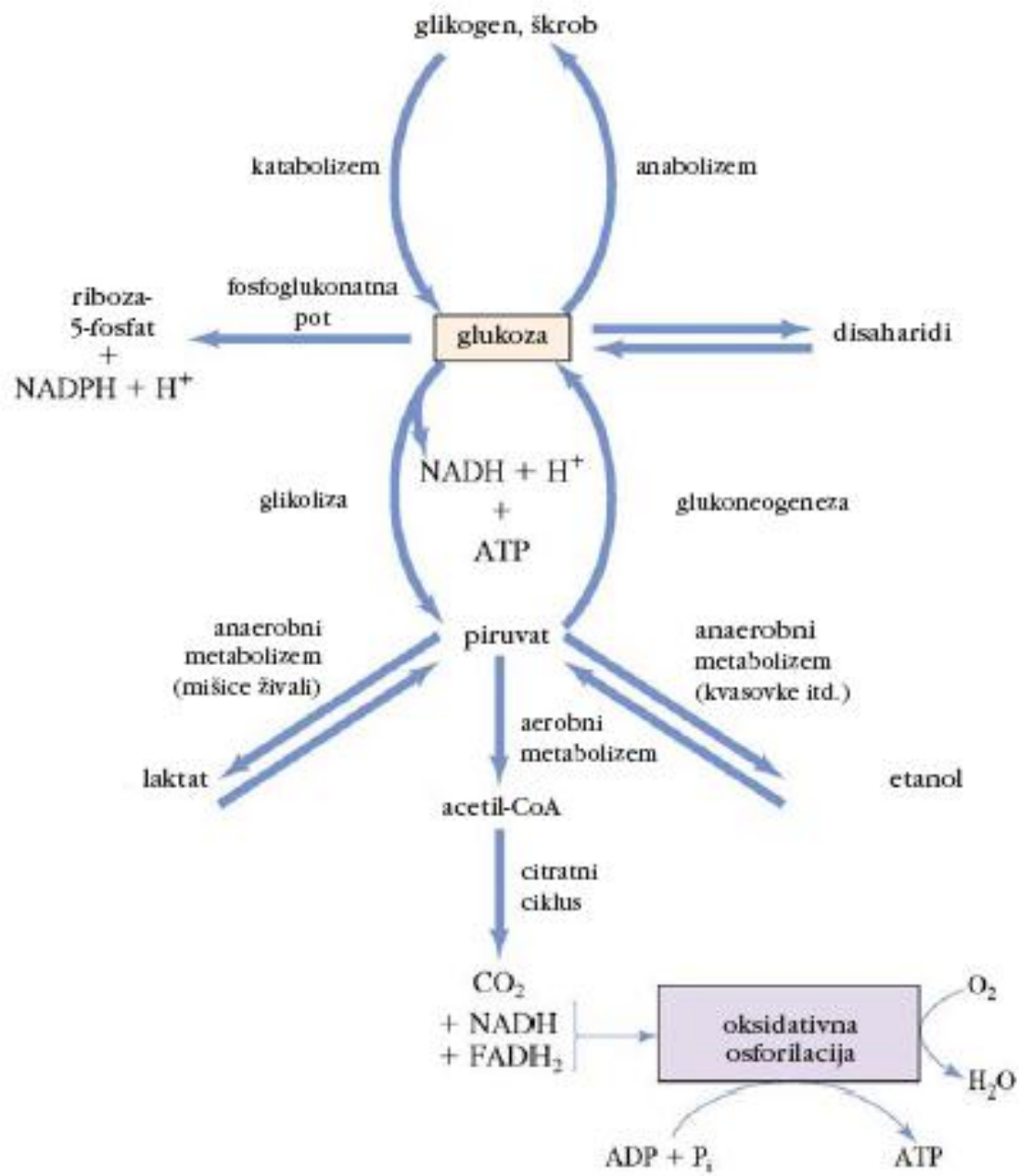


**GLIKOLIZA, GLUKONEOGENEZA IN
FOSFOGLUKONATNA POT**





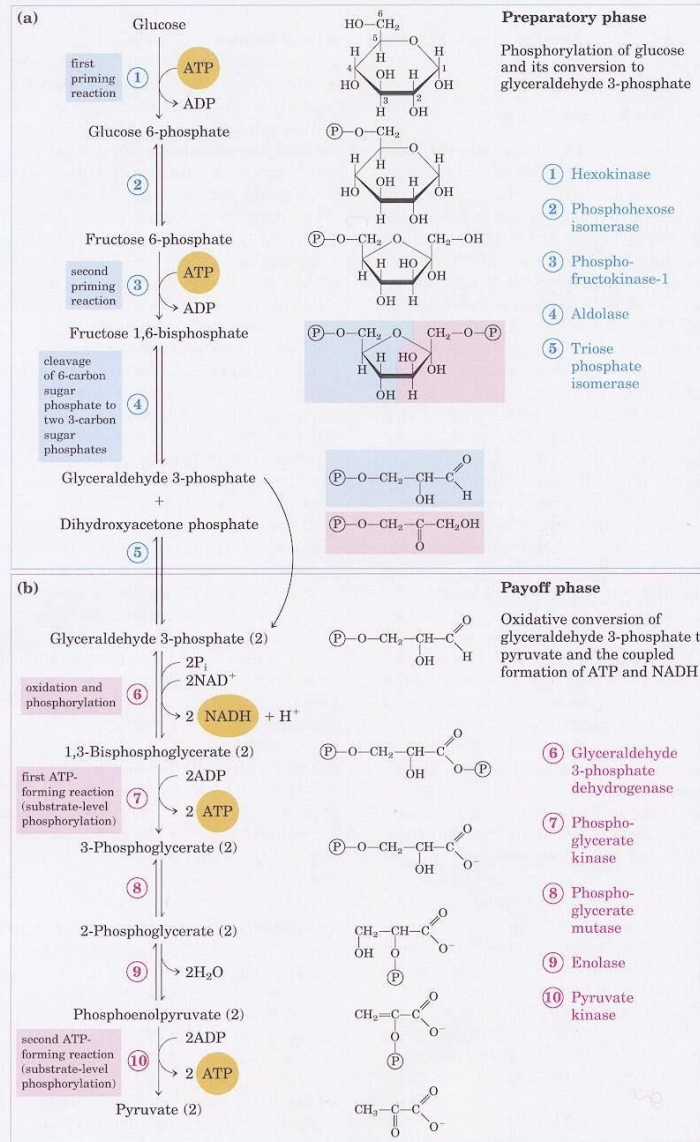
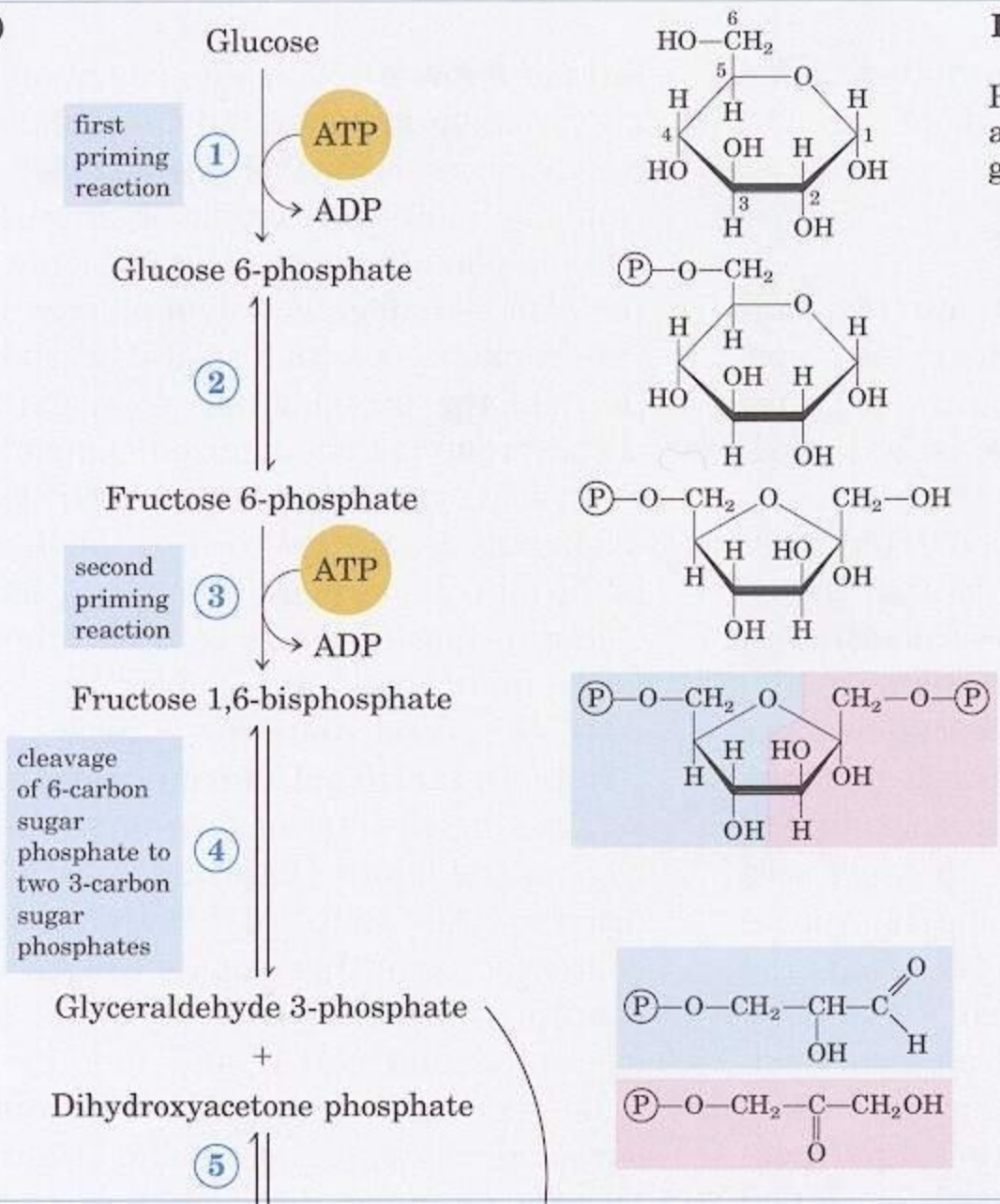


FIGURE 14-2 The two phases of glycolysis. For each molecule of glucose that passes through the preparatory phase (a), two molecules of glyceraldehyde 3-phosphate are formed; both pass through the payoff phase (b). Pyruvate is the end product of the second phase of glycolysis. For each glucose molecule, two ATP are consumed in the preparatory phase and four ATP are produced in the payoff phase, giving a

net yield of two ATP per molecule of glucose converted to pyruvate. The numbered reaction steps are catalyzed by the enzymes listed on the right, and also correspond to the numbered headings in the discussion. Keep in mind that each phosphoryl group, represented here as P-O- , has two negative charges ($-\text{PO}_3^{2-}$).

