnitine
(Enzyme : Carnitine acyltransferase I - outer membrane)

2). Palmitoyl-carnitine enters mitochondrial matrix via translocase.

3). In the matrix,
Palmitoyl-carnitine ⟶ Palmitoyl-CoA + carnitine
(Enzyme : Carnitine acyltransferase II)

3. β-Oxidation Cycle (in Mitochondrial Matrix)

- β-oxidative is a cyclic degradation of fatty acids, where two-carbon units are removed at a time as acetyl-CoA.
- Each cycle includes 4 steps:

Step No.	Reaction	Enzyme	Product
1.	Oxidation	Acyl-CoA dehydrogenase	$FADH_2$
2.	Hydration	Enoyl-CoA hydratase	–
3.	Oxidation	β-hydroxyacyl-CoA dehydrogenase	NADH
4.	Thiolysis	β-Ketothiolase	Acetyl-CoA

- Palmitoyl-CoA (C_{16}) undergoes 7 cycles of β-oxidation
- Final products:
- 8 Acetyl-CoA
- 7 NADH
- 7 $FADH_2$

4. Fate of Acetyl-CoA

- The 8 molecules of Acetyl-CoA enters the Citric Acid cycle (TCA / Krebs cycle) to produce ATP, CO_2 and water.
- In liver, acetyl coA may also be used to form ketone bodies during fasting / starvation.

- **ATP Yield from Complete Oxidation of Palmitic Acid**

Step	Molecules formed	ATP Yield
From 7 NADH	7	7 x 2.5 = 17.5 ATP
From 7 $FADH_2$	7	7 x 1.5 = 10.5 ATP
From 8 Acetyl-CoA (via TCA cycle)	8	8 x 10 = 80 ATP
Total ATP		108 ATP
Minus Activation Cost	- 2 ATP	
NET ATP Yield		106 ATP

- Modern calculation uses P:O ratio of 2.5 NADH and 1.5 for $FADH_2$

Significance of β-oxidation of Palmitic Acid:

- Major energy source during fasting, prolonged exercise or low carbohydrate intake.
- More energy efficient than glucose oxidation (Glucose = 30-32 ATP vs Palmitate = 106 ATP)
- Important for maintaining blood glucose (via gluconeogenesis) by sparing glucose usage in muscles.
- In liver, excess acetyl-CoA is used for ketogenesis, supplying energy to brain during starvation.

Conclusion:

- Oxidative of saturated fatty acid like palmitic acid is an essential metabolic process for energy production.
- It involves activation, transport and mitochondrial β-oxidation, resulting in high ATP yield.
- It plays a crucial role in energy homeostasis, especially when carbohydrates are limited.

Q.2. Explain De-novo synthesis of fatty acids

ANSWER: De Novo Synthesis of Fatty Acids

- De novo Synthesis means the new formation of fatty acids from non-lipid precursors mainly acetyl-CoA.
- This process occurs mainly in the cytosol of liver, adipose tissue, lactating mammary glands and kidneys.
- The major end product of this pathway is palmitic acid (C_{16}) a saturated fatty acid.
- Site, Requirements and Overview

Factor	Description
Site	Cytosol of liver, adipose tissue, lactating mammary glands & kidney.
Starting Molecule	Acetyl-CoA
End product	Palmitic acid (C_{16})
Main Enzyme	Fatty acid synthase complex
Coenzyme	NADPH (from HMP shunt)
Energy Requirement	ATP
Carbon donor	Malonyl-CoA

- **Phases of Fatty Acid Synthesis:**

- **Phase 1 : Formation of Malonyl-CoA**

- Acetyl-CoA is converted into malonyl-CoA by Acetyl-CoA carboxylase (ACC).

- This is the rate-limiting step and requires biotin (Vitamin B7) and ATP.

$$\text{Acetyl-CoA} + CO_2 + \text{ATP} \xrightarrow[\text{biotin}]{\text{Acetyl-CoA carboxylase}} \text{Malonyl-CoA} + \text{ADP} + \text{Pi}$$

- **Regulation:**

- Activated by : Citrate, insulin

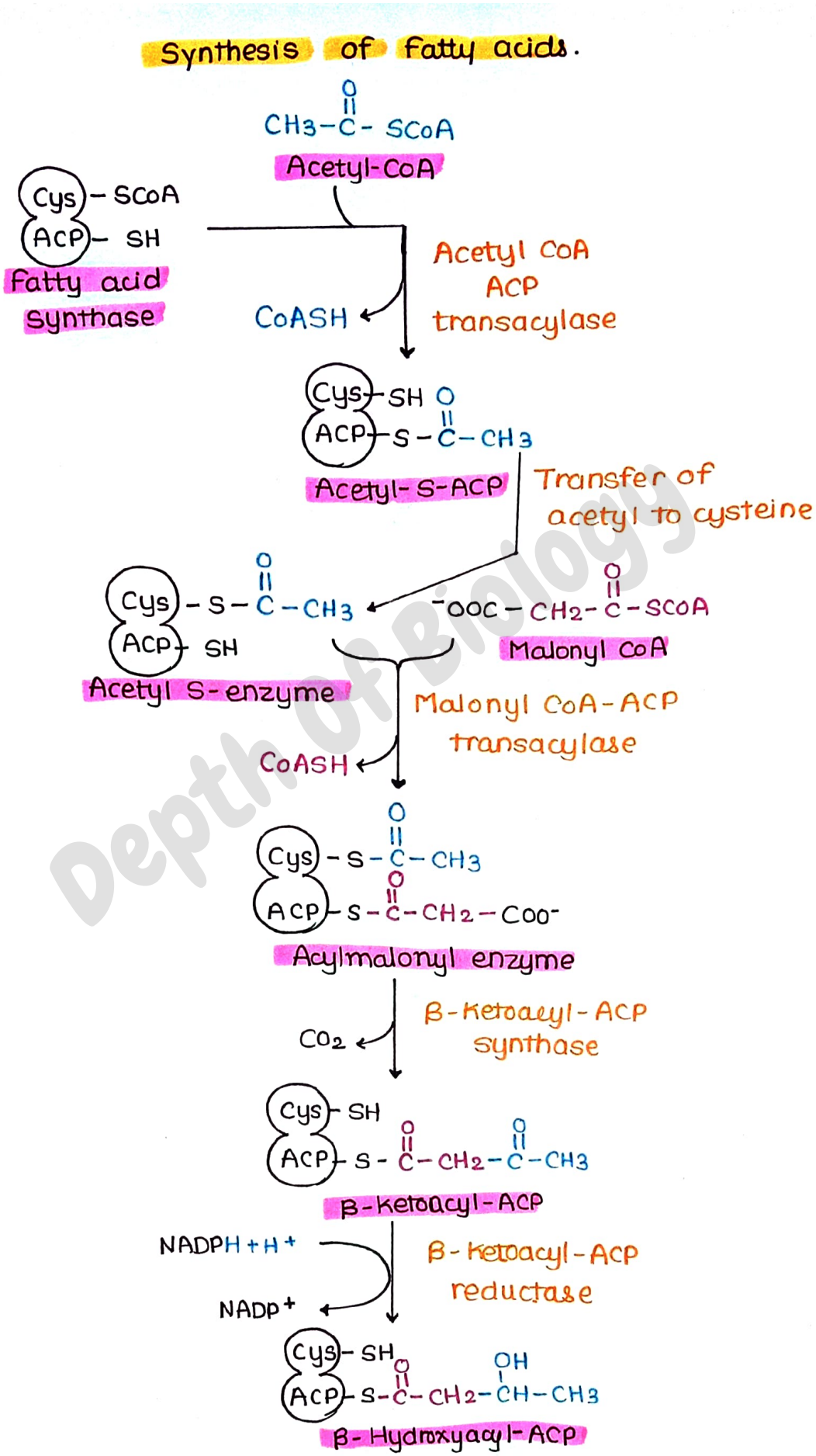
- Inhibited by : Long chain fatty acyl-CoA, glucagon.

