Pentose Phosphate Pathway (PPP)

Glucose is catabolised by way of glycolytic pathway in to two molecules of pyruvate , then pyruvate is oxidized by citric acid cycle to produce ATP In animal tissue .

There is an another metabolic pathway, called as the Pentose Phosphate Pathway (PPP), which is also termed as Hexose Monophosphate Pathway (HMP shunt) -or Phosphogluconate pathway .

this pathway generate Ribose sugar, ATP, two NADPH.

Pentose Phosphate Pathway, is a metabolic pathway parallel to glycolysis. is special because no energy in the form of ATP is produced or used up in this pathway.

Site in the body: liver, adipose tissue, lactating mammary gland, cortex of adrenal gland.

Site in the cell : Occurs in the cytosol of the Cells.

$$\text{Glucose 6-phosphate} + 2\text{NADP}^+ + \text{H}_2\text{O} \longrightarrow \text{ribose 5-phosphate} + \text{CO}_2 + 2\text{NADPH} + 2\text{H}^+$$

Function of pathway

- The generation of reducing equivalents, in the form of NADPH, used in reductive biosynthesis reactions within cells (e.g. fatty acid synthesis).
- Production of ribose 5-phosphate (R5P), used in the synthesis of nucleotides and nucleic acids.
- Production of erythrose 4-phosphate (E4P) used in the synthesis of aromatic amino acids.

The PPP can be divided into following phases

1.The oxidative (non- reversible) phase

2.The non oxidative (reversible) phase

First phase: oxidative- non, reversible phase. In this phase, glucose 6- phosphate undergoes dehydrogenation and decarboxylation to yield a pentose, ribulose 5-phosphate.

Second phase: a non-oxidative, reversible phase. In this phase, ribulose 5-phosphate is converted back to glucose 6-phosphate by a series of reactions involving mainly two enzymes: transketolase and transaldolase .

- 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. For most organisms

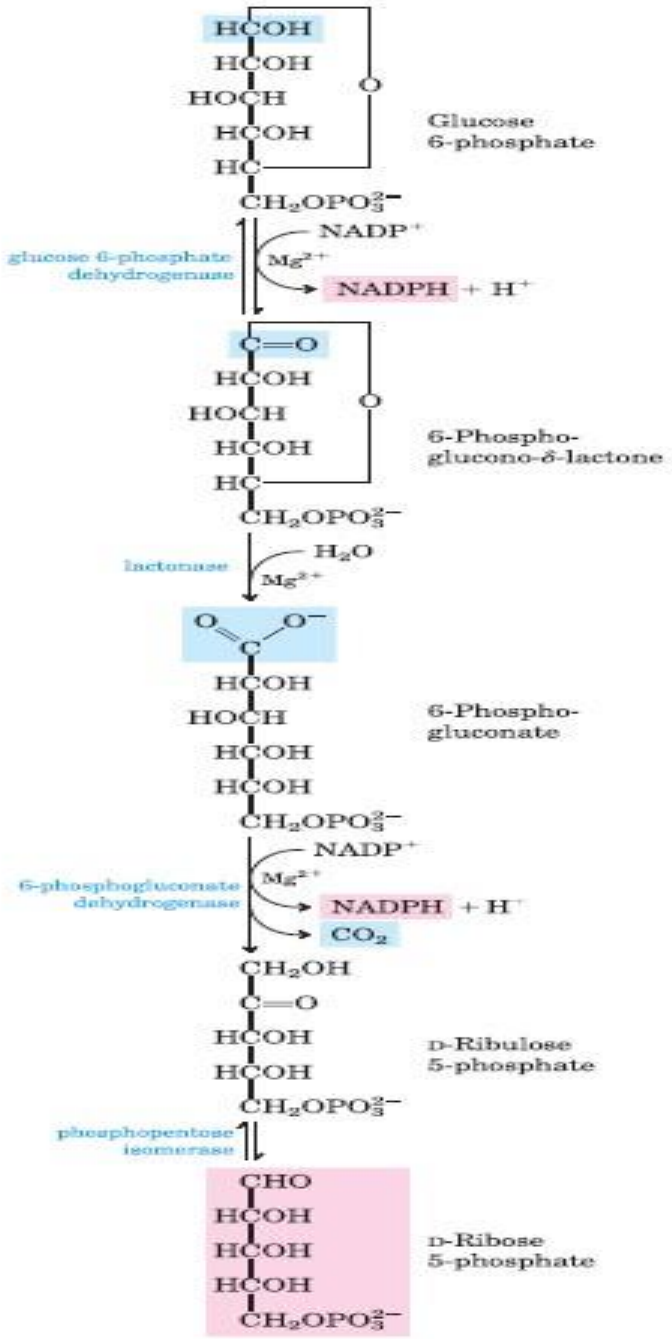
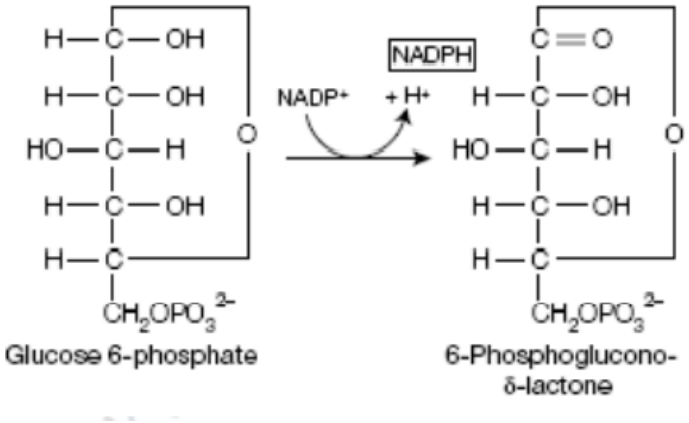


