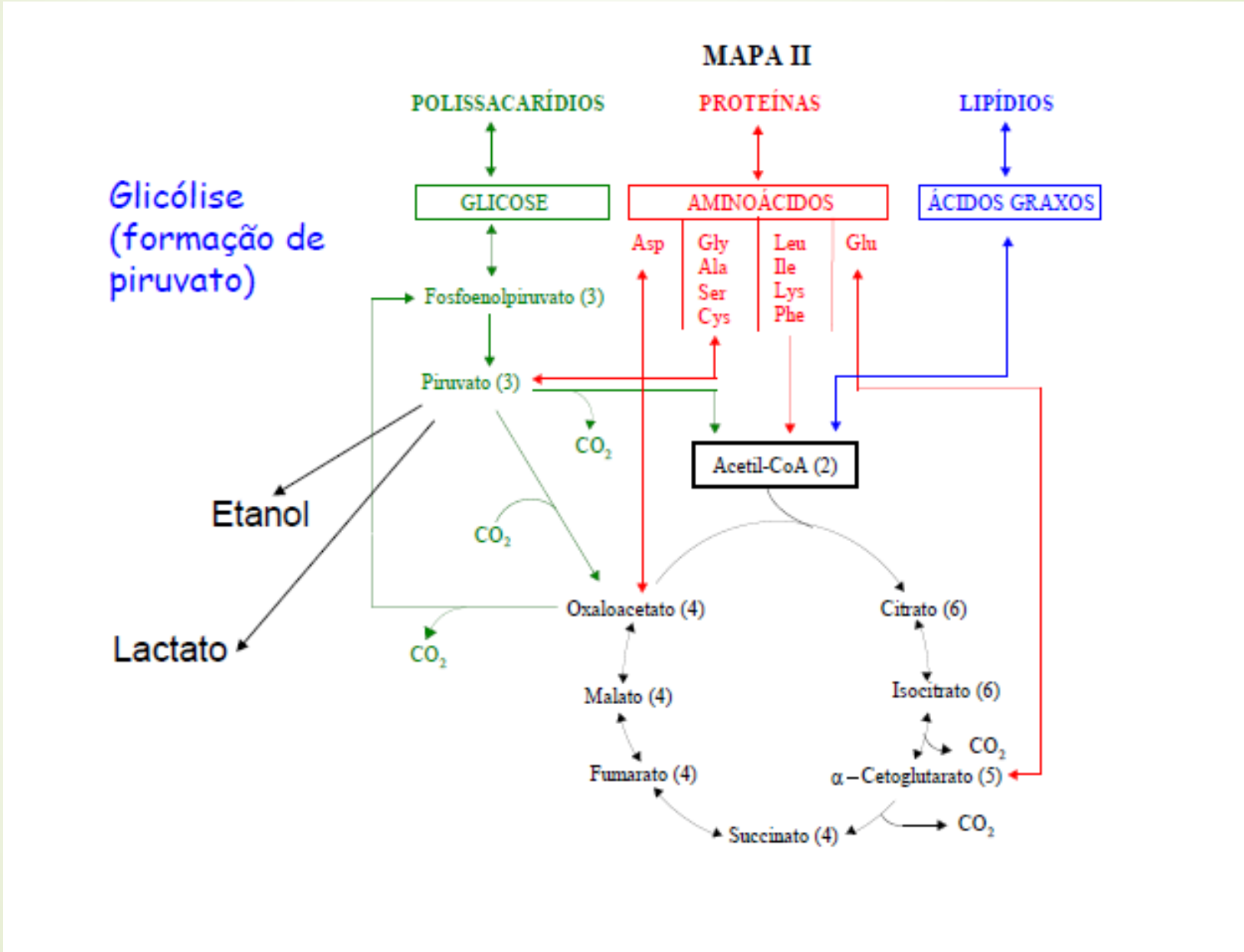
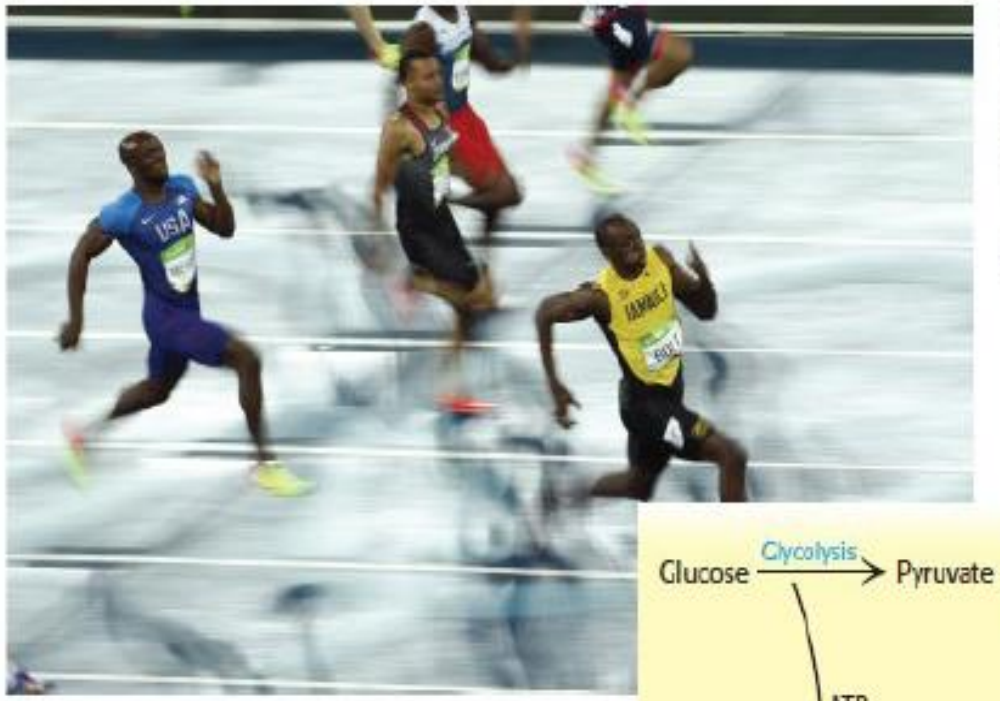
Via Glicolítica

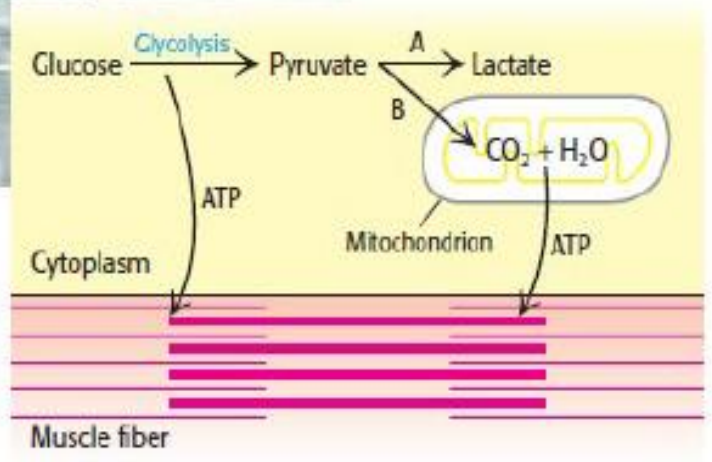
Utilização da glicose pelas células


MAPA II
POLISSACARÍDIOS
PROTEÍNAS
LIPÍDIOS
Glicólise (formação de piruvato)
GLICOSE
AMINOÁCIDOS
ÁCIDOS GRAXOS
Asp
Gly
Ala
Ser
Cys
Leu
Ile
Lys
Phe
Glu
Fosfoenolpiruvato (3)
Piruvato (3)
CO2
Acetil-CoA (2)
Etanol
Lactato
CO2
Oxaloacetato (4)
Citrato (6)
CO2
Malato (4)
Isocitrato (6)
CO2
Fumarato (4)
α – Cetoglutarato (5)
Succinato (4)
CO2

Vias de degradação da glicose



Usain Bolt sprints to a win in the 200-meter finals at the Olympics in Rio de Janerio in 2016. Glucose metabolism can generate the ATP to power muscle contraction. During a sprint, when the ATP needs outpace oxygen delivery, as would be the case for Bolt, glucose is metabolized to lactate. When oxygen delivery is adequate, glucose is metabolized more efficiently to carbon dioxide and water. [Odd Andersen/Getty Images.]



A. Low O_2
(last seconds of a sprint)

B. Normal
(long, slow run)

https://www.youtube.com/watch?v=hDq1rhUkV-g

http://www.iubmb-nicholson.org/mp4/glycolysis.mp4

https://www.youtube.com/watch?v=WlSpTBUDXoI

Importância da Glicólise

1 – Principal meio de degradação da glicose.

2 – Obtenção de Energia mesmo em condições anaeróbias.

3 - Principal via de obtenção de energia nos eritrocitos, medula renal, cérebro e esperma.