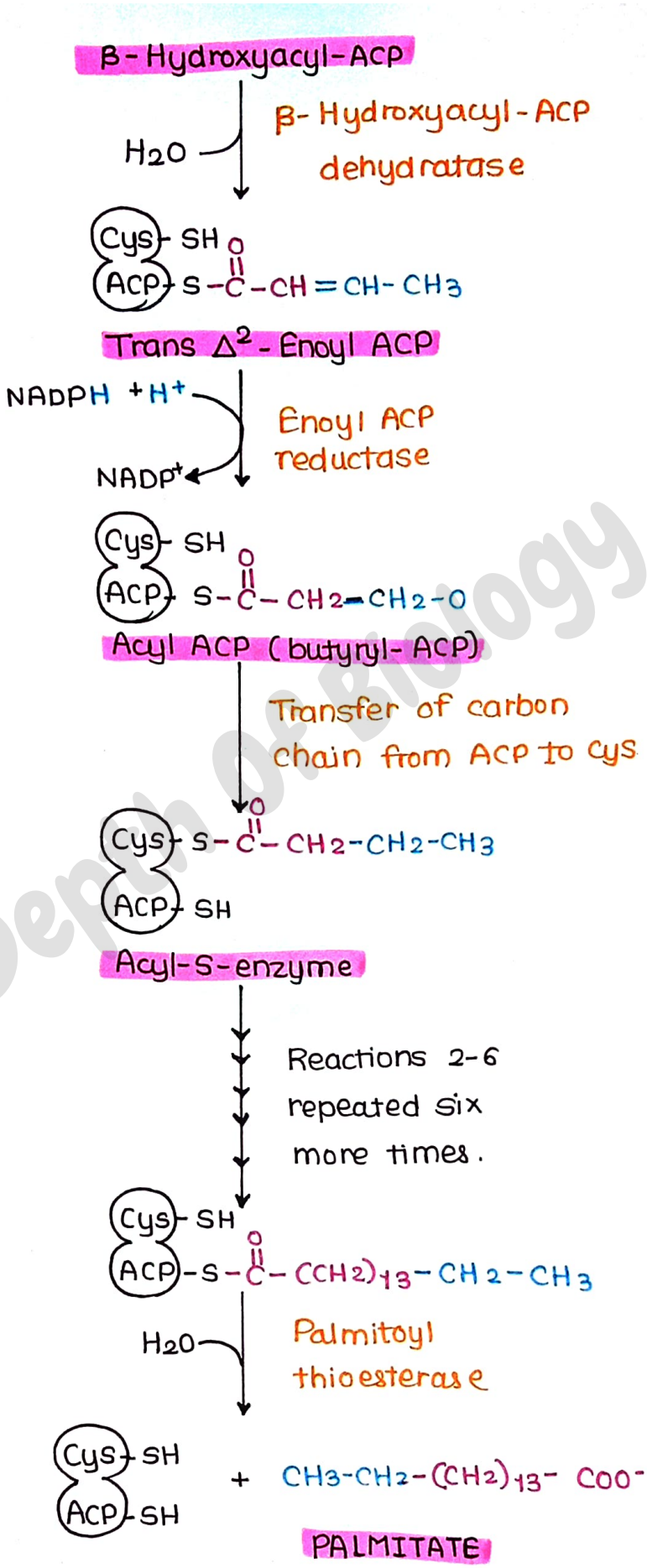
- **Phase 2 : Fatty Acid Chain Elongation**

- Fatty acid synthase (FAS) is a large multifunctional enzyme with 7 enzymatic activities in a single polypeptide chain.

- Each round adds 2 carbons from malonyl-CoA.

- One acetyl-CoA + seven malonyl-CoA ⟶ Palmitic acid (C_{16})





- **Steps in One Cycle of Chain Elongation:**

1. **Priming:**

Acetyl-CoA and malonyl-CoA are attached to ACP (acyl carrier protein).

2. **Condensation:**

Acetyl group (2C) and malonyl group (3C) combine, releasing CO_2, forming a 4C unit.

3. **Reduction:**

NADPH reduces the β-keto group to β-hydroxy.

4. **Dehydration:**

Water is removed to form a double bond.

5. **Second Reduction:**

NADPH reduces the double bond to form a saturated acyl group.

