

Pentose Phosphate Pathway

Chapter 26, Stryer Short Course

Glucose Metabolism Overview

- Gluconeogenesis
- Glycogen metabolism
- **Pentose Phosphate Pathway**

Pentose Phosphate Pathway

- Dual Purpose
 - Synthesis of “reducing potential”
 - Synthesis of 5-carbon sugars
- At cost of one carbon worth of carbohydrate
- Net reaction:

Table 26.1 Pathways requiring NADPH

Synthesis
Fatty acid biosynthesis
Cholesterol biosynthesis
Neurotransmitter biosynthesis
Nucleotide biosynthesis
Detoxification
Reduction of oxidized glutathione
Cytochrome P450 monooxygenases

$$\text{Glucose 6-phosphate} + 2 \text{NADP}^{\oplus} + \text{H}_2\text{O} \longrightarrow \text{Ribulose 5-phosphate} + 2 \text{NADPH} + \text{CO}_2 + 2 \text{H}^{\oplus}$$

2-Stage Process

- Oxidative Stage
 - Generates reducing power and ribose
- Non-oxidative stage
 - Regenerates 3- and 6-carbon sugars from 5 carbon sugars



Oxidative Stage

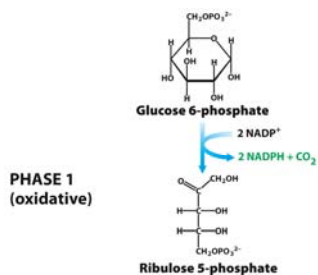
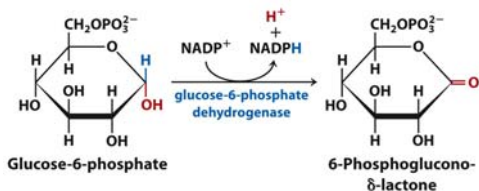


Figure 26.7 panel 1
Principles of Biochemistry, Third Edition
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Oxidative Stage Step 1:

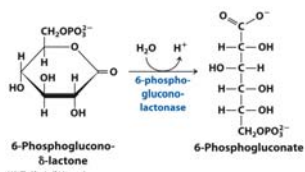
- G-6-P DH
- Lactone formation



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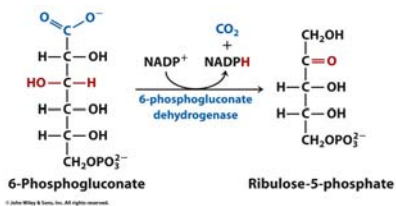
Oxidative Stage Step 2:

- Also a spontaneous hydrolysis
- Recognize hydrolysis
- Predict carbohydrate orientation

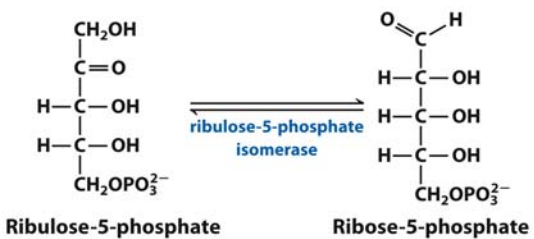


Oxidative Stage Step 3:

- Oxidative decarboxylation
- We will see this process again

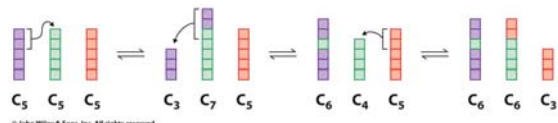


Biosynthesis of Ribose



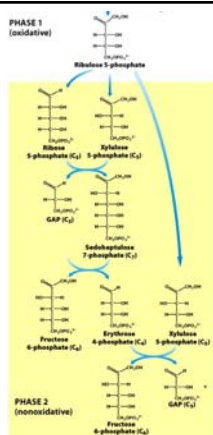
Non-oxidative Stage

- To understand purpose, realize that we generally need to make much more NADPH than ribose
- Problem: stuck with C5, but need C6 and C3
- Solution: "Shunt" C5 back to C6 through near-equilibrium reactions

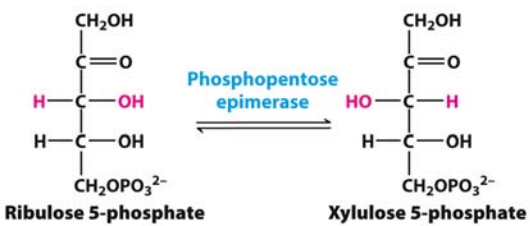


PPP Reactions

- Epimerase
- Isomerase
- Transketolase
- Transaldolase

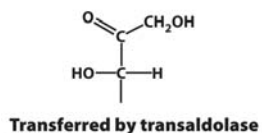
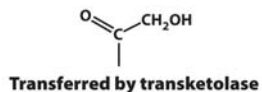


Epimerase



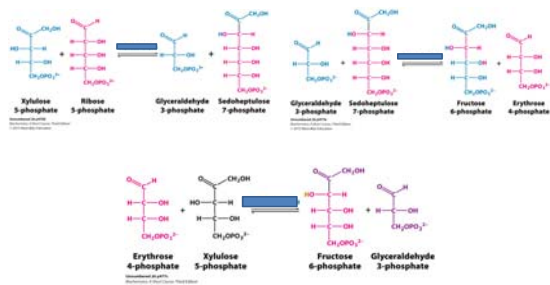
Transketalase, Transaldolase

- Transketalase
 - Transfer of an acyl anion
 - Requires TPP to stabilize unstable anion
- Transaldolase
 - Transfer of somewhat stable enolate ion
 - Schiff base helps
- Be able to recognize need for TK vs. TA



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Transketalase or transaldolase?



Mechanism (just FYI...)

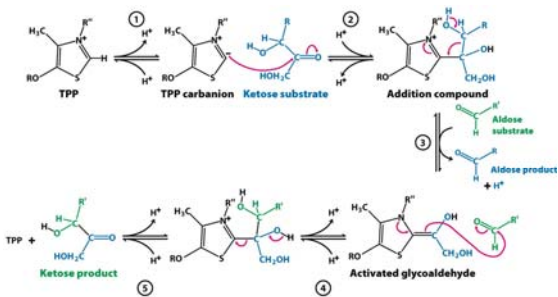
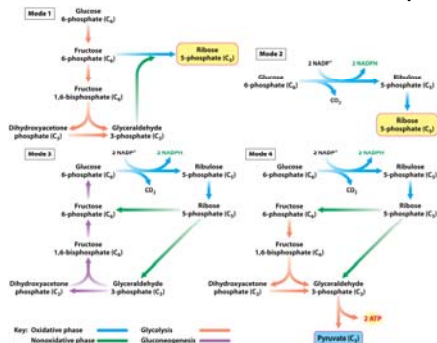


Figure 20.20 Biochemistry, Seventh Edition © 2012 W. H. Freeman and Company

Different Modes for Different Purposes



Physiological Purposes

Table 26.3 Tissues with active pentose phosphate pathways

Tissue	Function
Adrenal gland	Steroid synthesis
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

Table 26.3
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Glutathione: Protection from Oxidation

- Glutathione is the redox buffer of the cell
- Regenerated by NADPH
- PPP especially important in RBC because it is only means to generate reducing power (no mitochondria)

