Faculty Science
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M.Sc. III Sem Paper- H3002 (Phytochemistry and Metabolism),

Topic- The Pentose Phosphate Pathway

The pentose phosphate pathway or the hexose monophosphate pathway or 6-phosphogluconate pathway is an alternative pathway occurs in the cytosol of the cell. Besides ATP, cells require the reducing power of NADPH for the biosynthesis of macromolecules (anabolism). **NADPH is used in biosynthesis (anabolism), whereas NADH is used in oxidative metabolism (catabolism)**. Cells keep the NAD^+/NADH ratio near 1000 (which favors metabolite oxidation) and the $NADP^+$/NADPH ratio near 0.01 (which favors reductive biosynthesis). The pathway provides NADPH for reductive biosynthesis and ribose-5-phosphate for nucleotide biosynthesis in the quantities that the cell requires. The oxidation of glucose by the pentose phosphate pathway generates NADPH. It includes two, irreversible oxidative reactions, followed by a series of reversible sugar–phosphate interconversions. **No ATP is directly consumed or produced in the cycle. First carbon of glucose 6-phosphate is released as CO2 and two NADPH are produced for each glucose 6-phosphate molecule entering the oxidative part of the pathway. The rate and direction of the reversible reactions of the pentose phosphate pathway are determined by the supply of and demand for intermediates of the cycle.** The pentose phosphate pathway consists of three stages the production of NADPH, isomerization of pentoses and formation of glycolytic intermediates.

The first stage of the pentose phosphate pathway consists of three steps, its oxidative reactions:

(a) Glucose-6-phosphate is oxidized to 6-phosphoglucono-δ-lactone by glucose-6- phosphate dehydrogenase, producing the first NADPH.

(b) 6-Phosphogluconolactonase hydrolyzes the lactone (cyclic ester) to yield 6-phosphogluconate.

(c) 6-Phosphogluconate dehydrogenase then catalyzes the oxidative decarboxylation of 6- phosphogluconate by $NADP^+$ to yield ribulose-5-phosphate, CO_2, and the second NADPH.

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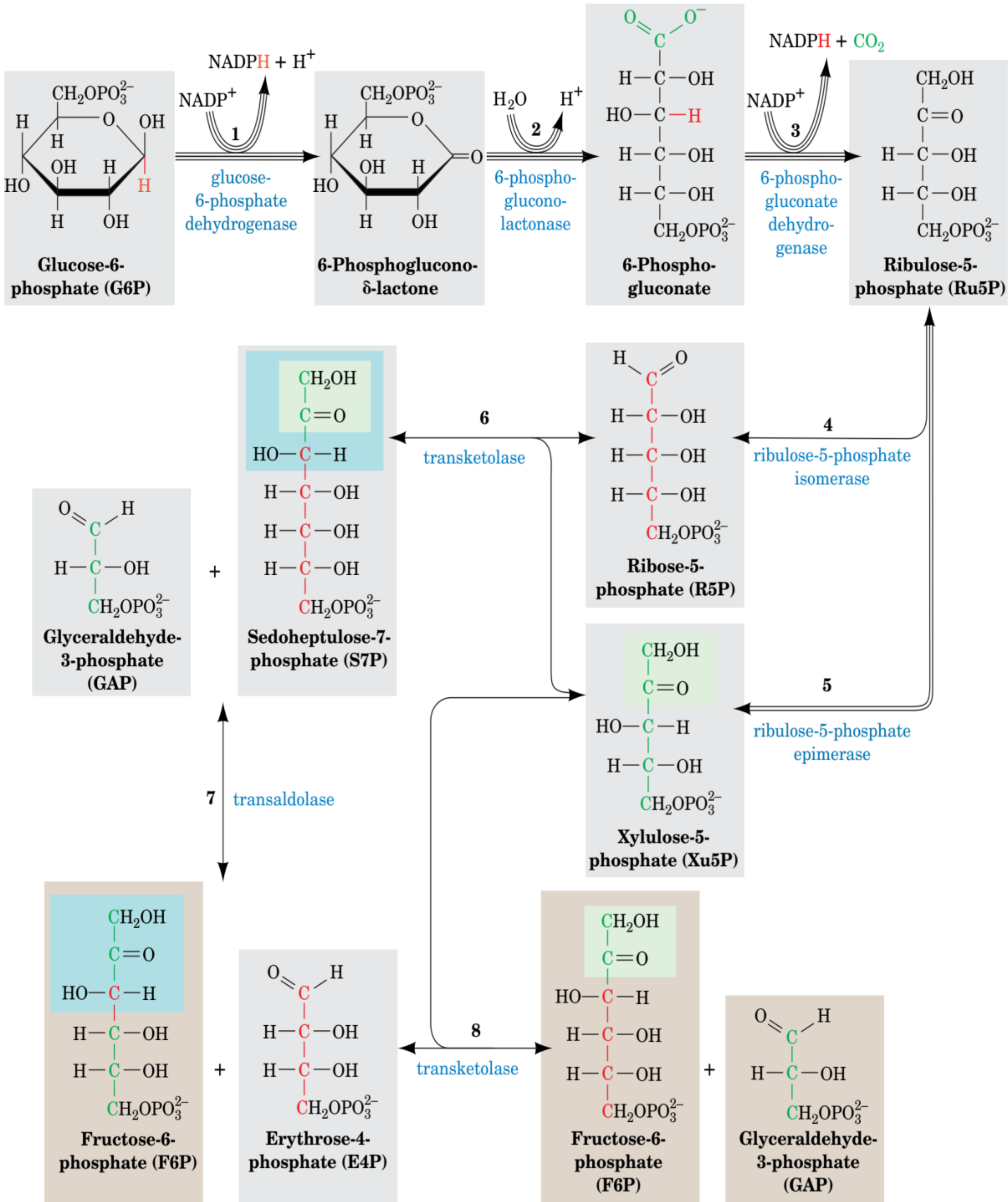


