

Pentose phosphate pathway
So far we have discussed the glucose catabolism with major emphasis on generation of ATP. Oxidation of Glucose to carbon dioxide via glycolysis, PDC, CAC generates ATP and reducing equivalents such as NADH and FADH2 which are further oxidized in ETC generating ATP by oxidative phosphorylation.

Cells require ATP as well as reducing power for exergonic synthetic reactions. In most mammalian cells NADH produced by glycolysis and CAC is efficiently utilized by oxidative phosphorylation for ATP generation.

Thus the NAD⁺/NADH ratio is always around 1000 (i.e. high concentrations of NAD⁺). Therefore NADH is not the best reducing equivalent for synthetic reaction.

In order providing reducing power for synthetic reactions, cells produce NADPH in a special pathway of oxidation of glucose 6 phosphate called **pentose phosphate shunt**.

NADP⁺/NADPH ration is 0.01 in most cells as it is not used in oxidative phosphorylation and it is available exclusively for reduction reactions required for synthetic purposes.

NADPH: an other currency for reducing power in synthetic reaction. This pathway generates NADPH and Ribose-5-P which is used for synthetic reactions including nucleic acid synthesis.

Pentose phosphate pathway

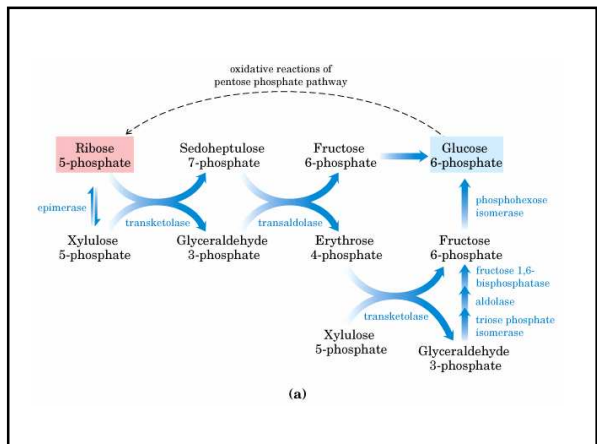
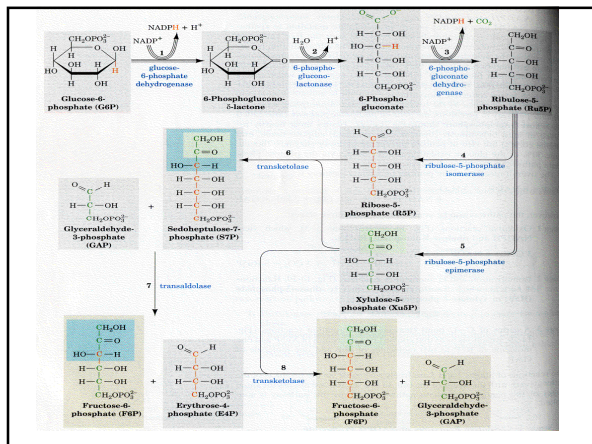
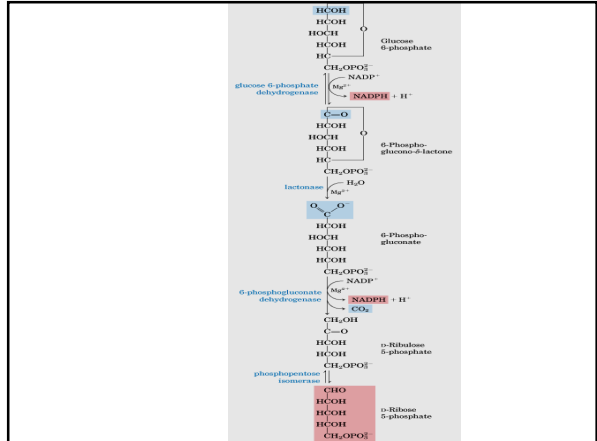
This pathway also leads to the formation of pentose sugar intermediates such as Ribose 5 phosphate, Riulose 5 phosphate that are essential for nucleic acid synthesis.

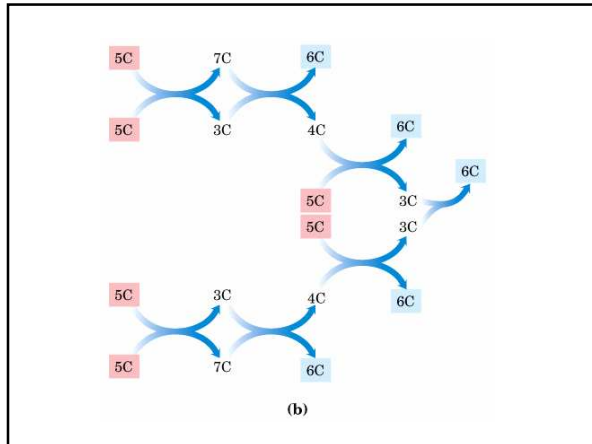
The overall reaction:

$$3G6P + 6NADP^+ + 3H_2O = 6NADPH + 6H^+ + 3CO_2 + 2F6P + GAP$$

There are seven enzymes involved in three different steps of this pathway;

- Oxidative reactions:**
 - Glucose 6 phosphate dehydrogenase
 - 6-phosphogluconolactonase
 - 6-phosphogluconate dehydrogenase
- Isomerization and epimerization reactions**
 - Ribulose 5 phosphate isomerase
 - Ribulose 5 phosphate epimerase
- C-C bond cleavage and formation reactions**
 - Transketolase
 - Transaldolase



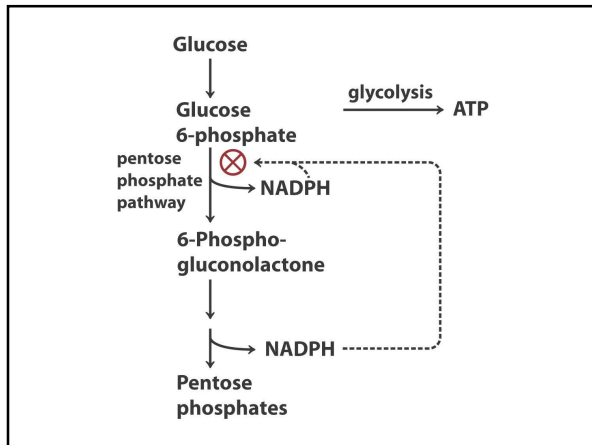


Regulation of pentose phosphate pathway

The major specific product of this pathway are NADPH and Ribose 5P which are used as reducing power for synthetic reactions and nucleic acid synthesis respectively.

Glucose 6 phosphate dehydrogenase (G6P DH) is the main enzyme that controls the flux (overall rate) of this pathway.

G6P DH is strongly inhibited by NADPH. Thus if the NADPH concentration decreases, the G6PDH is activated.



NADPH is used to generate reduced glutathione (GSH). GSH plays a critical role in quenching the oxyradicals in the cells.

If NADPH generation is inhibited due to the mutations in G6PDH, cells become susceptible to oxidative damage.

Malaria parasite is very sensitive to Oxy-radicals, and people with G6PDH defect are resistant to malaria as the parasite is killed by oxy-radicals.