FIGURE 14–21 Oxidative reactions of the pentose phosphate pathway. The end products are ribose 5-phosphate, CO_2, and NADPH.

oxidative phase

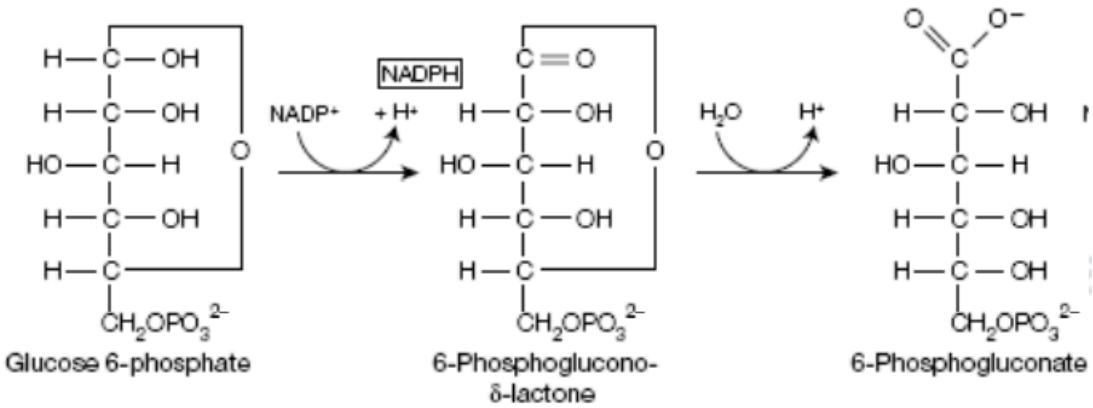
1- **Enzyme: Glucose -6-phosphate dehydrogenase**

The first reaction of the pentose phosphate pathway is the oxidation of glucose 6-phosphate by **glucose 6-phosphate dehydrogenase (G6PD)** to form 6-phosphoglucono-lactone,and formation NADPH.



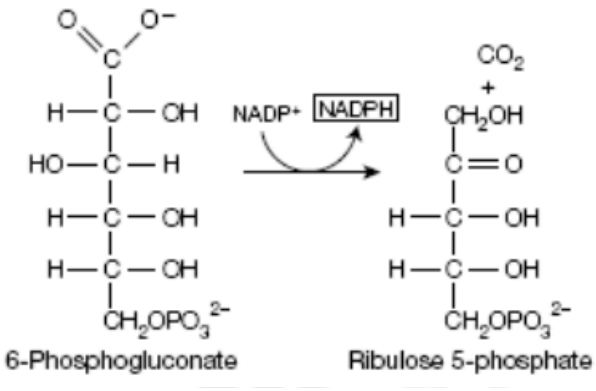
2- **Enzyme: Lactonase**

The lactone is hydrolyzed to the free acid 6-phosphogluconate by a specific **lactonase.**



