Pentose Phosphate Pathway

-Dr. Ekta Khare
Department of Microbiology
Institute of Biosciences & Biotechnology,
CSJM University, Kanpur

Pentose Phosphate Pathway

- The pentose phosphate pathway (also called the phosphogluconate pathway, Warburg-Dicken's pathway and the hexose monophosphate shunt) is a metabolic pathway parallel to glycolysis.
- Occurs in cytoplasm of procaryotes and eucaryotes as an alternative pathway to glycolysis.
- In this pathway glucose 6-phosphate is directly oxidised without entering glycolysis, hence also known as 'Direct oxidation pathway' or 'HMP shunt'.
- The pentose phosphate pathway is a process of glucose turnover that produces NADPH as reducing equivalents and pentoses as essential parts of nucleotides.
- There are two different phases in the pathway:
- One is irreversible **oxidative phase** in which glucose-6P is converted to ribulose-5P by oxidative decarboxylation, and NADPH is generated.

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

- The other is **reversible non-oxidative phase** in which there is non-oxidative synthesis of 5-carbon sugars.

Non-oxidative phase

- Ribulose-5-phosphate can reversibly isomerize to ribose-5-phosphate.
- Ribulose-5-phosphate can alternatively undergo a series of isomerizations as well as transaldolations and transketolations that result in the production of other pentose phosphates including fructose-6-phosphate, erythrose-4-phosphate, and glyceraldehyde-3-phosphate.
- The overall result is that six glucose 6-phosphates are converted to four fructose 6-phosphates, two glyceraldehyde 3-phosphate, and six CO_2 molecules, as shown in the following equation (Figure 1).

$$6 \text{ glucose 6-phosphate} + 12\ NADP^{+} + 6\ H_2O \longrightarrow$$
$$4 \text{ fructose 6-phosphate} + 2 \text{ glyceraldehyde 3-phosphate} +$$
$$6\ CO_2 + 12\ NADPH + 12\ H^{+}$$

