Pentose Phosphate Pathway (Warburg-Dicken's Pathway):

TIG

It involves the oxidation of Glucose-6-Phosphate to 6-Phosphogluconic acid which in turn is converted into pentose phosphates. In this pathway glucose-6-phosphate is directly oxidised without entering glycolysis, hence it is also known as Direct Oxidation Pathway or Hexose Monophosphate Shunt.

Reactions of Pentose Phosphate Pathway:

(1) 6 molecules of glucose-6-phosphate in the presence of coenzyme NADP are converted (oxidised) into 6 molecules of 6-phosphogluconolactone by the enzyme glucose-6-phosphate dehydrogenase. 6 molecules of NADP are reduced in the reaction which is reversible.

(2) 6-Phosphogluconolactone is hydrolysed by the enzyme Lactonase to produced 6 molecule of 6-phosphogluconic acid.

(3) 6-Phosphogluconic acid is oxidatively decarboxylated by the enzyme 6-Phosphogluconic acid dehydrogenase. 6 molecules of NADP are reduced, 6 molecules of CO_2 are released and 6 mols, of Ribulose-5-Phosphate are produced.

(4) 6 mols. of Ribulose-5-P isomerise into 4 mols. of XyIuIose-5-Phosphate and 2 mols. of Ribose-5-Phosphate in the presence of Ribulose phosphate-3-epimerase and Pentose phosphate isomerase respectively.

(5) 2 mols. of xylulose-5-Phosphate and 2 mols. of Ribose-5-phosphate combine in the presence of Transketolase to form 2 mols. of Sedoheptulose-7-Phosphate and 2 mols. of 3- Phosphoglyceraldehyde.

(6) 2 mols. of Sedoheptulose-7-Phosphate and 2 mols. of 3-Phosphoglyceraldehyde combine in the presence of Transaldolase to form 2 mols. of Fructose-6-Phosphate and 2 mols. of Erythrose-4-Phosphate (4-carbon atoms sugar).

(7) 2 mols. of Erythose-4-Phosphate react with remaining two mols. of xylulose-5-Phosphate (see reaction No. 4 and 5) in the presence of Transketolase to form 2 mols. of Fructose- 6-Phosphate and 2 mols of 3-Phosphoglyceraldehyde.

(8) One mol. of 3-phosphoglyceraldehyde isomerises into dihydroxyacetone phosphate. The enzyme is Phosphotriose isomerase.

(9) Remaining one mole, of 3-Phosphoglyceraldehyde unites with Dihydroxyacetone phosphate in presence of Aldolase to form one mol. of Fructose 1, 6-bisphosphate. The latter, in the presence of Phosphatase forms one mol. of Fructose 6-Phosphate.

(10) 5 molecules of Fructose-6-phosphate produced in reactions 6, 7 and 9, isomerise into 5 mols. of Glucose-6-P in presence of Phosphohexose isomerase.

To summarise, 6 mols. of Glucose-6-P which enter into this pathway after oxidation produce 6 mols. of CO_2 (Reaction No. 3. CO_2 comes from C-No. 1 of the glucose molecule) and 12 mols. of reduced coenzymes $NADPH_2$ (reaction 1 and 3) while 5 mols of Glucose-6-Phosphate are regenerated (Reaction No. 10).

$$6\ (\text{Glucose-6-P}) + 12\ NADP^{+} \rightarrow 5\ (\text{Glucose-6-P}) + 12\ (NADPH + H^{+}) + 6\ CO_2$$

In other words one mol. of Glucose-6-P after oxidation produces 6-mols. of CO_2 and 12 ($NADPH + H^+$) molecules.

All the enzymes of pentose phosphate pathway are present in cytosol.

Significance of Pentose-Phosphate-Pathway:

(i) It provides alternative route for carbohydrate breakdown.

(ii) It generates NADPH molecules which are used as reductants in biosynthetic processes under conditions when NADPH molecules are not generated by photosynthesis. It is therefore, especially important in non-photosynthetic tissues such as in differentiating tissues, germinating seeds and during periods of darkness. Production of NADPH is not linked to ATP generation in pentose phosphate pathway.

(iii) It provides Ribose sugars for the synthesis of nucleic acids.

(iv) It plays important role in fixation of CO_2 in photosynthesis through Ribulose-5-Phosphate. (Ribulose 1, 5-bisphosphate derived from Ribulose-5-Phosphate is the primary acceptor of CO_2 in photosynthesis).
(v) It provides Erythrose-4-phosphate which is required for the synthesis of shikimic acid. The latter is precursor of aromatic ring compounds.

