

BIOCHEMISTRY

UNIT 2 NOTES

CARBOHYDRATE METABOLISM

- GLYCOLYSIS
- CITRIC ACID CYCLE
- HMP SHUNT
- GLUCONEOGENESIS
- DIABETES MELLITUS

BIOENERGETICS

- ETC
- OXIDATIVE PHOSPHORYLATION



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CARBOHYDRATE METABOLISM

- Carbohydrates are the most abundant organic molecule on this earth.
- Carbohydrates are the major source of energy in our body.
- All the biochemical processes that are involved in the synthesis, breakdown and interconversion of carbohydrates that ensures a constant supply of energy to all the living cells are known as Carbohydrate Metabolism.
- Carbohydrate metabolism is simpler than fat or amino acid metabolism, hence carbohydrates are used as instant source of energy.
- Glucose is the most important carbohydrate which takes part in the carbohydrate metabolism.

Major Pathway of Carbohydrate Metabolism

- Glycolysis
- Citric Acid Cycle
- Gluconeogenesis
- Glycogenesis
- Glycogenolysis
- HMP Shunt
- Uronic Acid Metabolism
- Galactose Metabolism
- Fructose Metabolism
- Amino Sugar & Mucopolysaccharide Metabolism

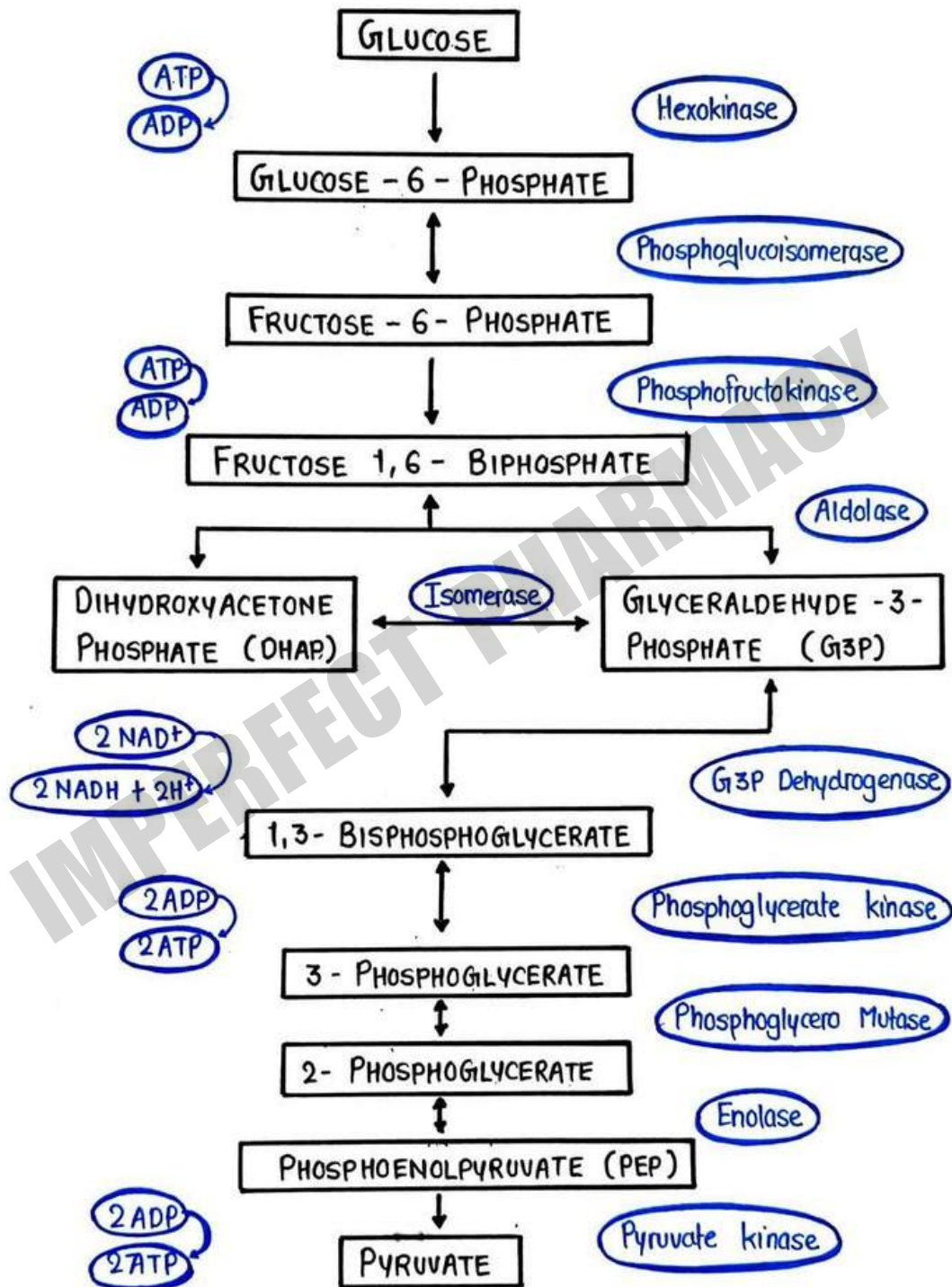


GLYCOLYSIS

- Glycolysis is one of the most important pathway of carbohydrate metabolism occurs in all types of living cells.
- It takes place in the cytoplasm (cytosol) of cells as all the enzymes involved in glycolysis pathway present in cytoplasm.
- It can takes place in both either aerobic or anaerobic conditions.
- Under Aerobic conditions one molecule of Glucose converted into Under Aer two molecules of Pyruvate along with the production of energy in the form of ATP and NADH.
- Under Anaerobic conditions Pyruvate is further converted into Lactate.
- Glycolysis is also known as EMP (Embden, Mayerhof, Parnas) Pathway.

Pathway Of Glycolysis (Significance)

- It is the only pathway that takes place in all the cells of body.
- From glycolysis pathway energy is obtained in the form of ATP which is further used for various metabolic pathways.
- It is the only source of energy in RBCs (Erythrocytes)
- During extreme exercise when muscle tissue lacks enough oxygen, Anaerobic glycolysis occurs that forms major source of energy for muscles.
- It also helps in the synthesis of Non - Essential Amino Acids.
- Glyceraldehyde - 3 - Phosphate is used in triglycerides and phospholipids synthesis.
- Glycolysis is first step of complete oxidation of glucose.



Steps of Glycolysis Pathway

- ① Glucose is converted into glucose-6-phosphate in the presence of hexokinase that breaks the ATP into ADP & P_i .
- ② Glucose-6-Phosphate isomerised into Fructose-6-Phosphate by the enzyme 'Phosphoglucose isomerase'.
- ③ Fructose-6-Phosphate is further converted into Fructose-1,6-bisphosphate in the presence of 'Phosphofructokinase'.
- ④ Fructose 1,6-bisphosphate is further cleaved into two compounds each having 3 carbon atoms, :
 - One is Glyceraldehyde-3-Phosphate (G3P)
 - Other is Dihydroxyacetone-Phosphate (DHAP)
 - DHAP is further isomerised to G3P, hence we get 2 molecules of G3P (Glyceraldehyde-3-Phosphate)
- ⑤ Glyceraldehyde-3-Phosphate is converted into 1,3-bisphosphoglycerate in the presence of G3P Dehydrogenase.
- ⑥ 1,3-bisphosphoglycerate is converted into 3-Phosphoglycerate by the enzyme (Phosphoglycerate kinase)
- ⑦ 3-Phosphoglycerate is isomerised to 2-Phosphoglycerate by the enzyme Phosphoglucomutase.
- ⑧ 2-Phosphoglycerate is converted into Phosphoenol Pyruvate by the enzyme enolase.
- ⑨ Phosphoenol pyruvate is finally converted into Pyruvate in the presence of 'Pyruvate kinase'.
- ⑩ During Anaerobic condition Pyruvate is further converted into Lactate in the presence of Lactate Dehydrogenase.