(a)



Preparatory phase

Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate

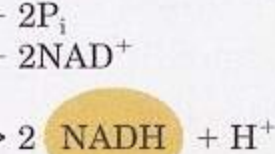
- ① Hexokinase
- ② Phosphohexose isomerase
- ③ Phosphofructokinase-1
- ④ Aldolase
- ⑤ Triose phosphate isomerase

(b)

Glyceraldehyde 3-phosphate (2)

oxidation and phosphorylation

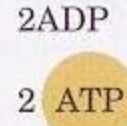
⑥



1,3-Bisphosphoglycerate (2)

first ATP-forming reaction (substrate-level phosphorylation)

⑦

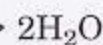


3-Phosphoglycerate (2)

⑧

2-Phosphoglycerate (2)

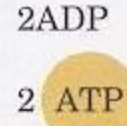
⑨



Phosphoenolpyruvate (2)

second ATP-forming reaction (substrate-level phosphorylation)

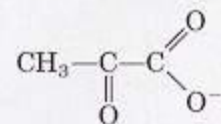
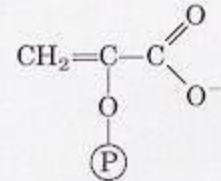
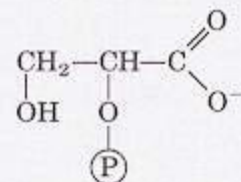
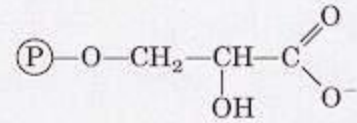
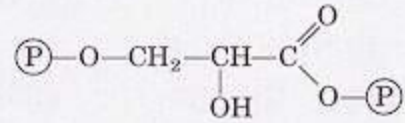
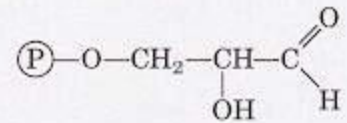
⑩



Pyruvate (2)

Payoff phase

Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH



⑥ Glyceraldehyde 3-phosphate dehydrogenase

⑦ Phosphoglycerate kinase

⑧ Phosphoglycerate mutase

⑨ Enolase

⑩ Pyruvate kinase

Reakcije glikolize z imeni običajnih encimov in vrsto reakcij

št. reakcije	reakcija	encim ^a	vrsta reakcije ^b
1	glukoza+ATP \rightarrow glukoza-6-fosfat + ADP	heksokinaza	2
2	glukoza-6-fosfat \rightleftharpoons fruktoza-6-fosfat	fosfoglukoizomeraza	5
3	fruktoza-6-fosfat + ATP \rightarrow fruktoza-1,6-bisfosfat + ADP	fosfofruktokinaza	2
4	fruktoza-1,6-bisfosfat \rightleftharpoons dihidroksiacetonfosfat+gliceraldehid-3-fosfat	aldolaza	4
5	dihidroksiacetonfosfat - gliceraldehid-3-fosfat	triozafosfat-izomeraza	5
6	gliceraldehid-3-fosfat+Pi+NAD ⁺ \rightleftharpoons 1,3-bisfosfoglicerat+NADH+H ⁺	gliceraldehid-3-fosfat-izomeraza	1,2
7	1,3-bisfosfoglicerat + ADP \rightleftharpoons 3-fosfoglicerat + ATP	fosfoglicerat-kinaza	2
8	3-fosfoglicerat \rightleftharpoons 2-fosfoglicerat	fosfoglicerat-mutaza	5
9	2-fosfoglicerat \rightleftharpoons fosfoenolpiruvat + H ₂ O	enolaza	4
10	fosfoenolpiruvat + ADP \rightarrow piruvat + ATP	piruvat-kinaza	2

^a Navedena so trivialna imena encimov.

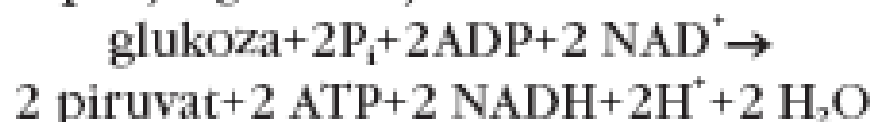
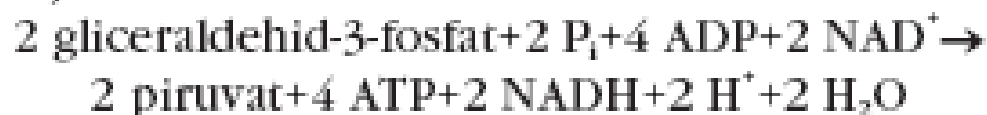
^b Vrsta reakcije:(1) oksidoredukcija, (2) prenos skupin, (3) hidroliza, (4) nehidrolitična cepitev, (5) izomerizacija in primestitev in (6) nastanek vezi z uporabo energije ATP.

Obračun števila nastalih oziroma porabljenih molekul ATP in NADH pri glikolizi

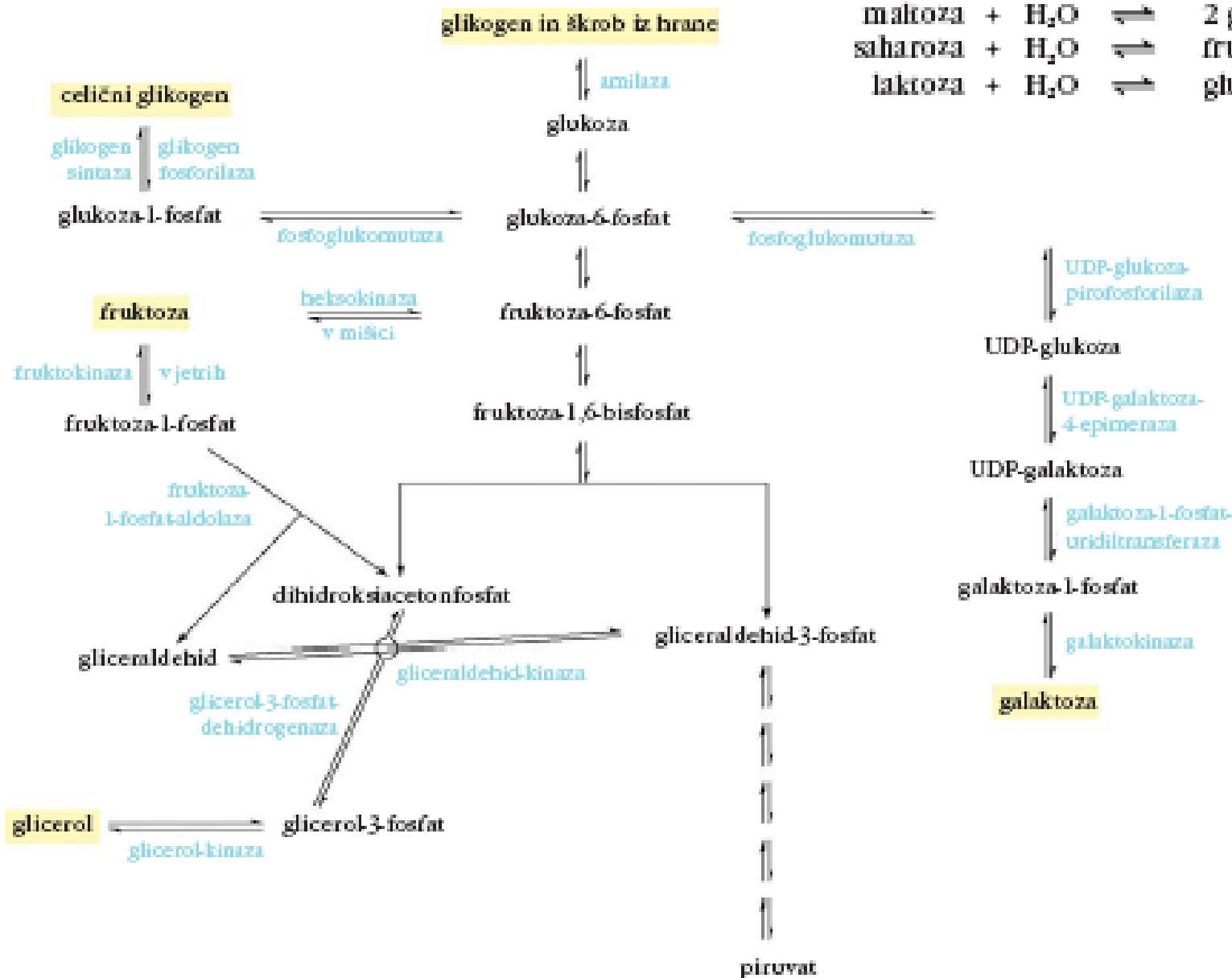
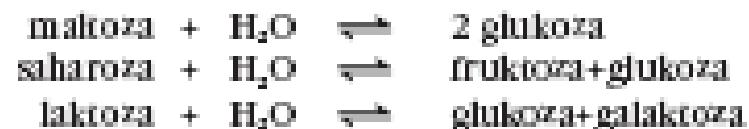
število ^a	reakcija (na molekulo glukoze) ^a	sprememba ATP (na molekulo glukoze) ^a	sprememba NADH (na molekulo glukoze) ^b
1	glukoza → 1 glukoza-6-fosfat	-1	0
3	fruktoza-6-fosfat → 1 fruktoza 1,6-bisfosfat	-1	0
6	2 gliceraldehid-3-fosfat - 2 1,3-bisfosfoglicerat	0	+2
7	2 1,3-bisfosfoglicerat - 2 3-fosfoglicerat	+2	0
10	2 fosfoenolpiruvat → 12 piruvat	+2	0
Skupaj		+2	+2

^a Številka ustreza številki reakcije v tabeli 15.1.