Pentose phosphate pathway (PPP) or Hexose mono-phosphate (HMP) shunt

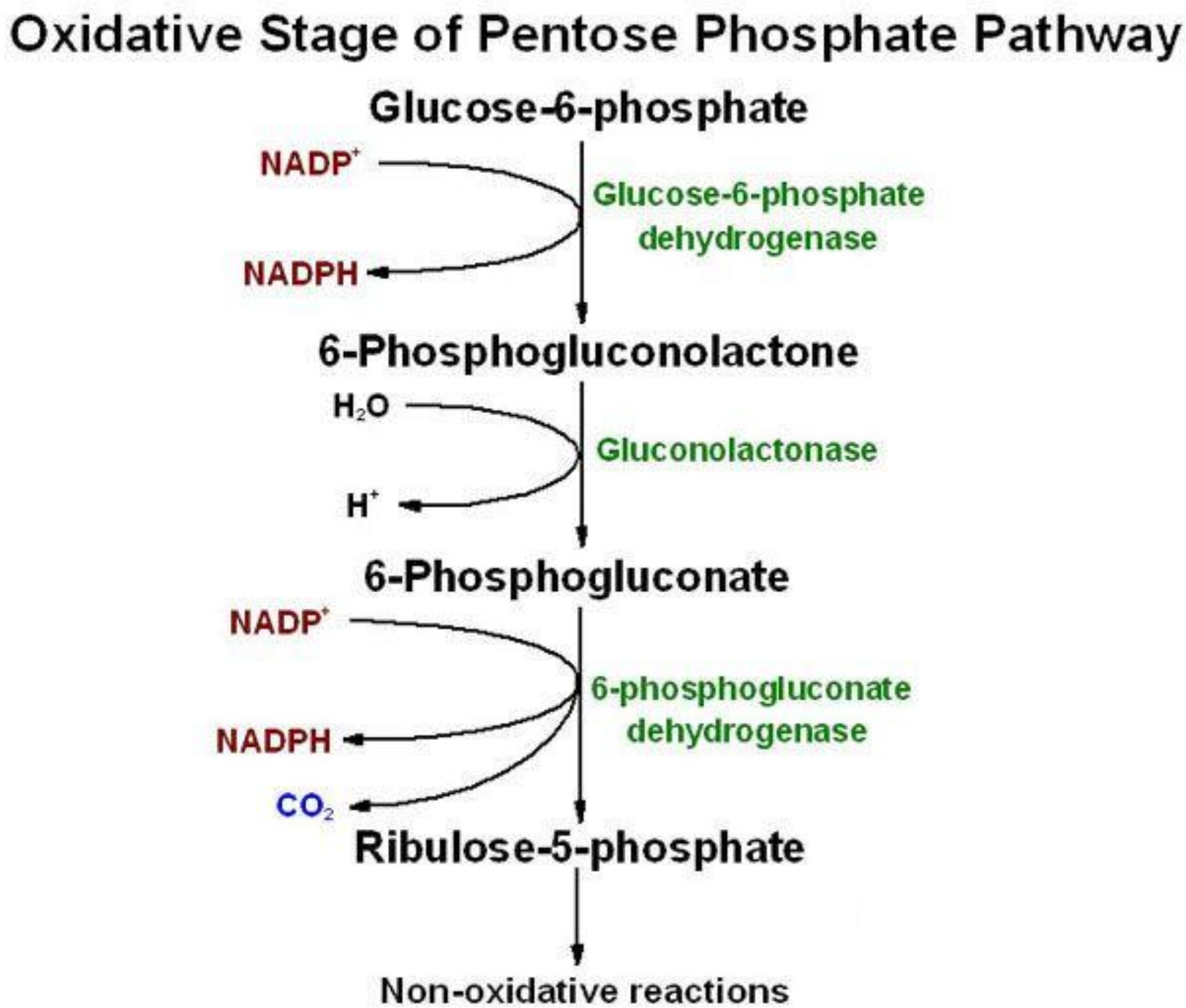
- Pentose phosphate pathway is an alternative pathway to glycolysis and TCA cycle for oxidation of glucose.
- It is a shunt of glycolysis
- It is also known as hexose monophosphate (HMP) shunt or phosphogluconate pathway.
- It occurs in cytoplasm of both prokaryotes and eukaryotes
- Pentose phosphate pathway starts with glucose and it is a multi-steps reaction.

The sequence of reactions are divided into two types:

I) oxidative reaction phase

II) Non-oxidative reaction phase

Oxidative phase:



First four reactions are irreversible and oxidative in which glucose molecule is oxidized twice generating two molecules of NADPH and glucose is converted into Ribose-5 phosphate.

1st reaction: conversion of glucose to glucose-6 phosphate.

This reaction is catalyzed by the enzyme hexokinase and a molecule of ATP is utilized. This reaction is actually a primary step of glycolysis.

2nd reaction: conversion of glucose-6 phosphate to 6-phosphogluconolactone.

This reaction is catalyzed by an enzyme glucose-6 phosphate dehydrogenase (G6PD) in the presence of Mg++ ion.

In this reaction a molecule of NADPH is produced.