ENERGETICS OF GLYCOLYSIS PATHWAY

① Molecules of ATP Gain (Synthesized)

- Glyceraldehyde-3-Phosphate $\rightarrow$ 1,3 Bisphosphoglycerate $\Rightarrow$ 6 (2 NADH)
- 1,3 Bisphosphoglycerate $\rightarrow$ 3 Phosphoglycerate $\Rightarrow$ 6 2
- Phosphoenolpyruvate $\rightarrow$ Pyruvate $\Rightarrow$ 2

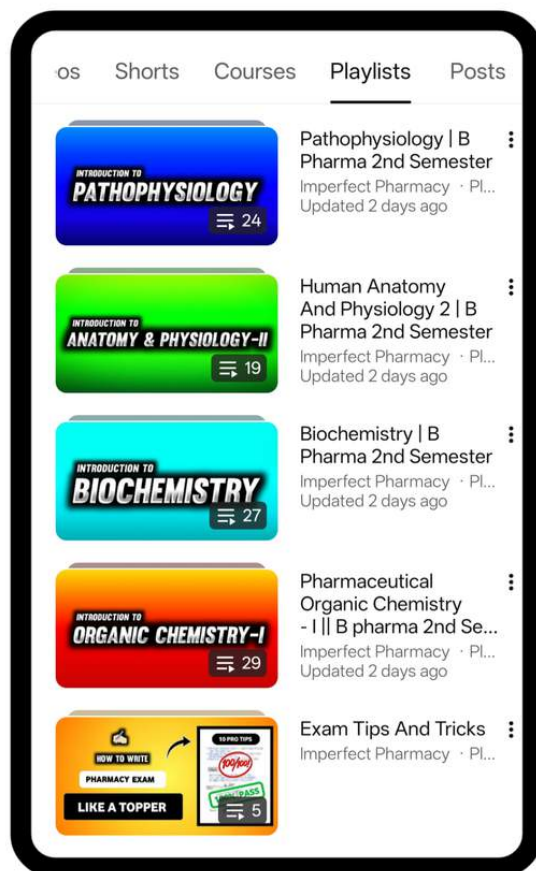
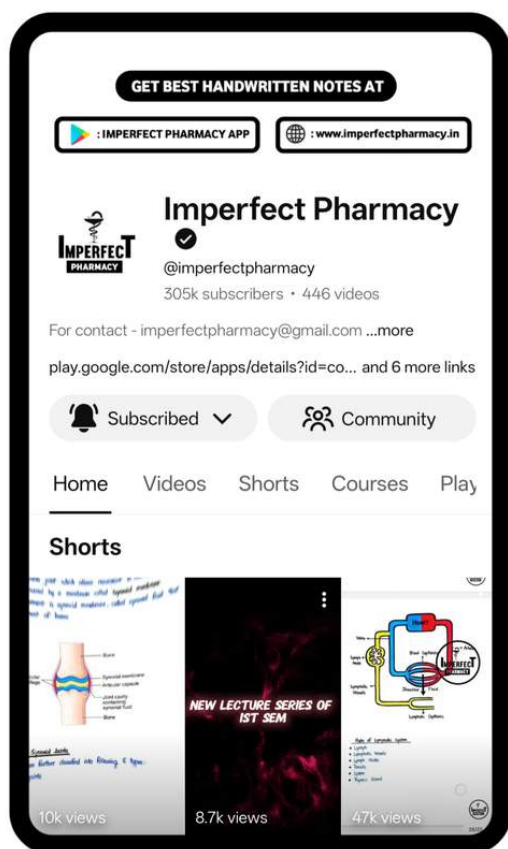
② Molecules of ATP Used (Utilized)

- Glucose $\rightarrow$ Glucose 6-Phosphate $\Rightarrow$ 1
- Fructose-6-Phosphate $\rightarrow$ Fructose-1,6-Diphosphate $\Rightarrow$ 1

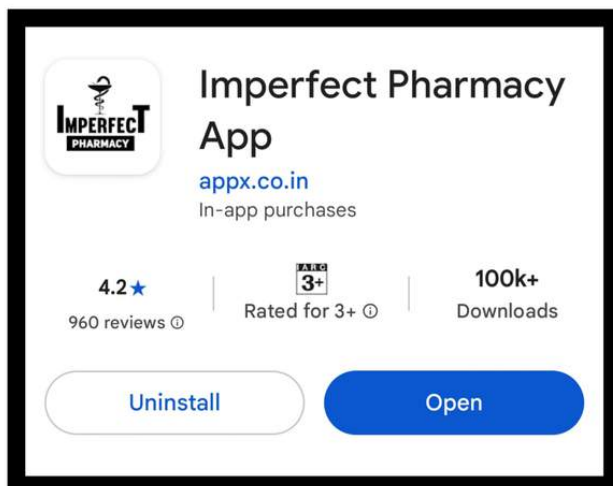
- No. of ATP Synthesized = 10
- No. of ATP Used = 2

Net ATP Synthesized $\rightarrow$ 8

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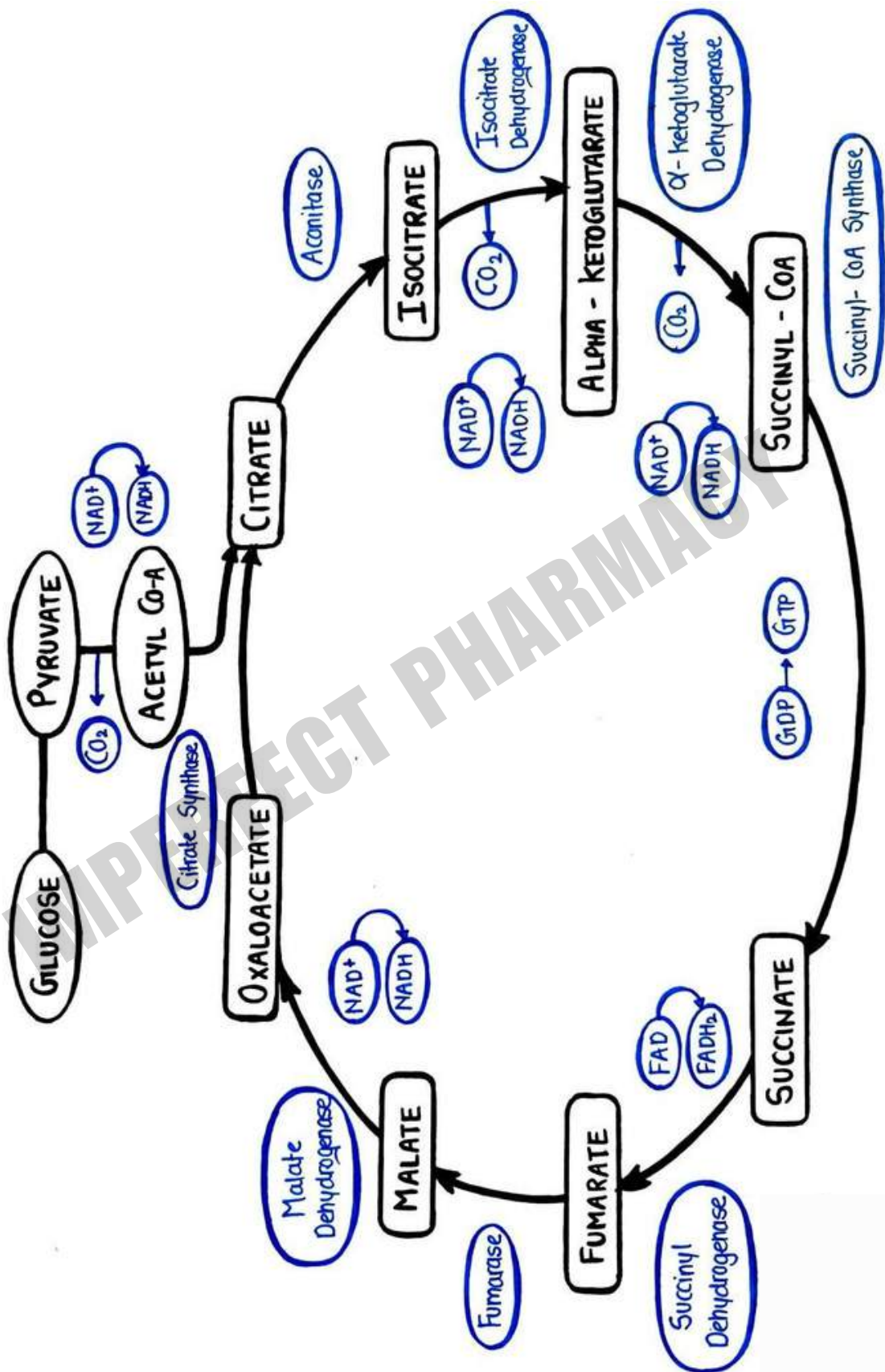


