Gliconeogênese e via das pentoses

A disponibilidade de glicose é central para o metabolismo energético

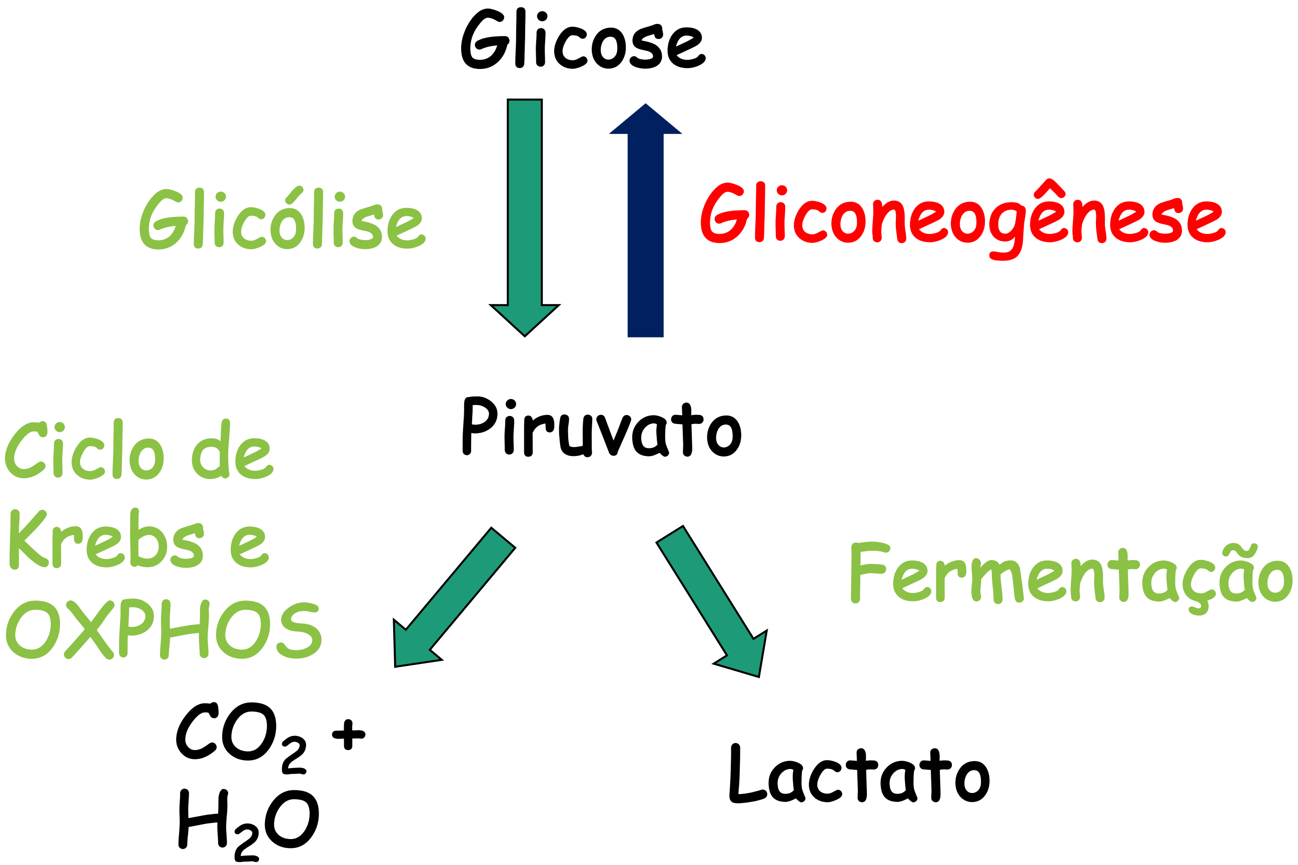
Alguns tecidos: cérebro, hemácias, medula renal,cristalino e córnea ocular, testículos e músculo em exercício → Suprimento contínuo de glicose

Necessidade diária de um adulto humano – glicose do cérebro 120g

Glicose presente - líquidos orgânicos 20g
Glicogênio -190g

Reservas suficientes para atender as necessidades por cerca de um dia

Período maior de jejum ? ? ?


Glicose
Glicólise
Gliconeogênese
Piruvato
Ciclo de Krebs e OXPHOS
Fermentação
CO_2 + H_2O
Lactato

