Pentose Phosphate Pathway

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Introduction

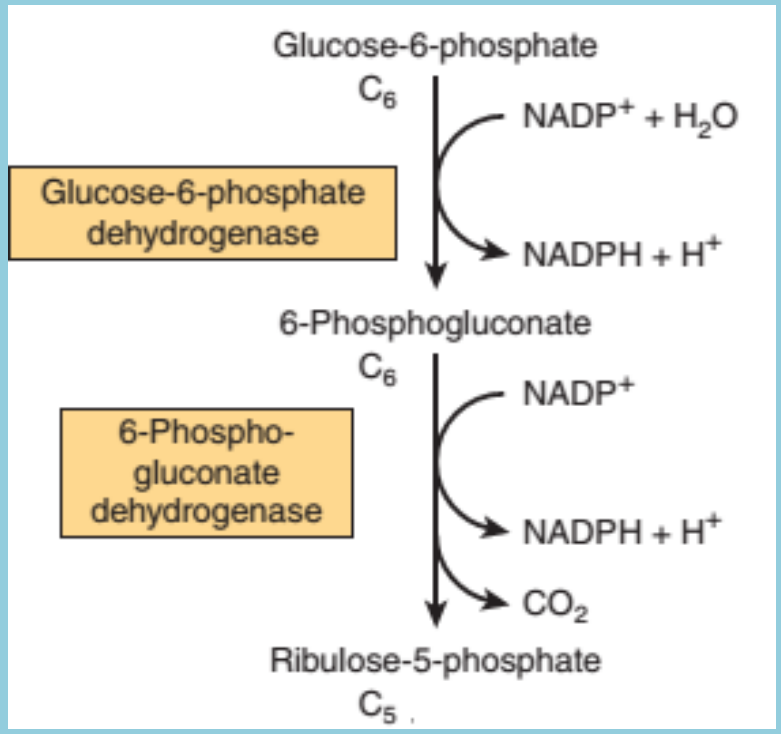
- Alternative route for the metabolism of glucose
- Also known as **Hexose Monophosphate (HMP) shunt**
- More complex pathway than glycolysis
- It helps in
  - formation of **NADPH** for synthesis of fatty acids, steroids,
  - maintaining reduced **glutathione** for antioxidant activity
  - synthesis of **ribose** for nucleotide and nucleic acid formation

Pentose Phosphate Pathway

- Like glycolysis it occurs in cytosol
- Oxidation is achieved by dehydrogenation using $NADP^+$, not NAD^+
- Its carried out in 2 step:
  - **Irreversible oxidative phase:** 3 molecules of **glucose-6-phosphate** give rise to 3 molecules of **CO_2** and 3 5-carbon sugars.
  - **Reversible nonoxidative phase:** Rearranged to regenerate 2 molecules of **glucose-6 phosphate** and 1 molecule of the **glyceraldehyde-3 phosphate**

Oxidative phase

- Dehydrogenation of **glucose-6-phosphate** to **6-phosphogluconate** catalyzed by *glucose 6-phosphate dehydrogenase*
- Followed by hydrolysis of **6- phosphogluconolactone** to **Ribulose-5-phosphate** catalyzed by 6-phosphogluconate dehydrogenase
- Decarboxylation follows with the formation of the ketopentose **ribulose-5-phosphate**
- Both this step requires $NADP^+$ as hydrogen acceptor