CITRIC ACID CYCLE

- The citric acid cycle is discovered or given by Sir Hans Krebs in 1937, hence it is also known as Krebs Cycle.
- The another name of citric acid cycle or Krebs cycle is TCA Cycle (Tricarboxylic Acid Cycle).
- The Citric Acid Cycle occurs inside Mitochondria and generates a high amount of chemical energy.
- The Citric Acid Cycle is nothing but the forward procedure of Aerobic Glycolysis Pathway.
- The end product of Aerobic Glycolysis Pathway 'Pyruvate' is converted into Acetyl-CoA, which starts the citric acid cycle.
- The citric acid cycle is the most important metabolic pathway for the energy supply to the body as about 65-70% of ATP is synthesized in this cycle.
- The major event of citric acid cycle is oxidation of Acetyl-CoA into CO_2 .
- The citric acid cycle occurs only in Aerobic Conditions.

Significance Of Citric Acid Cycle

- It is the major source of energy for body.
- It is the final common oxidative pathway.
- During Citric acid cycle complete oxidation of acetyl-CoA occurs.
- Excess of carbohydrates is converted into fat.
- It also helps in the synthesis of Non-Essential Amino Acids.
- High amount of ATP is generated.
- It is amphibolic in nature.
- Fat is burned on the wick of carbohydrates.



Steps of Citric Acid Cycle

- STEP-I** : In the first step the acetyl-CoA reacts with oxaloacetate (4 carbon compound) to form Citrate (6 C-compound).
- STEP-II** : In the second step the citrate undergoes isomerisation to form Isocitrate in the presence of Aconitase.
- STEP-III** : In the third step a CO_2 group is removed / released from Isocitrate and it is converted into α -ketoglutarate in the presence of Isocitrate Dehydrogenase.
- STEP-IV** : In the fourth step one more CO_2 group is released from α -ketoglutarate & Succinyl Co-A is formed in the presence of α -ketoglutarate Dehydrogenase.
- STEP-V** : In the fifth step succinyl-CoA is converted into succinate in the presence of succinyl-CoA synthase and also 1 molecule of GDP is converted into GTP.
- STEP-VI** : In the 6th step Succinate is converted into Fumarate by oxidation in the presence of Succinate dehydrogenase and also a molecule of FADH_2 is formed from FAD.
- STEP-VII** : In the 7th step Fumarate is converted into Malate in the presence of enzyme Fumarase.
- STEP-VIII** : In the last step Malate is again converted into Oxaloacetate in the presence of Malate Dehydrogenase and kreb's cycle continues.

ENERGETICS OF KREB'S CYCLE

Although conversion of Pyruvate into Acetyl Co-A is not actually the part of kreb's cycle but for energy calculation we also include this part.

Total ATP

• Pyruvate	→	Acetyl - CoA	⇒	3 (NADH)
• Isocitrate	→	α - ketoglutarate	⇒	3 (NADH)
• α - ketoglutarate	→	Succinyl - CoA	⇒	3 (NADH)
• Succinyl - CoA	→	Succinate	⇒	1 (GTP)
• Succinate	→	Fumarate	⇒	2 (FADH ₂)
• Malate	→	Oxaloacetate	⇒	3 (NADH)

Net ATP = 15 (From 1 PYRUVATE)

- Since, here are 2 molecules of Pyruvate or Acetyl - Co-A hence the total ATP formed in kreb's cycle = $15 \times 2 = 30$
- And if we talk about total ATP produced by 1 Glucose molecule :
- Total ATP from 1 Glucose = ATP Produced in Glycolysis + kreb's cycle
= $8 + 30$
= 38 ATP

HMP SHUNT

- The full form of HMP Shunt is 'Hexose Monophosphate Shunt'
- The another names of HMP Shunt are :
 - ① Pentose Phosphate Pathway
 - ② Phosphogluconate Pathway
 - ③ Warburg - Dickens Pathway
- It is an alternative pathway to glycolysis and TCA cycle for the oxidation of glucose.
- It is more complex pathway than glycolysis.
- It takes place in cytosol of cell.
- This pathway is mainly concerned with the synthesis of NADPH and Pentose Sugar.
- It is anabolic in nature.
- It contains two phase :
 - ① Oxidative Phase (NADPH Synthesis)
 - ② Non-oxidative Phase (Pentose Sugar Synthesis)

