Pentose phosphate pathway

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For M.sc 3rd sem Botany

The **pentose phosphate pathway** (also called the **phosphogluconate pathway** and the **hexose monophosphate shunt**) is a metabolic pathway parallel to glycolysis. It generates NADPH and pentoses (5-carbon sugars) as well as ribose 5-phosphate, a precursor for the synthesis of Nucleotides. While the pentose phosphate pathway does involve oxidation of glucose, its primary role is anabolic rather than catabolic. The pathway is especially important in red blood cells (erythrocytes).

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, the pentose phosphate pathway takes place in the cytosol; in plants, most steps take place in plastids.[1]

Similar to glycolysis, the pentose phosphate pathway appears to have a very ancient evolutionary origin. The reactions of this pathway are mostly enzyme-catalyzed in modern cells, however, they also occur non-enzymatically under conditions that replicate those of the Archean ocean, and are catalyzed by metal ions, particularly ferrous ions (Fe(II)).[2] This suggests that the origins of the pathway could date back to the prebiotic world.

The primary results of the pathway are:

- 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.

Aromatic amino acids, in turn, are precursors for many biosynthetic pathways, including the lignin in wood.[*citation needed*]

Dietary pentose sugars derived from the digestion of nucleic acids may be metabolized through the pentose phosphate pathway, and the carbon skeletons of dietary carbohydrates may be converted into glycolytic/gluconeogenic intermediates.

In mammals, the PPP occurs exclusively in the cytoplasm. In humans, it is found to be most active in the liver, mammary glands, and adrenal cortex.[citation needed] The PPP is one of the three main ways the body creates molecules with reducing power, accounting for approximately 60% of NADPH production in humans.[citation needed]

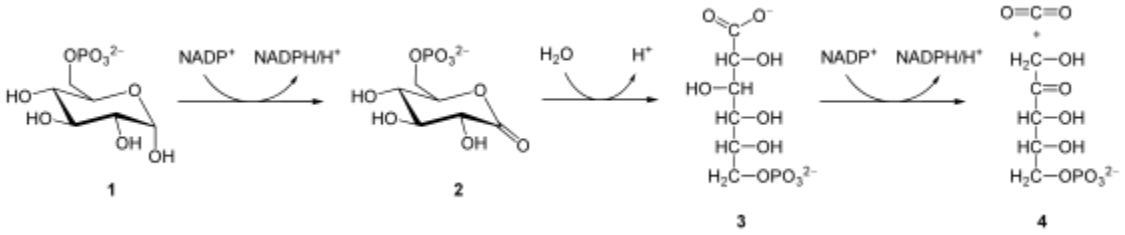
One of the uses of NADPH in the cell is to prevent oxidative stress. It reduces glutathione via glutathione reductase, which converts reactive H_2O_2 into H_2O by glutathione peroxidase. If absent, the H_2O_2 would be converted to hydroxyl free radicals by Fenton chemistry, which can attack the cell. Erythrocytes, for example, generate a large amount of NADPH through the pentose phosphate pathway to use in the reduction of glutathione.

Hydrogen peroxide is also generated for phagocytes in a process often referred to as a respiratory burst.[3]

Phases

Oxidative phase

In this phase, two molecules of $NADP^+$ are reduced to NADPH, utilizing the energy from the conversion of glucose-6-phosphate into ribulose 5-phosphate.



Oxidative phase of pentose phosphate pathway.
Glucose-6-phosphate (**1**), 6-phosphoglucono-δ-lactone (**2**), 6-phosphogluconate (**3**), ribulose 5-phosphate (**4**)

The entire set of reactions can be summarized as follows:

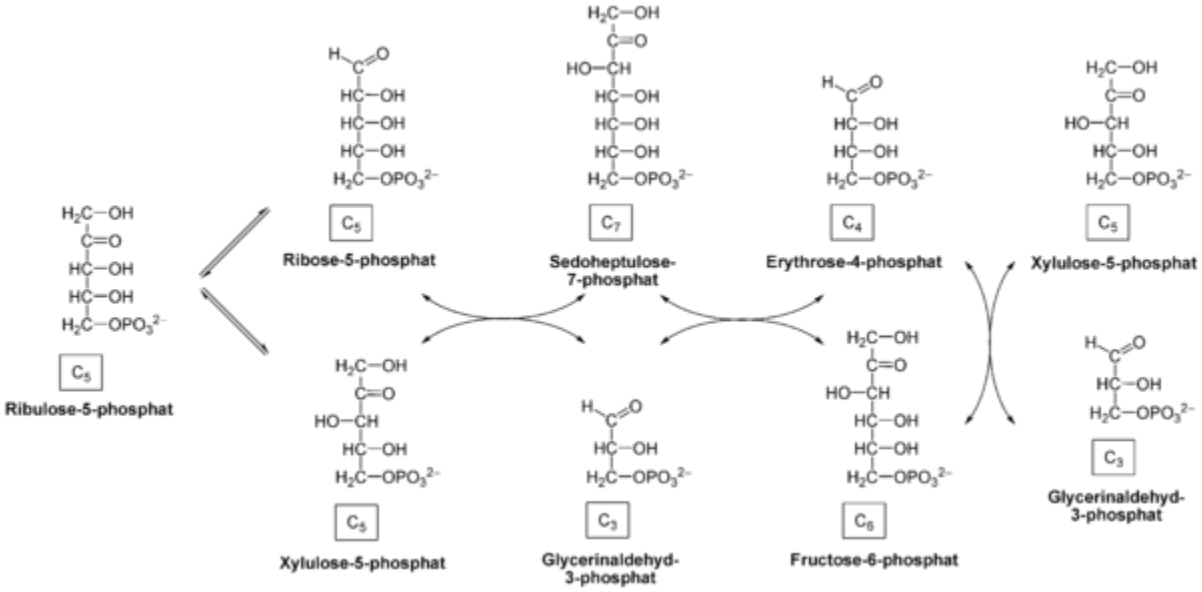
Reactants	Products	Enzyme	Description
Glucose 6-phosphate + NADP+	→ 6-phosphoglucono-δ-lactone + **NADPH**	glucose 6-phosphate dehydrogenase	Dehydrogenation. The hydroxyl on carbon 1 of glucose 6-phosphate turns into a carbonyl, generating a lactone, and, in the process, NADPH is generated.

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

Non-oxidative phase



The pentose phosphate pathway's nonoxidative phase

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

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