^b Negativen predznak označuje porabo ATP s cepitvijo fosfoanhidridne vezi; pozitiven predznak označuje nastanek ATP (iz ADP) ali NADH (iz NAD⁺).



Vstop drugih ogljikovih hidratov v glikolizo



Razgradnja glikogena

Nonreducing end

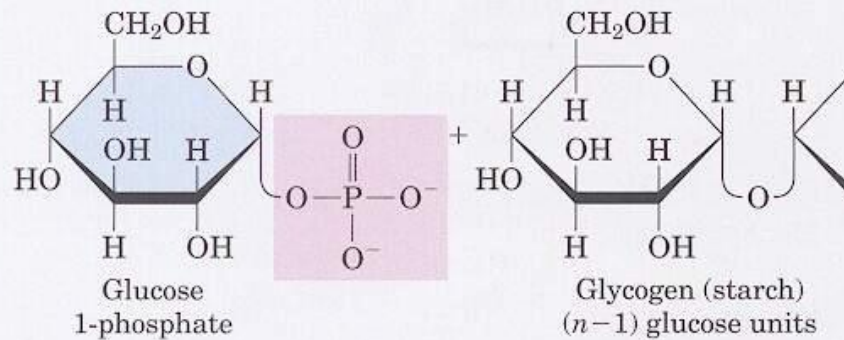
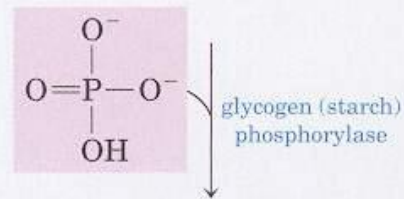
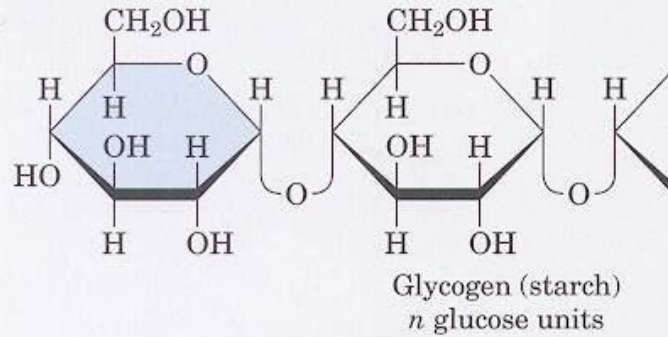


FIGURE 14-10 Glycogen breakdown by glycogen phosphorylase.

The enzyme catalyzes attack by inorganic phosphate (pink) on the terminal glucosyl residue (blue) at the nonreducing end of a glycogen molecule, releasing glucose 1-phosphate and generating a glycogen molecule shortened by one glucose residue. The reaction is a *phosphorolysis* (not hydrolysis).

Pretvorba galaktoze v glukozo-1-fosfat

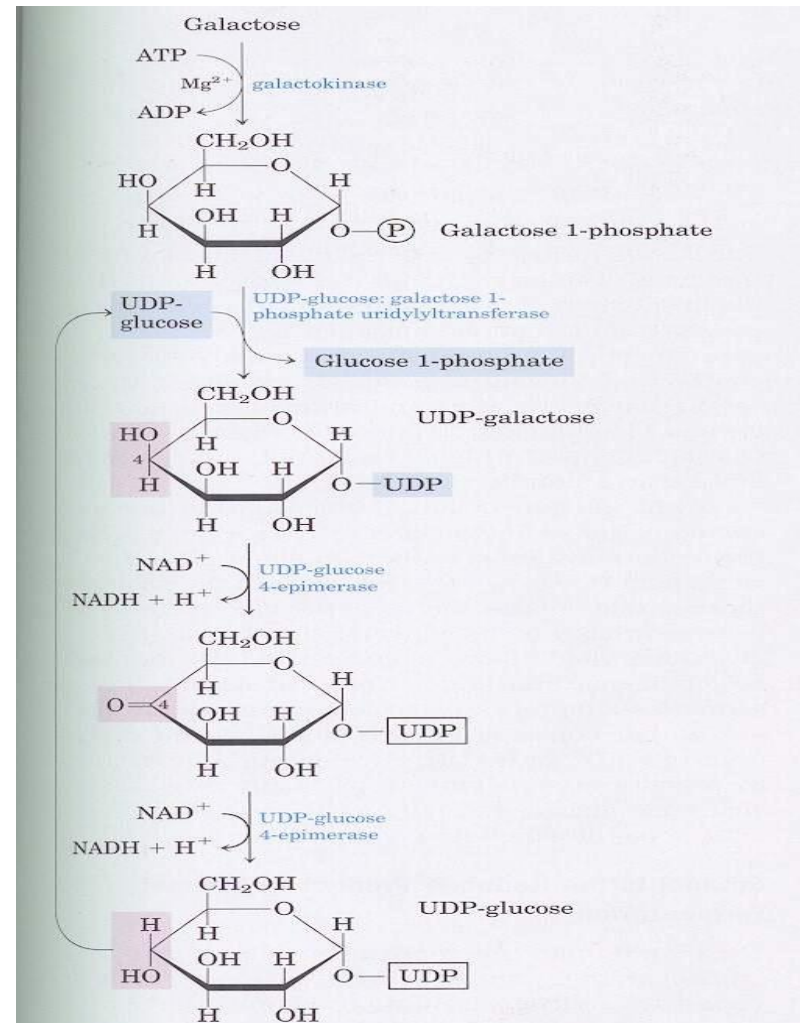
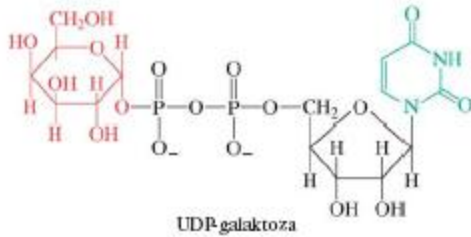
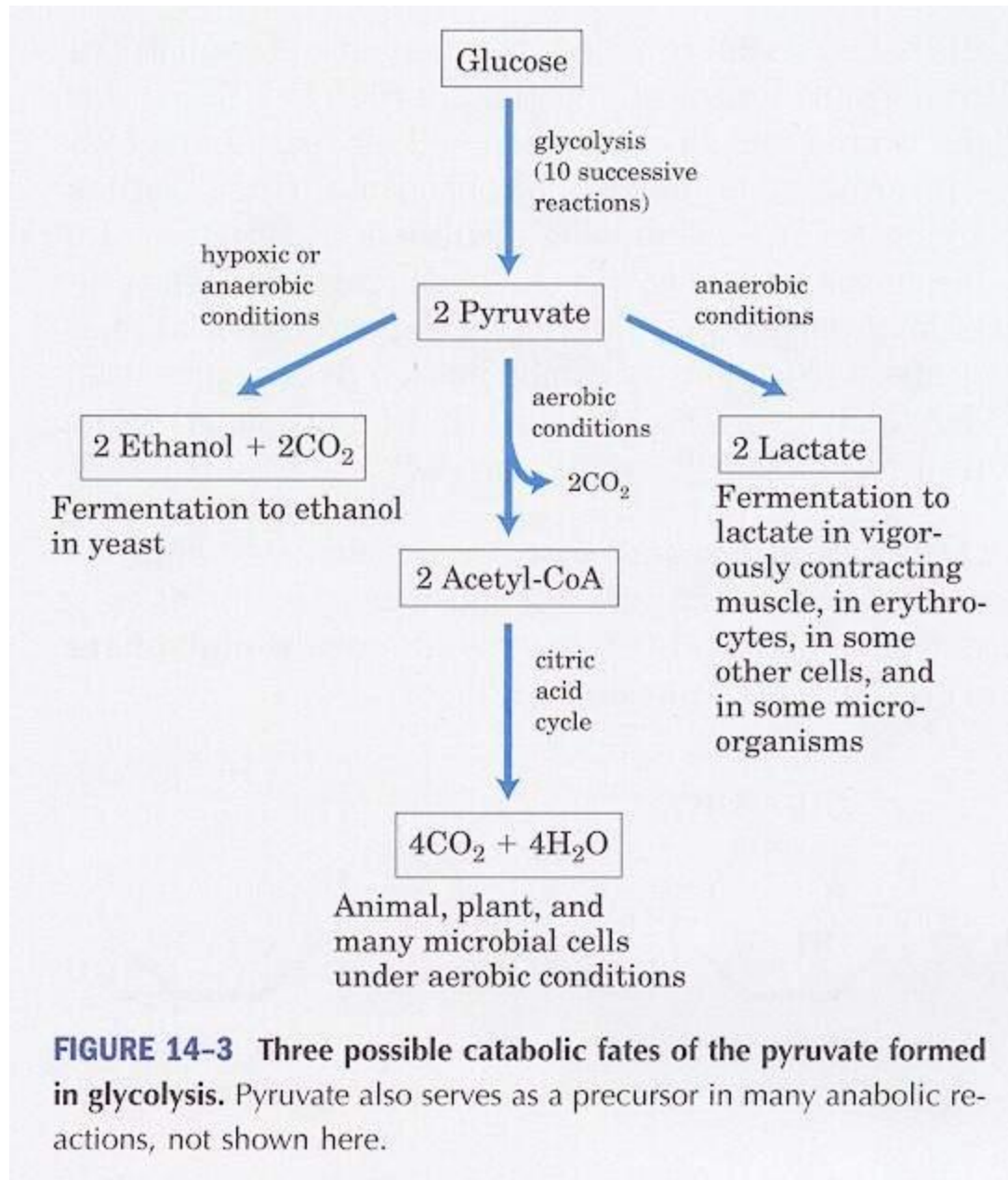
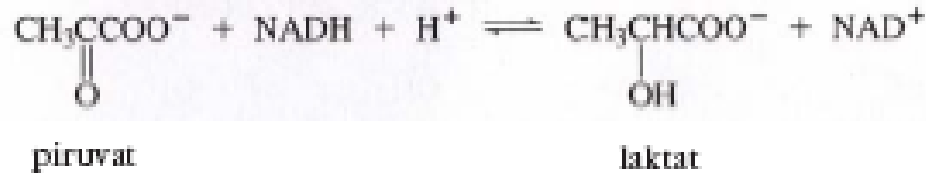