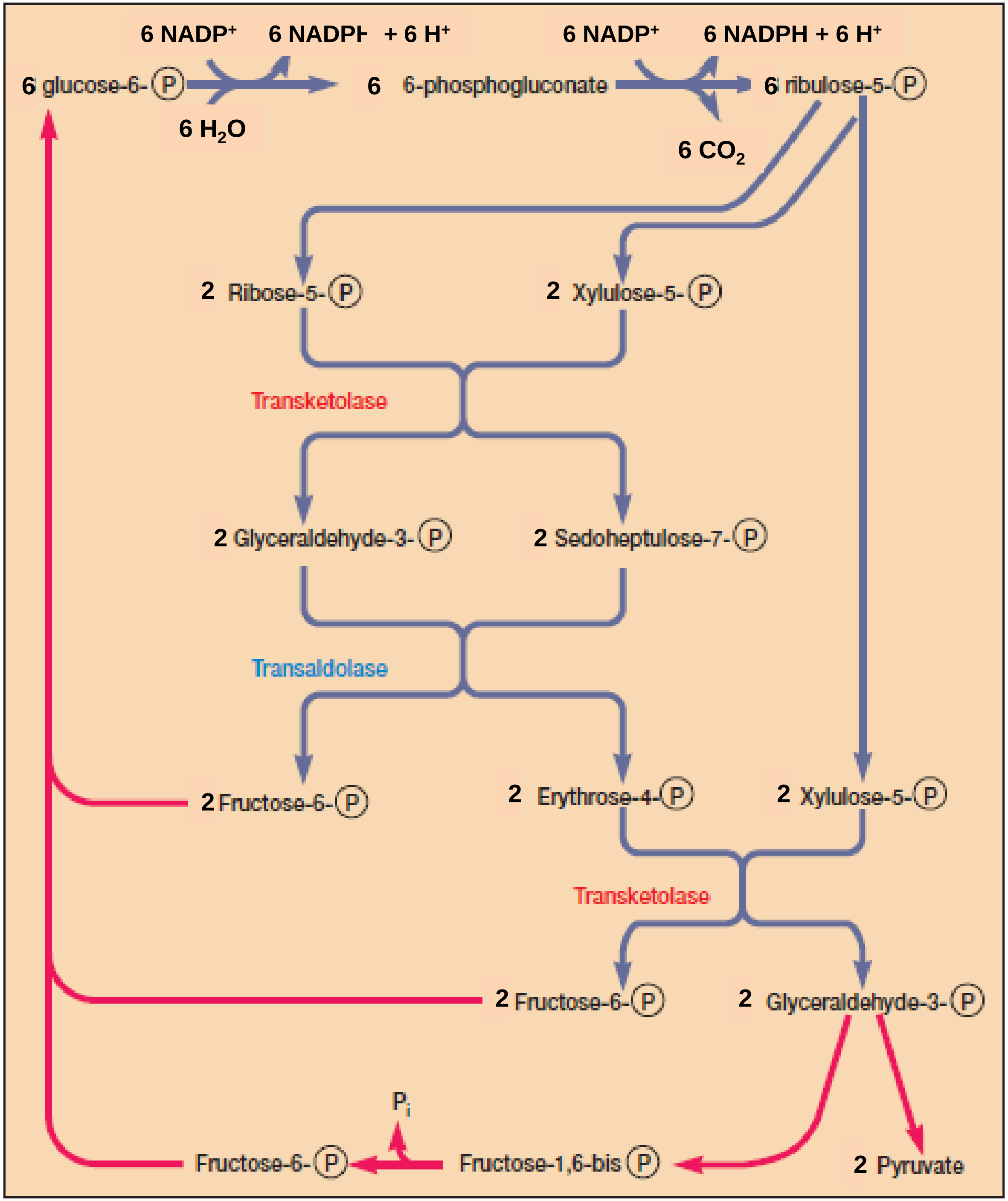
… Non-oxidative phase

- The fructose 6-phosphate can be changed back to glucose 6-phosphate while glyceraldehyde 3-phosphate is converted to pyruvate by glycolytic enzymes.
- The glyceraldehyde 3-phosphate also may be returned to the pentose phosphate pathway through glucose 6-phosphate formation.
- This results in the complete degradation of glucose 6- phosphate to CO_2 and the production of a great deal of NADPH.
- **In total, a series of PPP reactions cycle 6 molecules of glucose-6-phosphate to 5 molecules of glucose-6-phosphate, 12 NADPH and 6 CO_2 (Figure 2).**

$$\text{Glucose 6-phosphate} + 12NADP^{+} + 6\,H_2O \longrightarrow 6CO_2 + 12NADPH + 12H^{+} + P_i$$

