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PENTOSE PHOSPHATE PATHWAY

BY

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ZOOLOGY: SEM- III, PAPER- C7T: FUNDAMENTALS OF BIOCHEMISTRY, UNIT 1: CARBOHYDRATES

Pentose Phosphate Pathway Definition:

- The pentose phosphate pathway is a metabolic pathway parallel to glycolysis, which generates NADPH and pentoses (5-carbon sugars) as well as ribose 5-phosphate.
- The pentose phosphate pathway is also called as the phosphogluconate pathway or hexose monophosphate shunt.
- While it involves oxidation of glucose, its primary role is anabolic rather than catabolic.

- It is an important pathway that generates precursors for nucleotide synthesis and is especially important in red blood cells (erythrocytes).

Pentose Phosphate Pathway Location:

In animals, it takes place in the cytoplasm of cells of the liver, adrenal cortex, and lactating mammary glands. In plants, most steps take place in plastids.

The Pathway:

- **Substrate:** Glucose-6-phosphate.

There are two distinct phases in the pathway.

- The first is the oxidative phase, in which NADPH is generated, and
- The second is the non-oxidative synthesis of 5-carbon sugars.

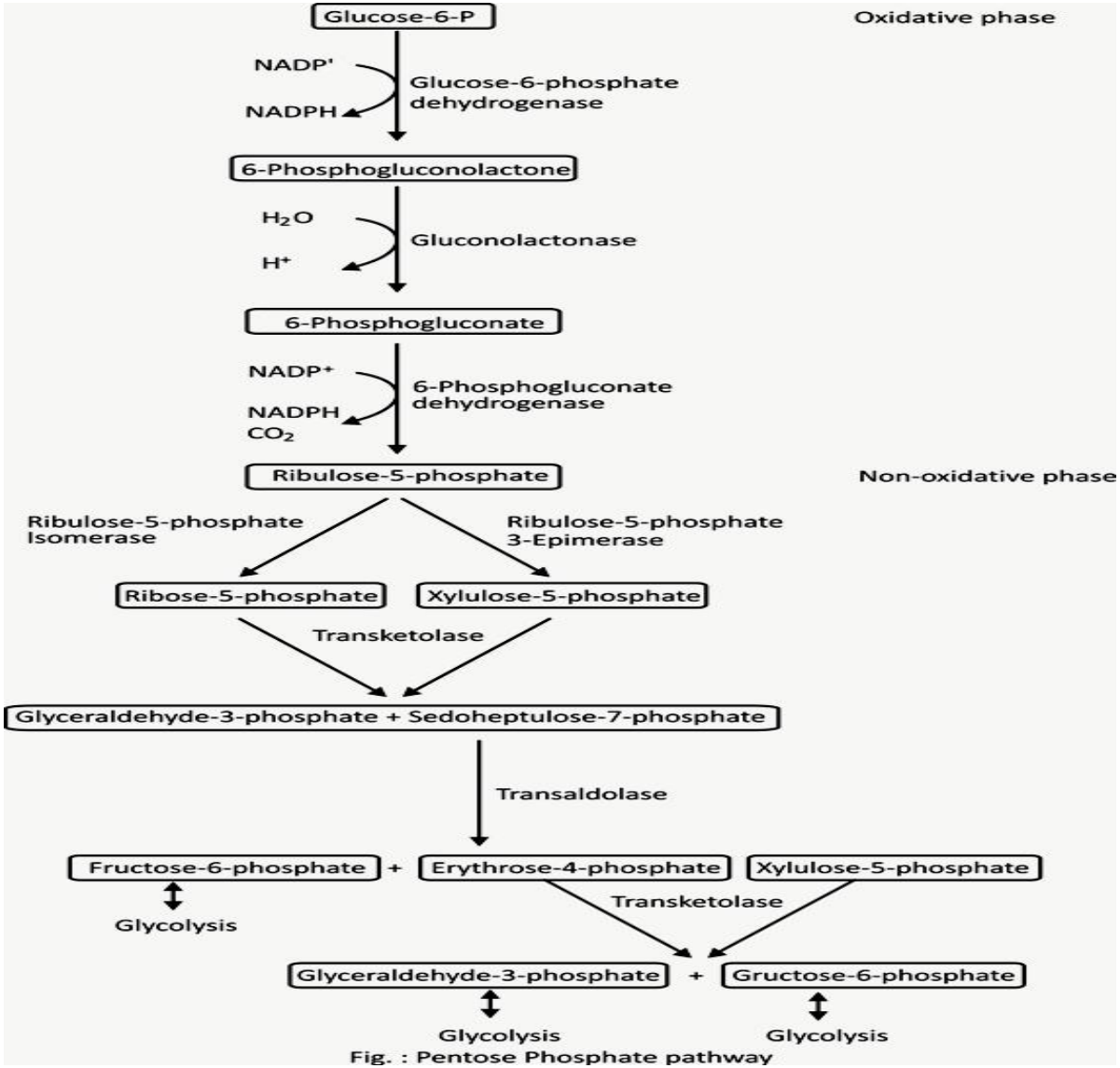

Fig. : Pentose Phosphate pathway

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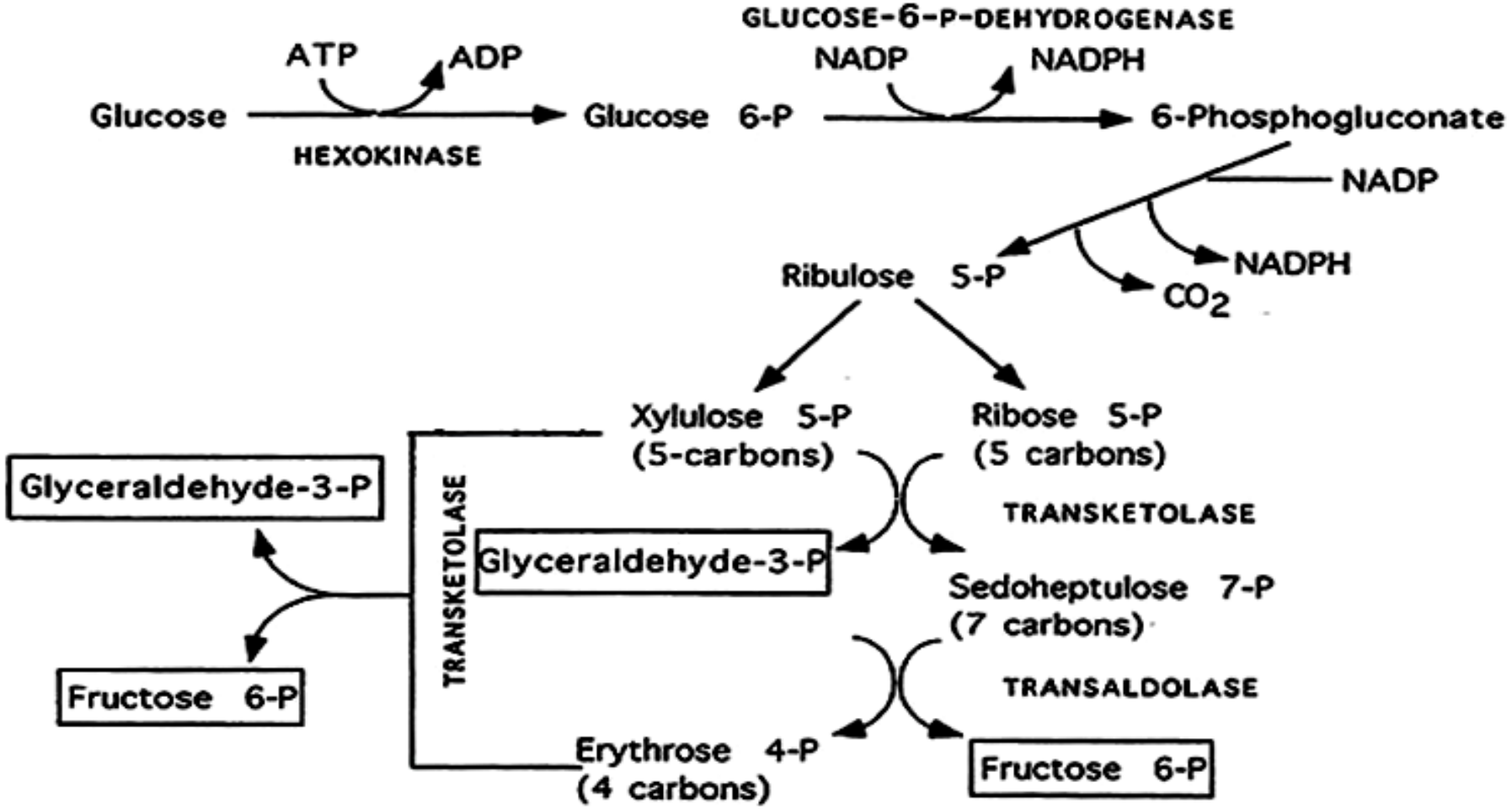