6. **Chain Transfer:**

The growing chain is transferred back to enzyme for next cycle.

- This cycle repeats 7 times, each time adding 2 carbons, resulting in a 16-carbon palmitate chain.

- **Overall Reaction for Palmitic Acid Synthesis:**

$$8\ \text{Acetyl-CoA} + 7\ \text{ATP} + 14\ \text{NADPH} + 14\ \text{H}^+ \rightarrow \text{Palmitic acid} + 8\ \text{CoA} + 7\ \text{ADP} + 7\ \text{Pi} + 14\ \text{NADP}^+ + 6\ \text{H}_2\text{O}$$

- **Source of NADPH:**
  - HMP shunt (Pentose phosphate pathway)
  - Malic enzyme (converts malate to pyruvate + NADPH).

- **Transport of Acetyl-CoA from Mitochondria to Cytosol**
  - Acetyl-CoA is produced in mitochondria but fatty acid synthesis occurs in cytosol.
  - Acetyl-CoA is converted to citrate, transported to cytosol and reconverted to Acetyl-CoA by ATP-citrate lyase.

- **Regulation of Fatty Acid synthesis:**

Regulator	Effect
Insulin	Stimulates (activates Acetyl-CoA carboxylase)
Glucagon, Epinephrine	Inhibit synthesis
Citrate	Activates ACC
Long-chain fatty acyl-CoA	Feedback inhibition.

- **Significance of De Novo fatty Acid synthesis :**
- Provides fatty acids for :
  - Energy storage (triglycerides)
  - Membrane phospholipids
  - Lipids signaling molecules
- Active in fed state when excess carbohydrates are converted to fats.
- Helps in lipogenesis especially in liver and adipose tissue.

- **Conclusion**
- De Novo fatty acid synthesis is a cytosolic anabolic process by which acetyl-CoA is converted to palmitate using ATP and NADPH, regulated by hormonal and nutritional status.
- It plays a vital role in energy storage and lipid metabolism and is tightly regulated to maintain energy balance in the body.

5 / 7 Marks Question

Q.1. Give a detailed note on Urea Cycle and its disorders.

ANSWER: UREA CYCLE

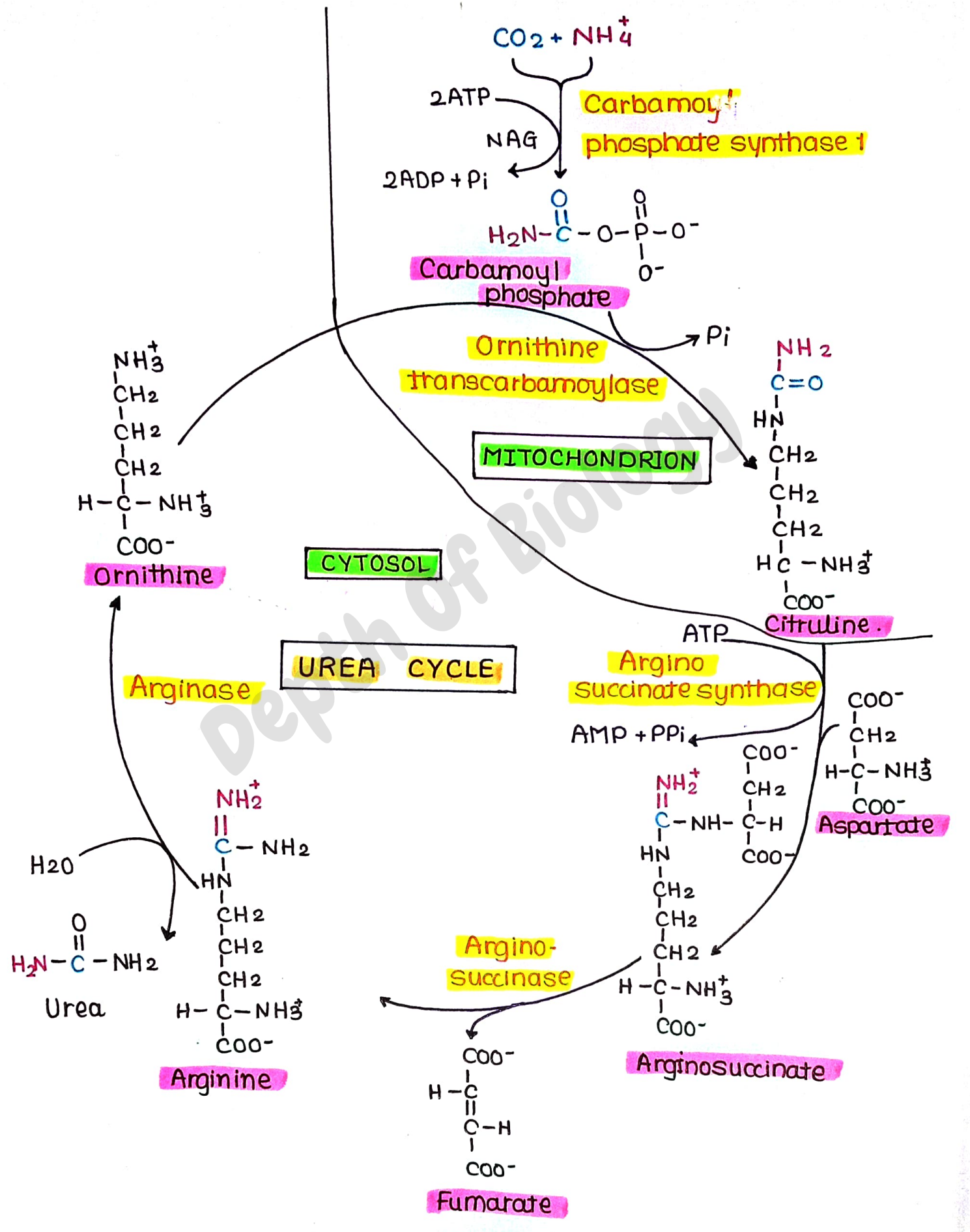
- The urea cycle (also known as the Krebs-Henseleit cycle) is the primary mechanism for the detoxification of ammonia, a toxic byproduct of amino acid metabolism.
- It occurs in the liver and converts ammonia to urea, which is excreted via urine.