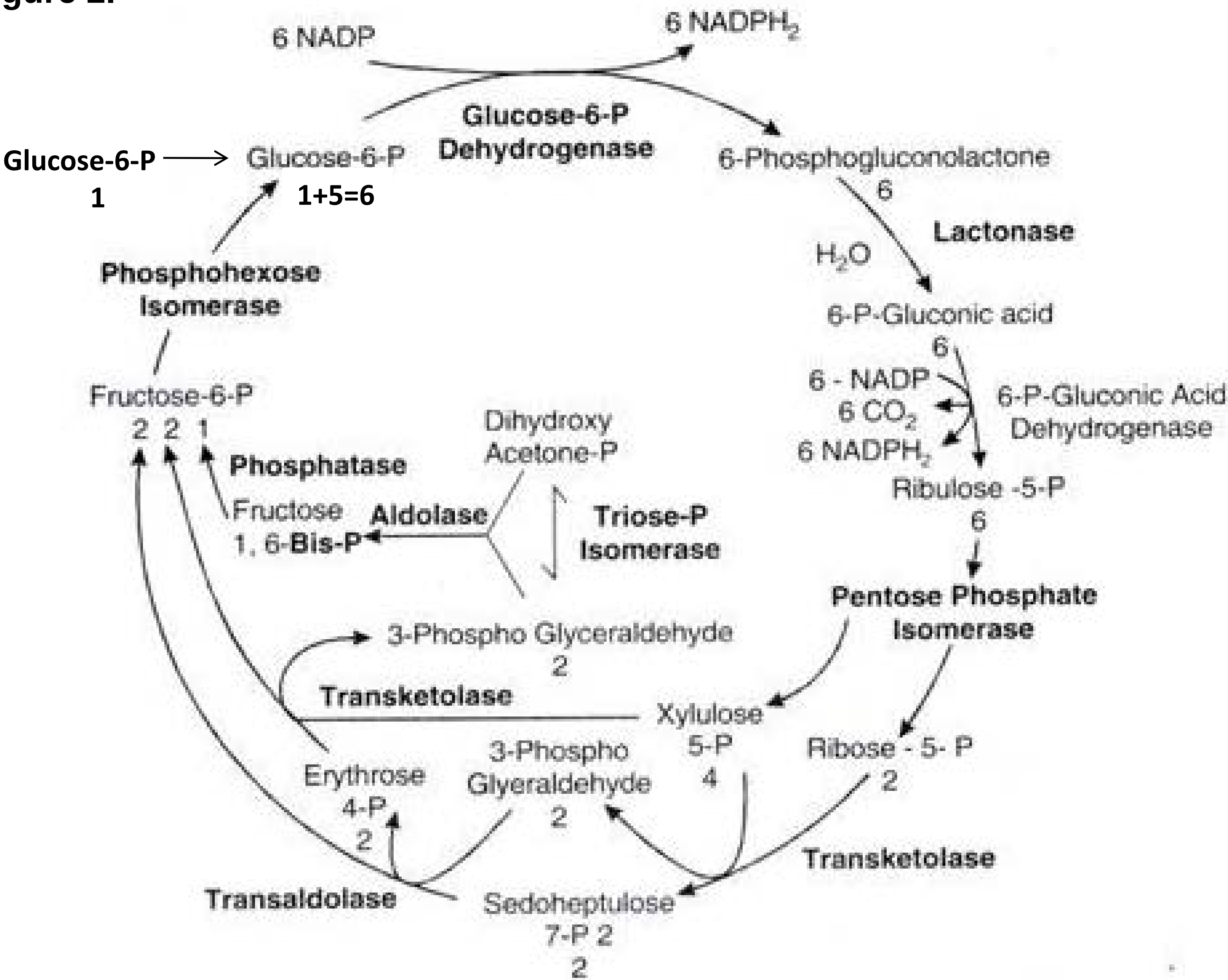
- These intermediate comps. are also used in a variety of different biological processes including production of nucleotides (ribose-5-phosphate), as well as synthesis of aromatic amino acids (erythrose-4-phosphate).
- Glucose-6-phosphate dehydrogenase is the rate-controlling enzyme in this pathway. It is allosterically stimulated by $NADP^+$.
- NADPH-utilizing pathways, such as fatty acid synthesis, generate $NADP^+$, which stimulates glucose-6-phosphate dehydrogenase to produce more NADPH.

Figure 1.



6 NADP+
6 NADPH + 6 H+
6 glucose-6-P
6 H2O
6 6-phosphogluconate
6 NADP+
6 NADPH + 6 H+
6 ribulose-5-P
6 CO2
2 Ribose-5-P
2 Xylulose-5-P
Transketolase
2 Glyceraldehyde-3-P
2 Sedoheptulose-7-P
Transaldolase
2 Fructose-6-P
2 Erythrose-4-P
2 Xylulose-5-P
Transketolase
2 Fructose-6-P
2 Glyceraldehyde-3-P
Pi
Fructose-6-P
Fructose-1,6-bis P
2 Pyruvate

Figure 2.


Glucose-6-P
1
6 NADP
6 NADPH2
Glucose-6-P
1+5=6
Glucose-6-P
Dehydrogenase
6-Phosphogluconolactone
6
Lactonase
H2O
6-P-Gluconic acid
6
6 - NADP
6 CO2
6 NADPH2
6-P-Gluconic Acid
Dehydrogenase
Ribulose -5-P
6
Pentose Phosphate
Isomerase
Phosphohexose
Isomerase
Fructose-6-P
2 2 1
Phosphatase
Fructose
1, 6-Bis-P
Aldolase
Dihydroxy
Acetone-P
Triose-P
Isomerase
3-Phospho Glyceraldehyde
2
Transketolase
Xylulose
5-P
4
Ribose - 5- P
2
Erythrose
4-P
2
3-Phospho
Glyeraldehyde
2
Transketolase
Transaldolase
Sedoheptulose
7-P 2
2