Gliconeogênese: é a síntese de glicose a partir de precursores não glicídicos

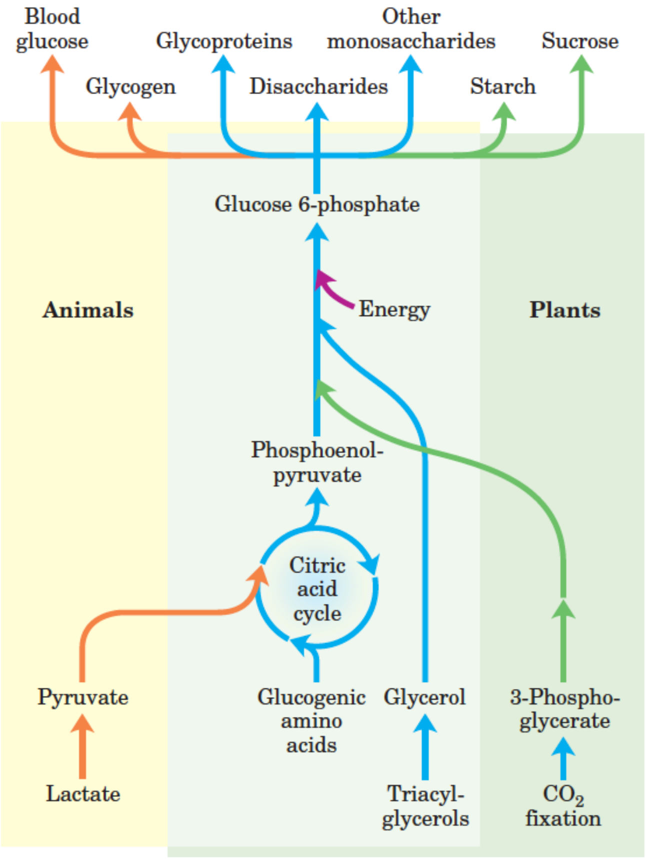


TABLE 14–4 Glucogenic Amino Acids, Grouped by Site of Entry

Pyruvate	**Succinyl-CoA**
Alanine	Isoleucine*
Cysteine	Methionine
Glycine	Threonine
Serine	Valine
Threonine	**Fumarate**
Tryptophan*	Phenylalanine*
α-Ketoglutarate	Tyrosine*
Arginine	**Oxaloacetate**
Glutamate	Asparagine
Glutamine	Aspartate
Histidine	
Proline	

A maioria das reações da glicólise é reversível

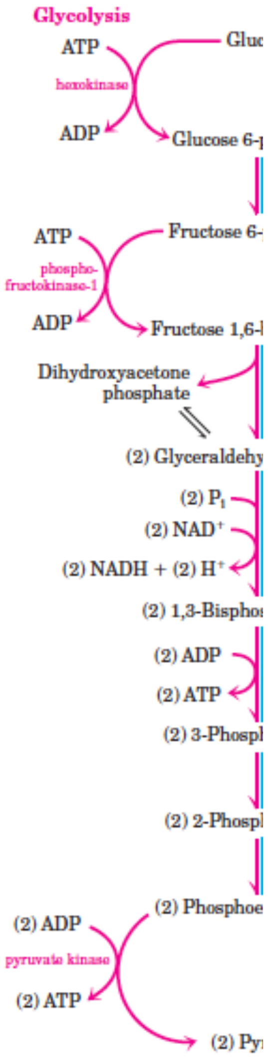


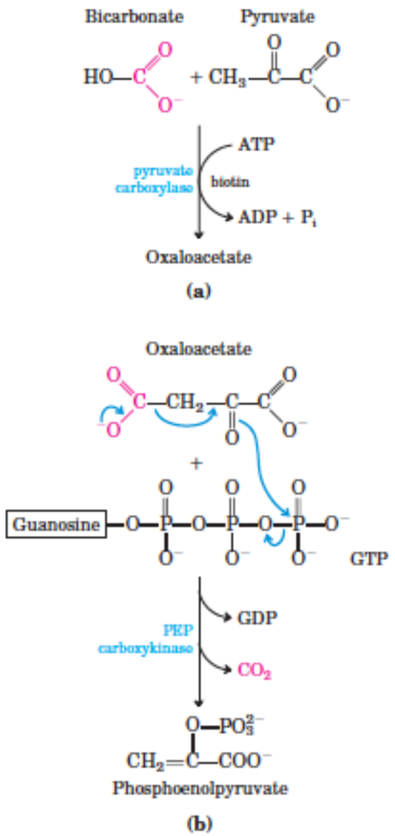
TABLE 14–2 Free-Energy Changes of Glycolytic Reactions in Erythrocytes

Glycolytic reaction step	$\Delta G'^{\circ}$ *(kJ/mol)*	ΔG *(kJ/mol)*
(1) Glucose + ATP $\longrightarrow$ glucose 6-phosphate + ADP	−16.7	−33.4
(2) Glucose 6-phosphate $\rightleftharpoons$ fructose 6-phosphate	1.7	0 to 25
(3) Fructose 6-phosphate + ATP $\longrightarrow$ fructose 1,6-bisphosphate + ADP	−14.2	−22.2
(4) Fructose 1,6-bisphosphate $\rightleftharpoons$ dihydroxyacetone phosphate + glyceraldehyde 3-phosphate	23.8	0 to −6
(5) Dihydroxyacetone phosphate $\rightleftharpoons$ glyceraldehyde 3-phosphate	7.5	0 to 4
(6) Glyceraldehyde 3-phosphate + P_i + NAD^+ $\rightleftharpoons$ 1,3-bisphosphoglycerate + NADH + H^+	6.3	−2 to 2
(7) 1,3-Bisphosphoglycerate + ADP $\rightleftharpoons$ 3-phosphoglycerate + ATP	−18.8	0 to 2
(8) 3-Phosphoglycerate $\rightleftharpoons$ 2-phosphoglycerate	4.4	0 to 0.8
(9) 2-Phosphoglycerate $\rightleftharpoons$ phosphoenolpyruvate + H_2O	7.5	0 to 3.3
(10) Phosphoenolpyruvate + ADP $\longrightarrow$ pyruvate + ATP	−31.4	−16.7