The pentose phosphate pathway

(The carbon skeleton of R5P and the atoms derived from it are drawn **in red** and those from Xu5P are drawn **in green**. The C2 units transferred by transketolase are shaded **in green**, and the C3 units transferred by transaldolase are shaded **in blue**.)

The second stage of the pentose phosphate pathway is catalyzed by two enzymes that act on ribulose-5-phosphate (Ru5P):

(a) Ribulose-5-phosphate epimerase converts Ru5P to xylulose5-phosphate (Xu5P).

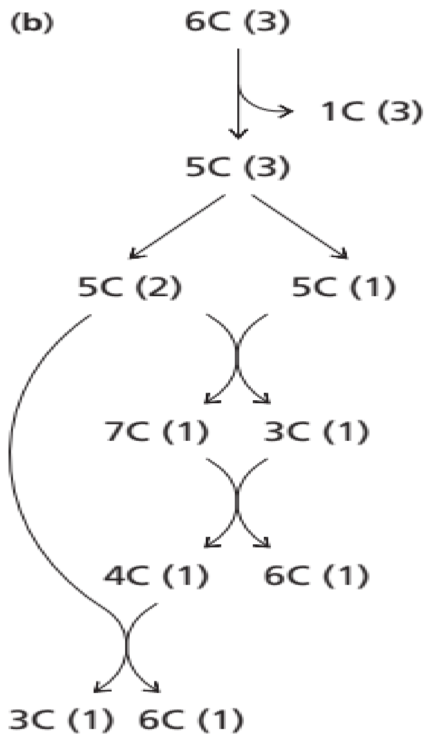
(b) Ribulose-5-phosphate isomerase converts Ru5P to ribose-5- phosphate (R5P). The R5P can be used to produce nucleosides for RNA and DNA synthesis.

The third stage of the pentose phosphate pathway, 3 five-carbon sugars are converted to 2 fructose-6-phosphate and 1 glyceraldehyde-3-phosphate. These interconversions are catalyzed by two enzymes known as transketolase and transaldolase.

Transketolase is also called glycoaldehydetransferase. It is a thiamine diphosphate (TDP) dependent enzyme that **catalyzes the transfer of a two-carbon glycoaldehyde group from a ketose phosphate to an aldose phosphate.** The ketose phosphate is shortened by two carbons and the aldose phosphate is lengthened by two carbons. Transketolase transfers a two-carbon unit from Xu5P to R5P yielding the seven-carbon sugar sedoheptulose-7-phosphate (S7P) and glyceraldehyde-3-phosphate (GAP).

Transaldolase is also called dihydroxyacetonetransferase. It **catalyzes the transfer of a three-carbon dihydroxyacetone group from a ketose phosphate to an aldose phosphate.** The transaldolase converts sedoheptulose-7-phosphate and glyceraldehyde-3-phosphate to the four-carbon erythrose-4-phosphate and fructose 6-phosphate. The finally transketolase converts Xu5P and E4P to F6P and GAP.

Figure (b)- The path of carbon in the pentose phosphate pathway. In the oxidative stage, three molecules of a six-carbon compound are converted to three molecules of a five carbon sugar (ribulose 5-phosphate) with release of three molecules of CO2. In the non-oxidative stage, three molecules of five carbon sugars are interconverted to produce two molecules of a six-carbon sugar (fructose 6-phosphate) and one molecule of a three-carbon compound (glyceraldehyde 3-phosphate).