FIGURE 14-11 Conversion of galactose to glucose 1-phosphate. The conversion proceeds through a sugar-nucleotide derivative, UDP-galactose, which is formed when galactose 1-phosphate displaces glucose 1-phosphate from UDP-glucose by UDP-glucose 4-epimerase to UDP-glucose, in a reaction that involves oxidation of C-4 (pink) by NAD⁺, then reduction of C-4 by NADH; the result is inversion of the configuration at C-4. The UDP-glucose is recycled through another round of the same reaction. The net effect of this cycle is the conversion of galactose 1-phosphate to glucose 1-phosphate; there is no net production or consumption of UDP-galactose or UDP-glucose.



Mlečnokislinska fermentacija

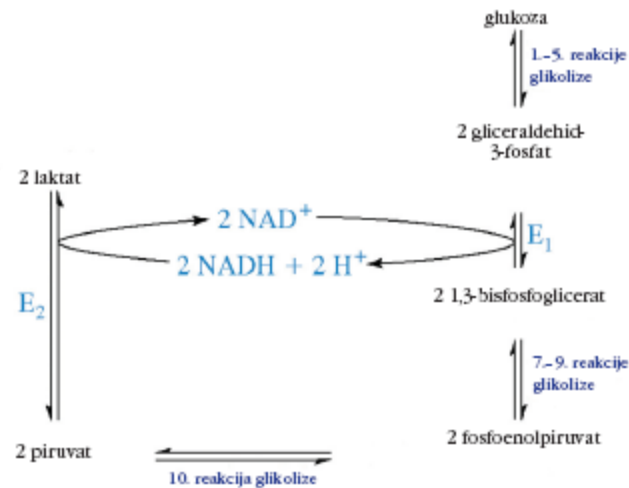


Neto reakcija pri mlečnokislinski fermentaciji (glukoza → 2 laktata) je:



Slika 15.6

Sklopitev glikolize in mlečnokislinske fermentacije. Redukcija piruvata reciklira NADH v NAD⁺. E1 = gliceraldehid-5-fosfat-dehidrogenaza, E2 = laktat-dehidrogenaza. Neto izkoristek nastanka NADH pri pretvorbi glukoze v mlečno kislino je nič.

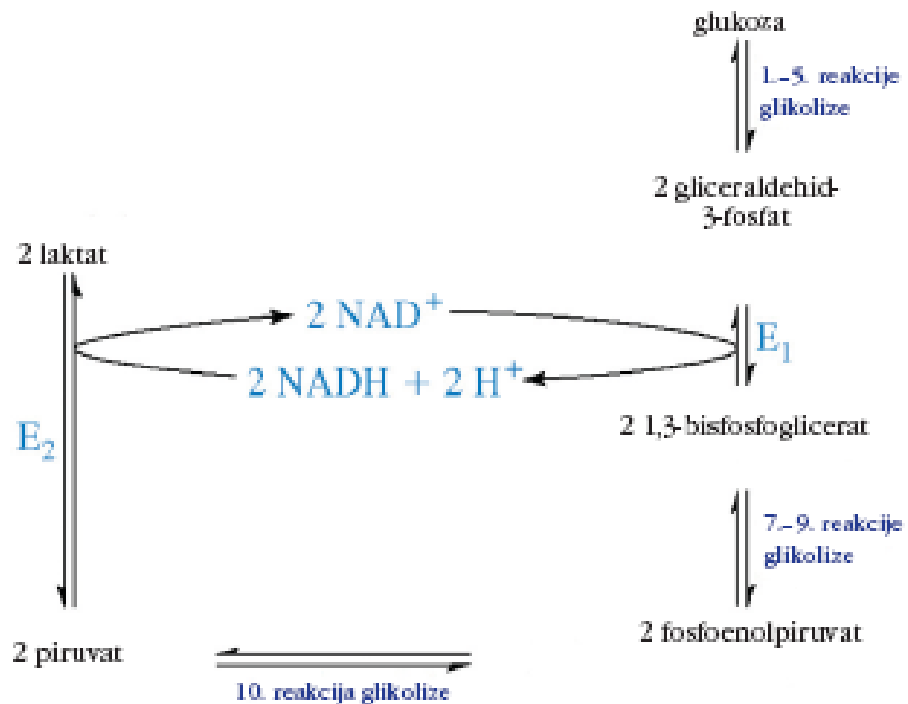


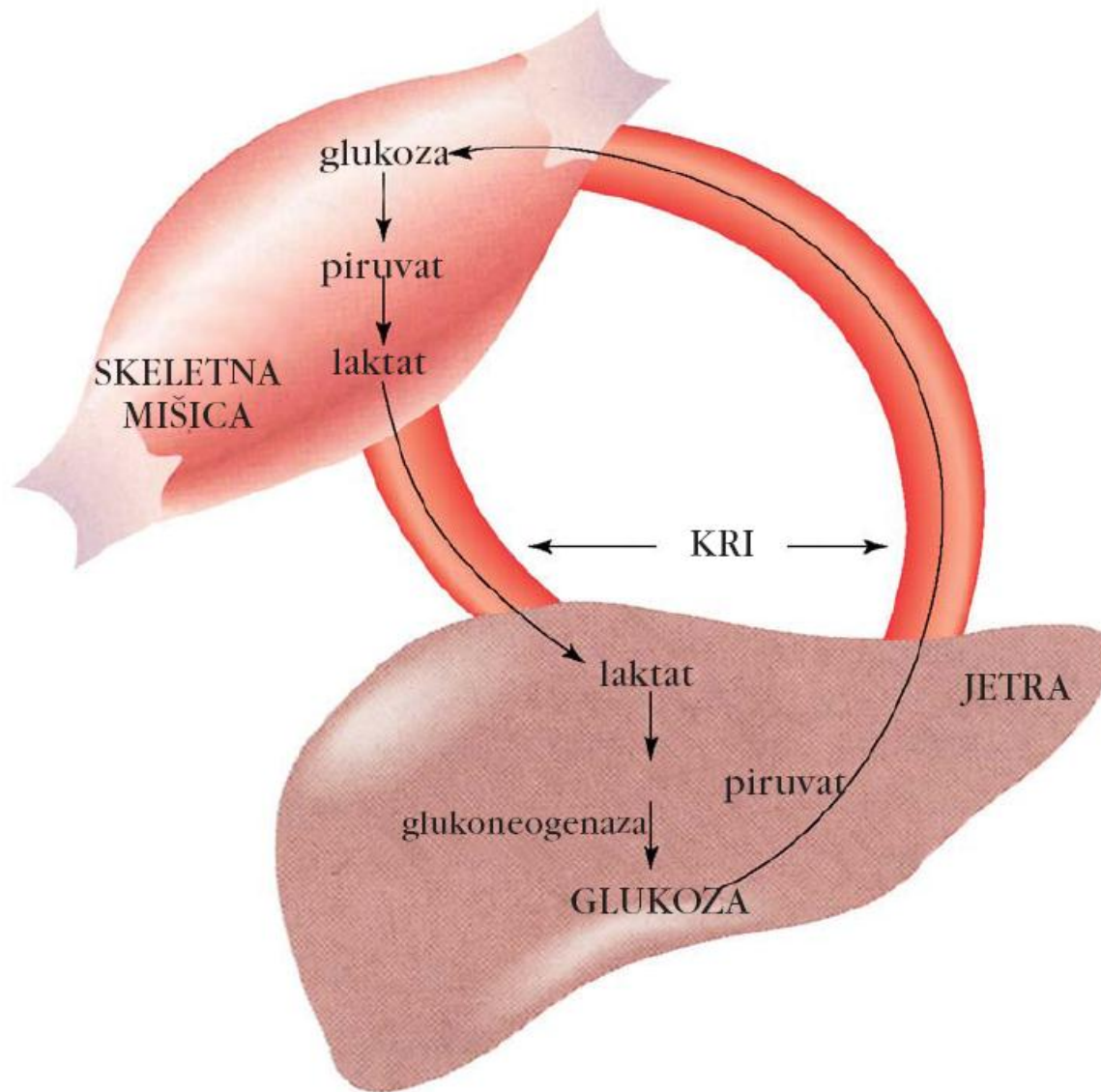
Cori ciklus

Slika 15.6

Sklopitev glikolize in mlečnokislinske fermentacije

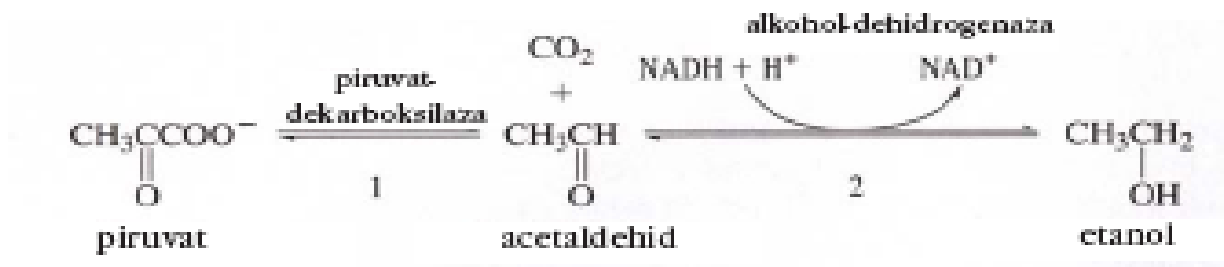
Redukcija piruvata reciklira NADH v NAD⁺. E1 = gliceraldehid-3-fosfat-dehidrogenaza, E2 = laktat-dehidrogenaza. Neto izkoristek nastanka NADH pri pretvorbi glukoze v mlečno kislino je nič.