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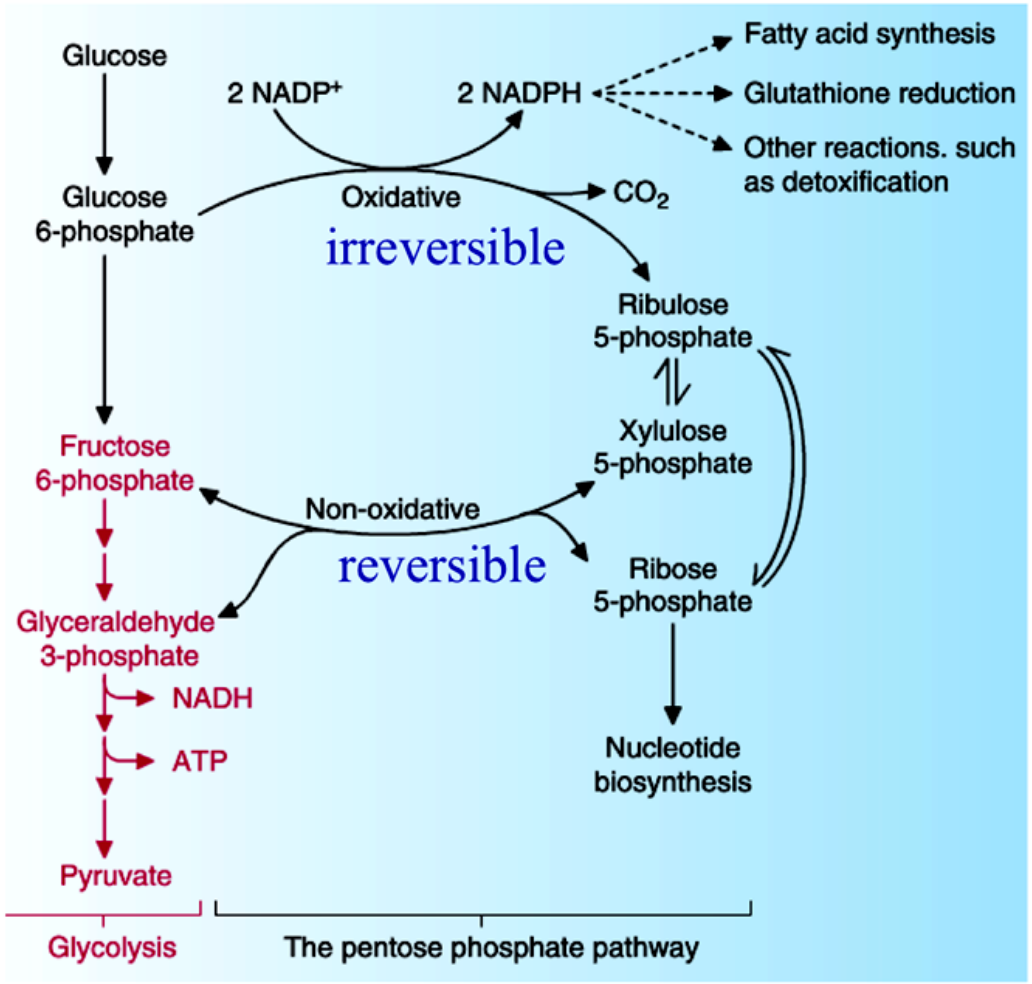
Pentose phosphate pathway and its link to glycolysis



- NADPH
- Ribose 5-P
- Glucose 6-P dehydrogenase deficiency

Reactions of Pentose Phosphate Pathway:

1. The Oxidative Reactions:

- Glucose-6-phosphate is converted to 6-phosphogluconolactone, and NADP+ is reduced to NADPH + H+.
  - **Enzyme:** glucose-6-phosphate dehydrogenase
- 6-Phosphogluconolactone is hydrolyzed to 6-phosphogluconate.
  - **Enzyme:** Gluconolactonase

- 6-Phosphogluconate undergoes an oxidation, followed by a decarboxylation. CO_2 is released, and a second NADPH + H+ is generated from NADP+.
- The remaining carbons form ribulose-5-phosphate.
  - Enzyme: 6-phosphogluconate dehydrogenase