Como a glicose e transportada para dentro das celulas

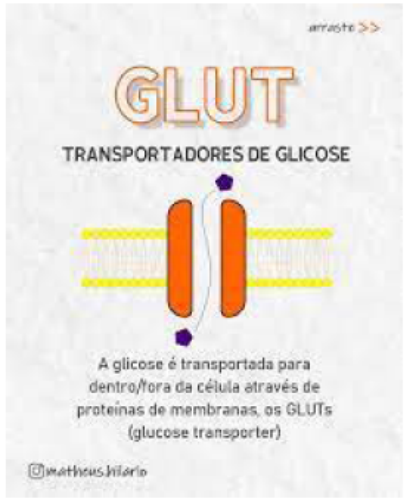


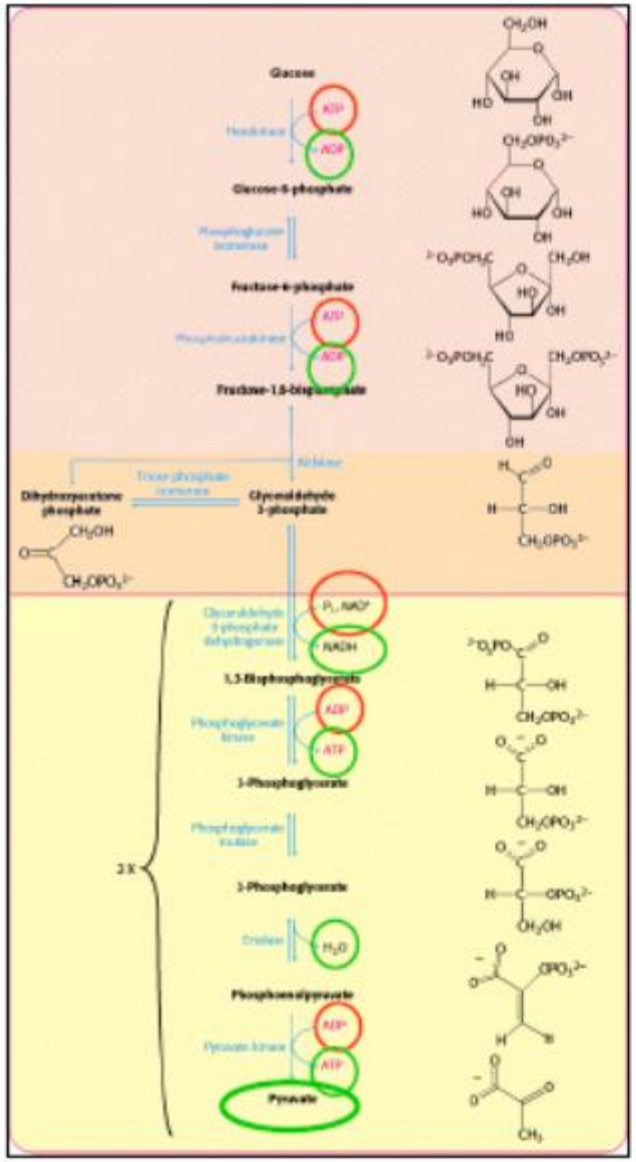
TABLE 16.4 Family of glucose transporters

Name	Tissue location	K_M	Comments
GLUT1	All mammalian tissues	1 mM	Basal glucose uptake
GLUT2	Liver and pancreatic β cells	15–20 mM	In the pancreas, plays a role in the regulation of insulin In the liver, removes excess glucose from the blood
GLUT3	All mammalian tissues	1 mM	Basal glucose uptake
GLUT4	Muscle and fat cells	5 mM	Amount in muscle plasma membrane increases with endurance training
GLUT5	Small intestine	—	Primarily a fructose transporter

$$Glicose + 2NAD + 2ADP + 2Pi \rightarrow 2Piruvato + 2NADH + 2H^{+} + 2ATP + 2H2O$$

1- Ativação ou Fosforilação da Glicose

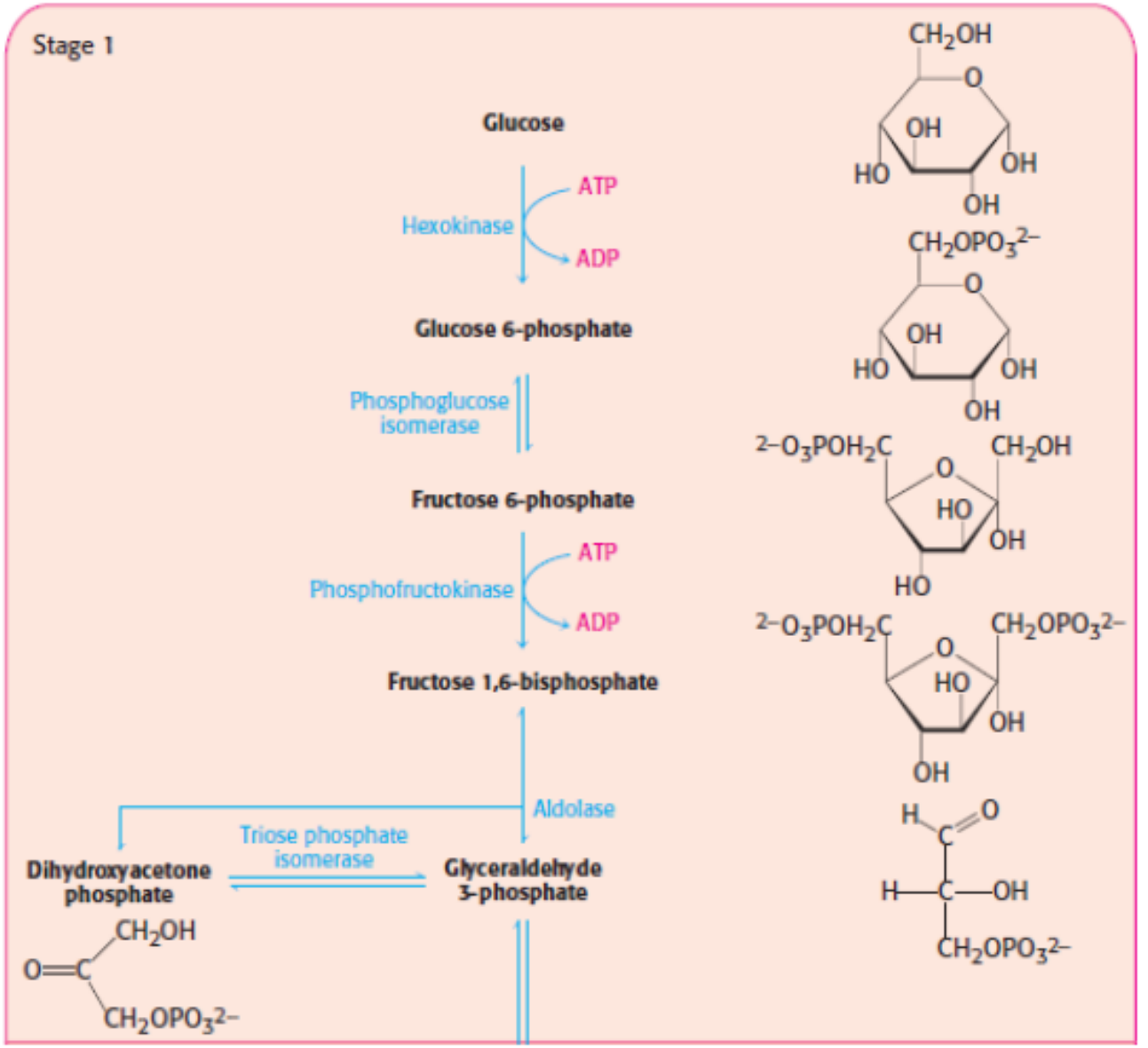
2- Transformação do Gliceraldeído em Piruvato