- **Net Reaction:**

$$NH_3 + CO_2 + \text{Aspartate} + 3\,ATP \rightarrow \text{Urea} + \text{Fumarate} + 2ADP + AMP + 2Pi + PPi$$

- The main precursors of the cycle are:
  - Ammonia (NH_3): from deamination of amino acids
  - Carbon dioxide (CO_2): from cellular respiration.
  - Aspartate: provides the second Nitrogen atom in urea.

These substrates are essential for the formation of urea, the main nitrogenous waste product in humans.



- **Steps of Urea Cycle**

Step	Reaction	Enzyme	Location
1.	$NH_3 + CO_3 + 2ATP \rightarrow$ Carbamoyl phosphate	Carbamoyl phosphate synthetase I	Mitochondrion
2.	Carbamoyl phosphate + Ornithine → Citrulline	Ornithine transcarbamo--ylase	Mitochondria
3.	Citrulline + Aspartate + ATP → Arginino--succinate	Arginino-succinate synthetase	Cytosol
4.	Argininosuccinate → Arginine + fumarate	Argininosuccinate lyase	Cytosol
5.	Arginine → Urea + Ornithine	Arginase	Cytosol.

- **Net Reaction**:

$NH_3 + CO_2 +$ Aspartate $+ 3ATP \rightarrow$ Urea + Fumarate $+ 2ADP + AMP + 2Pi + PPi$

- **Energetics**:
- 3 ATP used (equivalent to 4 high-energy phosphate bonds)
- Very energy-consuming, but essential for life.
- **Urea Cycle Disorders**

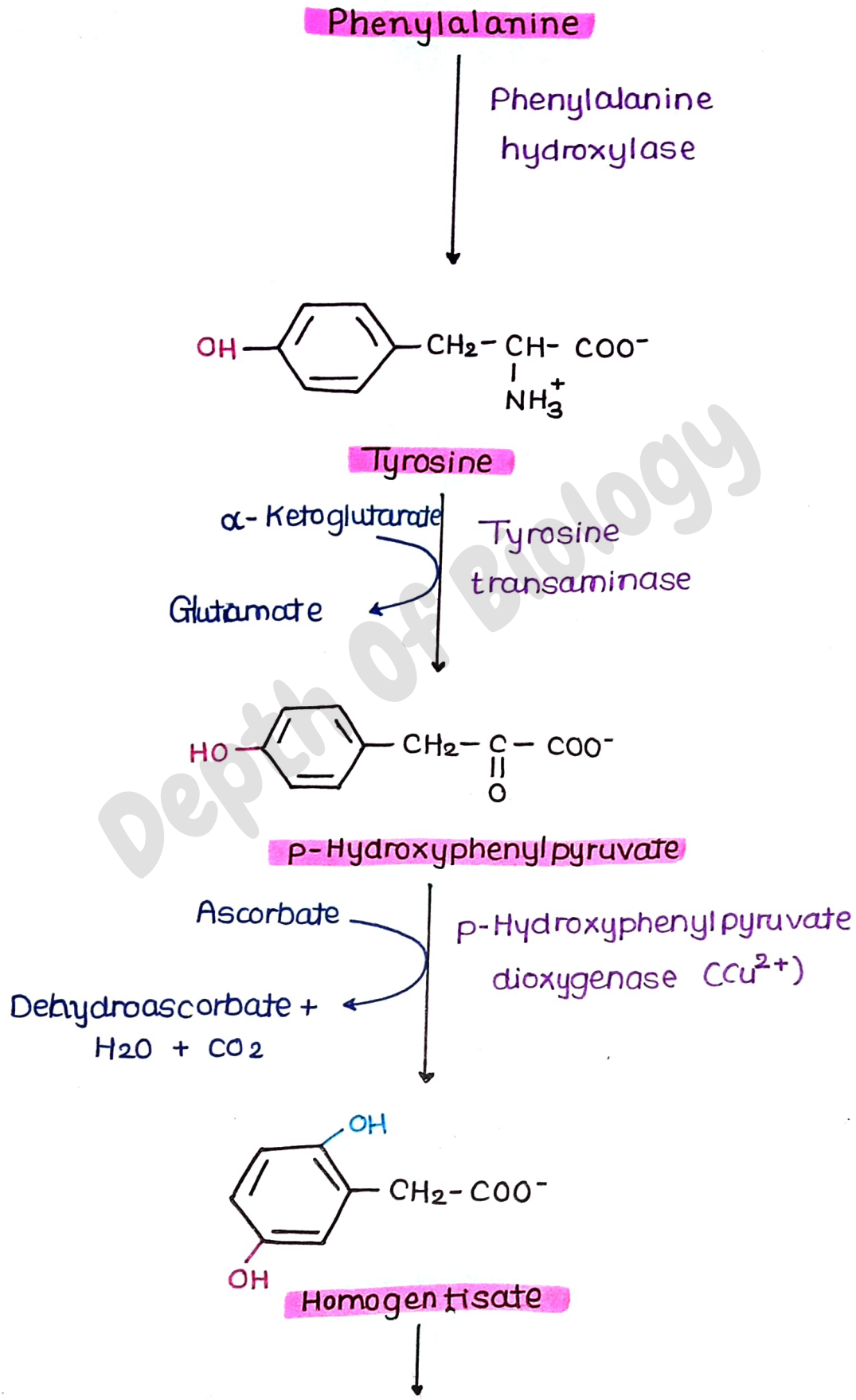
Disorder	Enzyme Deficiency	Features
CPS-I deficiency	Carbamoyl phosphate synthetase I	Hyperammonemia Type I
OTC Deficiency	Ornithine transcarbamoylase	Hyperammonemia Type II (x-linked)
Citrullinemia	Argininosuccinate synthetase	Citrulline in blood and urine.
Argininosuccinic aciduria	Argininosuccinate lyase	Hair abnormalities, hepatomegaly
Hyperargininemia	Arginase	Progressive spasticity and developmental delay