Alkoholna fermentacija in metabolizem etanola

Anaerobni pogoji



Aerobni metabolizem etanola

Pri ljudeh, ima pitje alkoholnih pijač pomembne biokemijske, klinične in socialne posledice. Zaužiti etanol se najprej v jetrih oksidira s citosolno alkohol-dehidrogenazo:



Drugo oksidacijsko stopnjo katalizira aldehyd-dehidrogenaza



GLUKONEOGENEZA

Sinteza ogljikovih hidratov iz enostavnih prekurzorjev

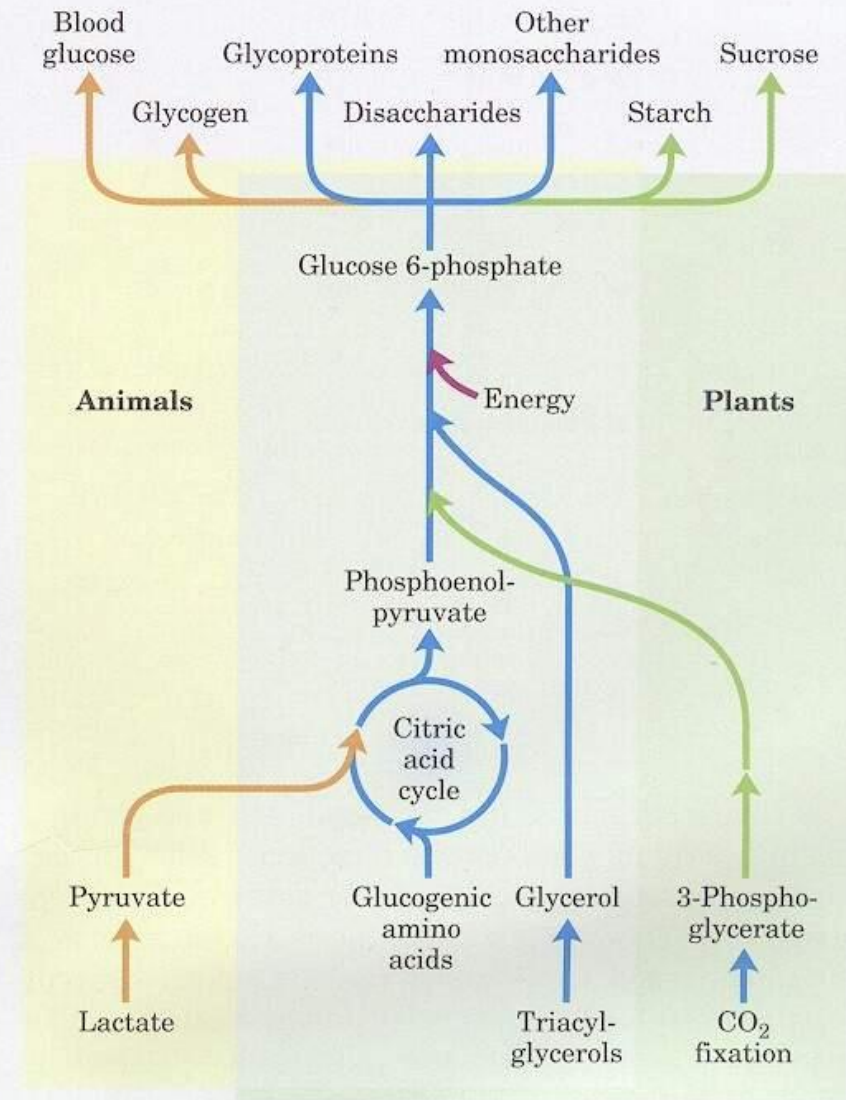
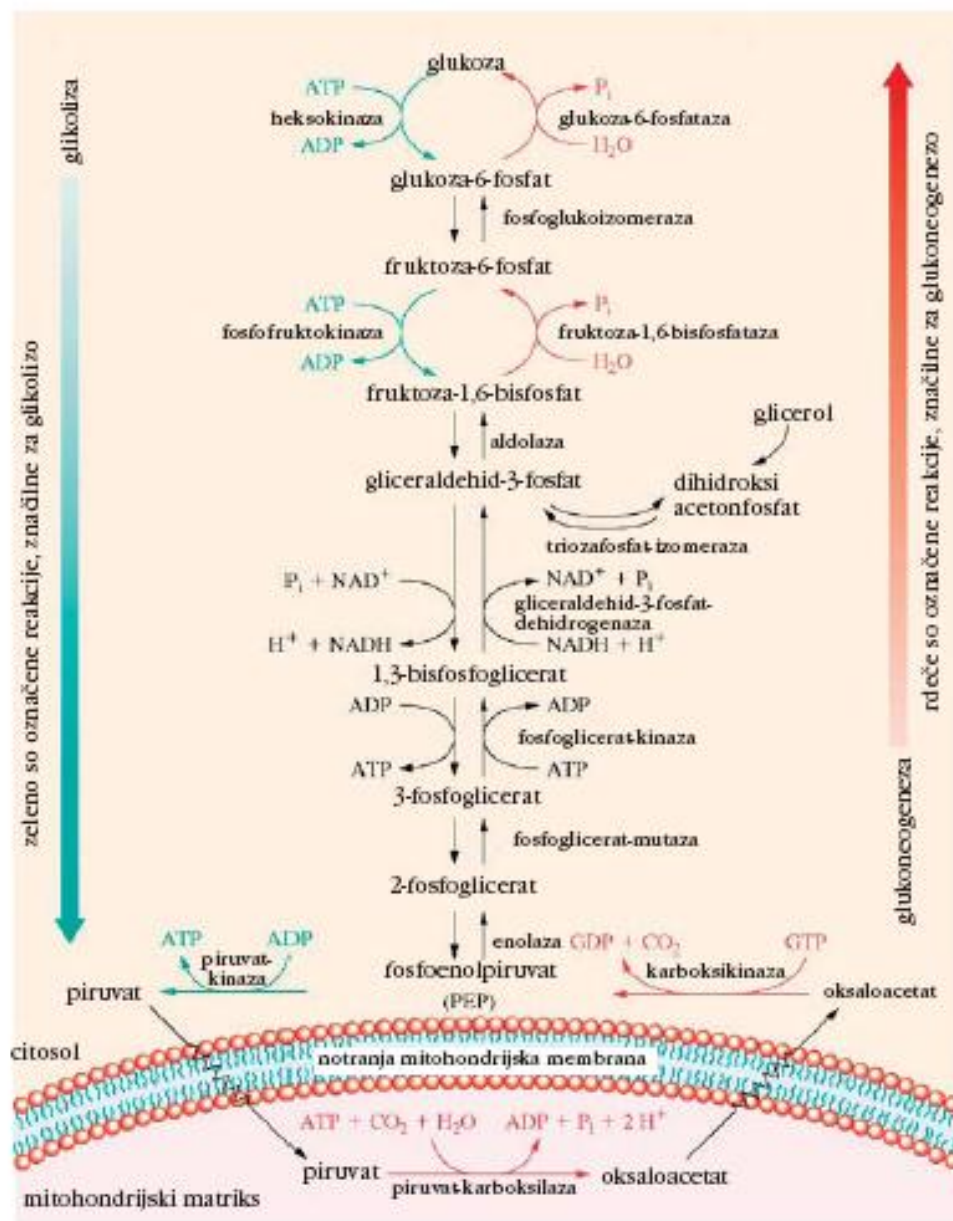


FIGURE 14-15 Carbohydrate synthesis from simple precursors. The pathway from phosphoenolpyruvate to glucose 6-phosphate is common to the biosynthetic conversion of many different precursors of carbohydrates in animals and plants. Plants and photosynthetic bacteria are uniquely able to convert CO₂ to carbohydrates.



Slika 15.9
Metabolizem glukoze; prikazane so reakcije glikolize in glukoneogeneze.

Irreverzibilne reakcije glikolize, ki jih v glukoneogenezi nadomeščajo druge reakcije

številka ^a	reakcija	encim	ΔG° [kJ/mol]
1	glukoza+ATP \rightarrow glukoza-6-fosfat+ADP	heksokinaza	-16,7
3	fruktoza-6-fosfat+ATP \rightarrow fruktoza-1,6-bisfosfat+ADP	fosfofruktokinaza	-14,2
10	PEP+ADP \rightarrow piruvat+ATP	piruvat-kinaza	-31,4

^a Številka se nanaša na številke reakcij v tabeli 15.1.

Reakcije glukoneogeneze z začetkom pri piruvatu

številka	reakcija
1	piruvat+CO ₂ +ATP \rightarrow oksaloacetat+ADP+Pi
2	oksalacetat+GTP \rightleftharpoons fosfoenolpiruvat+CO ₂ +GDP
3	fosfoenolpiruvat+H ₂ O \rightleftharpoons 2-fosfoglicerat
4	2-fosfoglicerat \rightleftharpoons 3-fosfoglicerat
5	3-fosfoglicerat+ATP \rightleftharpoons 1,3-bisfosfoglicerat
6	1,3-bisfosfoglicerat+NADH+H ⁺ \rightleftharpoons gliceraldehid-3-fosfat+NAD ⁺ +Pi
7	gliceraldehid-3-fosfat \rightleftharpoons dihidroksiacetonfosfat
8	gliceraldehid-3-fosfat+dihidroksiacetonfosfat \rightleftharpoons fruktoza-1,6-bisfosfat
9	fruktoza-1,6-bisfosfat+H ₂ O \rightarrow fruktoza-6-fosfat+Pi
10	fruktoza-6-fosfat \rightleftharpoons glukoza-6-fosfat
11	glukoza-6-fosfat+H ₂ O \rightleftharpoons glukoza+Pi

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).

