



HMP SHUNT PATHWAY

(Pentose phosphate pathway or Phospho gluconate pathway or Dickens-Horecker pathway)

Introduction:

It is an alternative route for the metabolism of glucose. It is more complex pathway than glycolysis. It is more anabolic in nature. It concerns with the biosynthesis of NADPH and pentoses. It is a minor metabolic pathway of glucose. It is a major catabolic pathway (Oxidative) next to glycolysis.

Occurrence

RBC, Adrenal Cortex, Liver, lactating mammary gland and adipose tissue, testes and ovaries, lens of eye

Operates in cytoplasm

TISSUES WITH ACTIVE HMP SHUNT PATHWAY

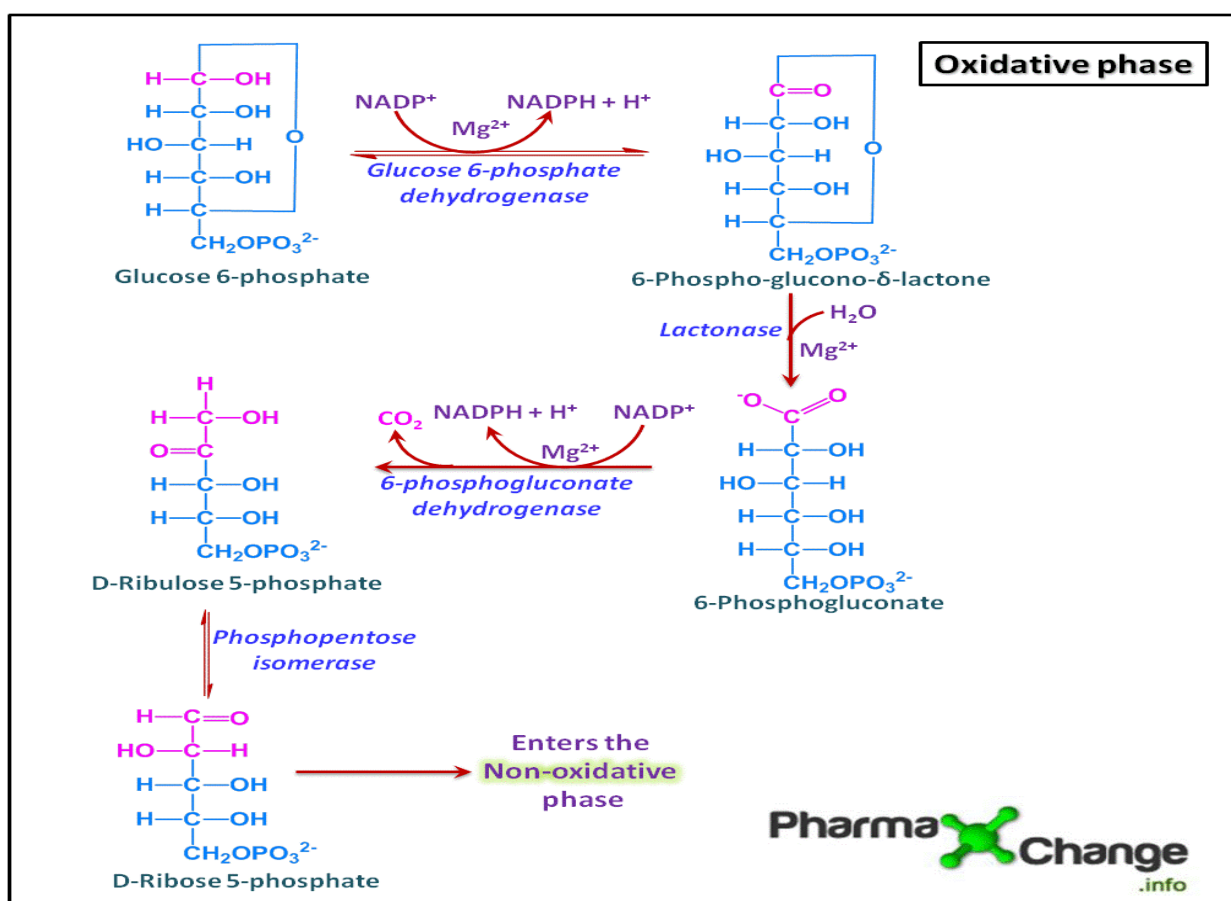
- Liver - Fatty acid and cholesterol synthesis
- Testes - Steroid synthesis
- Adipose tissue - Fatty acid synthesis
- Ovary - Steroid synthesis
- Mammary gland - Fatty acid synthesis
- Red blood cells - Maintenance of reduced glutathione