Importance Of HMP Shunt

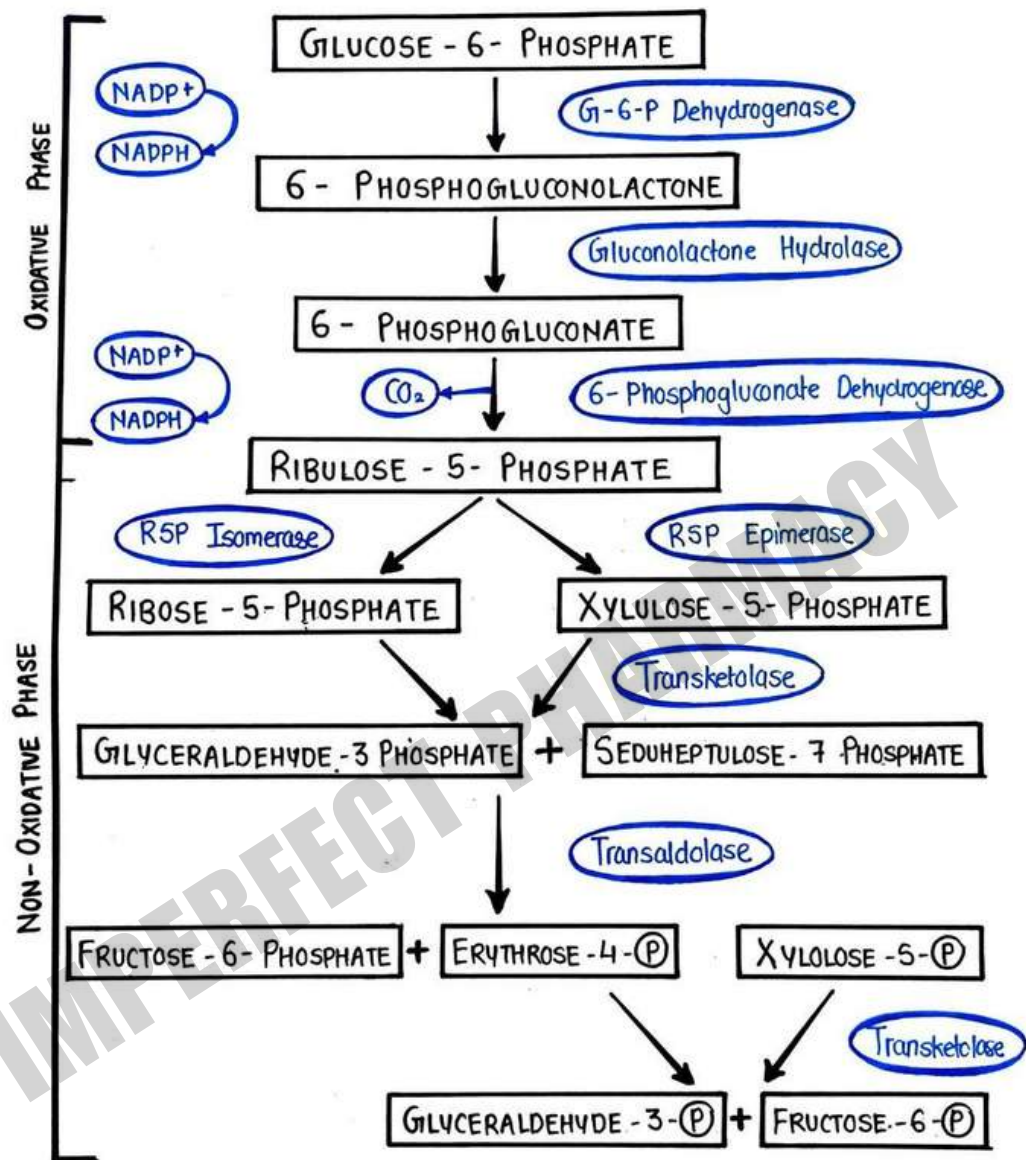
The NADPH produced in HMP Shunt use as :

- In the biosynthesis of Fatty acids and steroids.
- In the biosynthesis of certain amino acids.
- In the preservation or To preserve transparency of lenses.
- In many detoxification reaction.

The pentose sugar synthesized in HMP Shunt used as :

- It is used for synthesis of Nucleic acids (DNA & RNA)
- It is used for synthesis of many nucleotides i.e., ATP, NAD⁺, FAD etc.





Steps of HMP Shunt

- First glucose- 6- phosphate from 'Glycolysis Pathway' converted into 6- Phosphogluconate in the presence of Glucose- 6- Phosphate dehydrogenase.
- Now 6- Phosphogluconolactone further converted into 6- Phosphogluconate in the presence of Gluconolactone Hydrolase.
- In the third step 6- Phosphogluconate is converted into Ribulose -5 Phosphate by releasing one CO_2 group in the presence of 6- Phosphogluconate Dehydrogenase.
- Now this Ribulose - 5- Phosphate undergoes isomerisation & epimerisation & form Ribose - 5 phosphate & Xylulose - 5 Phosphate respectively.
- In the next step Ribose - 5- Phosphate and Xylulose - 5- Phosphate forms and Glyceraldehyde 3- Phosphate and Sedoheptulose - 7 - (P) in the presence of Transketolase.
- Now this G3P and S7P combines and forms Fructose - 6- Phosphate and Erythrose - 4 - Phosphate in the presence of Transaldolase.
- Erythrose - 4 - Phosphate combines with Xylulose - 5 Phosphate & forms Glyceraldehyde - 3 - Phosphate & Fructose - 6 - Phosphate.

ENERGETICS OF HMP SHUNT

- During HMP Shunt no ATP is directly produced or utilized but it is present in the form of NADPH.
- Now ATP Produced is :
 - ① Glucose - 6 - Phosphate $\rightarrow$ 6 - Phosphogluconolactone $\rightarrow$ 3 ATP (NADPH)
 - ② 6 - Phosphogluconate $\rightarrow$ Ribose - 5 - Phosphate $\rightarrow$ 3 ATP (NADPH)
- Now 6 ATP is produced by 1 molecule of Glucose - 6 - Phosphate but Here are 6 molecules of Gl-6-P.

$$\text{TOTAL ATP} = 6 \times 6 = 36$$

GLYCOGEN METABOLISM

- Glycogen is a stored form of glucose.
- It mainly stores in liver and muscles.
- Due to more muscle mass in our body, the quantity of glycogen in muscles (250 grams) is about 3 times higher than that in Liver (75 grams).
- Glycogen metabolism is a process of synthesis and breakdown of glycogen.
- Glycogen metabolism takes place in cytosol (cytoplasm).

Functions of Glycogen

- Liver glycogen maintains blood - glucose level.
- Muscle glycogen supplies energy during muscle contraction.
- It supplies energy during starvation.

Why Glycogen is the major source of stored energy

- Glycogen can be rapidly mobilized
- It can generate energy even in the absence of oxygen.
- Brain needs continuous glucose supply that mostly comes from glycogen breakdown.
- Fat is also a stored form of energy but its mobilization is slow and it also needs O_2 for energy production.

TYPES OF GLYCOGEN METABOLISM

Glycogen metabolism is basically of two types :

- ① Glycogenesis
- ② Glycogenolysis

GLYCOGENESIS

- The synthesis of Glycogen from Glucose is known as Glycogenesis.
- Glycogenesis takes place in cytosol & requires ATP & UTP.
- Glycogenesis → Glyco + Genesis