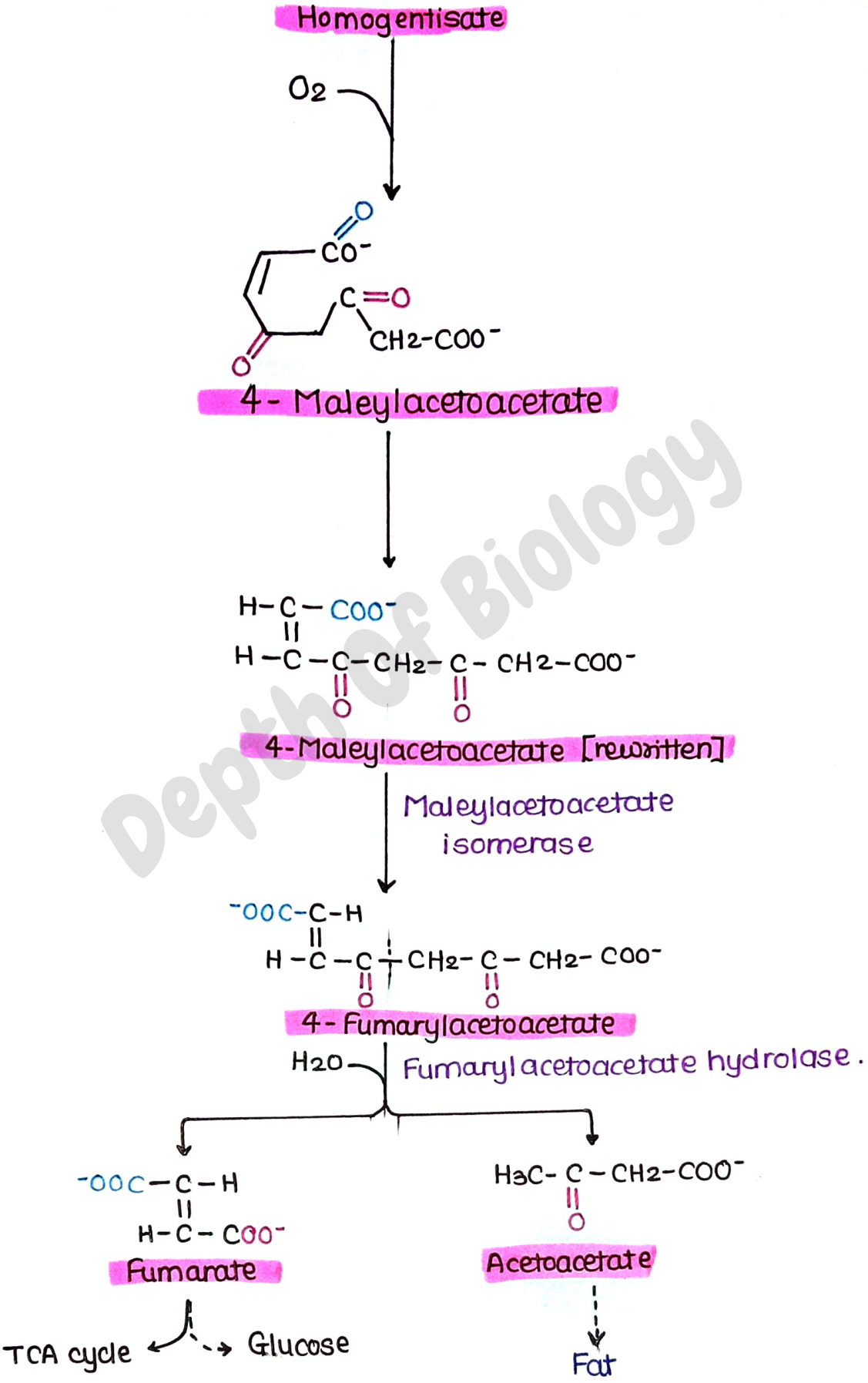
- **Clinical Features of UCDs:**
  - Lethargy
  - Vomiting
  - Hyperammonemia
  - Seizures
  - Coma (in severe cases)
- **Treatment:**
  - Low-protein diet, sodium benzoate, phenylbutyrate, arginine supplementation.

Q.2 Explain catabolism of Phenylalanine and Tyrosine

⇨ **ANSWER:** Phenylalanine and tyrosine are aromatic amino acids.

- Phenylalanine is essential, while
- Tyrosine is non-essential, synthesized from Phenylalanine.
- Both are glucogenic and ketogenic and they are catabolized through a common pathway to form fumarate (glucogenic) and acetoacetate (ketogenic).





Stepwise Catabolism:

1. Phenylalanine → Tyrosine

- Enzyme: Phenylalanine hydroxylase
- Cofactor: Tetrahydrobiopterin (BH_4)
- Hydroxylation of phenylalanine at para-position.

2. Tyrosine → p-Hydroxyphenylpyruvate

- Enzyme: Tyrosine transaminase (also called amino-transferase)
- Requires PLP (pyridoxal phosphate)
- α-Ketoglutarate acts as amino group acceptor → forms glutamate.

3. p-Hydroxyphenylpyruvate → Homogentisate

- Enzyme: p-Hydroxyphenylpyruvate dioxygenase
- Oxidative decarboxylation and hydroxylation occur.

4. Homogentisate → Maleylacetoacetate

- Enzyme: Homogentisate oxidase
- Aromatic ring is cleaved.

5. Maleylacetoacetate ⟶ Fumarylacetoacetate

- Enzyme: Maleylacetoacetate isomerase
- Isomerization reaction.

6. Fumarylacetoacetate ⟶ Fumarate + Acetoacetate

- Enzyme: Fumarylacetoacetate hydrolase
- Final step of cleavage into:
  - Fumarate ⟶ enters TCA cycle ⟶ Glucose.
  - Acetoacetate ⟶ Ketone body.

- **Physiological importance**:

- Maintains energy balance during fasting.
- Provides intermediates for TCA cycle and ketogenesis.
- Forms neurotransmitter precursors: Dopamine, norepinephrine, epinephrine

Q.3 Metabolic Disorders of Catabolism of Phenylalanine and Tyrosine

ANSWER: Phenylalanine and tyrosine are metabolized through a common pathway that produces fumarate and acetoacetate.