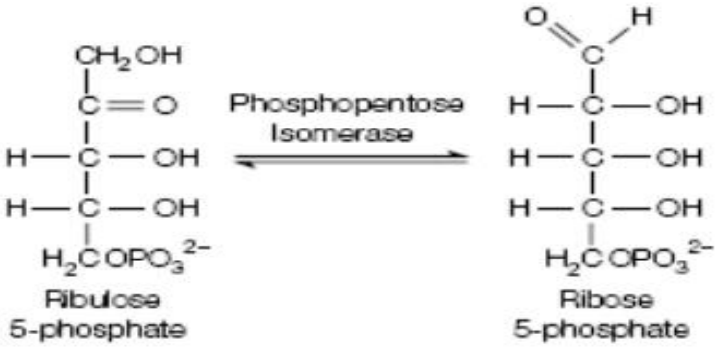
3- **Enzyme: 6-Phospho gluconate dehydrogenase**

6-phosphogluconate undergoes oxidation and decarboxylation by **6-phosphogluconate dehydrogenase** to form the D ribulose 5-phosphate.so as NADPH.



4- **Enzyme: Phosphopentose isomarase**

D ribulose 5-phosphate convert to D ribose 5- phosphopentose by isomerase . it's the only reaction is reversible in phospho pentos bathway.

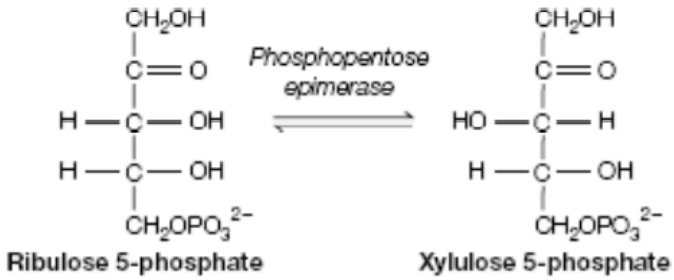


NON OXIDATIVE PHASE

Conversion of pentose phosphate to glucose -6 phosphate

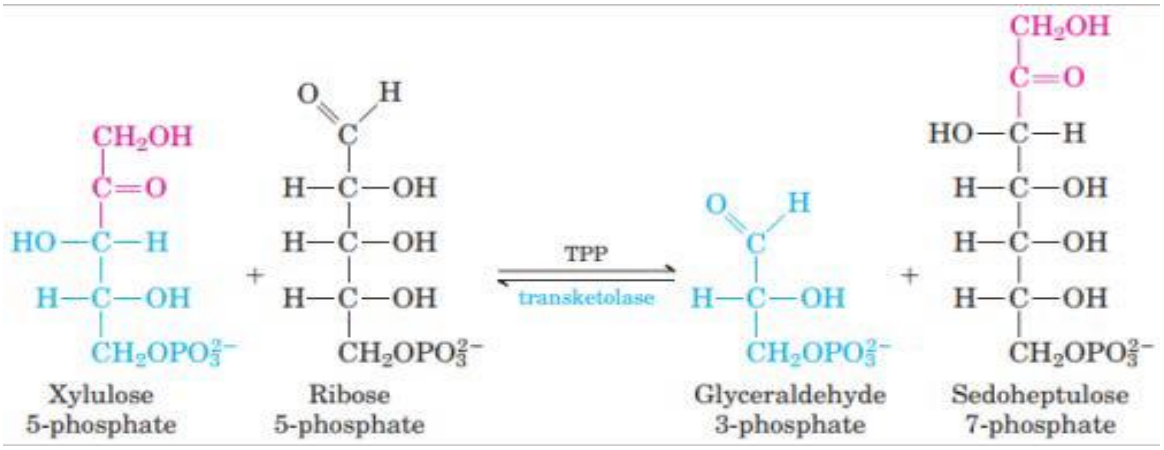
- In cell that require high level of NADPH for biosynthetic reaction, the ribulose -5P produced in the oxidative phase need to be a turn back in to a glucose -6 phosphate to maintain flux through the glucose -6P dehydrogenase reaction
- The carbon shuffle reaction of non-oxidative phase which ultimately are used to regenerate glucose -6P using transketolase and trans aldolase enzyme.