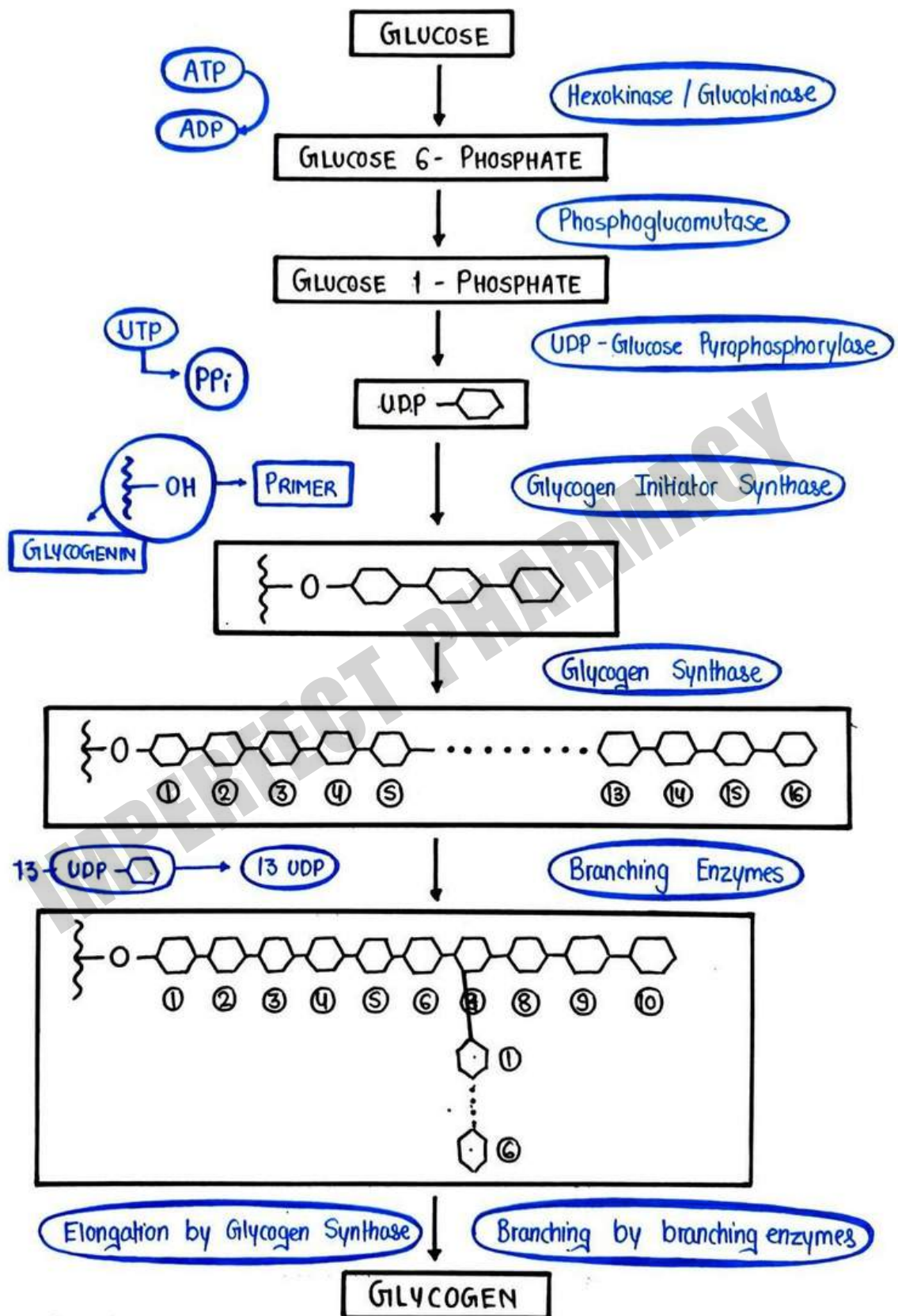
Glycogen

Formation

STEPS OF GLYCOGENESIS

Glycogenesis occurs in 4 major steps :

- Synthesis of UDP glucose
- Requirement of Glycogen Primer.
- Elongation of chain
- Glycogen Branching



GLYCOGENOLYSIS

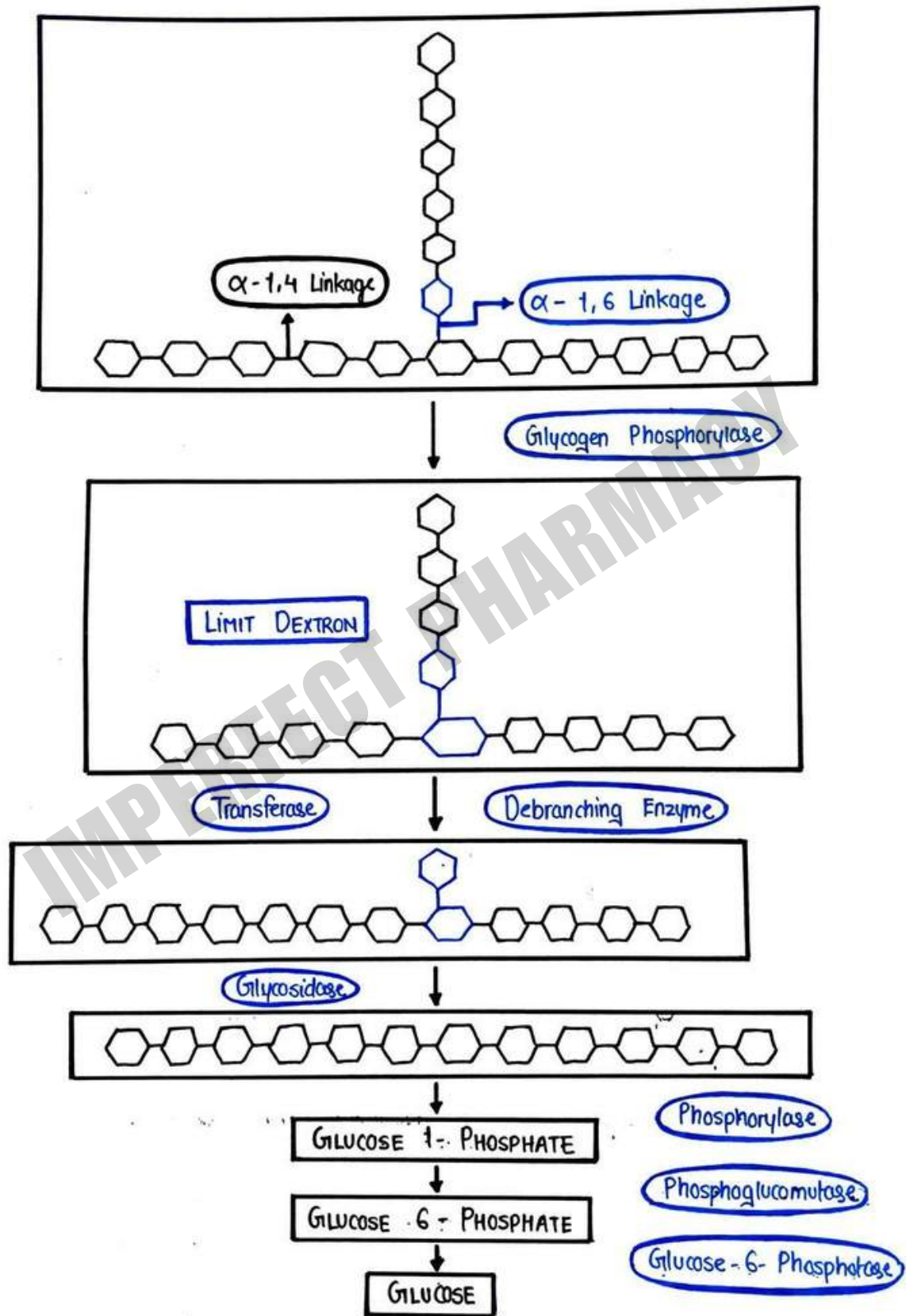
- The conversion or breakdown of stored glycogen into Glucose is known as Glycogenolysis
- Glycogenolysis mainly takes place in liver & muscles.
- It doesn't require ATP or UTP
- Glycogenolysis → Glycogen + Lysis

Glycogen

Breakdown

SIGNIFICANCE OF GLYCOGENOLYSIS

- Glycogenolysis maintains blood glucose level during starvation or Fasting.
- Glycogenolysis fulfill energy requirement of body when necessary.
- It provides energy for muscle contraction
- Abnormal accumulation of glycogen can lead to Glycogen storage disease.



GLYCOGEN STORAGE DISEASE

- Glycogen storage disease as the name suggest occurs due to accumulation / storage of large amount of glycogen.
 - These disorders are occurs due to defect in enzymes.
 - These are genetic disorders.
 - Not all but few of them are very serious disorders.
 - Glycogen storage diseases are as follows :
- ① Von Girke's Disease
 - ② Pompe's Disease
 - ③ Cori's Disease
 - ④ Anderson's Disease
 - ⑤ McArdle's Syndrome
 - ⑥ Her's Disease

VON GIRKE'S DISEASE

- It is glycogen storage disease type - I (GSD-I)
- It occurs due to deficiency of 'Glucose-6-Phosphatase'.
- Due to this abnormal storage of glycogen occurs in kidney & liver, that causes enlarged liver.