- Any enzyme deficiency in this catabolic pathway leads to inborn errors of metabolism, many of which are autosomal recessive disorders.
- These disorders cause accumulation of toxic intermediates, leading to severe clinical symptoms.

- **Major Disorders:**

1. **Phenylketonuria (PKU)**

- Enzyme Deficiency: Phenylalanine hydroxylase (also may be due to deficiency of BH_4 cofactor).
- Metabolic Defect:
  Phenylalanine is not converted to tyrosine and accumulates in the blood and tissues.
- The excess is converted to phenylpyruvate and other phenylketones, which are excreted in urine.
- Clinical features include severe mental retardation, developmental delay, seizures, eczema, hypopigmentation.

of skin and hair and a characteristic mousy odor of urine.

- Early diagnosis by newborn screening and dietary restriction of phenylalanine prevents complications.

2. Tyrosinemia Type I

- This is due to deficiency of fumarylacetoacetate hydrolase, the final enzyme in tyrosine degradation.
- As a result, fumarylacetoacetate and its toxic derivatives (like succinylacetone) accumulate.
- Clinical manifestations include liver failure, renal tubular dysfunction, growth retardation, rickets and a cabbage-like odor of urine.

3. Tyrosinemia Type II

- This disorder is caused by deficiency of tyrosine aminotransferase.
- It leads to high levels of tyrosine in blood and tissues.
- Patients present with painful corneal ulcers, keratitis, hyperkeratotic skin lesions on palms and soles and intellectual disability.

4. Alkaptonuria

- It results from deficiency of homogentisic acid oxidase.
- Homogentisic acid accumulates and is excreted in urine, which turns black on standing due to oxidation.
- Long-term deposition of homogentisic pigment in connective tissues produces ochronosis (bluish-black discoloration) and degenerative arthritis of large joints and spine.

5. Albinism

- Although primarily a defect in pigment synthesis, it is related to tyrosine metabolism.
- It is caused by absence or deficiency of tyrosinase an enzyme needed to convert tyrosine to melanin.
- This results in partial or complete lack of pigmentation in skin, hair and eyes with assosicated photophobia and visual defects.

- These are mostly autosomal recessive and present early in life.
- They lead to accumulation of toxic metabolites that can affect the nervous system, skin, eyes, liver, kidneys and skeletal system.
- Early detection by newborn screening and prompt dietary or medical management can prevent irreversible complications.

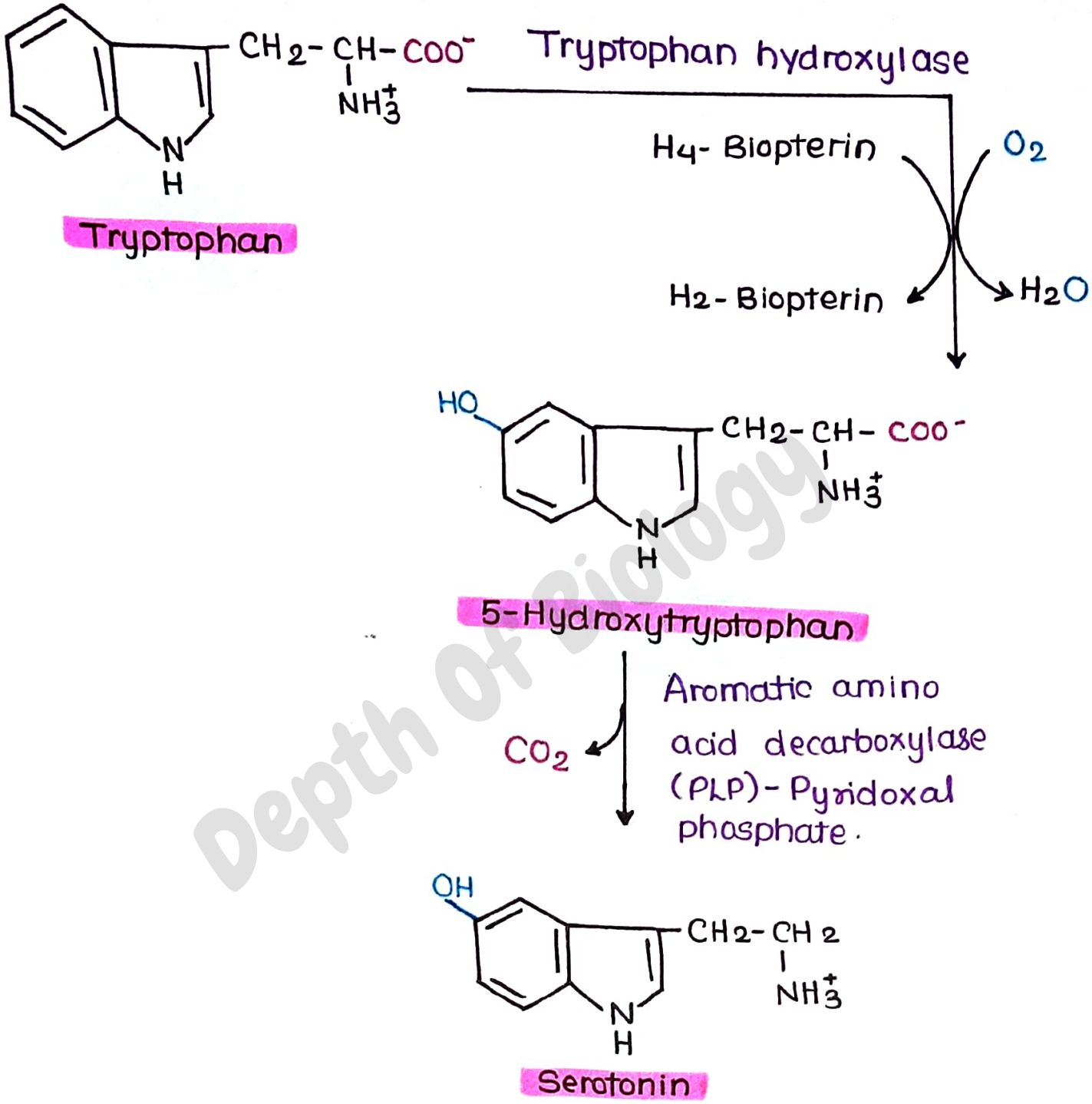
Q.4. Write down the synthesis and biological significance of 5HT and dopamine

ANSWER :

- **Serotonin** (5-Hydroxytryptamine, 5-HT)
- **Synthesis**:

1. Tryptophan → 5-hydroxytryptophan
   - enzyme: tryptophan hydroxylase, needs BH_4, O_2

2. 5-hydroxytrptophan → Serotonin
   - enzyme: aromatic L-amino acid decarboxylase, needs PLP- Pyridoxal phosphate.