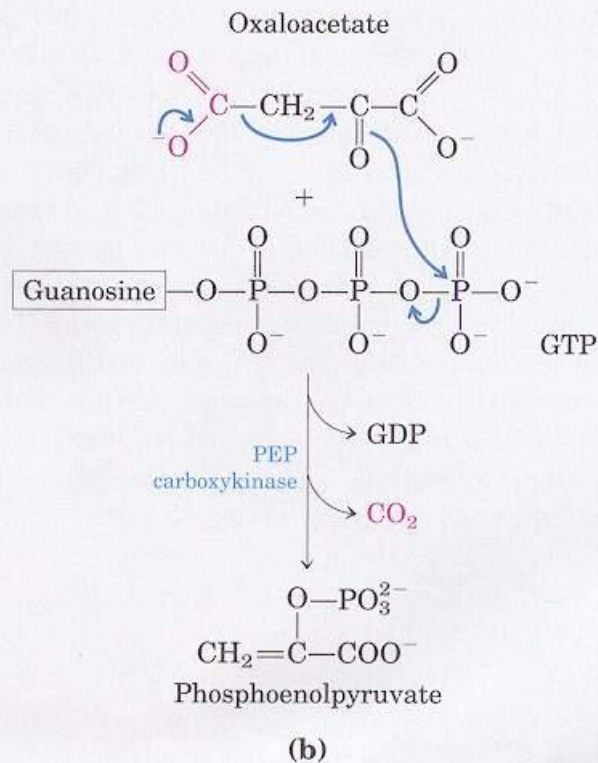
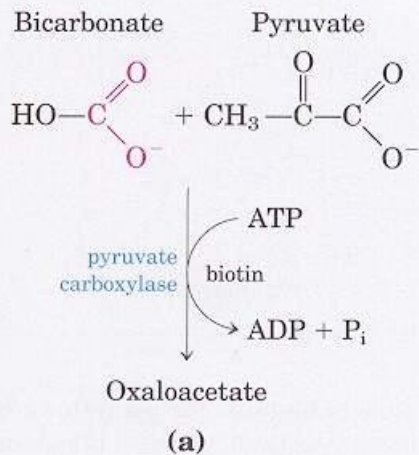


FIGURE 14-17 Synthesis of phosphoenolpyruvate from pyruvate. (a) In mitochondria, pyruvate is converted to oxaloacetate in a biotin-requiring reaction catalyzed by pyruvate carboxylase. (b) In the cytosol, oxaloacetate is converted to phosphoenolpyruvate by PEP carboxykinase. The CO₂ incorporated in the pyruvate carboxylase reaction is lost here as CO₂. The decarboxylation leads to a rearrangement of electrons that facilitates attack of the carbonyl oxygen of the pyruvate moiety on the γ phosphate of GTP.

I. obvoz



Reakcije glukoneogeneze. I. obvoz. Citosolni piruvat ali laktat se lahko uporabita za sintezo fosfoenolpiruvata s citosolnimi in mitohondrijskimi encimi.

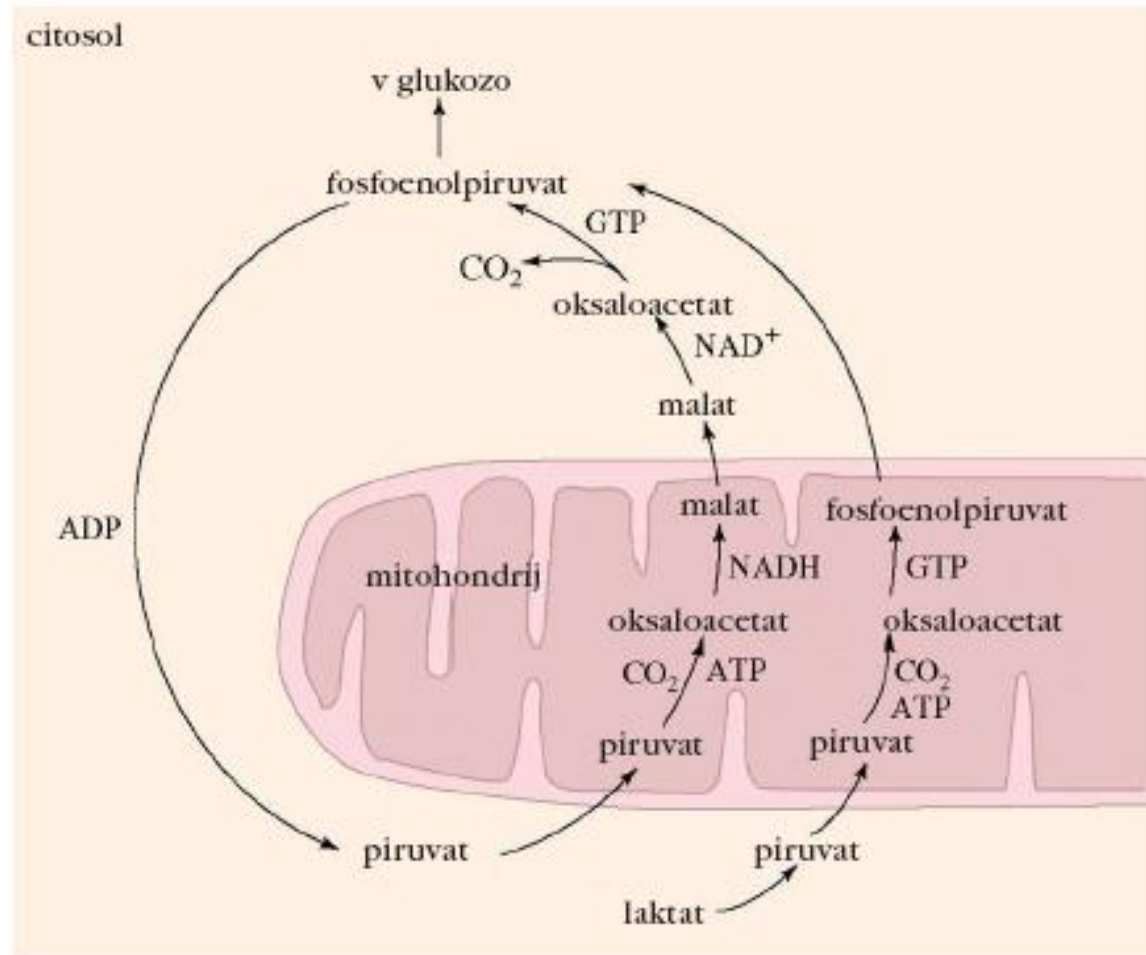
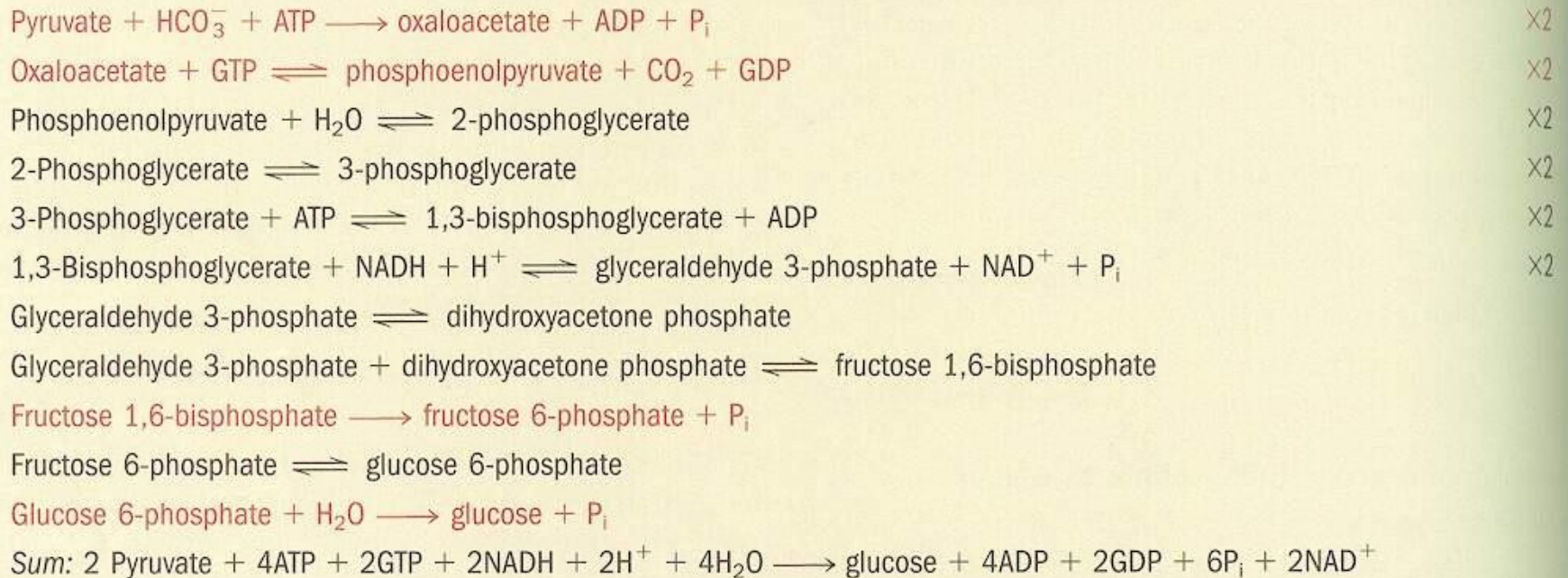


TABLE 14-3 Sequential Reactions in Gluconeogenesis Starting from Pyruvate



I. obvoz



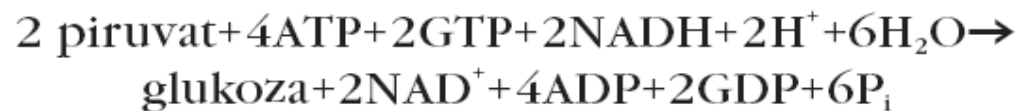
II. obvoz



III. obvoz



Povzetek glukoneogeneze:



Aktivacija glukoze in galaktoze za biosintezo

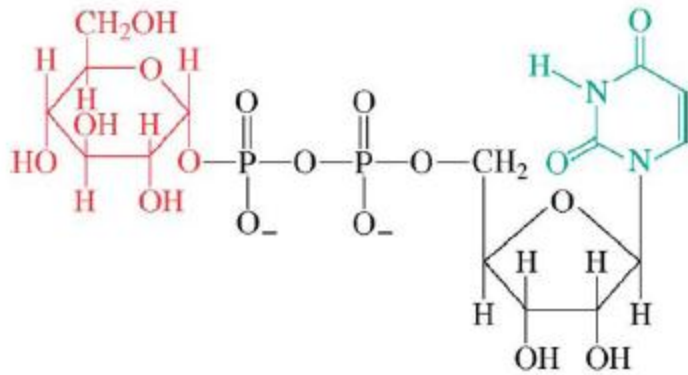
Nastanek NDP-glukoze

Nastanek NDP-glukoze lahko zapišemo s splošno reakcijo:

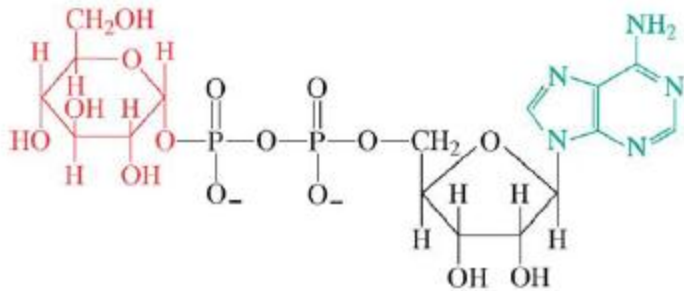


NTP = nukleozidtrifosfat, ATP ali UTP ali GTP

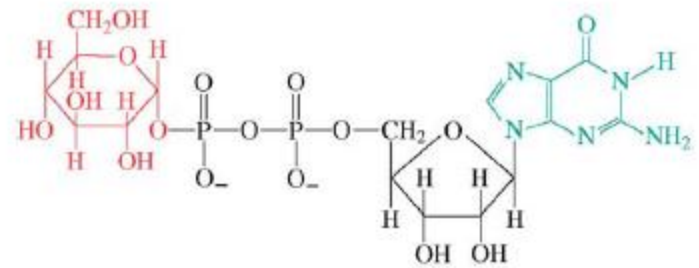
NDP-glukoza = nukleoziddifosfat-glukoza, ADP-glukoza ali UDP-glukoza ali GDP-glukoza



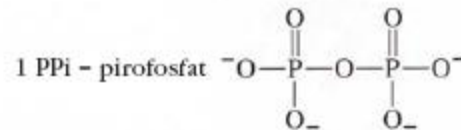
(a) UDP-glukoza



(b) ADP-glukoza



(c) GDP-glukoza



Encim: ADP-glukoza-pirofosforilaza ali
 UDP-glukoza-pirofosforilaza ali
 GDP-glukoza-pirofosforilaza

Nastanek UDP-galaktoze

Sinteza UDP-galaktoze poteka po dveh možnih poteh:

1. Izomerizacija UDP-glukoze



Encim = UDP-glukoza-4-epimeraza

2. Izmenjava UDP



Encim = galaktoza-1-fosfat-uridiltransferaza

Sinteza disaharidov

Laktoza

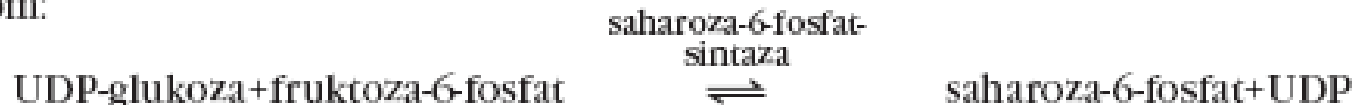
Disaharid laktoza (mlečni sladkor) se po porodu aktivno sintetizira v mlečni žlezi sesalcev. Laktoza nastane s povezavo aktivirane galaktoze z glukozo:



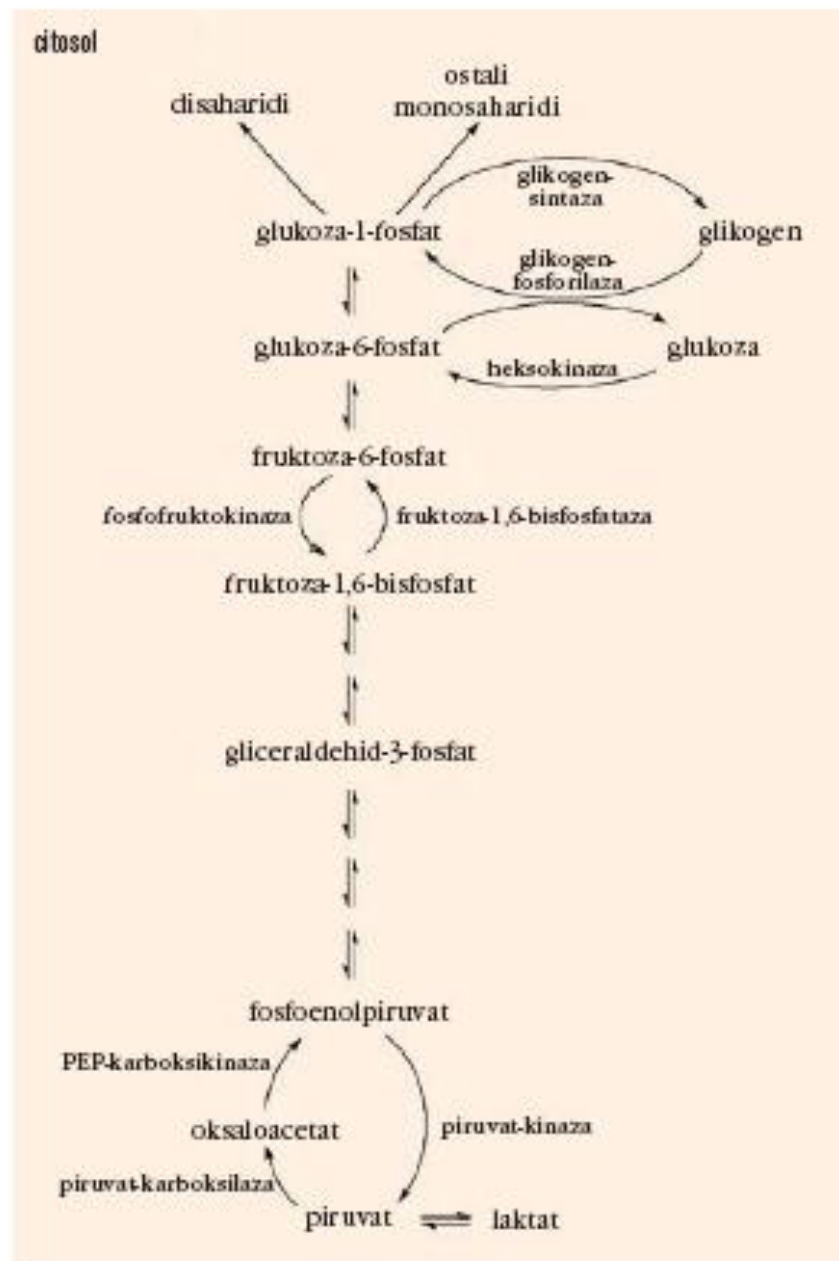
Encimski sistem laktoza-sintaza katalizira nastanek $\beta(1 \rightarrow 4)$ glikozidne vezi med dvema monosaharidoma (glej Okno v biokemijo 15.1).

Saharoza

Disaharid saharoza je glavni sladkor pri večini vrst sadja in zelenjave, zlasti veliko pa ga vsebujeta sladkorni trs in sladkorna repa. Saharoza, transportna oblika monosaharidov, potrebnih za pridobivanje energije in biosintetske procese, se prenaša po rastlini preko floema (sekundarnega žilnega sistema rastlin). Disaharid se sintetizira v dveh stopnjah iz glukoze, aktivirane z UDP, in iz fruktoze, aktivirane s fosfatom:



REGULACIJA METABOLIZMA OGLJIKOVIH HIDRATOV



Regulatorni encimi v metabolizmu ogljikovih hidratov

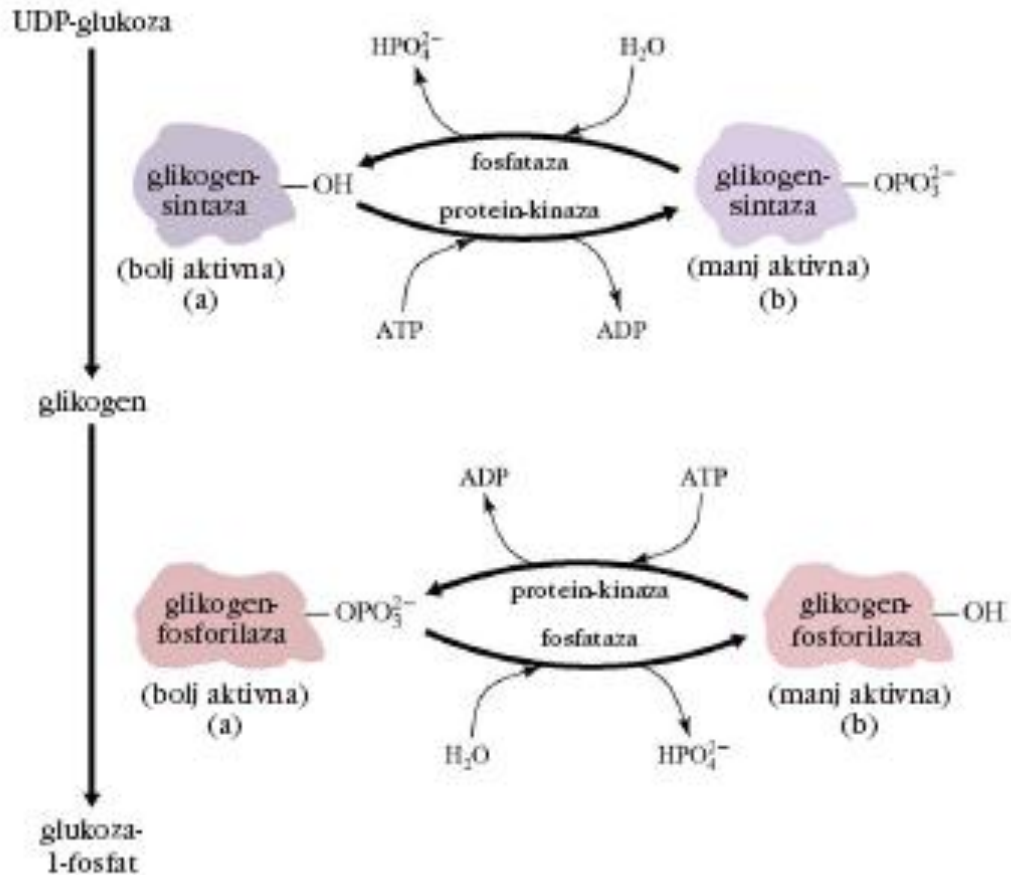
ime encima	⊕ modulator ^a	⊖ modulator ^a	komentar
glikogen-fosforilaza			
oblika (a)	-	-	aktivna v vseh razmerah
oblika (b)	AMP	G6P ^b	razmerje med oblikama (a) in (b) uravnavajo hormoni
glikogen-sintaza			
oblika (a)	-	-	aktivna v vseh razmerah
oblika (b)	G6P ^b	-	razmerje med oblikama (a) in (b) uravnavajo hormoni
heksokinaza	-	G6P ^b	inhibicija s povratno zvezo
fosfofruktokinaza	AMP, F2,6BP ^c	ATP, citrat	glavna kontrolna točka glikolize
fruktoza-1.6-bisfosfataza	-	AMP, F2,6BP ^c	regulacijska stopnja v sintezi glukoze
piruvat-kinaza	-	ATP, acetil-CoA	uravnavana tudi z izoencimskimi oblikami
piruvat-karboksilaza	acetil-CoA	-	pomaga vzdrževati stalno koncentracijo glukoze in oksaloacetata

^a + alosterični modulatorji stimulirajo encim; -alosterični modulatorji inhibirajo encim.

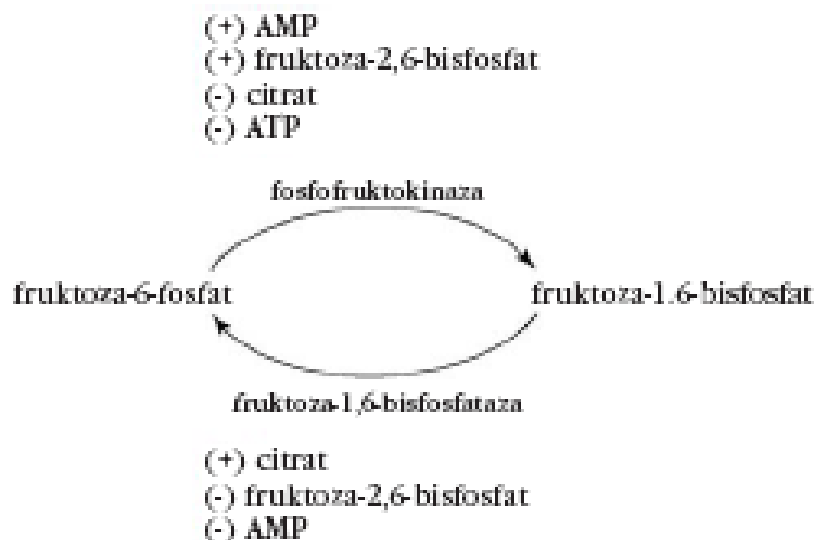
^b G6P = glukoza-6-fosfat

^c F2,6-BP = fruktoza-2,6-bisfosfat

GLIKOGEN SINTAZA IN GLIKOGEN FOSFORILAZA

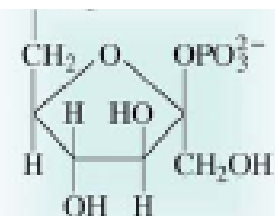


Fruktoza-1,6-bisfosfataza



Recipročno uravnavanje fosfofruktokinaze in fruktoza-1,6-bisfosfataze.

Struktura fruktoza-2,6-bisfosfata, alosteričnega modulatorja, ki stimulira delovanje fosfofruktokinaze



fruktoza-2,6-bisfosfat

Piruvat-kinaza in piruvat-karboksilaza

Piruvat-kinaza (PK) je tetrameren protein, ki za svojo aktivnost potrebuje Na^+ ali K^+ ione. ATP inhibira piruvat-kinazo in tako upočasni nastanek piruvata.

Piruvat-karboksilaza (PC) je pomemben regulatorni encim glukoneogeneze. PC katalizira nastanek oksaloacetata z vezavo CO_2 na piruvat. PC je aktivna samo, kadar ima na razpolago intermediat acetil-CoA. Metabolične logike te stopnje ne boš

FOSFOGLUKOZNA POT

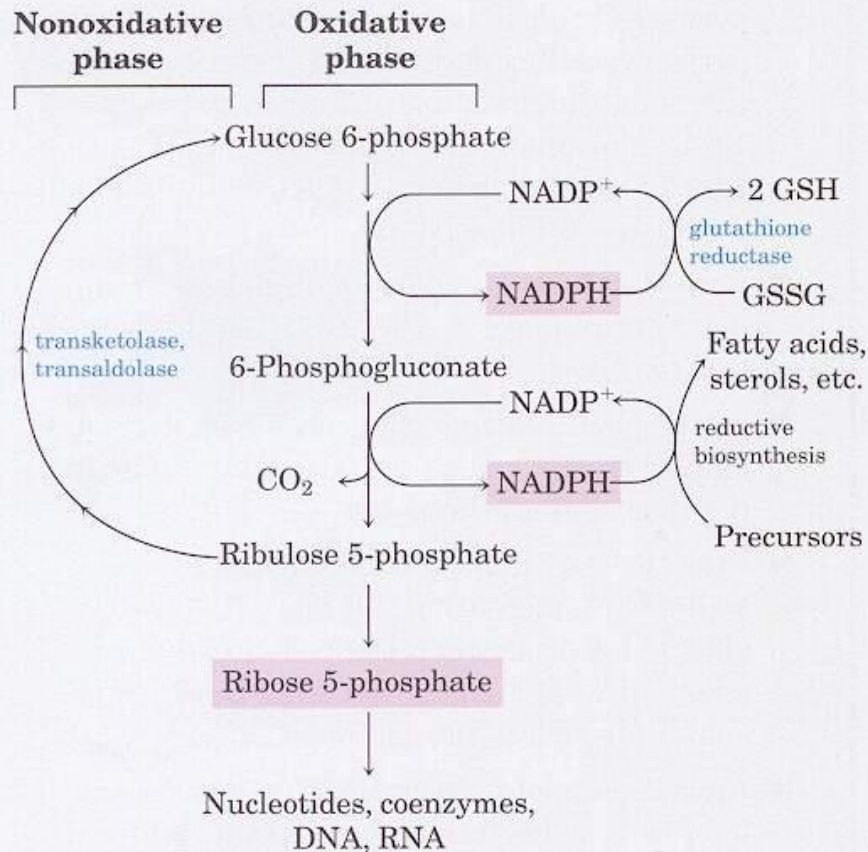


FIGURE 14-20 General scheme of the pentose phosphate pathway.

NADPH formed in the oxidative phase is used to reduce glutathione, GSSG (see Box 14-3) and to support reductive biosynthesis. The other product of the oxidative phase is ribose 5-phosphate, which serves as precursor for nucleotides, coenzymes, and nucleic acids. In cells that are not using ribose 5-phosphate for biosynthesis, the nonoxidative phase recycles six molecules of the pentose into five molecules of the hexose glucose 6-phosphate, allowing continued production of NADPH and converting glucose 6-phosphate (in six cycles) to CO₂.

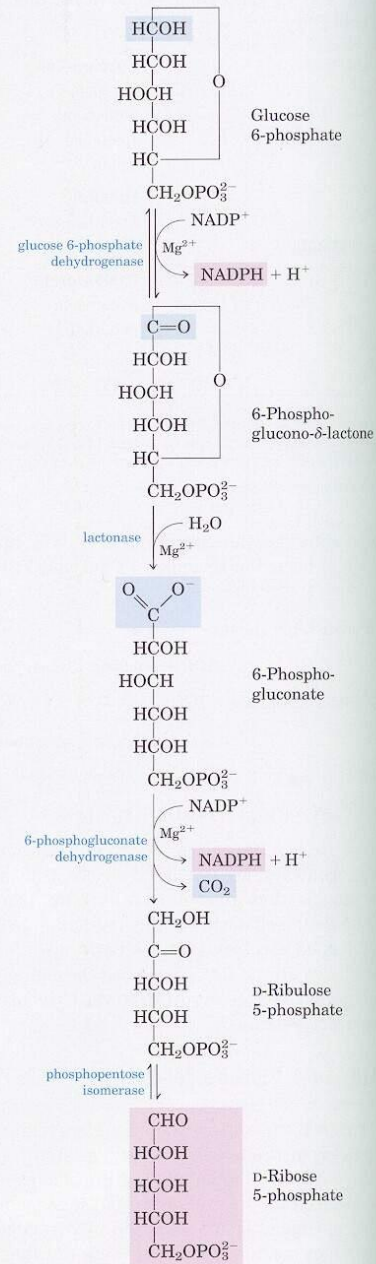


FIGURE 14-21 Oxidative reactions of the pentose phosphate pathway. The end products are ribose 5-phosphate, CO₂, and NADPH.