POMPE'S DISEASE

- It is glycogen storage disease type - II (GSD-II)
- It occurs due to deficiency of Acid Maltase.
- It can leads to heart failure.

CORI'S DISEASE

- It is Glycogen storage Disease type III (GSD-III)
- It occurs due to deficiency of 'Glycogen Debranching Enzymes'
- It leads to abnormalities in the functions of liver and muscles.

ANDERSON'S DISEASE

- It is glycogen storage disease, type IV (GSD-IV)
- It occurs due to deficiency of 'Glycogen Branching Enzymes'
- In this disease, an abnormal form of glycogen called amylopectin is produced and accumulates in body tissues, mainly in Heart & Liver.

McARDLE'S DISEASE

- It is glycogen storage disease type V (GSD-V)
- It occurs due to deficiency of Muscle Phosphorylase.
- In this lactic acid production is decreased in muscles that cause muscle pain after heavy exercise.

HER'S DISEASE

- It is glycogen storage disease type VI (GSD-VI)
- It occurs due to deficiency of Liver Phosphorylase.
- It cause disturbance in the functioning of liver cell

GLUCONEOGENESIS

- Gluconeogenesis → Gluco + Neo + Genesis
 Glucose New Formation

- The synthesis or formation of Glucose from non-carbohydrate compounds is known as Gluconeogenesis.
- Gluconeogenesis is not a common process and occurs only during prolonged fasting, starvation & intense exercise.
- It is an energy consuming process.
- Gluconeogenesis is almost the reversible pathway of Glycolysis but not the exact reversal of glycolysis.

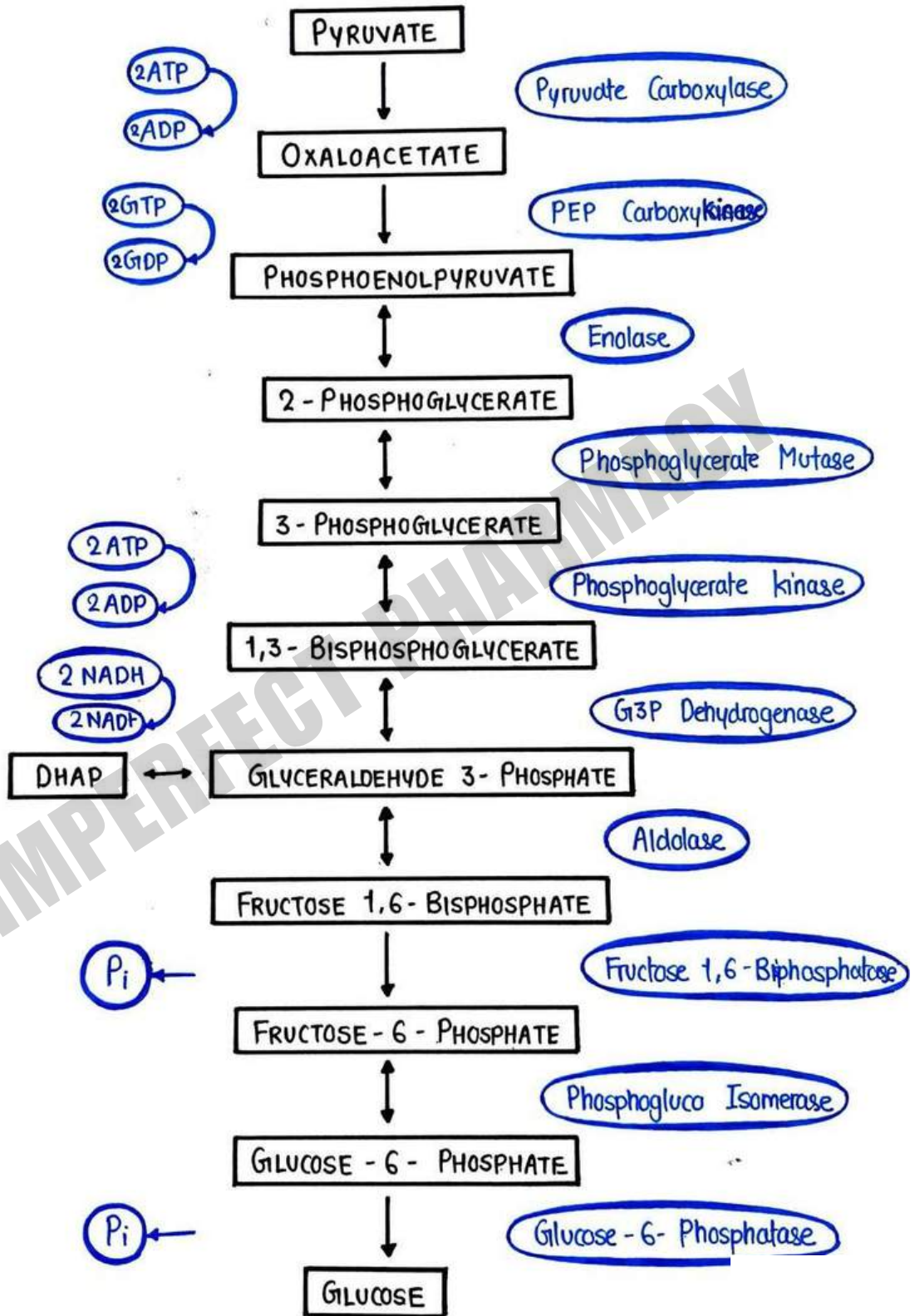
LOCATION OF GLUCONEOGENESIS

Gluconeogenesis takes place in cytosol and mitochondria of

- ① Liver
- ② Kidney (Renal Cortex)

MAJOR SUBSTRATES / NON CARBOHYDRATES FOR GLUCONEOGENESIS

- Pyruvate
- Lactate
- Glycerol
- Glucogenic Amino Acids
- Intermediates of TCA cycle
- Propionate



MAJOR EVENTS OF GLUCONEOGENESIS

- Pyruvate is first converted into oxaloacetate in the presence of Pyruvate carboxylase
- Oxaloacetate after that converted into Phosphoenolpyruvate in the presence of Phosphoenolpyruvate (PEP) Carboxykinase.
- Fructose 1,6 Bisphate is converted into Fructose 6 - Phosphate in the presence of Fructose 1,6 - Biphosphatase .
- Glucose 6 - Phosphate is finally converted into Glucose in the presence of Glucose 6 - Phosphatase

SIGNIFICANCE OF GLUCONEOGENESIS

- When carbohydrate is not available in sufficient amount from diet , Gluconeogenesis fulfills the requirement of body for glucose & maintains homeostasis .
- During prolong fasting , excessive exercise and starvation , when glycogen stores also gets exhausted , Gluconeogenesis starts and fulfil energy requirement of body .
- Some tissues like brain , RBCs , lens , kidney medulla , testes needs continuous supply of energy that is fulfilled by Gluconeogenesis
- It maintains blood glucose level when required .
- It is used to clear metabolic products of other tissues from blood such as Lactate , Glycerol etc .