Reactions of the pathway

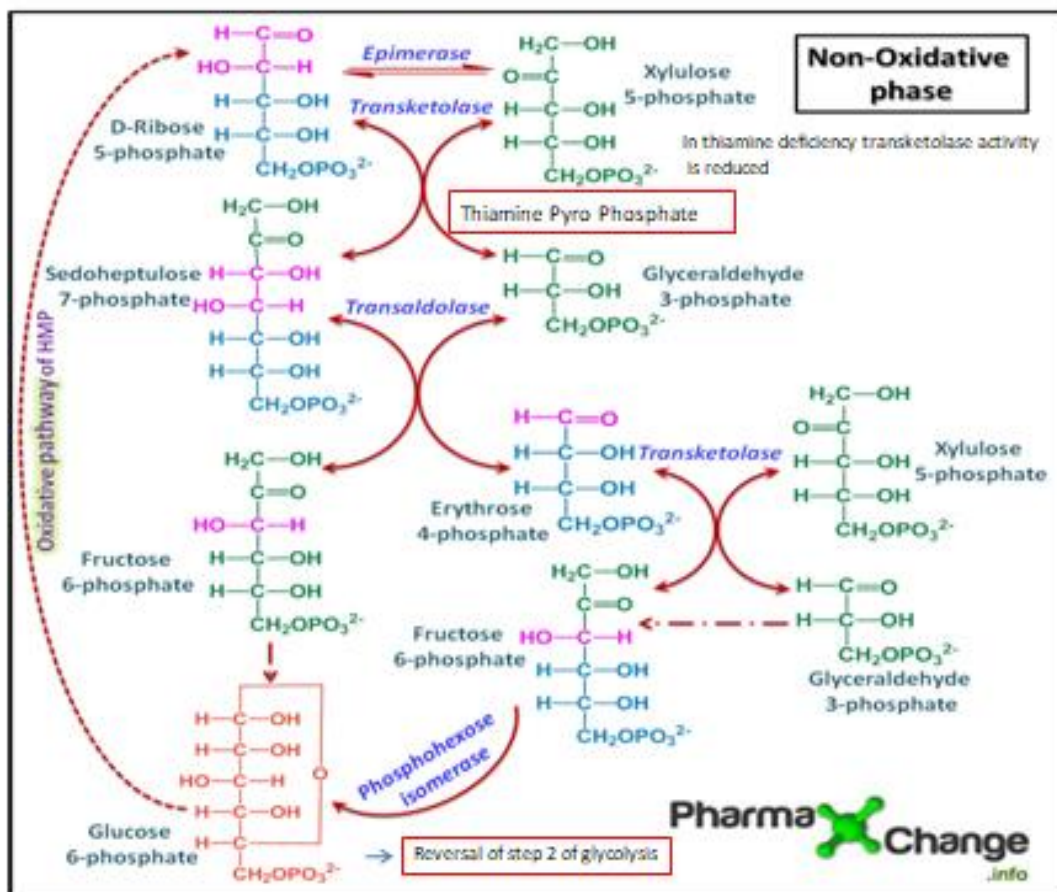
The sequence of reactions of HMP shunt is divided into two phasesoxidative and non-oxidative phase.

Oxidative phase:





Non-oxidative phase:





Regulation :

The regulatory enzymes of HMP shunt pathway are glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase.

The synthesis of both enzymes is induced by insulin.

The entry of glu-6-p into the ppp is controlled by the cellular concentration of NADPH. So the oxidative phase is controlled by NADPH.

The non-oxidative phase is controlled by pentoses

SIGNIFICANCE OF HMP SHUNT PATHWAY

I Produce NADPH and pentose phosphates

NADPH is required for Reductive biosynthesis of fatty acids, cholesterol and steroid hormones

Free Radical scavenging

Maintains RBC membrane integrity by keeping GSH in reduced state

NADPH protects RBC from oxidative damage by H_2O_2

To keep the ferrous iron of haemoglobin in the reduced state and to prevent accumulation of met-haemoglobin.

Detoxification by hydroxylation

Maintain the transparency of lens

Bactericidal activity of macrophages

II. Ribose 5 phosphate is required for nucleic acid synthesis

III Clinical importance

a. Glu 6 phosphate dehydrogenase deficiency

b. Drug induced hemolytic anemia



c. Methemoglobinemia

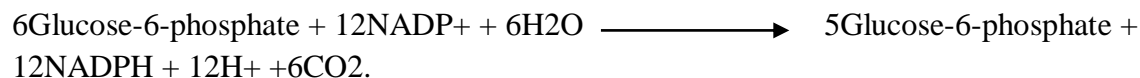
d. Thiamine deficiency leads to reduced transketolase activity

- NADPH seen in lens of eye for preserving the transparency of lens.
- NADPH is required for production of superoxide anion by macrophages to kill bacteria.
- Most of the drugs and other foreign substances are detoxified by liver microsomal P450 enzymes with the help of NADPH

ENERGETICS

- ATP is neither utilized nor produced by the HMP shunt pathway. Cells do not use the shunt pathway for energy production

The overall reaction may be represented as



WHY IS PENTOSE PHOSPHATE PATHWAY IMPORTANT FOR RBC?

Highly oxidizing environment

- Susceptible to oxygen-induced free radical damage .
- Free radicals are neutralized by glutathione peroxidase