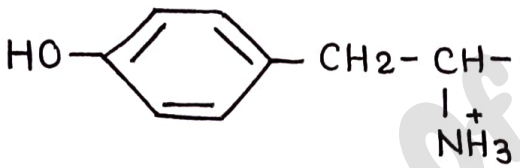


- **Sites of synthesis** :
- CNS neurons
- Enterochromaffin cells in intestine
- Platelets (uptake from plasma)

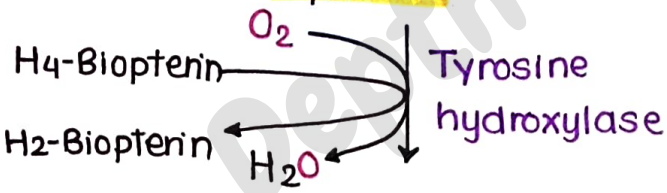
- **Biological roles:**

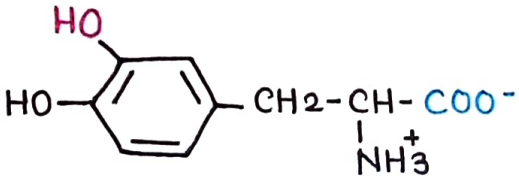
- Neurotransmitter : mood , appetite , sleep regulation
- Controls intestinal motility.
- Vasoconstrictor role in platelets
- Precursor for melatonin in pineal gland.

- **Dopamine ~ Synthesis**

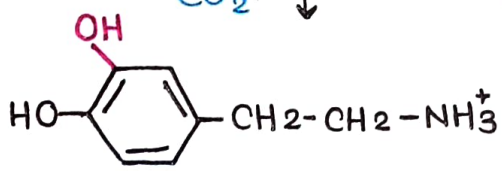


Tyrosine





Dihydroxyphenylalanine (DOPA)



Dopamine

- **Synthesis**

1. Tyrosine ⟶ L-DOPA

   Enzyme : tyrosin hydroxylase, needs BH_4

2. L-DOPA ⟶ Dopamine

   Enzyme: aromatic L-amino acid decarboxylase, needs PLP Pyridoxal phosphate

- **Sites**

- CNS : substantia nigra, hypothalamus.
- Peripheral sympathetic neurons

- **Biological Roles**:

- CNS neurotransmitter : movement control, reward, mood.
- Precursor for norepinephrine and epinephrine.
- Deficiency leads to Parkinson's disease.
- Excess: Schizophrenia (mesolimbic pathway overactivity)

- **Clinical Significance:**
- Levodopa used for Parkinson's disease boosts dopamine synthesis.

Q.5. Explain Jaundice

⇨ **ANSWER:**

- **Jaundice** (also called icterus) is a yellow discolouration of the skin, sclera (white of eyes), and mucous membranes due to increased bilirubin levels in blood.
  - Normal serum bilirubin : 0.3 - 1.2 mg/dL
  - Jaundice becomes visible when bilirubin > 2 mg/dL.

- **Pigment Responsible**
- **Bilirubin**: a yellow pigment formed from the breakdown of heme in hemoglobin from old red blood cells (RBCs).

- Exists in two forms :
  a. **Unconjugated bilirubin**
  water-insoluble, bound to albumin.

b. **conjugated bilirubin** -
water-soluble, formed in liver by conjugated with glucoronic acid.

Normal Bilirubin Metabolism

- **Causes of jaundice**

1. **Production**

- Senescent RBCs destroyed in reticuloendothelial system (spleen, liver, bone marrow).
- Heme → Biliverdin (green) → Bilirubin (yellow).

2. **Transport**

- Unconjugated bilirubin binds to albumin in blood.

3. **Hepatic Uptake**

- Liver cells take bilirubin from blood.

4. **Conjugation**

- Enzyme: UDP-glucaronyl transferase.
- Converts bilirubin → bilirubin diglucoronide [water-soluble].

5. Excretion into Bile

- Conjugated bilirubin secreted into bile → Intestine.

6. Intestinal Changes

- Bacteria convert bilirubin → urobilinogen.
- Some urobilinogen reabsorbed, rest excreted as:
  - ▷ Urobilin in urine (yellow)
  - ▷ Stercobilin in feces (brown)

- **Types of Jaundice**

1. Pre-hepatic (Hemolytic) Jaundice

- Cause: Excess RBC breakdown → excess unconjugated bilirubin.
- Examples: Hemolytic anemia, malaria, sickel cell anemia.
- ↑ Unconjugated bilirubin
- Urine: No bilirubin (not water-soluble)
- Urine urobilinogen: ↑
- Stool: Dark brown (↑ stercobilin)

2. Hepatic (Hepatocellular) Jaundice

- Cause: Liver cell damage → impaired uptake, conjugated & excretion.

- Examples: Viral hepatitis, alcoholic liver disease, drug-induced hepatitis.
- ↑ Both conjugated and unconjugated bilirubin.
- Urine bilirubin: Present (dark urine)
- Urine urobilinogen: Variable
- Stool: Pale if cholestasis present.

3. **Post-hepatic (Obstructive) Jaundice**

Cause: Obstruction in bile ducts → conjugated bilirubin cannot reach intestine.

Examples: Gallstones, pancreatic cancer, bile duct.

- ↑ conjugated bilirubin
- Urine bilirubin: Present (dark urine)
- Urine urobilinogen: Absent
- Stool: Clay-colored
- Itching due to bile salts in skin.

4. **Neonatal Jaundice**.

Cause: Immature liver enzyme (UDP-glucoronyl transferase) in newborns → reduced conjugated.