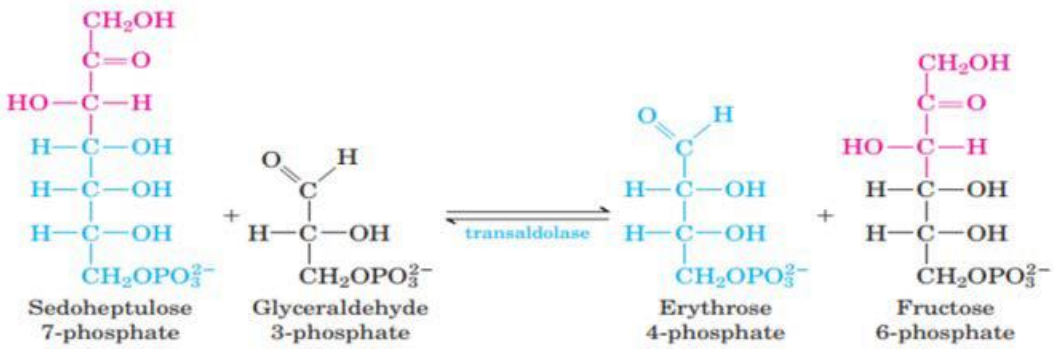
5- **Enzyme: Ribulose -5 phosphate epimerase**

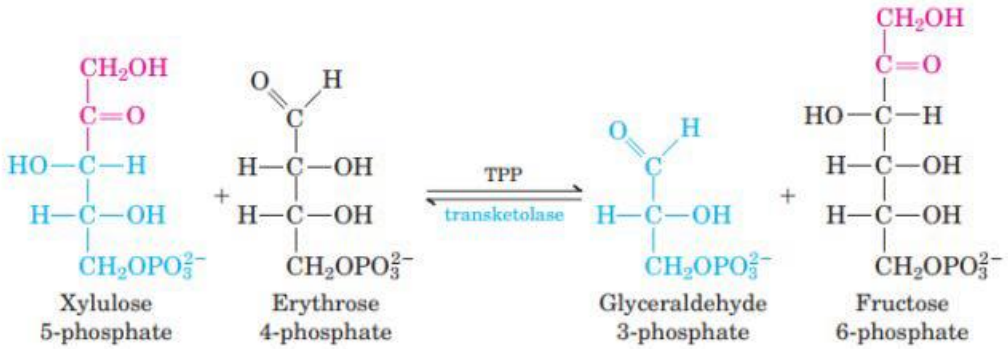


6- **Enzyme: Trans ketolase and trans aldolase**

This step isessential to change pentose back to glucose ,but beside to epimarase, two enzymes namely (i) Trans ketolase and (ii) Transaldolase are needed .

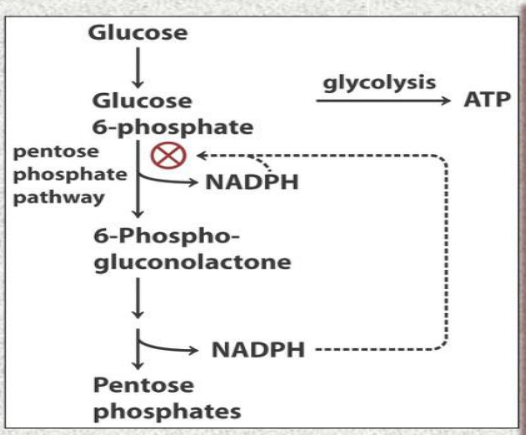






Note: Transketolase requires the cofactor thiamine pyrophosphate (TPP)

Regulation of the pentose phosphate pathway



- Glucose-6-P dehydrogenase (Rate Limiting Reaction) is controlled by:
  - Allosteric Regulation
    -Feedback inhibited by NADPH
  - Inducible enzyme
    -The synthesis of glucose 6-phosphate dehydrogenase is induced by the increased insulin/glucagon ratio after a high carbohydrate meal.