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Gluconeogenesis vs Glycolysis (Unit-III)

* Glycolysis and gluconeogenesis are two metabolic processes found in glucose metabolism of cells.

* Glycolysis is the first step in glucose breakdown where two pyruvate molecules are produced. Glycolysis occurs in the cytoplasm of both prokaryotic & eukaryotic cells.

* Gluconeogenesis is the reverse reaction of glycolysis where 2 pyruvate molecule come together to form a glucose molecule. It occur in all animals, plants, fungi & microorganisms. In mammals, it takes place mainly in the liver and to a lesser extent in renal cortex, ultimately storing glucose in the form of glycogen.

* The main difference between glycolysis and glyconeogenesis is that glycolysis is involved in glucose catabolism whereas glyconeogenesis is involved in glucose anabolism.

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Glycolysis

* The set of reactions that convert glucose into two pyruvate molecule is known as glycolysis.
* It is the major pathway for glucose metabolism, occur in the cytosol of cells.
* It is an unique pathway occur aerobically as well as anaerobically & does not involved molecular oxygen
* Glycolysis is composed of ten reactions that occur in the cytoplasm.

Step - 1 Phosphorylation

* Glucose is phosphorylated to glucose 6-phosphate by hexokinase. This is an irreversible reaction, dependent on ATP and Mg^{++}.
* Glucose 6 phosphate is impermeable to cell membrane. It is a central molecule with a variety of metabolic fates - glycolysis, glycogenesis & PPP.

Step - 2 Isomerization

* Glucose-6 phosphate undergoes isomerization to give fructose 6 phosphate in the presence of enzyme phosphohexose isomerase & Mg^{++}.

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Step - 3 Phosphorylation

* Fructose 6 phosphate is phosphorylated to fructose 1,6 diphosphate by phosphofructokinase with Mg^{++}. This is an irreversible & a regulatory step in glycolysis.

Step - 4 Aldose

* Fructose 1,6 diphosphate is split to yield two three carbon, molecule, glyceraldehyde 3 phosphate, and dihydroxyacetone phosphate by the enzyme aldolase.

Step - 5 Isomerization

* Dihydroxyacetone phosphate is isomerized to form glyceraldehyde 3 phosphate

* Isomerization of these 3-carbon phosphorylated sugar is catalyzed by triose phosphate isomerase.

Step - 6

* 2 molecules of glyceraldehyde 3 phosphate are oxidized. Glyceraldehyde-3 phosphate dehydrogenase catalyzed the conversion of glyceraldehyde 3 phosphate into 1,3 diphosphoglycerate.

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This step is important as it is involved in the formation of $NADH + H^+$ & a high energy compound 1,3 diphosphoglycerate.

Step - 7

- The enzyme phosphoglycerate Kinase acts on 1,3 diphosphoglycerate resulting in the synthesis of ATP and formation of 3 phosphoglycerate
- Since ATP is synthesized from the substrate without the involvement of ETC.

Step - 8

- 3 phosphoglycerate is converted to 2-phosphoglycerate by phosphoglycerate mutase. This is an isomerization reaction

Step - 9

- The high energy compound phosphoenol pyruvate is generated from 2-phosphoglycerate by the enzyme enolase. This enzyme require Mg^{2+} and is inhibited.

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Step-10

* The enzyme pyruvate kinase catalyse the transfer of high energy phosphate from phosphoenol pyruvate to ADP, leading to the formation of ATP.
* Pyruvate kinase requires either K^+ or Mg^{++}.

Net reaction

$$Glucose + 2NAD^+ + 2ADP + 2H_2PO_4 \rightarrow 2\,Pyruvate + 2NADH + 2H^+ + 2ATP + 2H_2O$$

Function

* Its function is to breakdown glucose to form NADH & ATP as source of energy in cells
* As a part of aerobic respiration pyruvate is made available for the citric acid cycle

Significance

* It is present in nearly all living organisms. Glucose is the source of almost all energy used by cells.
* It is a pathway through which the largest flux of carbon occurs in most cells.