HARMONAL REGULATION OF BLOOD GLUCOSE L

- Regulation of blood- glucose level is very important for maintaining Homeostasis.
- The normal range of blood glucose level is approx 70 mg/dl - 110 mg/dl
- The blood glucose level above normal is termed as Hyperglycemia
- The blood glucose level ~~above normal~~ below normal is termed as Hypoglycemia.
- The blood- glucose (Blood- sugar) level is maintained by hormones secreted by pancreas.

REGULATORY HORMONES

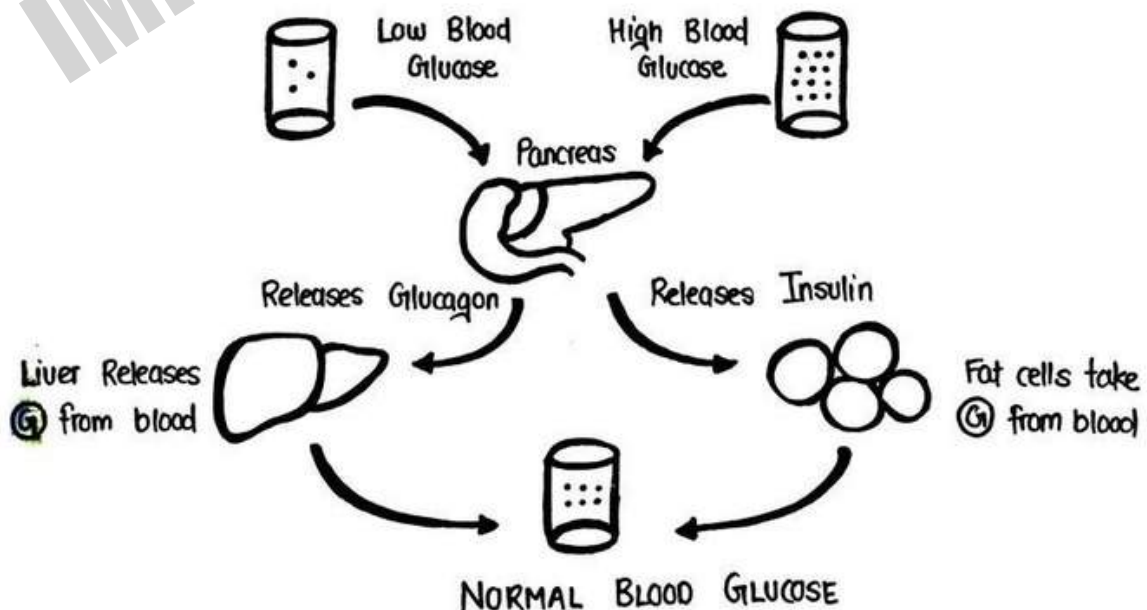
- Endocrine tissues of pancreas known as Islets of Langerhans contains 3 major types of cells :
 - ① α (Alpha) cells : Secretes Glucagon
 - ② β (Beta) cells : Secretes Insulin
 - ③ δ (Delta) cells : Secretes Somatostatin
- Now Glucagon and Insulin are two major hormones secreted by α & β cells of pancreas regulates the Blood- Glucose level.

INSULIN

- It is secreted by β cells of pancreas.
- It decreases the blood-glucose level.
- Secretion of insulin is depends upon blood-glucose level
 - Blood- Glucose Level $\uparrow \rightarrow$ Insulin Secretion $\uparrow$
 - Blood- Glucose Level $\downarrow \rightarrow$ Insulin Secretion $\downarrow$
- Along with insulin one more hormone is secreted by β cells called Amylin.

GLUCAGON

- It is secreted by α cells of pancreas.
- It increases the blood-glucose level.
- Pancreas release glucagon when concentration of glucose in blood falls too low.
- Glucagon converted the Glycogen into Glucose that is stored in liver $\leftarrow$ release them into the blood stream.



DIABETES MELLITUS

Diabetes Mellitus is defined as a condition in which body doesn't produce enough insulin or didn't respond to insulin normally that leads to increase in blood-glucose (blood-sugar) level abnormally high.

Types of Diabetes Mellitus

It is of mainly two types :

- ① Type - 1 Diabetes
- ② Type - 2 Diabetes

TYPE 1 DIABETES

- Earlier it was known as Insulin Dependent Diabetes.
- It occurs due to destruction of β -cells of pancreas due to autoimmune disorders.
- It leads to deficiency of insulin that leads to increase in Blood-Glucose Level.

TYPE 2 DIABETES

- Earlier it was known as Non-insulin dependent diabetes.
- It occurs when the cells does not respond to insulin properly.

SYMPTOMS

- Presence of glucose in urine
- Increased thirst
- Increase in frequency of urination
- Extreme Hunger.
- Fatigue & Headache
- Unknown Weight Loss
- Blurred Vision

TREATMENT

There is no any permanent treatment of diabetes, once it occurs it can only be controlled by various methods :

- Diet Control
- Physical Activity
- Healthy Lifestyle
- Insulin Therapy

BIOLOGICAL OXIDATION

- In Chemistry, Loss of electrons is termed as
Gain of electrons is termed as
- The phenomenon of oxidation - reduction is also applied to biological system, termed as Biological Oxidation.
- In simple words, Biological oxidation involves transfer of electrons through oxidation - reduction reaction to produce energy in the form of ATP.
- Electron Transport Chain and Oxidative Phosphorylation are the major events of biological oxidation.

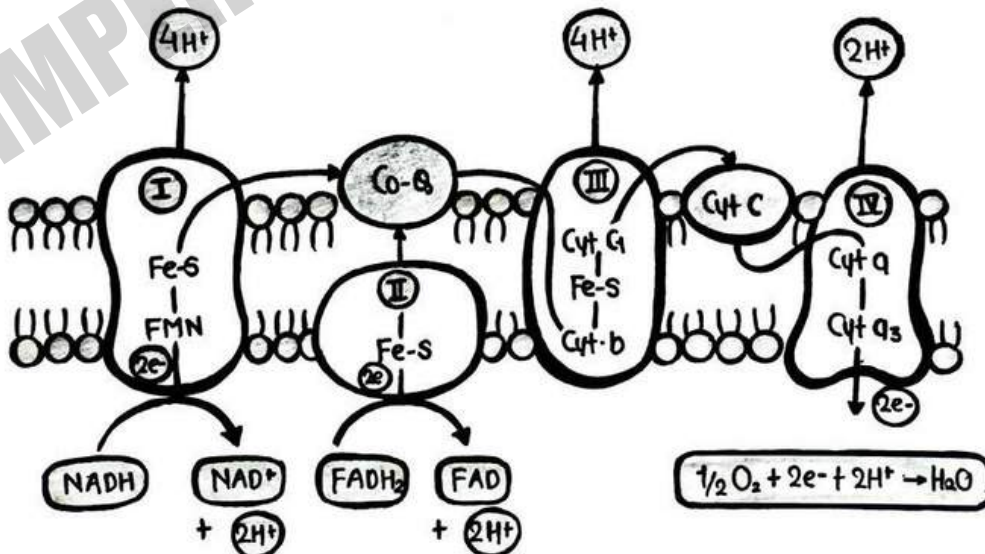
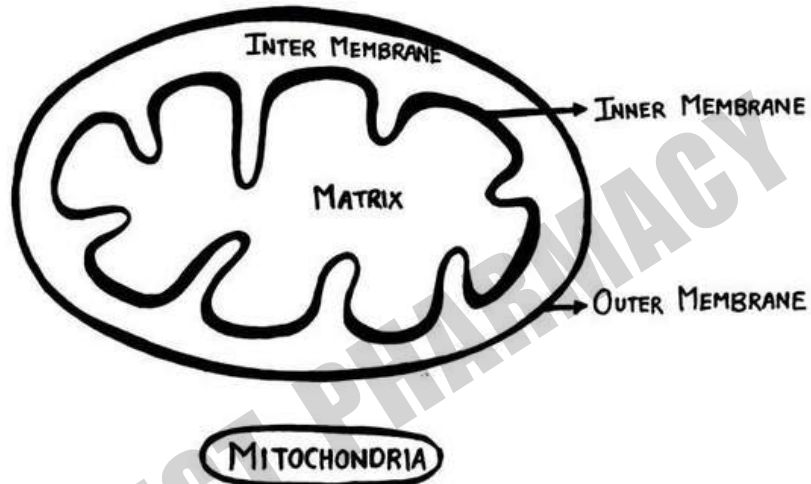
ELECTRON TRANSPORT CHAIN