Note: $\Delta G'^{\circ}$ is the standard free-energy change, as defined in Chapter 13 (p. 491). ΔG is the free-energy change calculated from the actual concentrations of glycolytic intermediates present under physiological conditions in erythrocytes, at pH 7. The glycolytic reactions bypassed in gluconeogenesis are shown in red. Biochemical equations are not necessarily balanced for H or charge (p. 506).

Reações distintas entre as vias glicolítica e gliconeogênese

1. A síntese de fosfoenolpiruvato a partir de piruvato



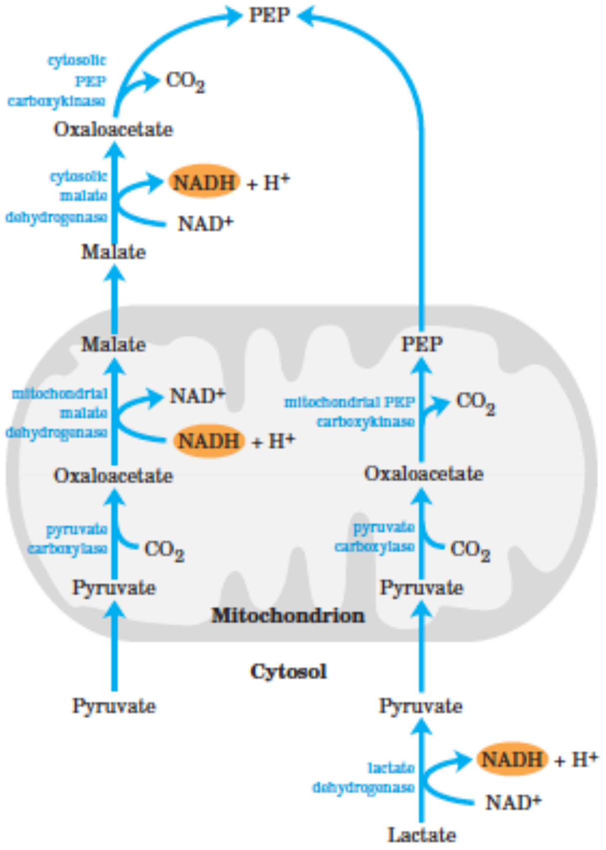


FIGURE 14–19 Alternative paths from pyruvate to phosphoenolpyruvate. The path that predominates depends on the glucogenic precursor (lactate or pyruvate). The path on the right predominates when lactate is the precursor, because cytosolic NADH is generated in the lactate dehydrogenase reaction and does not have to be shuttled out of the mitochondrion (see text). The relative importance of the two pathways depends on the availability of lactate and the cytosolic requirements for NADH by gluconeogenesis.

2. Conversão de frutose 1,6-bifosfato em frutose 6-fosfato

$$\text{Fructose 1,6-bisphosphate} + H_2O \longrightarrow \text{fructose 6-phosphate} + P_i \qquad \Delta G'^{\circ} = -16.3 \text{ kJ/mol}$$

3. Conversão de glicose-6-fosfato em glicose

$$\text{Glucose 6-phosphate} + H_2O \longrightarrow \text{glucose} + P_i \qquad \Delta G'^{\circ} = -13.8 \text{ kJ/mol}$$

TABLE 14–3 Sequential Reactions in Gluconeogenesis Starting from Pyruvate

Pyruvate + HCO_3^- + ATP $\longrightarrow$ oxaloacetate + ADP + P_i	×2
Oxaloacetate + GTP $\rightleftharpoons$ phosphoenolpyruvate + CO_2 + GDP	×2
Phosphoenolpyruvate + H_2O $\rightleftharpoons$ 2-phosphoglycerate	×2
2-Phosphoglycerate $\rightleftharpoons$ 3-phosphoglycerate	×2
3-Phosphoglycerate + ATP $\rightleftharpoons$ 1,3-bisphosphoglycerate + ADP	×2
1,3-Bisphosphoglycerate + NADH + H^+ $\rightleftharpoons$ glyceraldehyde 3-phosphate + NAD^+ + P_i	×2
Glyceraldehyde 3-phosphate $\rightleftharpoons$ dihydroxyacetone phosphate	
Glyceraldehyde 3-phosphate + dihydroxyacetone phosphate $\rightleftharpoons$ fructose 1,6-bisphosphate	
Fructose 1,6-bisphosphate $\longrightarrow$ fructose 6-phosphate + P_i	
Fructose 6-phosphate $\rightleftharpoons$ glucose 6-phosphate	
Glucose 6-phosphate + H_2O $\longrightarrow$ glucose + P_i	
Sum: 2 Pyruvate + 4ATP + 2GTP + 2NADH + $2H^+$ + $4H_2O$ $\longrightarrow$ glucose + 4ADP + 2GDP + $6P_i$ + $2NAD^+$	