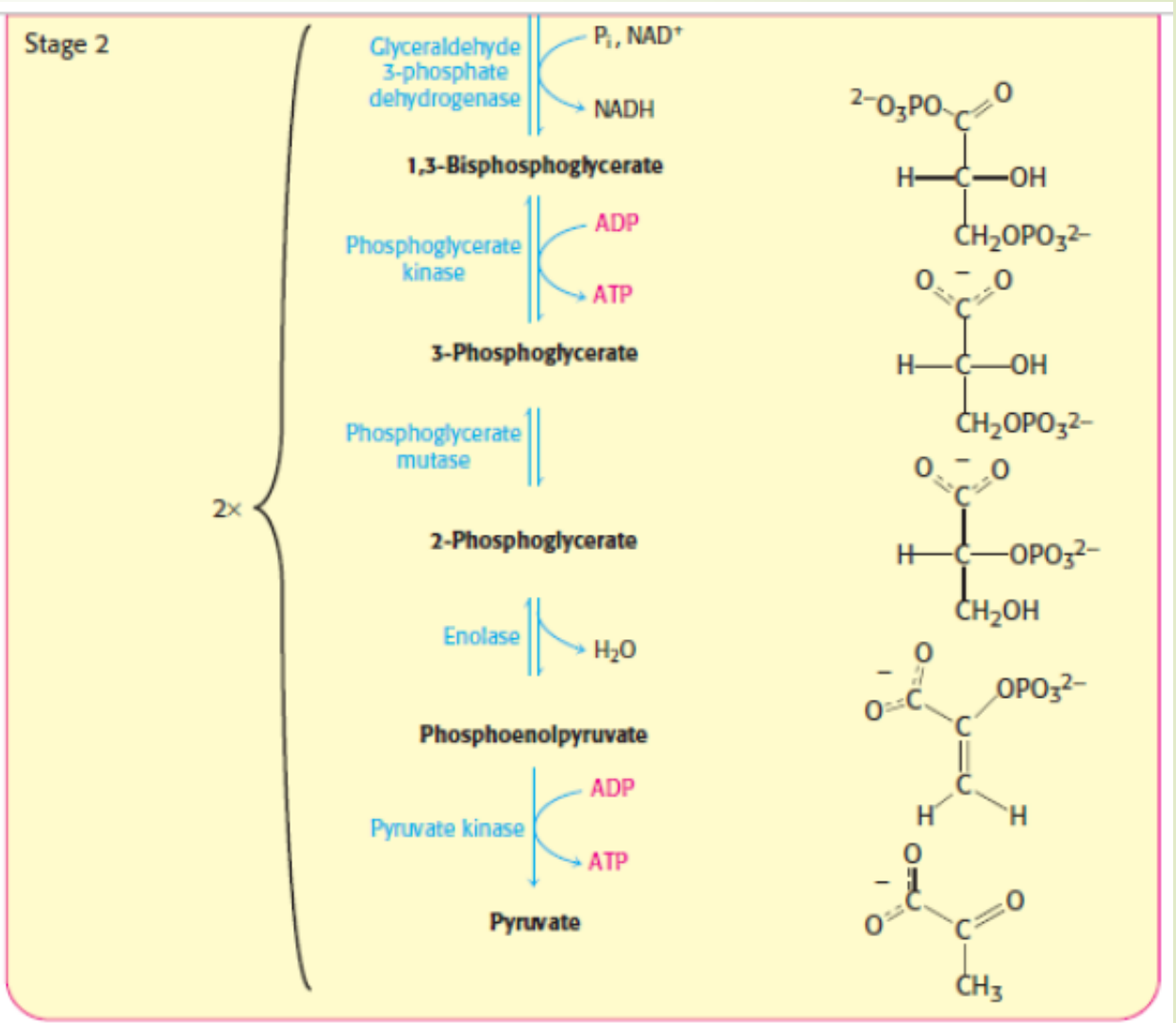
Fase preparatória

Fase compensatória

Fase preparatoria



Fase compensatoria



Como a glicose e transportada para dentro das celulas

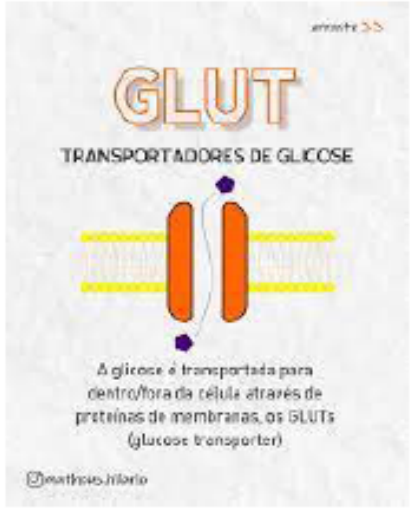


TABLE 16.4 Family of glucose transporters

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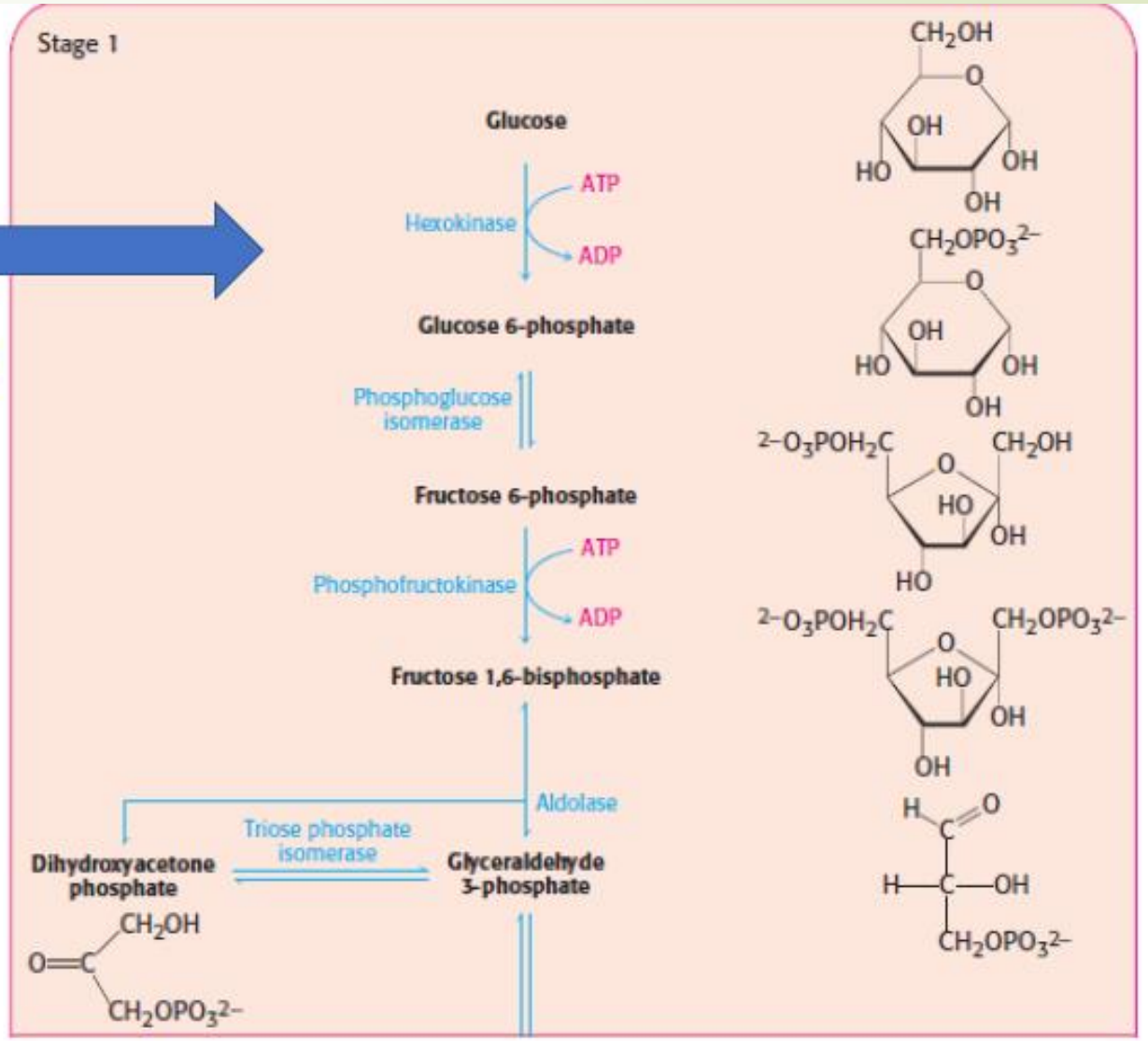
GLUT4	Muscle and fat cells	5 mM	Amount in muscle plasma membrane increases with endurance training
GLUT5	Small intestine	—	Primarily a fructose transporter

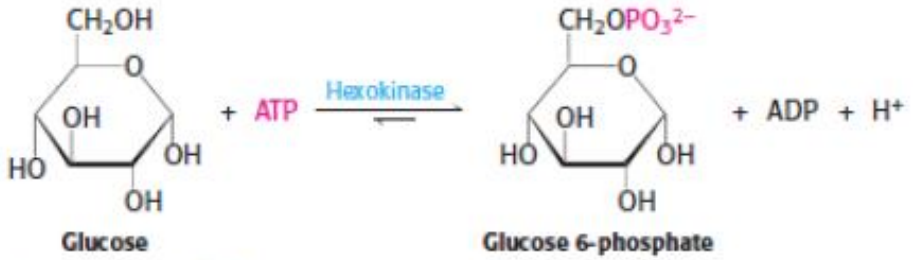
Activação ou Fosforilação da Glicose



Permite a entrada da Glicose no Metabolismo Intracelular

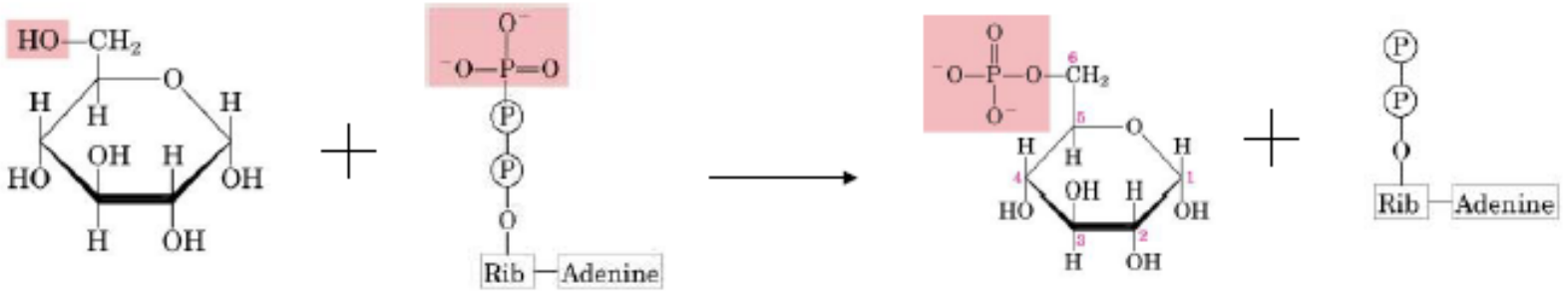
A Glicose-6-P não passa pela membrana plasmática