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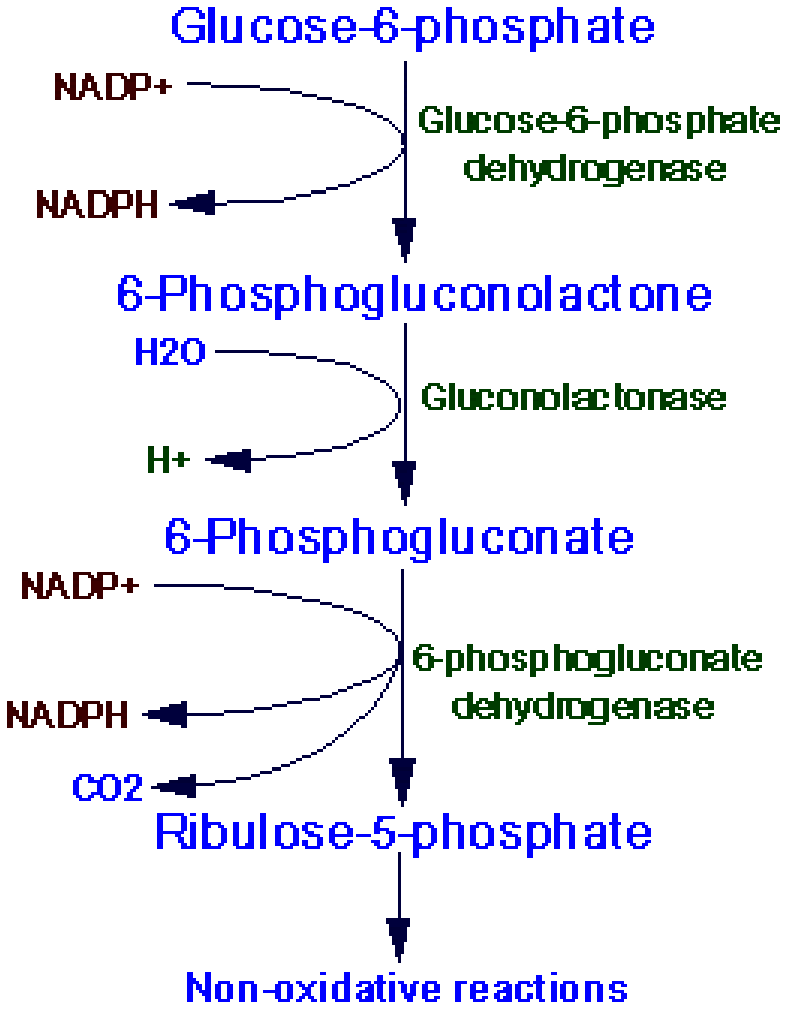
Oxidative Stage of Pentose Phosphate Pathway



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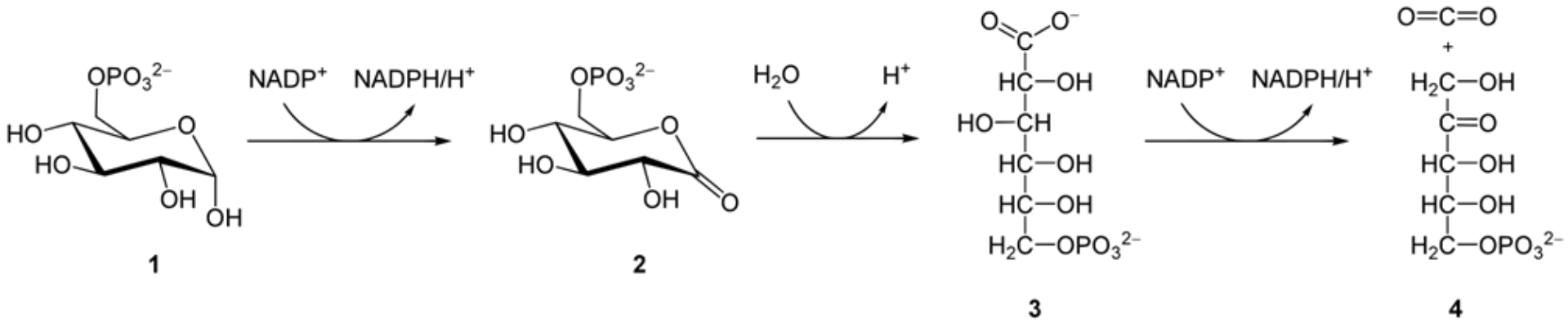

Oxidative phase of pentose phosphate pathway.