A glicólise e a gliconeogênese têm que ser reciprocamente reguladas

$$\text{ATP} + \text{fructose 6-phosphate} \xrightarrow[\text{PFK-1}]{} \text{ADP} + \text{fructose 1,6-bisphosphate}$$

$$\text{Fructose 1,6-bisphosphate} + H_2O \xrightarrow[\text{FBPase-1}]{} \text{fructose 6-phosphate} + P_i$$

The sum of these two reactions is

$$\text{ATP} + H_2O \longrightarrow \text{ADP} + P_i + \text{heat}$$

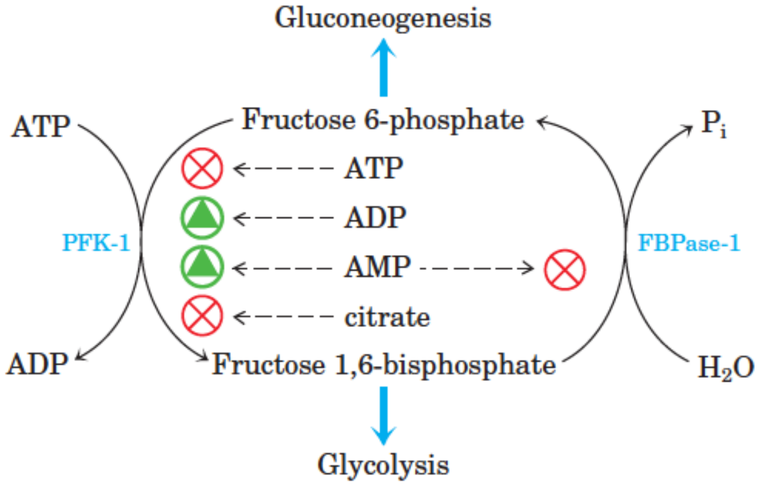
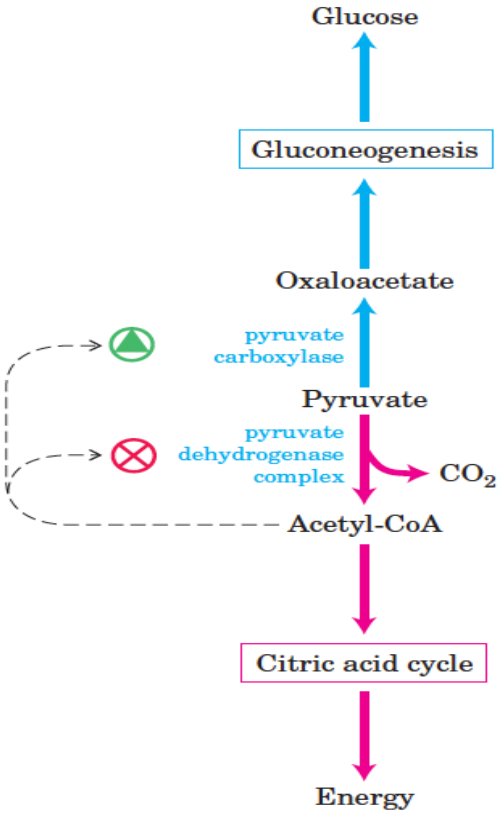
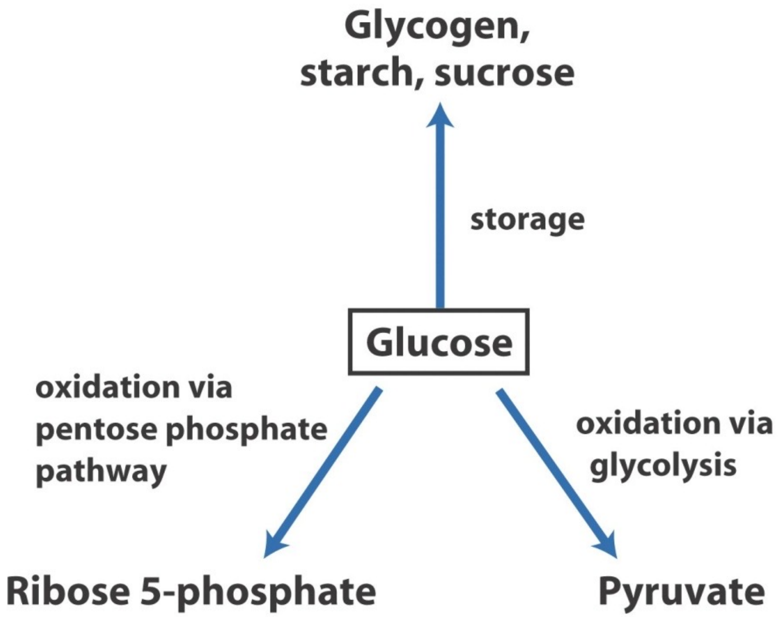


FIGURE 15–21 Regulation of fructose 1,6-bisphosphatase-1 (FBPase-1) and phosphofructokinase-1 (PFK-1). The important role of fructose 2,6-bisphosphate in the regulation of this substrate cycle is detailed in subsequent figures.