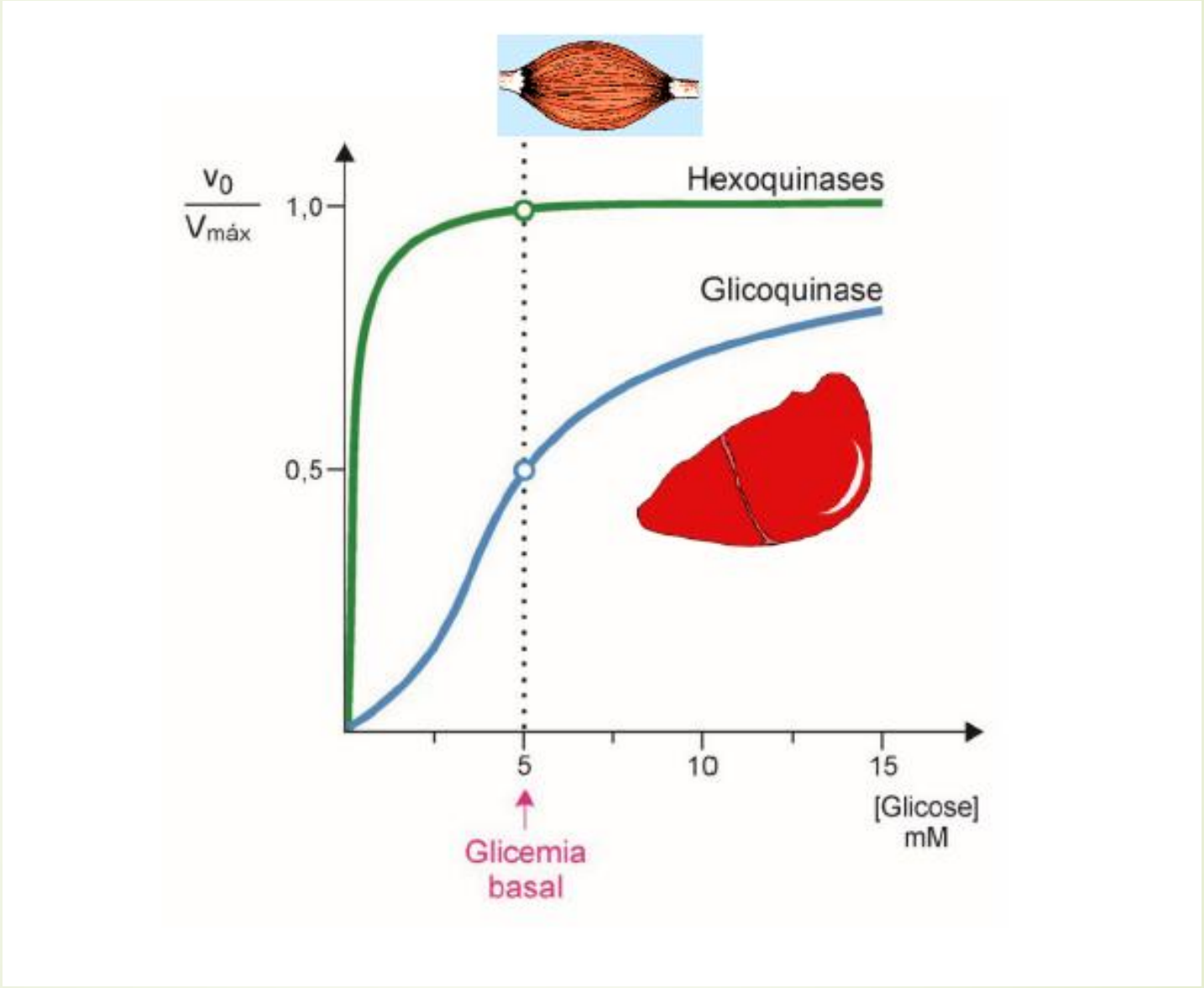
→ Reação irreversível

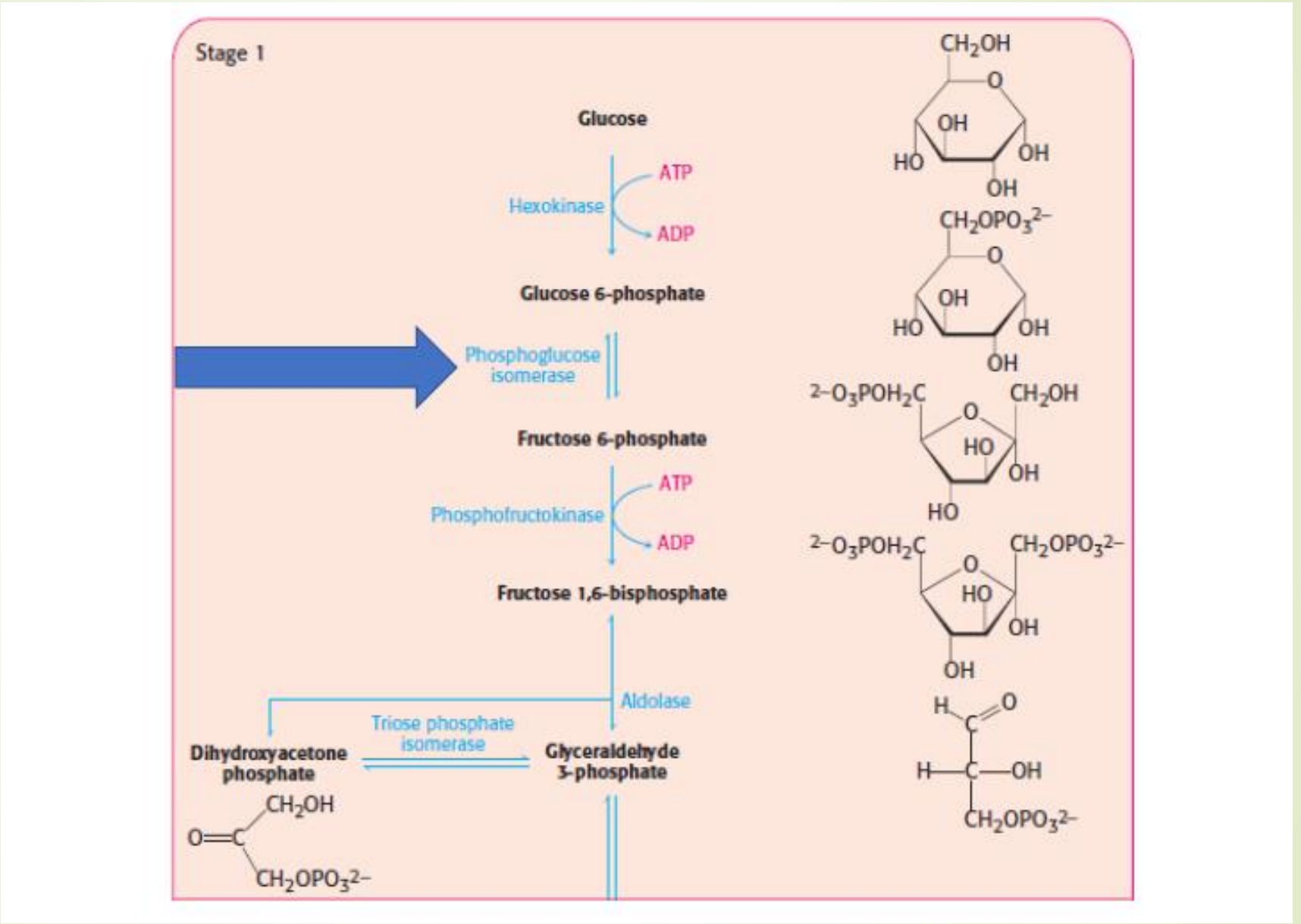


hexoquinase

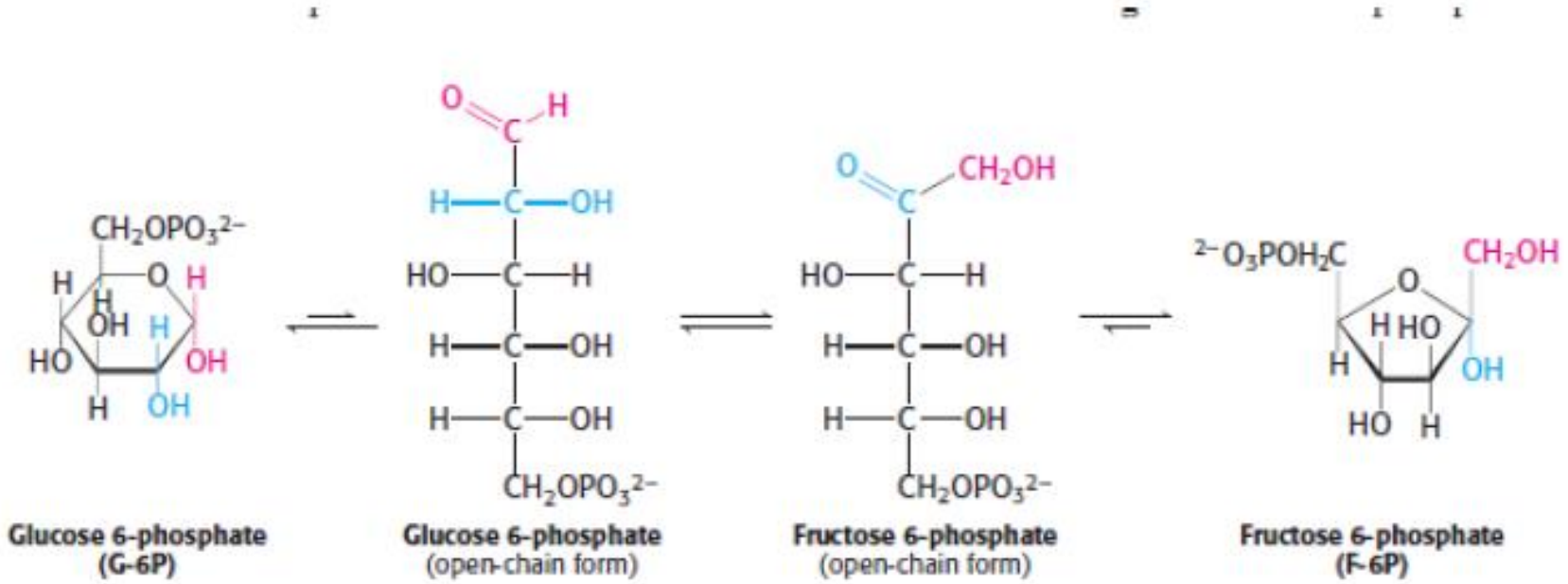
- Glicose + ATP → Glicose -6-Fosfato + ADP