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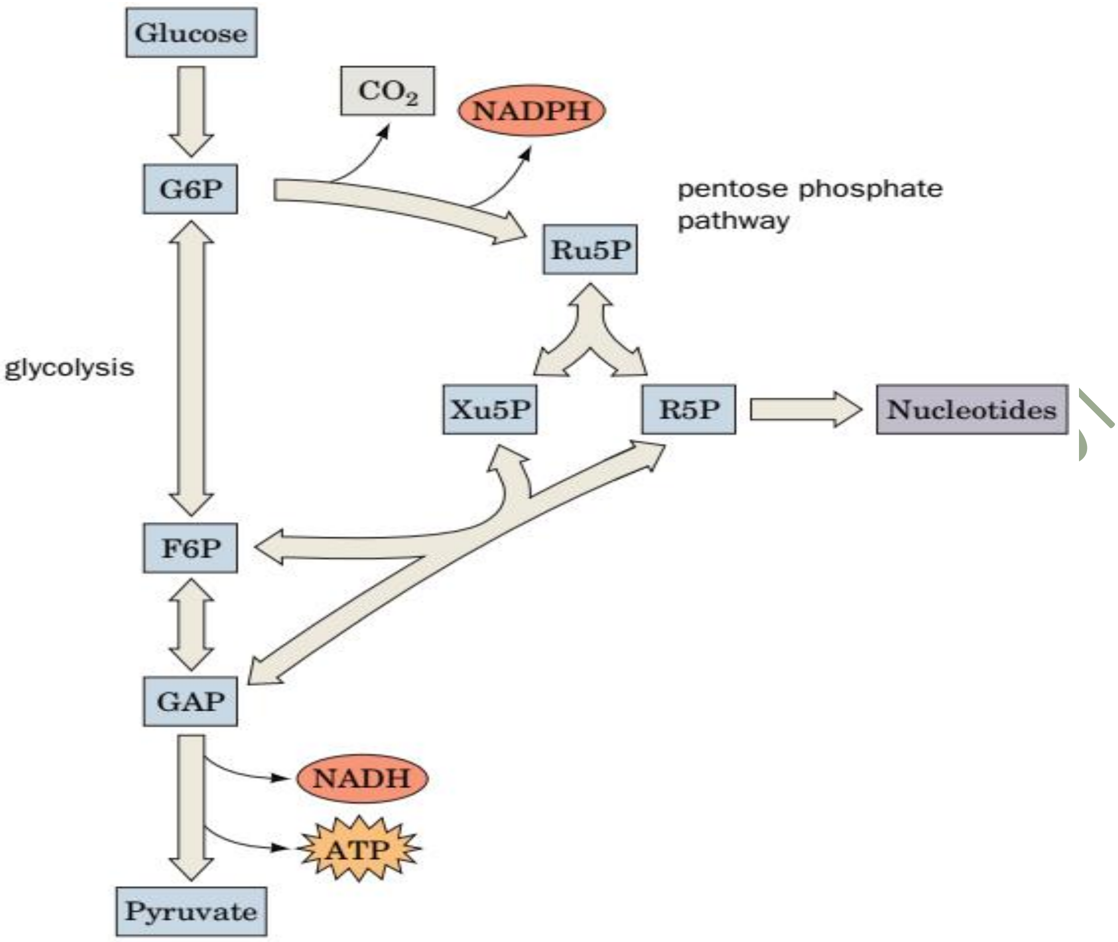

Relationship between glycolysis and the pentose phosphate pathway

The reversible nature of the second and third stages of the pentose phosphate pathway permits the cell to meet its need for R5P (a nucleic acid precursor) and NADPH. For example, if the need for NADPH is greater than that for R5P, the excess R5P is converted to F6P and GAP for consumption via glycolysis. Conversely, if the demand for R5P outstrips the need for NADPH, the glycolytic intermediates F6P and GAP can be diverted to the pentose phosphate pathway to synthesize R5P. The flux of glucose-6-phosphate through the pathway is regulated by the rate of the glucose-6-phosphate dehydrogenase (G6PD) reaction. This enzyme is controlled by the availability of its substrate NADP$^+$ so that the pathway flux increases in response to increasing levels of NADP$^+$ (which indicates increased cellular demand for NADPH).

Reference

1.Voet D, Voet J (2018) in "Biochemistry". 5th edition. J. Wiley & Sons, USA
2. Richard A. Harvey, Denise R Ferrier (2014) in "Lippincott's Illustrated Reviews: Biochemistry". 6th edition, Lippincott Williams &Wilkins, USA.

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