Via das Pentoses



- Síntese de ribose 5P $\rightarrow$ DNA, RNA

- Metabolismo de açúcares com 7, 5 e 4 carbonos

- Redução de $NADP^+$ a NADPH
    - doador de elétrons para biossíntese
    - doa elétrons para defesa contra radicais livres

NADH x NADPH

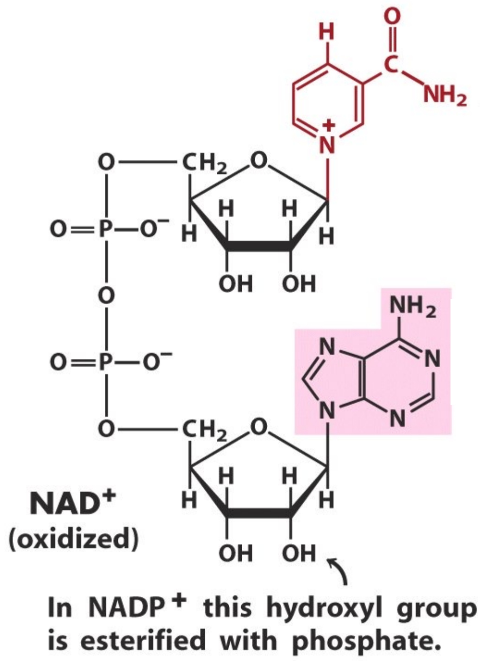
NADH: participa da conversão de energia liberada pela oxidação de metabólitos em ATP (fosforilação oxidativa)

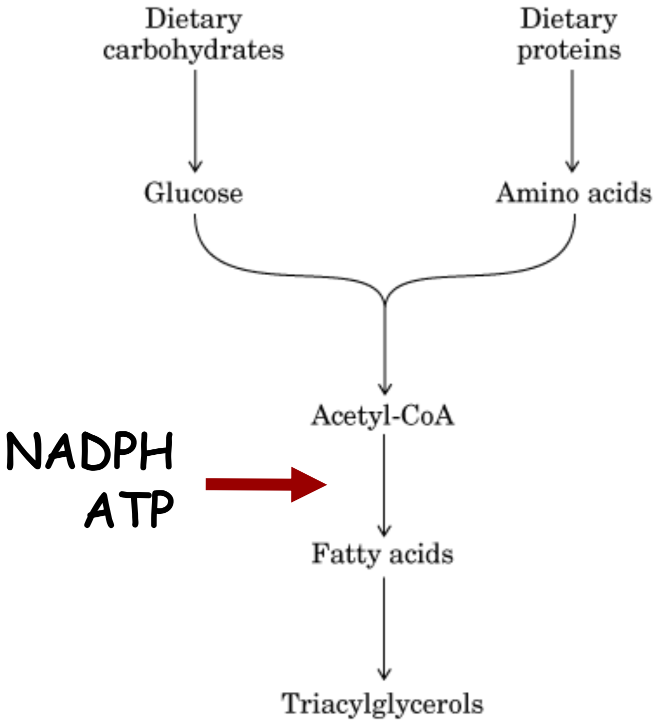
NADPH: fonte de potencial redox em processos de biossíntese redutora

Em condições fisiológicas:

razão $NAD^+/NADH = 1000$

razão $NADP^+/NADPH = 0.1$





Glicólise + Krebs + Fosforilação Oxidativa

$C_6H_{12}O_6 + 6\ O_2 + n\ ADP + n\ Pi \rightarrow 6\ CO_2 + 6\ H_2O + n\ ATP$

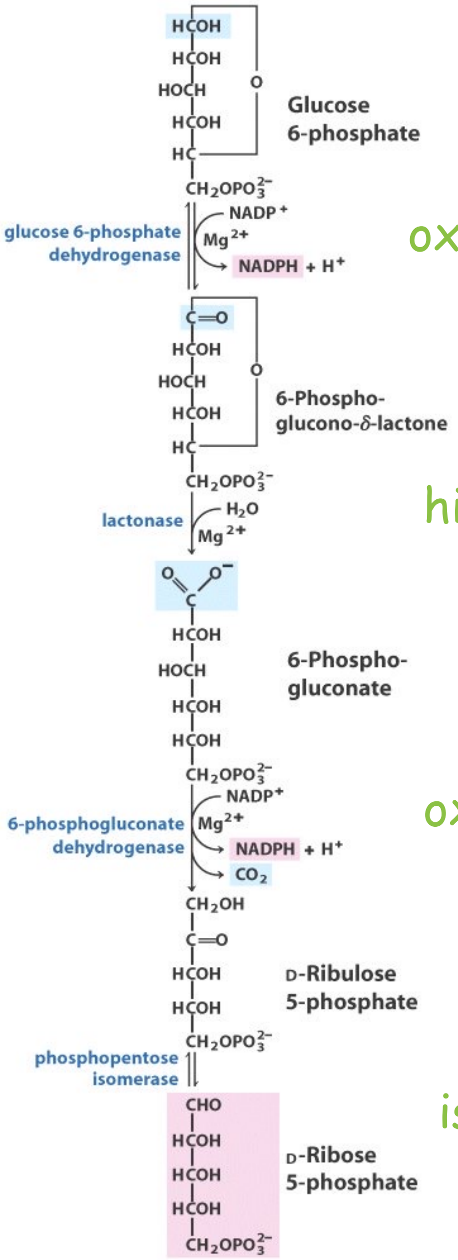
n ~ 30 ou 32

(NADH como intermediário)

Via das Pentoses

$C_6H_{12}O_6 + 6\ H_2O + 12\ NADP^+ \rightarrow 6\ CO_2 + 12\ NADPH + 12\ H^+$

Via das Pentoses – Fase Oxidativa



oxi-redução

hidrólise

oxidação + descarboxilação

isomerização

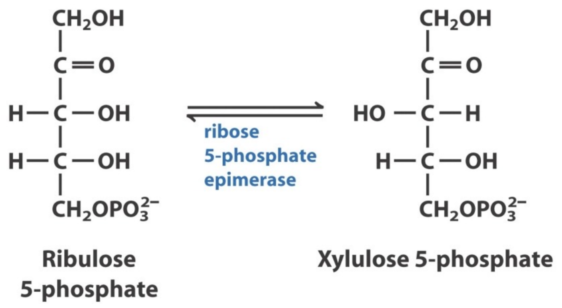
$$\text{Glicose-6P} + 2\ NADP^+ + H_2O$$