Glucose-6-phosphate (1), 6-phosphoglucono-δ-lactone (2), 6-phosphogluconate (3), ribulose 5-phosphate (4)

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The entire set of reactions can be summarized as follows:

Reactants	Products	Enzyme	Description
Glucose 6-phosphate + NADP+	→ 6-phosphoglucono-δ-lactone + NADPH	glucose 6-phosphate dehydrogenase	Dehydrogenation. The hydroxyl on carbon 1 of glucose 6-phosphate turns into a carbonyl, generating a lactone, and, in the process, NADPH is generated.
6-phosphoglucono-δ-lactone + H_2O	→ 6-phosphogluconate + H^+	6-phosphogluconolactonase	Hydrolysis
6-phosphogluconate + $NADP^+$	→ ribulose 5-phosphate + NADPH + CO_2	6-phosphogluconate dehydrogenase	Oxidative decarboxylation. $NADP^+$ is the electron acceptor, generating another molecule of NADPH, a CO_2, and ribulose 5-phosphate.

The overall reaction for this process is:

Glucose 6-phosphate + 2 NADP+ + H_2O → ribulose 5-phosphate + 2 NADPH + 2 H+ + CO_2

2. The Non-oxidative Reactions:

- Ribulose-5-phosphate is isomerized to ribose-5-phosphate or epimerized to xylulose-5-phosphate.
- Ribose-5-phosphate and xylulose-5-phosphate undergo reactions, catalyzed by transketolase and transaldolase, that

transfer carbon units, ultimately forming fructose 6-phosphate and glyceraldehyde-3-phosphate.

- Transketolase, which requires thiamine pyrophosphate, transfers two-carbon units.
- Transaldolase transfers three-carbon units.

The overall reaction for this process is:

3 ribulose-5-phosphate → 1 ribose-5-phosphate + 2 xylulose-5-phosphate → 2 fructose-6-phosphate + glyceraldehyde-3-phosphate

The entire set of reactions can be summarized as follows:

Reactants	Products	Enzymes
ribulose 5-phosphate	→ ribose 5-phosphate	Ribose-5-phosphate isomerase
ribulose 5-phosphate	→ xylulose 5-phosphate	Ribulose 5-Phosphate 3-Epimerase
xylulose 5-phosphate + ribose 5-phosphate	→ glyceraldehyde 3-phosphate + sedoheptulose 7-phosphate	transketolase
sedoheptulose 7-phosphate + glyceraldehyde 3-phosphate	→ erythrose 4-phosphate + fructose 6-phosphate	transaldolase
xylulose 5-phosphate + erythrose 4-phosphate	→ glyceraldehyde 3-phosphate + fructose 6-phosphate	transketolase