- Usually physiological (normal), appears after 24 hours, resolves in 1-2 weeks.
- Pathological if severe → may cause kernicterus (bilirubin in brain).
- Treatment: Phototherapy, exchange transfusion.

5. **Hereditary Disorders Related to Jaundice.**

- **Gilbert's syndrome**: mild decrease in bilirubin conjugation.
- **Crigler-Najjar syndrome**: severe absence of conjugated enzyme.
- **Dubin-Johnson syndrome**: defect in excretion of conjugated bilirubin.

- **Complications**

- Chronic liver disease
- Fat malabsorption
- Vitamin K deficiency → Bleeding
- Brain damage in newborns (kernicterus)

- Jaundice is not a disease by itself but a sign of underlying liver, blood or bile duct disorder.

2/3 Mark Question / MCQ

Q.1. Define obesity.

ANSWER : **OBESITY**

- Obesity is a medical condition in which there is an excessive accumulation of body fat that may harm health.
- It is most commonly measured by the Body Mass Index (BMI). A person is considered obese with BMI is equal to or greater than 30 kg/m^2.
- **Obesity may cause due to :**
- Excessive intake of high-calorie food.
- Lack of physical activity.
- Genetic factors and hormonal imbalances.
- Thus, obesity is both a nutritional and metabolic disorder affecting millions worldwide.

Q.2. Describe Ketoacidosis

ANSWER : **KETOACIDOSIS**

- Ketoacidosis is a serious metabolic complication where there is excessive production of ketone bodies, leading to increased acidity (low pH) of blood.
- It mainly occurs in uncontrolled diabetes mellitus, especially type 1 diabetes, due to lack of insulin.

- **Process** :
- In absence of insulin, fat breakdown increases.
- This leads to formation of large amounts of ketone bodies (acetoacetate, β-hydroxybutyrate, and acetone).
- Accumulation of these acids lowers blood pH.

- **Symptoms** :
- Nausea, vomiting.
- Deep and rapid breathing.
- Dehydration, confusion and in severe cases, coma.

- **Significance** :
- Ketoacidosis requires immediate medical treatment to restore acid-base balance and correct blood glucose levels.

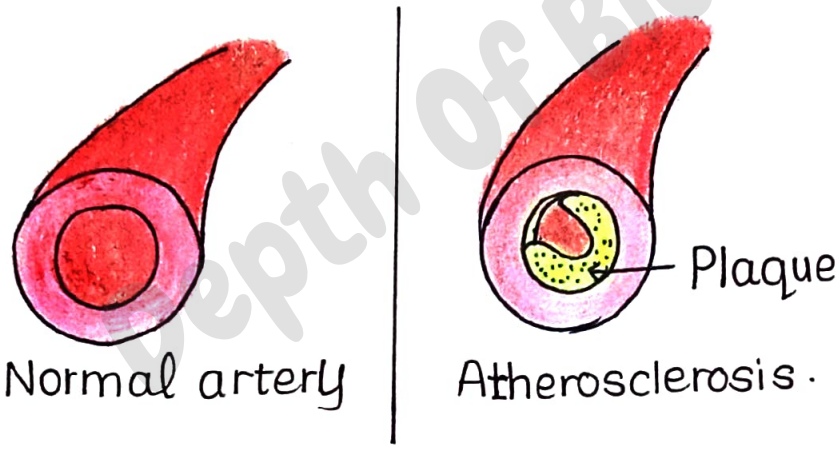
Q.3. Define atherosclerosis

⇨ **ANSWER** : **ATHEROSCLEROSIS** :

- Atherosclerosis is a chronic disease of the arteries in which there is buildup of fatty deposits called plaques on the inner walls of arteries.
- This process leads to thickening and hardening of arteries, narrowing the vessel lumen and reducing blood flow.

- **Steps involved** :
- Injury to endothelium (inner lining of artery).
- Accumulation of lipids (mainly cholesterol).
- Infiltration by white blood cells (macrophages).
- Formation of fibrous plaque.

- **Consequences** :
- Reduced blood supply to organs.
- Can cause heart attack (myocardial infarction), stroke and peripheral vascular disease



Normal artery | Atherosclerosis.

Q.4. Define transmutation [Transamination/ Deamination/ Decarboxylation]

⇨ **ANSWER** : **TRANSMUTATION**

Definition : · Transmutation is the process of changing one chemical element or isotope into another by altering the number of protons in its atomic nucleus.

- **Transamination**: Transfer of amino group from an amino acid to a keto acid.
  (enzyme : aminotransferase, needs PLP).
  - Example: Alanine + α-Ketoglutarate ⟷ pyruvate + glutamate.

- **Deamination**: Removal of amino group as ammonia.
  - Example: Glutamate → α-ketoglutarate + NH_3
    (Enzyme : glutamate dehydrogenase).

- **Decarboxylation**: Removal of CO_2 from amino acids forming amines.
  - Example: Histidine → Histamine
  - Enzyme : histidine decarboxylase, needs PLP

Q.5. What is Albinism

⇨ **ANSWER**:

- Genetic disorder with complete or partial lack of melanin in skin, hair, eyes.
- Cause: Deficiency of tyrosinase enzyme in melanine synthesis.

- Features: Pale skin, white hair, pink eyes, photophobia, poor vision.
- Complications: Sunburn, high risk of skin cancer.

Q.6. Biological Significance of Chloesterol and Vitamin D

⇨ **ANSWER**:

- **Significance of Cholesterol**:
- Cell membrane component (fluidity, stability)
- Precursor for bile acids, steroid hormones, vitamin D.
- Transported in plasma lipoproteins.
- **Significance of Vitamin D**:
- Regulates calcium and phosphorous absorption.
- Maintains bone mineralization.
- Deficiency: rickets (children), osteomalacia (adults).

Q.7. What is Hyperbilirubinemia

⇨ **ANSWER** :

- **Definition** : Elevated bilirubin in blood (> 1.2 mg/dL in adults).
- **Types** : Unconjugated (hemolysis, Gilbert's syndrome) and conjugated (obstruction, hepatitis).
- **Significance** : Main cause of jaundice; guides diagnosis of liver and biliary diseases.