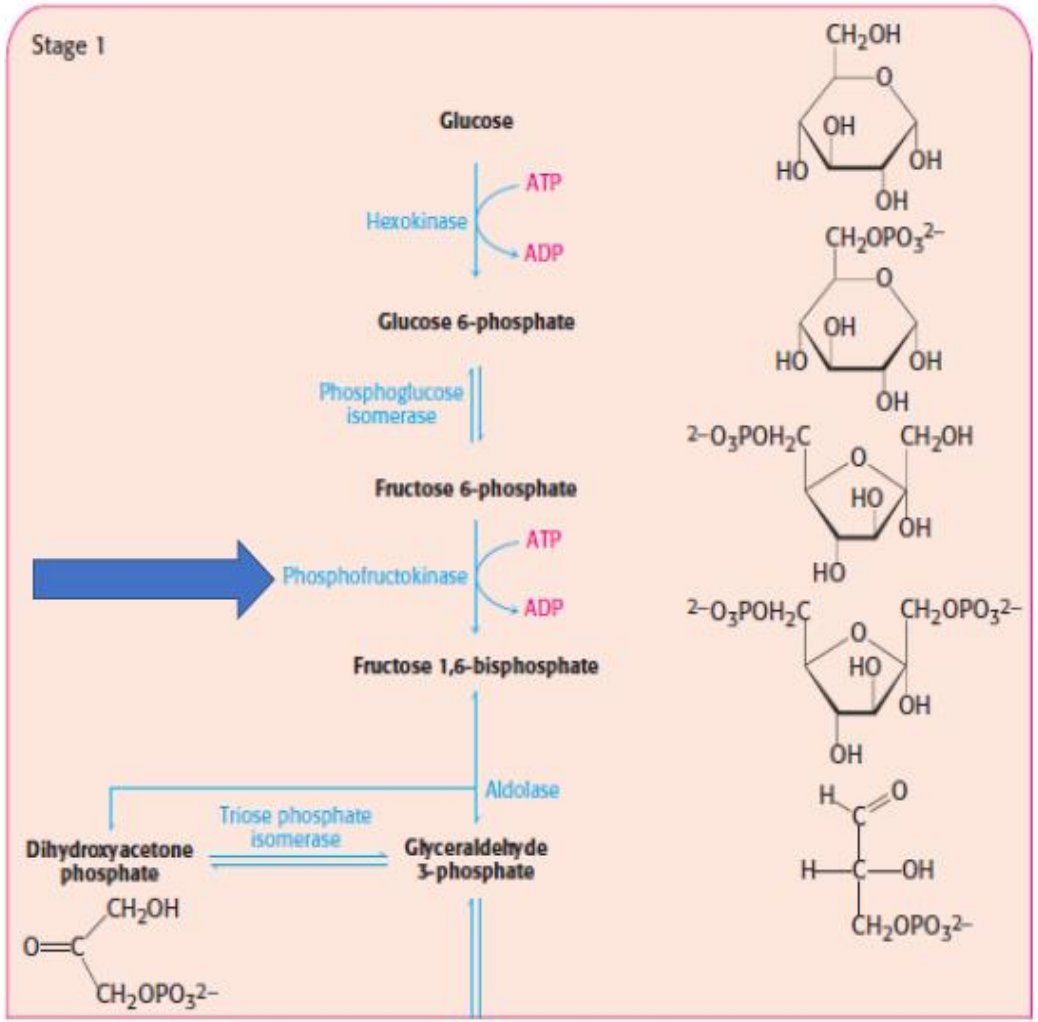


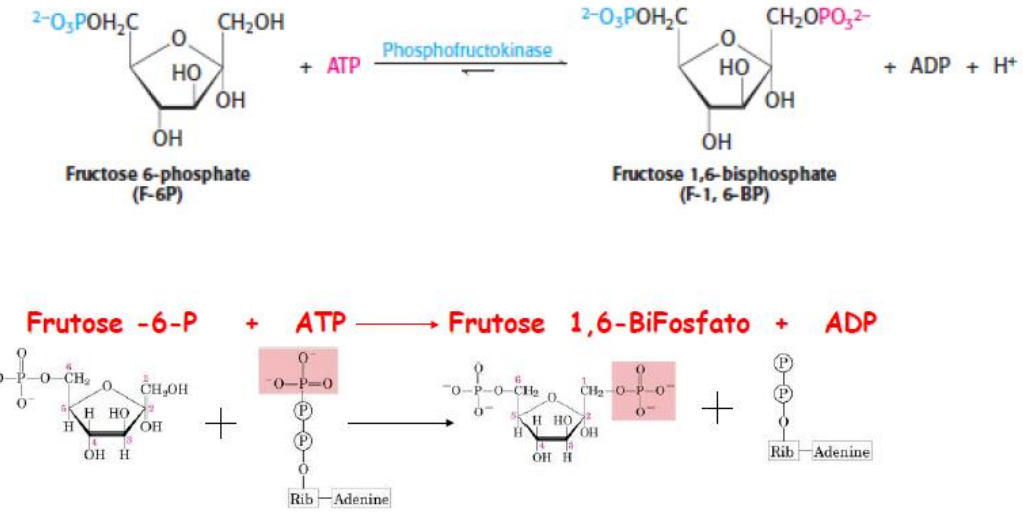

$\frac{v_0}{V_{máx}}$
1,0
0,5
Hexoquinases
Glicoquinase
5
10
15
[Glicose]
mM
Glicemia
basal

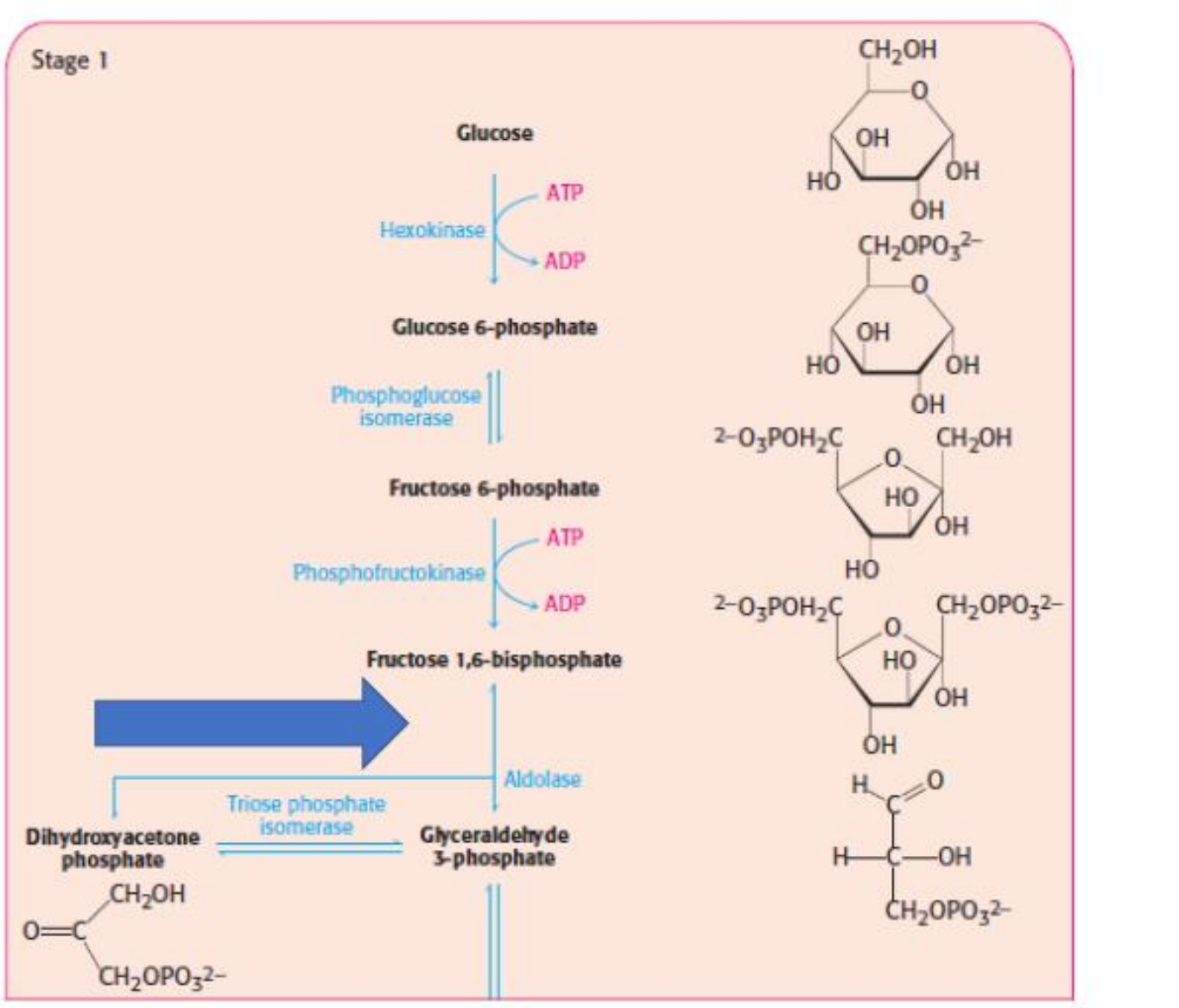

Stage 1
Glucose
ATP
Hexokinase
ADP
Glucose 6-phosphate
Phosphoglucose isomerase
Fructose 6-phosphate
ATP
Phosphofructokinase
ADP
Fructose 1,6-bisphosphate
Aldolase
Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate

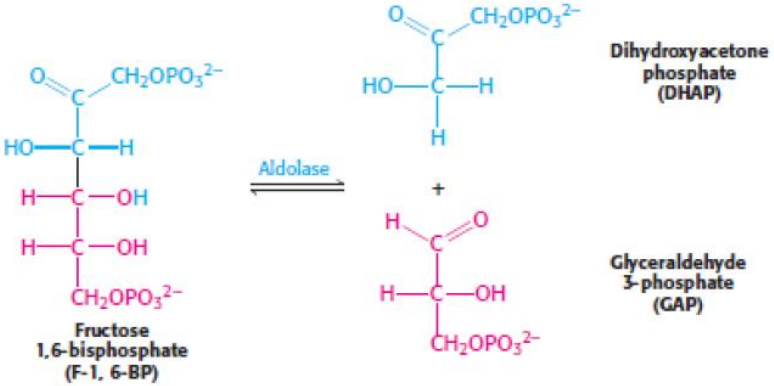
Fosfoglicose isomerase (Aldose para Cetose)