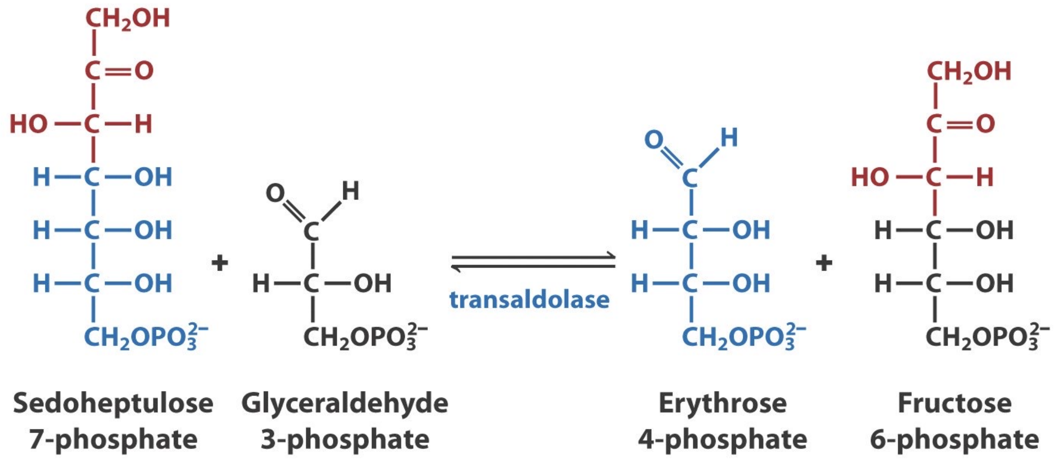
$$\downarrow$$

$$\text{Ribose-5P} + CO_2 + 2\ NADPH + 2H^+$$

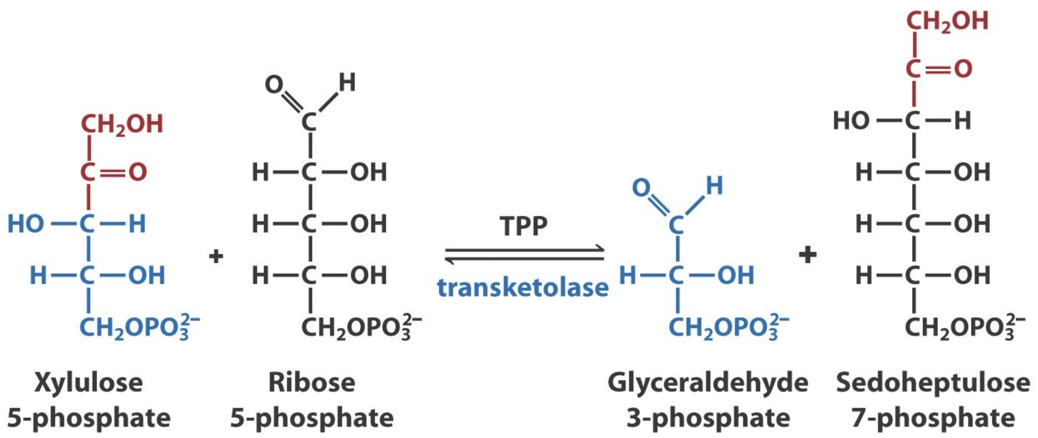
Nucleotídeos
Coenzimas
DNA
RNA

Via das Pentoses – Fase Não-Oxidativa

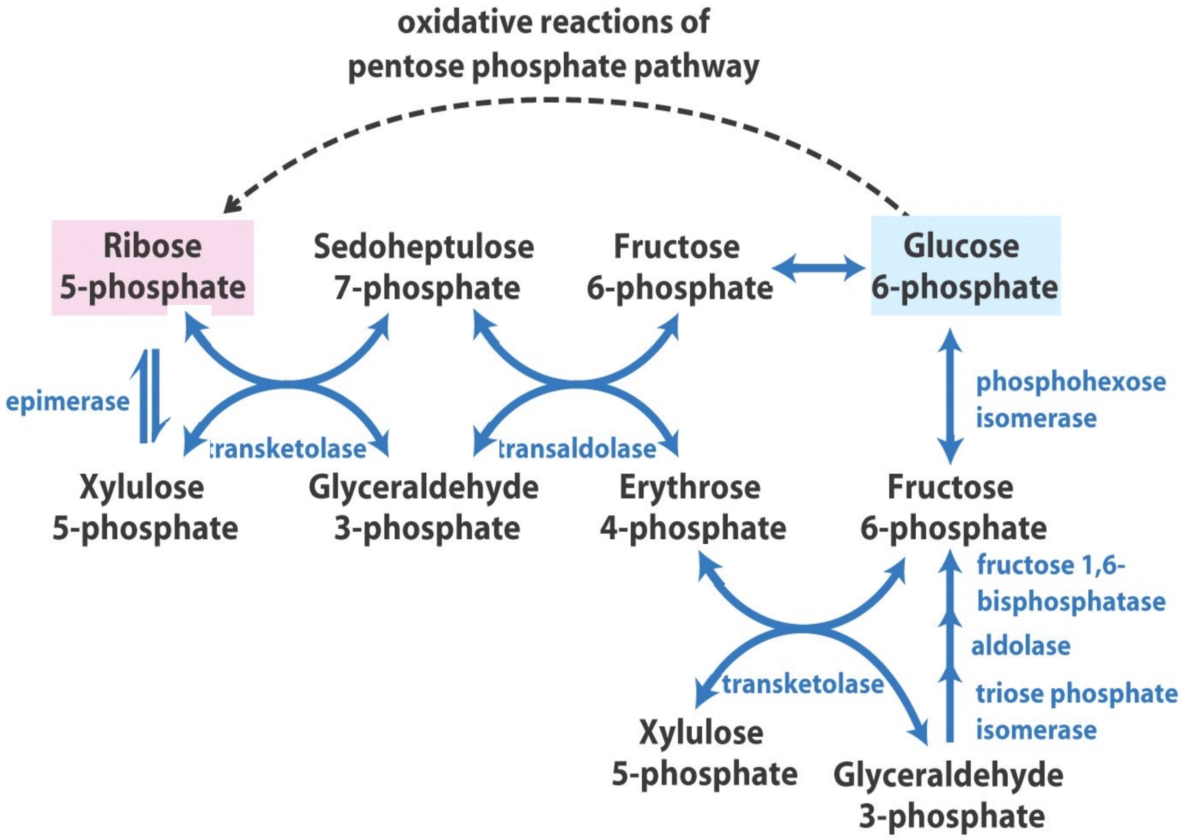


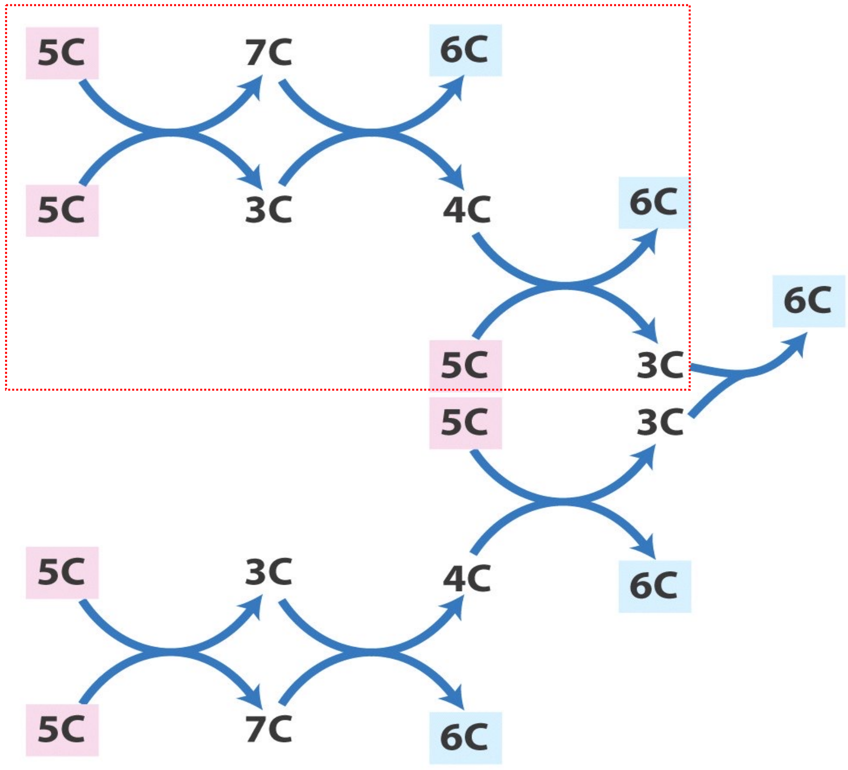


Transaldolase: Transfere 3C de uma cetose para uma aldose



Transcetolase: Transfere 2C de uma cetose para uma aldose