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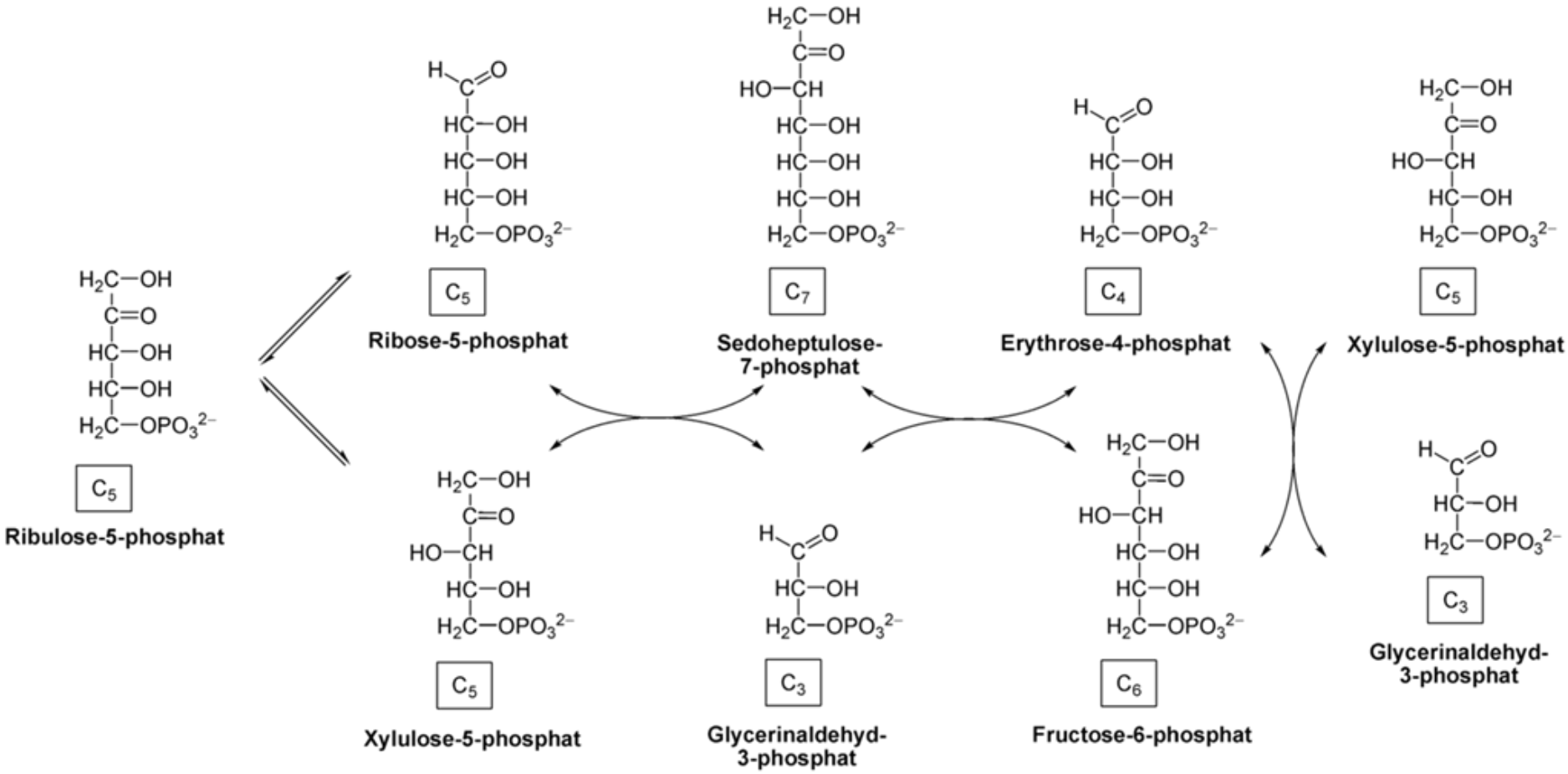

The pentose phosphate pathway's non-oxidative phase

Overall Reaction of Pentose Phosphate Pathway:

3 Glucose-6-P + 6 NADP+→ 3 ribulose-5-P + 3 CO2 + 6 NADPH

3 Ribulose-5-P → 2 xylulose-5-P + Ribose-5-P

2 Xylulose-5-P + Ribose-5-P → 2 fructose-6-P + Glyceraldehyde-3-P

Result of Pentose Phosphate Pathway:

- **Oxidative portion:** Irreversible.

Generates two NADPH, which can then be used in fatty acid synthesis and cholesterol synthesis and for maintaining reduced glutathione inside RBCs.

- **Nonoxidative portion:** Reversible.

Generates intermediate molecules (ribose-5-phosphate; glyceraldehyde-3-phosphate; fructose-6- phosphate) for nucleotide synthesis and glycolysis.

Regulation of Pentose Phosphate Pathway:

- Key enzyme in the pentose-phosphate pathway is glucose-6-phosphate dehydrogenase.
- Levels of glucose-6-phosphate dehydrogenase are increased in the liver and adipose tissue when large amounts of carbohydrates are consumed.
- Glucose-6-phosphate dehydrogenase is stimulated by NADP+ and inhibited by NADPH and by palmitoyl-CoA (part of the fatty acid synthesis pathway).

Purpose of Pentose Phosphate Pathway:

- Pentose phosphate pathway functions as an alternative route for glucose oxidation that does not directly consume or produce ATP.
- The pentose phosphate pathway produces NADPH for fatty acid synthesis. Under these conditions, the fructose-6-phosphate and glyceraldehyde-3-phosphate generated in the pathway reenter glycolysis.

- NADPH is also used to reduce glutathione (γ-glutamylcysteinylglycine).
- Glutathione helps to prevent oxidative damage to cells by reducing hydrogen peroxide (H2O2).
- Glutathione is also used to transport amino acids across the membranes of certain cells by the γ-glutamyl cycle.
- Generation of ribose-5-phosphate
- When NADPH levels are low, the oxidative reactions of the pathway can be used to generate ribose-5-phosphate for nucleotide biosynthesis.

- When NADPH levels are high, the reversible nonoxidative portion of the pathway can be used to generate ribose-5-phosphate for nucleotide biosynthesis from fructose-6-phosphate and glyceraldehyde-3-phosphate.

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THANK YOU

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