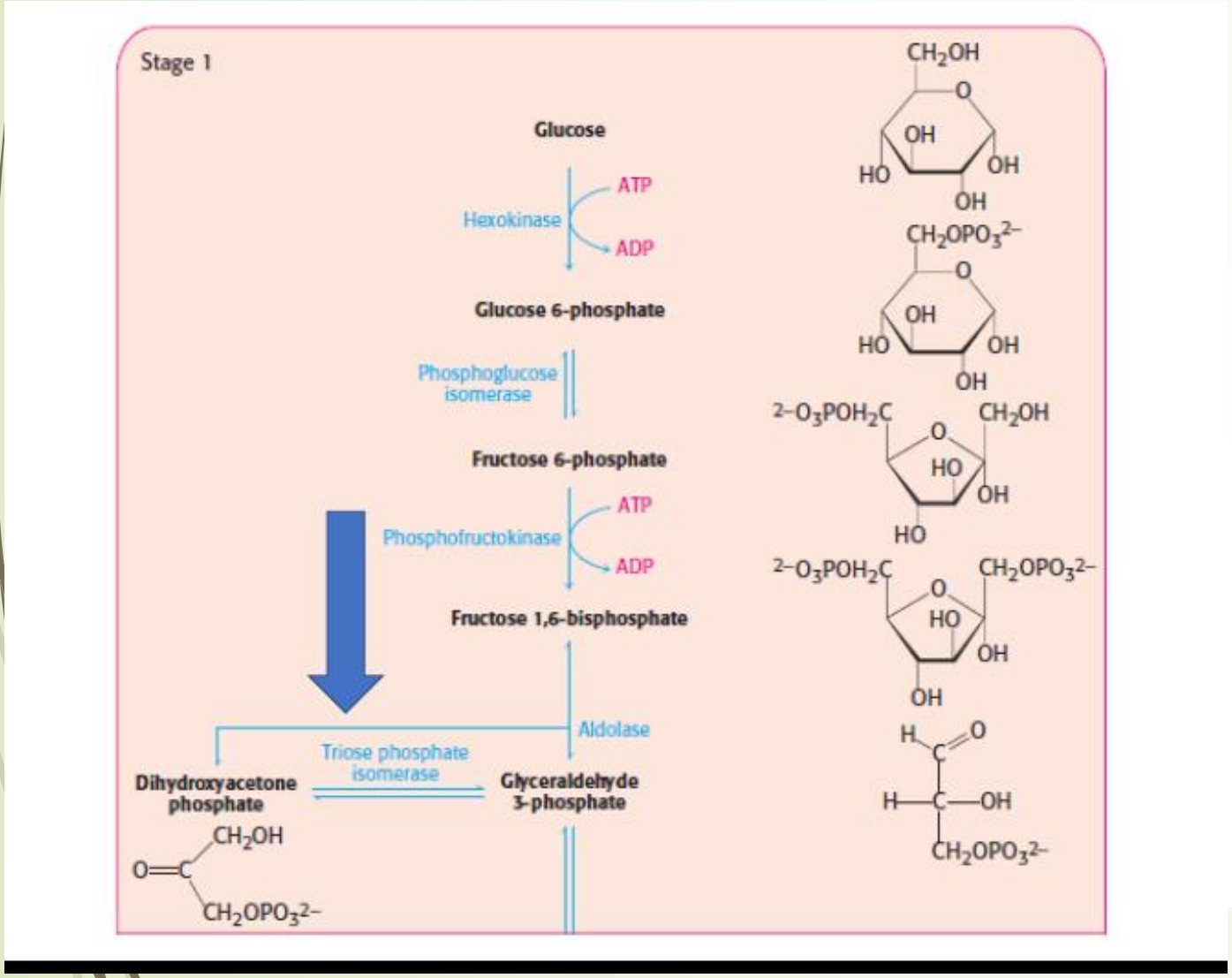


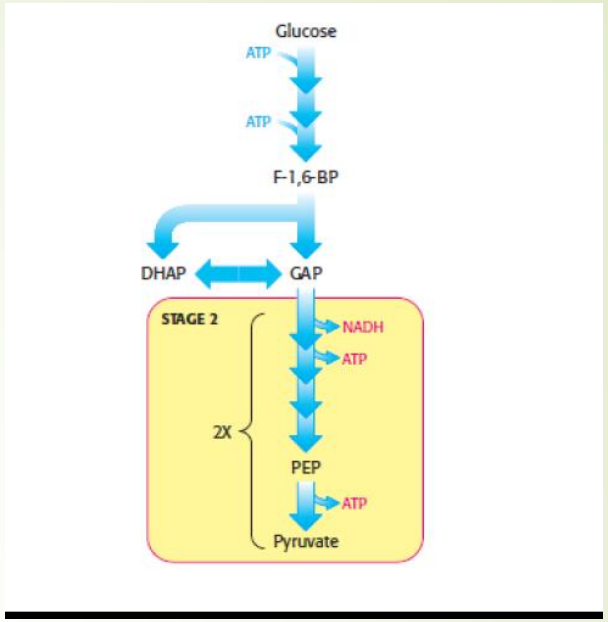

Stage 1
Glucose
Hexokinase
ATP
ADP
Glucose 6-phosphate
Phosphoglucose isomerase
Fructose 6-phosphate
Phosphofructokinase
ATP
ADP
Fructose 1,6-bisphosphate
Aldolase
Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate

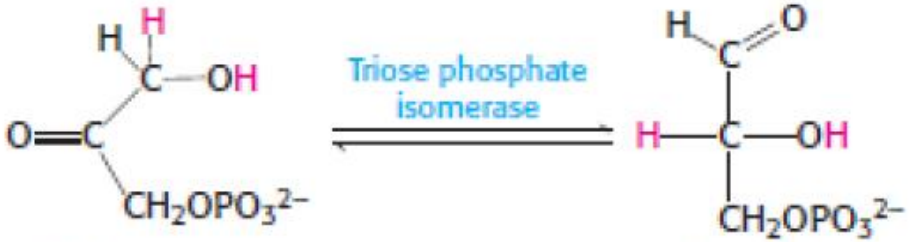

Phosphofructokinase
+ ATP
+ ADP + H+
Fructose 6-phosphate (F-6P)
Fructose 1,6-bisphosphate (F-1, 6-BP)
Frutose -6-P + ATP → Frutose 1,6-BiFosfato + ADP
Rib
Adenine


Stage 1
Glucose
ATP
Hexokinase
ADP
Glucose 6-phosphate
Phosphoglucose isomerase
Fructose 6-phosphate
ATP
Phosphofructokinase
ADP
Fructose 1,6-bisphosphate
Aldolase
Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate

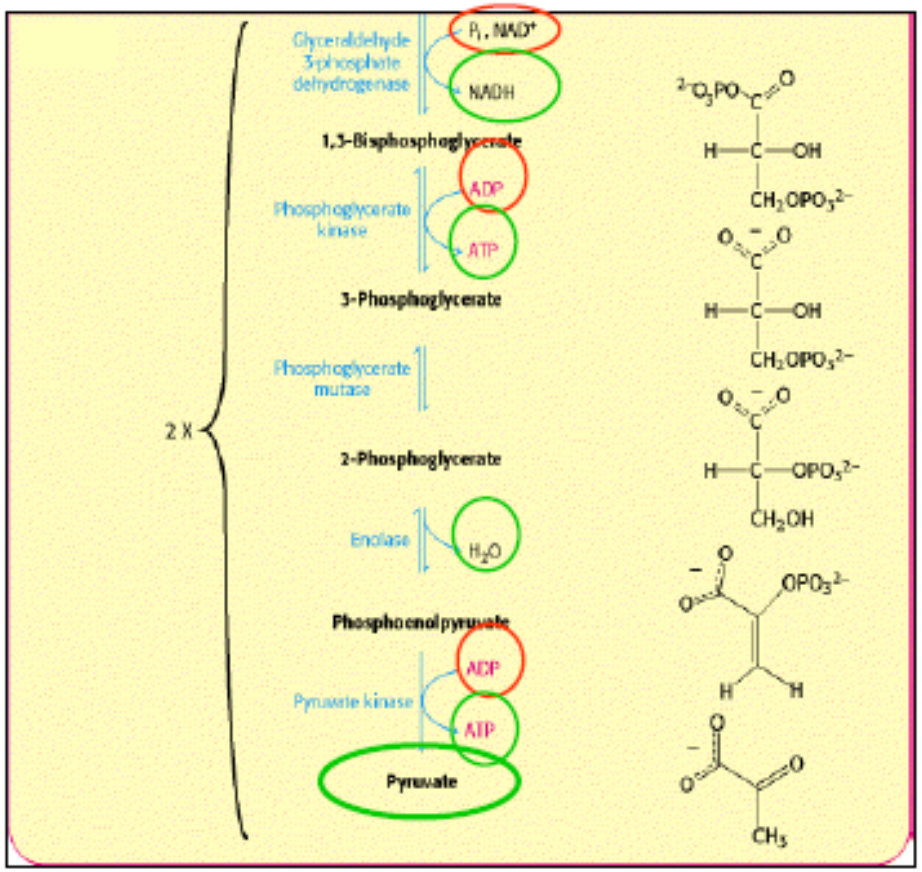

Aldolase
Fructose 1,6-bisphosphate (F-1, 6-BP)
Dihydroxyacetone phosphate (DHAP)
Glyceraldehyde 3-phosphate (GAP)


Stage 1
Glucose
ATP
Hexokinase
ADP
Glucose 6-phosphate
Phosphoglucose isomerase
Fructose 6-phosphate
ATP
Phosphofructokinase
ADP
Fructose 1,6-bisphosphate
Aldolase
Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate

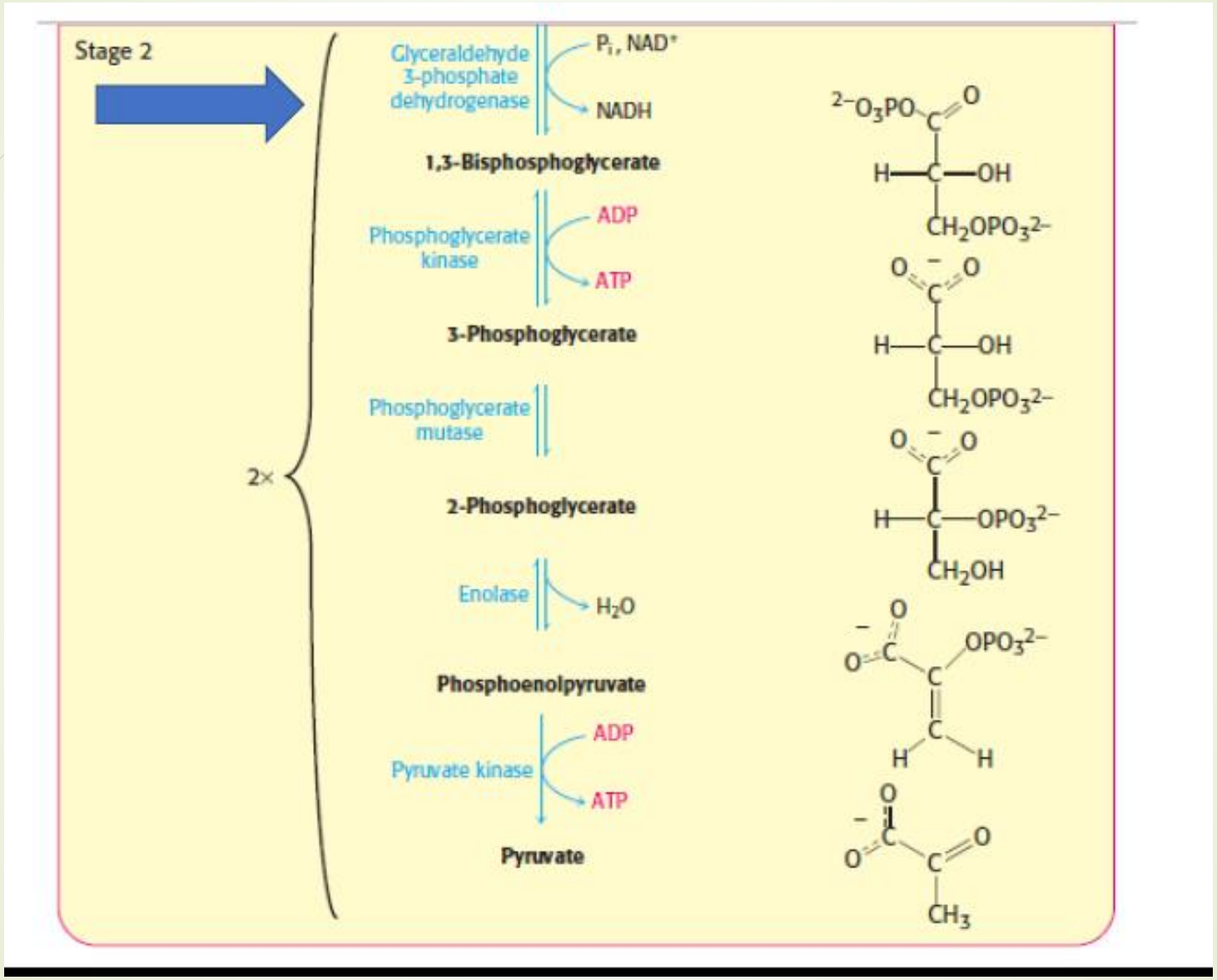

Glucose
ATP
ATP
F-1,6-BP
DHAP
GAP
STAGE 2
NADH
ATP
2X
PEP
ATP
Pyruvate


Triose phosphate isomerase
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate

Transformação do Gliceraldeído em Piruvato



Fase compensatória


Stage 2
2×
Glyceraldehyde 3-phosphate dehydrogenase
P_i, NAD+
NADH
1,3-Bisphosphoglycerate
Phosphoglycerate kinase
ADP
ATP
3-Phosphoglycerate
Phosphoglycerate mutase
2-Phosphoglycerate
Enolase
H_2O
Phosphoenolpyruvate
Pyruvate kinase
ADP
ATP
Pyruvate

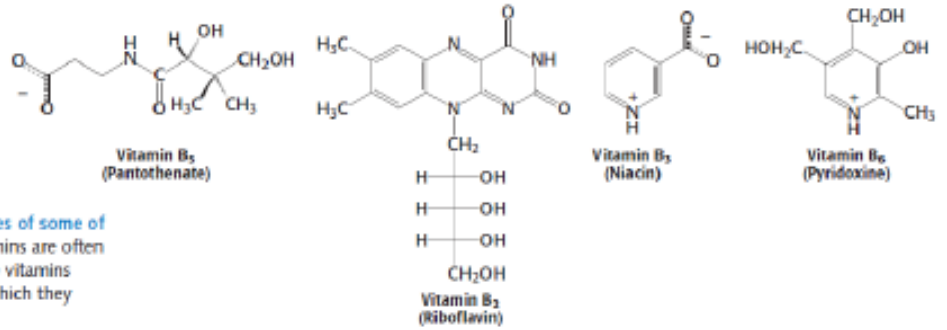
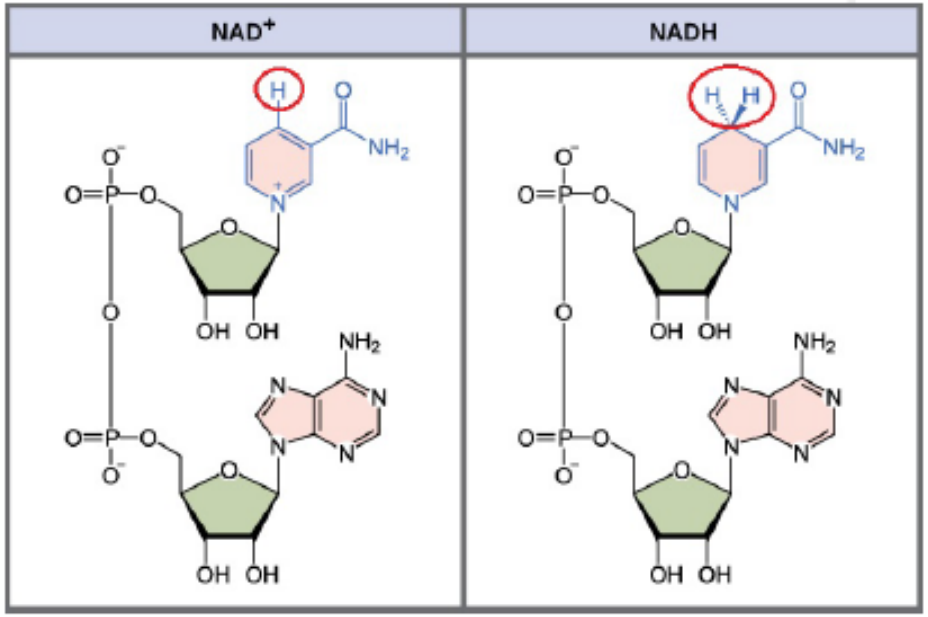
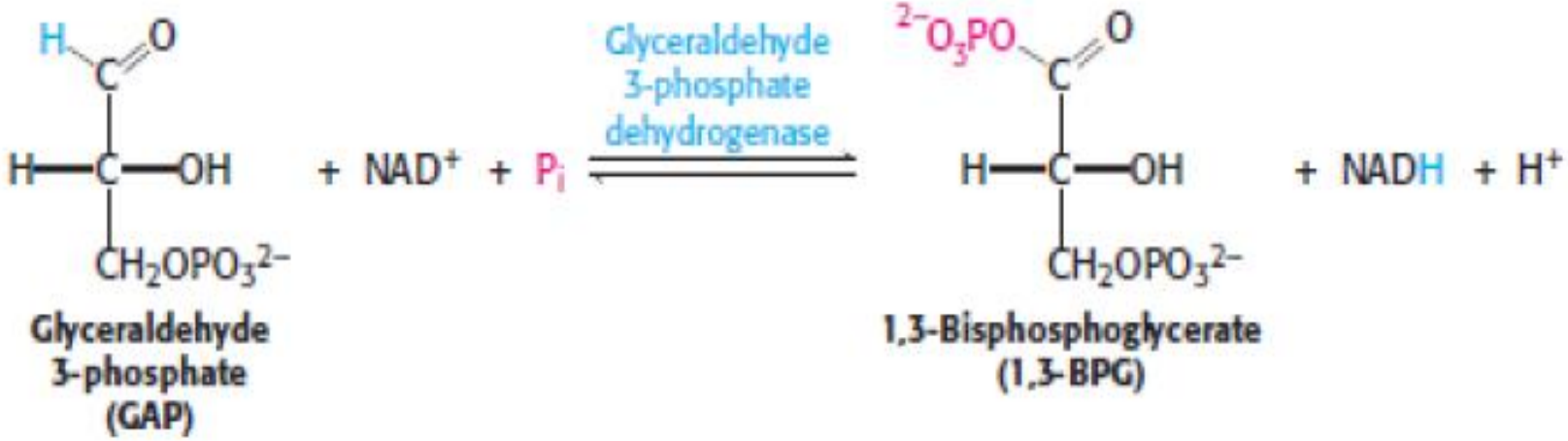
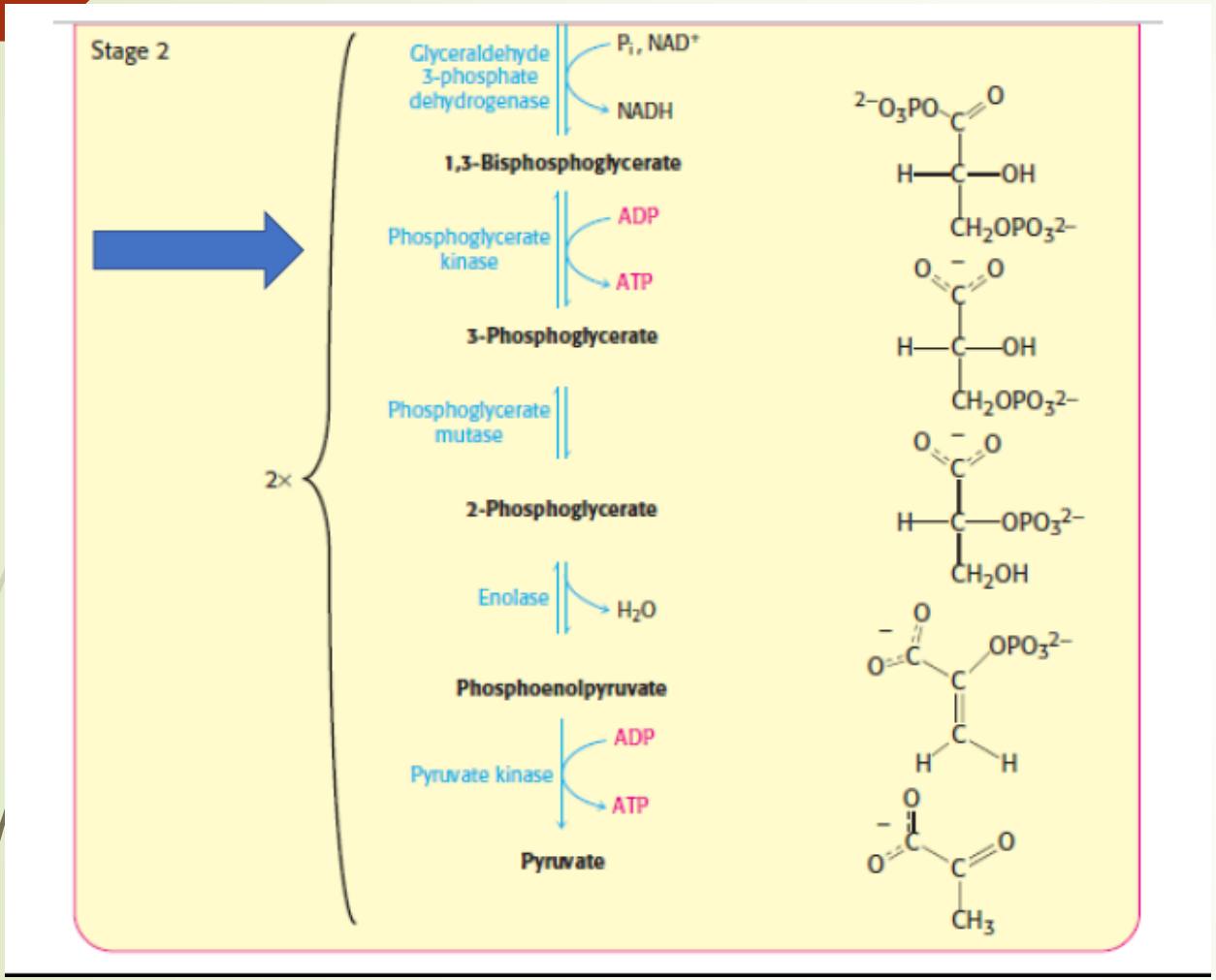


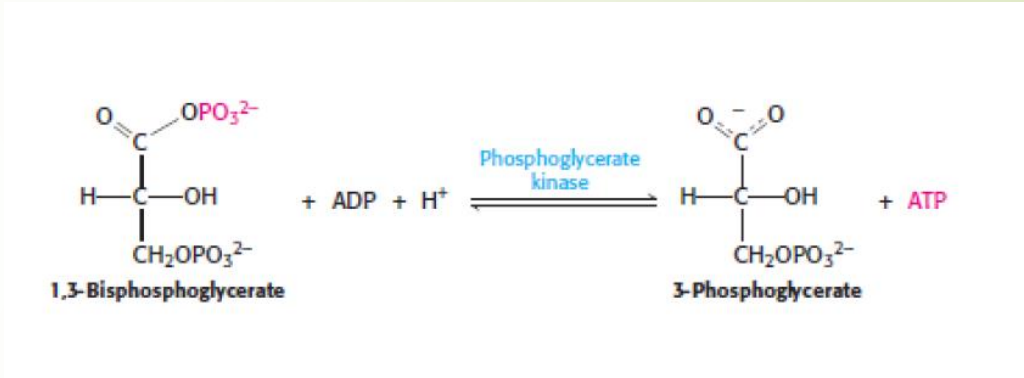
FIGURE 15.17 Structures of some of the B vitamins. These vitamins are often referred to as water-soluble vitamins because of the ease with which they dissolve in water.