- It is the final step of Aerobic respiration
- It is also known as 'Electron Transport System'
- It occurs in the inner membrane of Mitochondria.
- Electron Transport Chain is a series of protein complexes that involves transfer of electrons from Low Redox Potential compounds to High Redox Potential compounds that ultimately leads to formation of ATP.

COMPLEXES OF ELECTRON TRANSPORT CHAIN

There are mainly 4 complexes of Electron Transport Chain :

- Complex I
- Complex II
- Complex III
- Complex IV



COMPLEX - I

- It is also known as NADH Co-Q Oxidoreductase or NADH Dehydrogenase
- It contains FMN (Flavoprotein) with Fe-S (iron sulfur clusters)
- It transfer electrons from NADH to Co-Q via FMN & Fe-S.
- 4 protons are pumped from matrix to intermembrane space using energy released by transfer of electrons.

COMPLEX - II

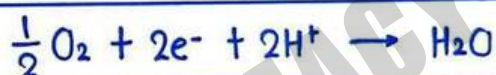
- It is also known as Succinate Co-Q Oxidoreductase or Succinate Dehydrogenase.
- It contains FAD & Fe-S clusters
- It transfer electrons from FADH₂ to Co-Q using Fe-S clusters.
- No proton is pumped in complex -II as it doesn't produce sufficient energy.

COMPLEX - III

- It is also known as Co-QH₂ cytochrome C Oxidoreductase or cytochrome reductase or Cytochrome bc₁ complex.
- It contains cytochrome b, cytochrome c₁ & Fe-S clusters.
- It takes electrons from Co-Q & transfer to cytochrome c using cytochrome b, c₁ & Fe-S.
- 4 protons are pumped in complex -III

COMPLEX IV

- It is also known as cytochrome C oxidase or simply Cytochrome c oxidase.
- It contains cytochrome a & cytochrome a₃
- It takes electrons from cytochrome c & transfer to oxygen molecule to form H₂O
- 2 protons are pumped in complex - IV
- Formation of H₂O : In complex O₂ takes e⁻ & converted into H₂O



Redox Potential of Various Components Involved in ETC

• NADH	:	- 0.32 V	MOVEMENT OF ELECTRON ↓
• FMN	:	- 0.12 V	
• CoQ	:	+ 0.04 V	
• Cytochrome b	:	+ 0.07 V	
• Cytochrome c ₁	:	+ 0.23 V	
• Cytochrome c	:	+ 0.25 V	
• Cytochrome a	:	+ 0.29 V	
• Cytochrome a ₃	:	+ 0.55 V	
• O ₂	:	+ 0.82 V	

NOTE : Electron transfers from Low Redox Potential component towards high redox potential component.

OXIDATIVE PHOSPHORYLATION

- It is the final step in which finally energy is synthesized in the form of ATP from NADH & FADH_2 molecules.
- It is the process in which ADP is phosphorylated to ATP using the energy released in electron transport chain.
- Oxidative Phosphorylation starts after the electron transport chain or we can say it is coupled with ETC for ATP synthesis.
- The complex V named ATP synthase is the major site for oxidative phosphorylation.
- The process occurs in mitochondria.

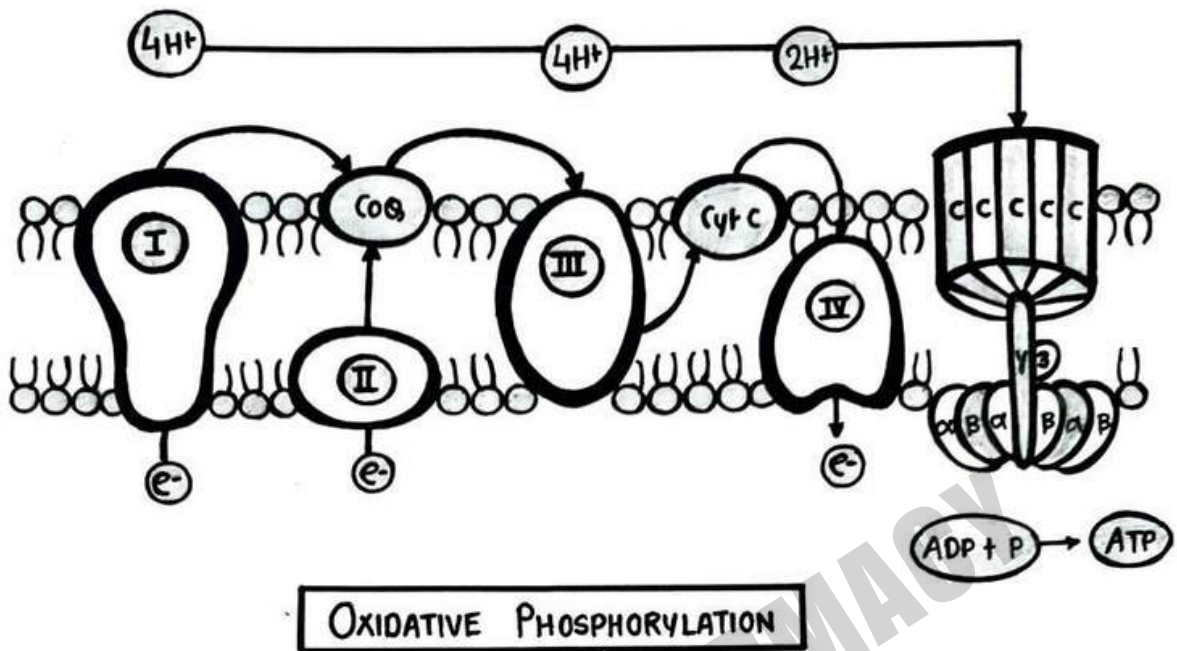
MECHANISM OF OXIDATIVE PHOSPHORYLATION

There are various hypothesis given to explain the mechanism of oxidative phosphorylation but among all of them, the Chemiosmotic Hypothesis is widely accepted given below :

CHEMIOSMOTIC HYPOTHESIS

- This hypothesis is proposed by Peter Mitchell in 1953.
- When electrons are transported through ETC then protons (H^+) are also pumped from matrix to intermembrane space that generates a proton gradient.
- Complex V uses this proton gradient as energy source for the synthesis of ATP.
- A total of 10 protons pumped into the intermembrane space that returns back into the matrix via ATP synthase, because membrane becomes impermeable for H^+ & this leads to the phosphorylation of ADP into ATP.





P:O RATIO

- The P/O ratio refers to the amount of ATP produced from movement of $2e^-$ through the electron transport chain.
- For NADH : P/O Ratio = 2.5 ATP
- For $FADH_2$: P/O Ratio = 1.5 ATP

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