3rd reaction: conversion of 6-phosphogluconolactone to 6-phosphogluconate

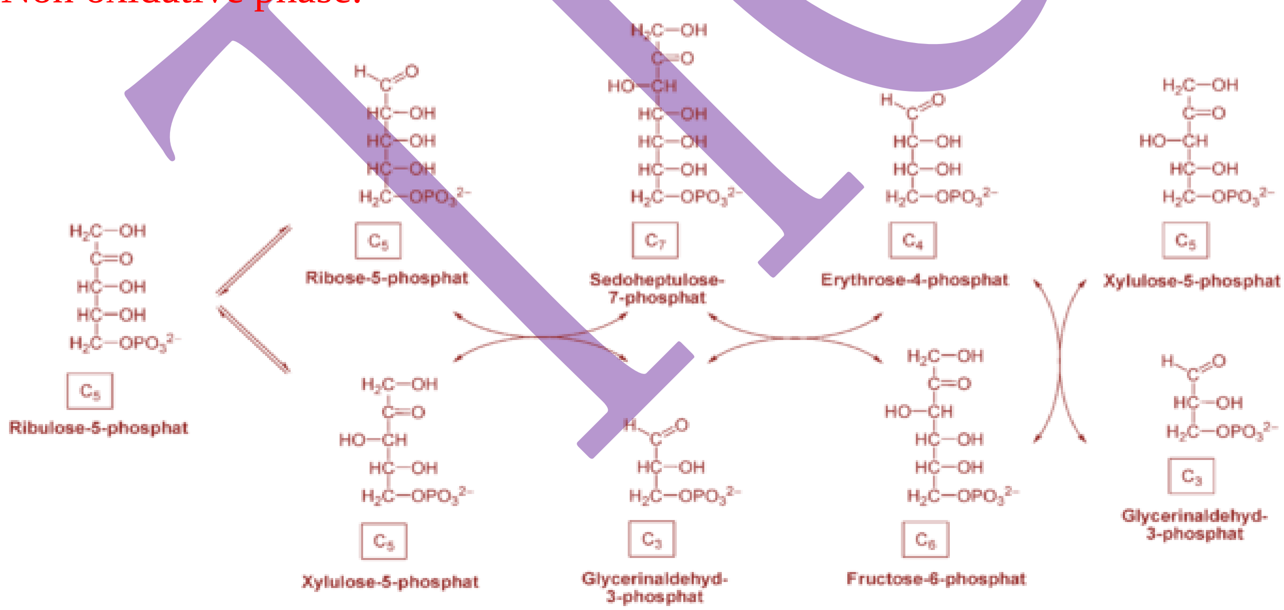
This reaction is a hydrolysis reaction catalyzed by hydrolase enzyme

4th reaction: conversion of 6-phosphogluconate to ribose-5 phosphate

This reaction is catalyzed by the enzyme 6-phosphogluconate dehydrogenase to produce 3-keto-6-phosphogluconate which undergoes decarboxylation to produce ribulose-5 phosphate.

In this reaction a molecule of NADPH is generated.

Non oxidative phase:



Oxidative reactions is followed by a series reversible sugar phosphate inter-conversion reaction:

1. Ribulose-5-phosphate is epimerized to produce xylulose 5-phosphate in the presence of enzyme phosphor pentose epimerase. Similarly ribulose-5-phosphate is also keto-isomerized into ribose 5-phosphate.
2. Xylulose-5-phsphate transfer two carbon moiety to ribose 5-phospahate in the presence of enzyme transketolase to form sedoheptulose-7-phosphate and glyceraldehyde 3—phosphate.
3. Sedoheptulose -7-phosphate transfer three carbon moiety to glyceraldehyde -3-phosphate to form fructose 6-phopsphate and erythrose 4-phosphate in the presence of enzyme transaldolase.
4. Transketolase enzyme catalyse the transfer of two carbon moiety from Xylulose-5-phsphate to erythrose-4- phosphate to form fructose-6-phosphate and glyceraldehyde-3-phosphate.
5. Fructose-6-phosphate and glyceraldehyde-3-phosphate is later enter into glycolysis and kreb's cycle.
6. The rate and direction of reversible reaction depends upon the needs of cell.
7. If cell needs only NADPH then fructose-phosphate and glyceraldehyde-3-phosphate are converted back to glucose by reverse glycolysis, otherwise converted to pyruvate and enter TCA cycle generating ATPs.

Significance of Pentose phosphate pathway:

- HMP is only the cytoplasmic pathway that generates NADPH

- NADPH is produced in this pathway acts as reducing agent during biosynthesis of various molecules eg. fattyacids.
- This pathway generates 3, 4, 5, 6 and 7 carbon compounds which are precursors for biosynthesis of other molecules. Eg nucleotides are synthesized from ribose-5-phsophate.
- Pentose phosphate pathway is very essential for cell lacking mitochondria (eg.RBCs) for generation of NADPH.
- Triose, tetrose, pentose, hexose and heptose sugar are generated as intermediate products in pentose phosphate pathway.
- NADPH is also used to reduce (detoxify) Hydrogen peroxide in cell.
- Resistance to malaria in some Africans are associated with deficiency of glucose-6-phosphate dehydrogenase enzyme because malarial parasites depend upon HMP shunt to reduce glutathione in RBCs.