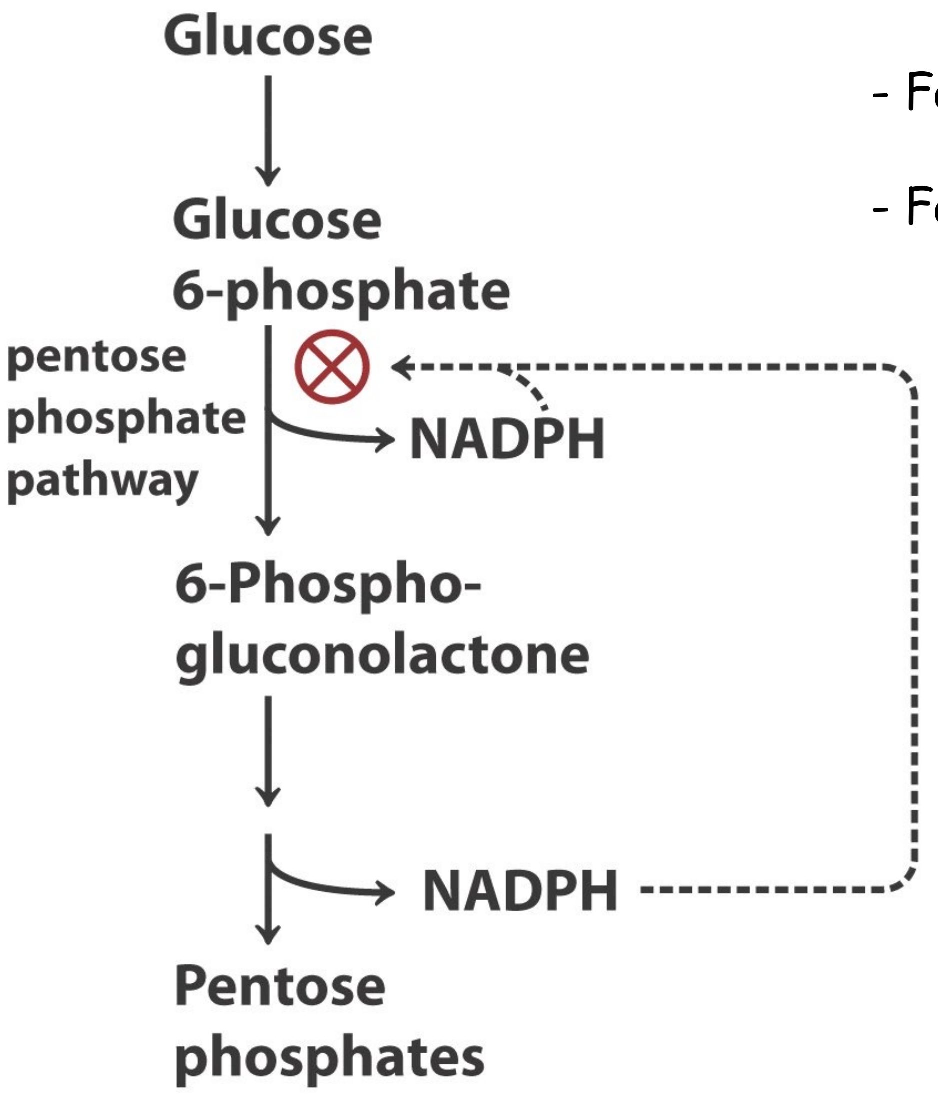


$$6\ \text{glicose-6P} + 12\ NADP^+ + 6\ H_2O$$

$$\downarrow$$

$$6\ \text{ribose-5P} + 6\ CO_2 + 12\ NADPH + Pi + 12\ H^+$$

Via das Pentoses - Regulação



- Fase oxidativa: retroalimentação negativa

- Fase não-oxidativa:
    - Consumo de ribose-5 fosfato
    - Consumo de outros açúcares
    - Consumo de NADPH

    - Ligação com glicólise!

NADPH e a detoxificação de espécies oxidantes