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Glycolysis

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Glucose

Hexokinase ↓ ATP / ADP

Glucose 6-phosphate

Phosphohexose isomerase ⇌

Fructose 6-phosphate

Phosphofructokinase ↓ Mg^{2+} ATP / ADP

Fructose 1,6 diphosphate

⇌

Glyceraldehyde 3-phosphate + Dihydroxyacetone phosphate

⇌

Glyceraldehyde 3 phosphate (2)

Glyceraldehyde 3-phosphate dehydrogenase ⇓ 2Pi, $2NAD^+$ → $2NADH + H^+$

1,3 diphosphoglycerate (2)

Phosphoglycerate kinase ↓ 2ADP → 2 ATP

3-Phosphoglycerate (2)

2-Phosphoglycerate (2)

↓ $2H_2O$

Phosphoenol pyruvate (2)

Pyruvate kinase ↓ 2ADP → 2ATP

Pyruvate (2)

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Gluconeogenesis

* It is the production of glucose from non-carbohydrate source like glycerol, amino acids and lactate.

* It is found in all animals, plants, fungi & microorganism.

* The three irreversible steps of glycolysis are catalysed by the enzyme namely :- hexokinase, phosphofructokinase, and pyruvate kinase.

1. Conversion of Pyruvate to phosphoenol pyruvate

* This takes place in 2 steps.

Pyruvate carboxylase is a biotin dependent mitochondrial enzyme that converts pyruvate to oxaloacetate in presence of ATP & CO_2. This enzyme regulates gluconeogenesis & requires acetyl CoA for its activity.

* Oxaloacetate is synthesized in the mitochondrial matrix. It has to be transported to the cytosol to be used in glyconeogenesis, where the rest of the pathway occurs.

* oxalo acetate is converted to malate & then transported to the cytosol. With in the cytosol, oxalo acetate is regenerated.

* The reversible conversion of oxaloacetate & malate is catalysed by malate dehydrogenase.

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* In the cytosol, phosphoenolpyruvate carboxykinase converts oxaloacetate to phosphoenolpyruvate. GTP is used in this reaction & the CO_2 is liberated

* For the conversion of pyruvate to phosphoenol pyruvate 2 ATP equivalent are utilized

2. Conversion of fructose 1,6 diphosphate to fructose 6-phosphate

* Phosphoenolpyruvate undergoes the reversal of glycolysis until fructose 1,6 diphosphate is produced.

* Fructose, 1,6 diphosphatase converts fructose 1,6 diphosphate to fructose 6-phosphate with Mg^{++} ions.

* This enzyme is absent in smooth muscle & heart muscle. This enzyme is regulatory in gluconeogenesis.

3. Conversion of glucose 6 phosphate to glucose

* Glucose 6 phosphate catalyse the conversion of glucose 6 phosphate to glucose.

* The presence or absence of this enzyme in a tissue determines whether the tissue is capable of contributing glucose to the blood or not

* It is present in liver & kidney but absent in muscle, brain & adipose tissue.

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Net reaction

2 Pyruvate + 2 NADH + 4 ATP + 2 GTP + $6H_2O$

↓

Glucose + 2 NAD + 2 GDP + 4 ADP

Function

* It maintain the level of intermediate of the TCA cycle even when fatty acids are the main source of acetyl CoA in the tissue
* It is essentially glycolysis, which is the process of converting glucose into energy, in reverse

Significance

* Removal of lactic acid
* Removal of glycerol producted by lipolysis
* It maintain the level of intermediates of the TCA cycle even when fatty acids are the main sources of acetyl CoA in the tissue