Non-oxidative Phase

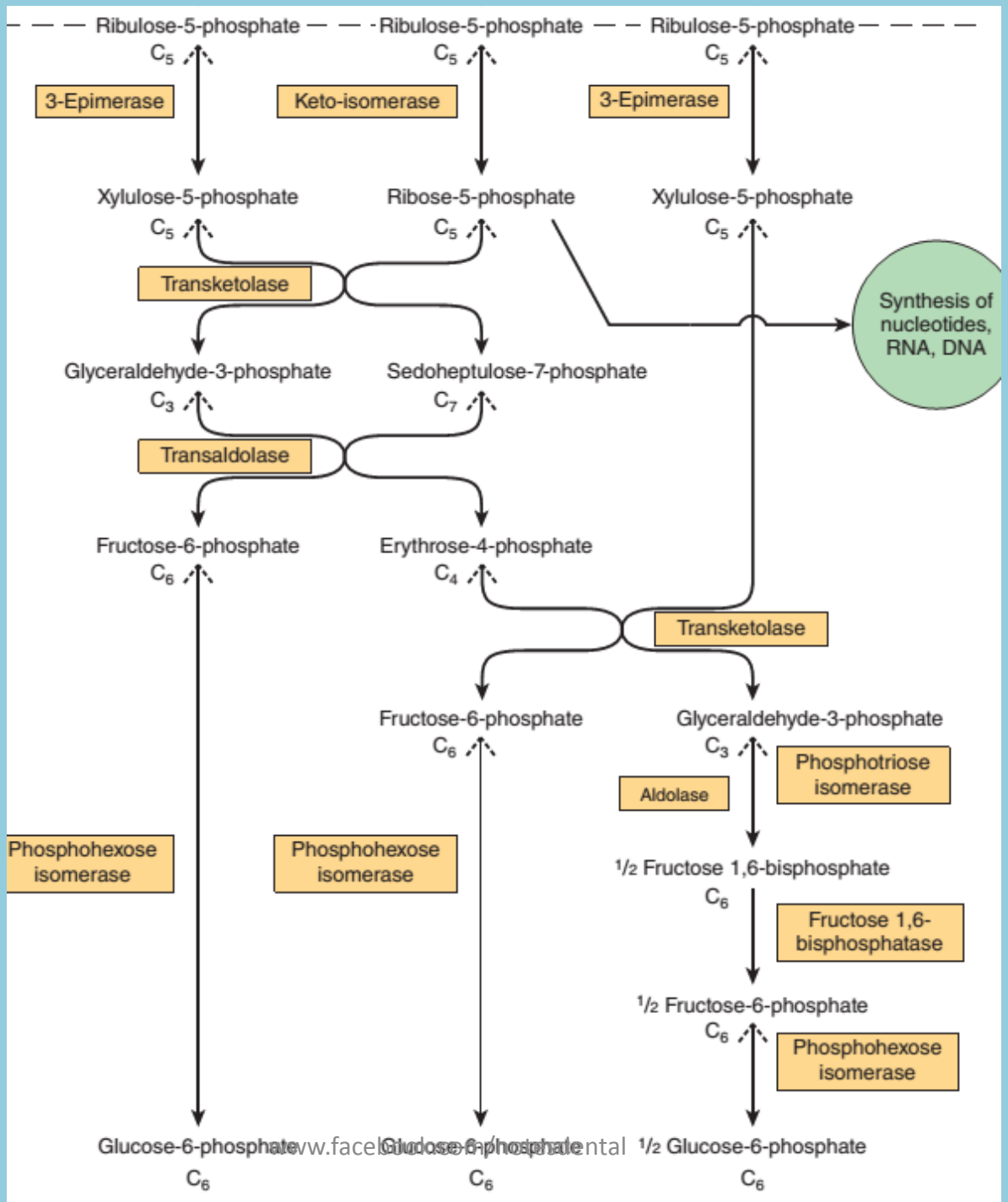
- Ribulose-5-phosphate is the substrate for two enzymes
  - **Ribose-5-phosphate ketoisomerase:** ribulose 5-phosphate to the corresponding ribose-5-phosphate - used for nucleotide and nucleic acid synthesis
  - **Ribulose-5-phosphate 3-epimerase:** alters the configuration about carbon giving xylulose 5-phosphate

Non-oxidative Phase

- **Xylulose-5-phosphate (5c)** and **Ribose-5-phosphate (5c)** reacts to give **Glyceraldehyde-3-phosphate (3c)** and **Sedoheptulose-7-phosphate (7c)** by the enzyme **Transketolase**
- **Glyceraldehyde-3-phosphate (3c)** and **Sedoheptulose-7-phosphate (7c)** is acted by **Transaldolase** to give **Fructose-6-phosphate** and **Erythrose-4-phosphate**

Non-oxidative Phase

- Erythrose-4-phosphate and Xylulose-5-phosphate reacts in the presence of enzyme **Transketolase** to give **Fructose-6-phosphate** and **Glyceraldehyde-3-phosphate**
  - **Mg^{2+}** and **thiamin diphosphate** (vitamin B1) as coenzyme
- Subsequently **Fructose-6 –phosphate** is isomerised to **Glucose-6-phosphate** by enzyme **Phosphohexose isomerase**
- **Glyceraldehyde-3-phosphate** - reversal of glycolysis and the gluconeogenic enzyme **fructose 1,6 bisphosphatase** or it proceeds to glycolysis.



Importance of NADPH

- Bio-synthesis of Fatty acid
- Certain amino acid involving the enzyme **glutamate dehydrogenase**
- **Antioxidant reaction** – **Glutathione** mediated reaction of H_2O_2
- **Detoxification** of drugs – **cytochrome P450**
- **Phagocytosis**
- Integrity of **RBC membrane**

Importance of Pentose Sugar

- **Ribose-5 phosphate** – useful for the synthesis of **nucleic acid** (RNA and DNA) and **nucleotide**
- **Skeletal muscles** capable of synthesizing pentoses

CLINICAL ASPECTS

- Genetic defects of **glucose-6-phosphate dehydrogenase**
- impairment of the generation of NADPH - X chromosome
- Mediterranean and Afro-Caribbean origin
- red cell hemolysis **(hemolytic anemia)**
- subjected to oxidative stress
  - Infection
  - Drugs such as the antimalarial primaquine, and sulfonamides
  - Fava beans - **favism**

References

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