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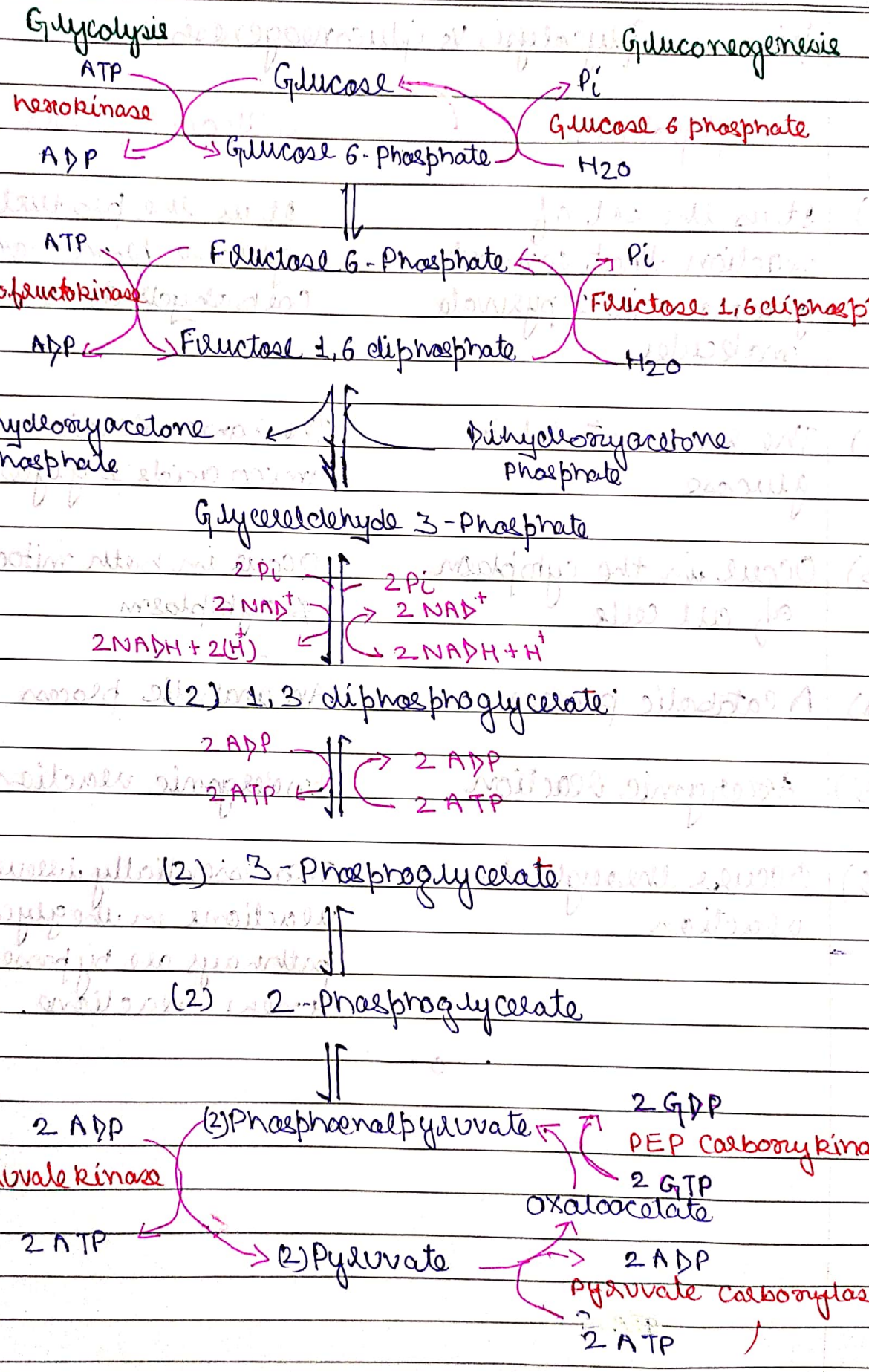

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Q. Glycolysis Vs Gluconeogenesis

	Glycolysis	Gluconeogenesis
1)	It is the set of reaction that convert glucose into 2 pyruvate molecules.	It is the production of glucose from non-carbohydrate sources.
2)	The raw material is glucose	The raw material is lactate, amino acids & glycerol
3)	Occur in the cytoplasm of all cells	Occur in both mitochondria & cytoplasm
4)	A catabolic process	An anabolic process
5)	Exergonic reaction	Endergonic reaction
6)	Occurs through ten reaction	Two essentially irreversible reactions in the glycolytic pathways are by passed by 4 new reactions.