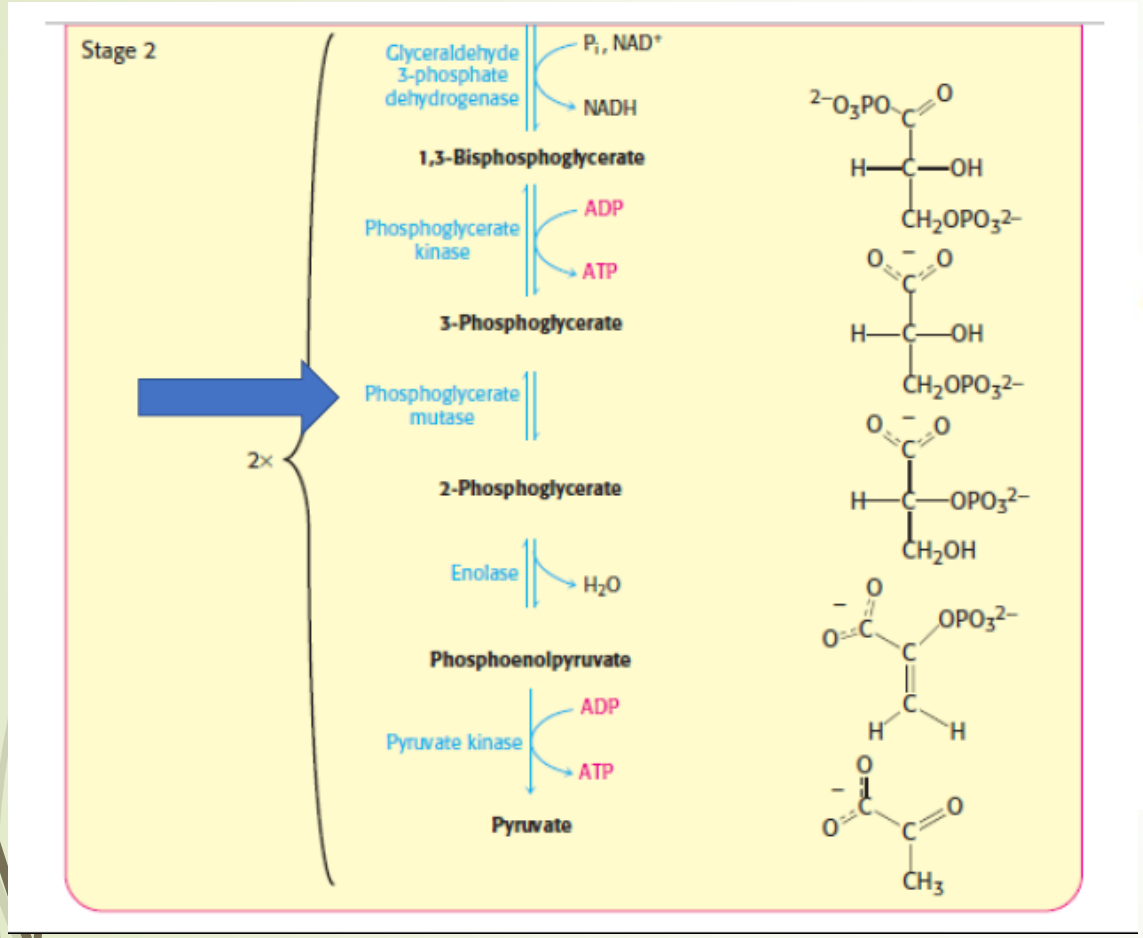
Dinucleótido de nicotinamida e adenina



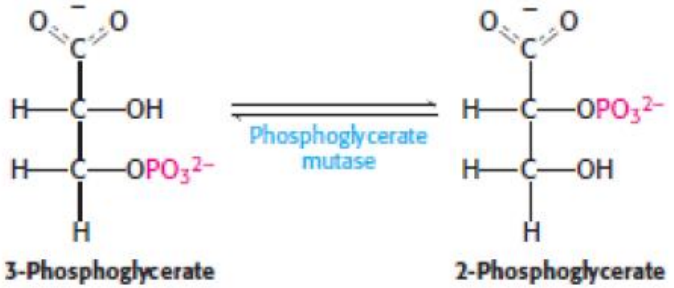

Glyceraldehyde 3-phosphate dehydrogenase
+ NAD+ + Pi
+ NADH + H+
Glyceraldehyde 3-phosphate (GAP)
1,3-Bisphosphoglycerate (1,3-BPG)

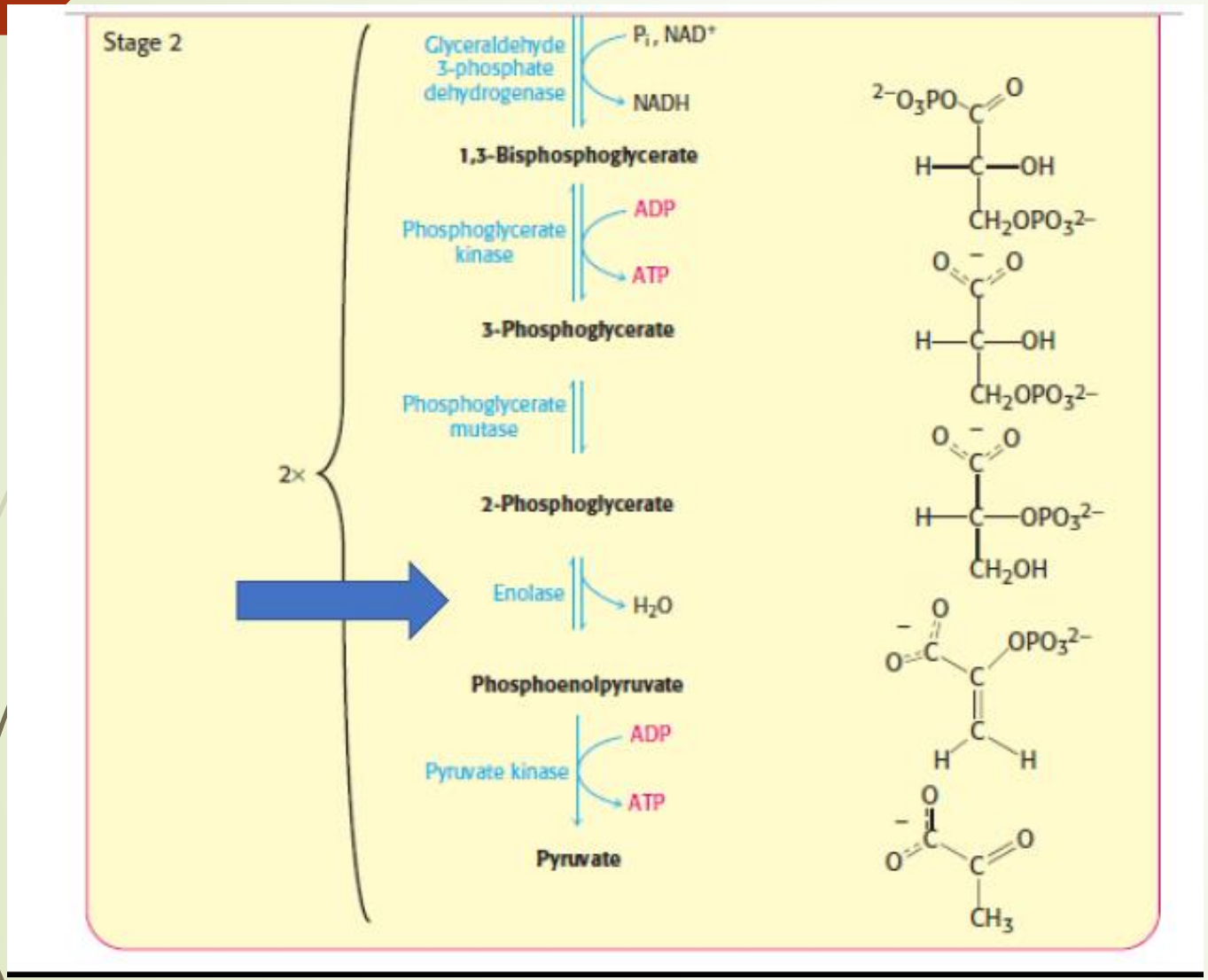

Stage 2
2×
Glyceraldehyde 3-phosphate dehydrogenase
P_i, NAD^+
NADH
1,3-Bisphosphoglycerate
Phosphoglycerate kinase
ADP
ATP
3-Phosphoglycerate
Phosphoglycerate mutase
2-Phosphoglycerate
Enolase
H_2O
Phosphoenolpyruvate
Pyruvate kinase
ADP
ATP
Pyruvate

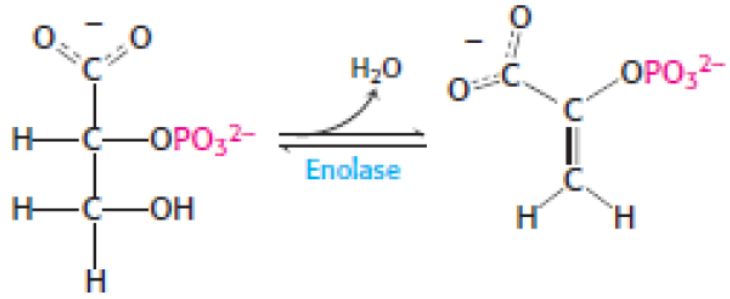

Phosphoglycerate kinase
+ ADP + H^+
+ ATP
1,3-Bisphosphoglycerate
3-Phosphoglycerate

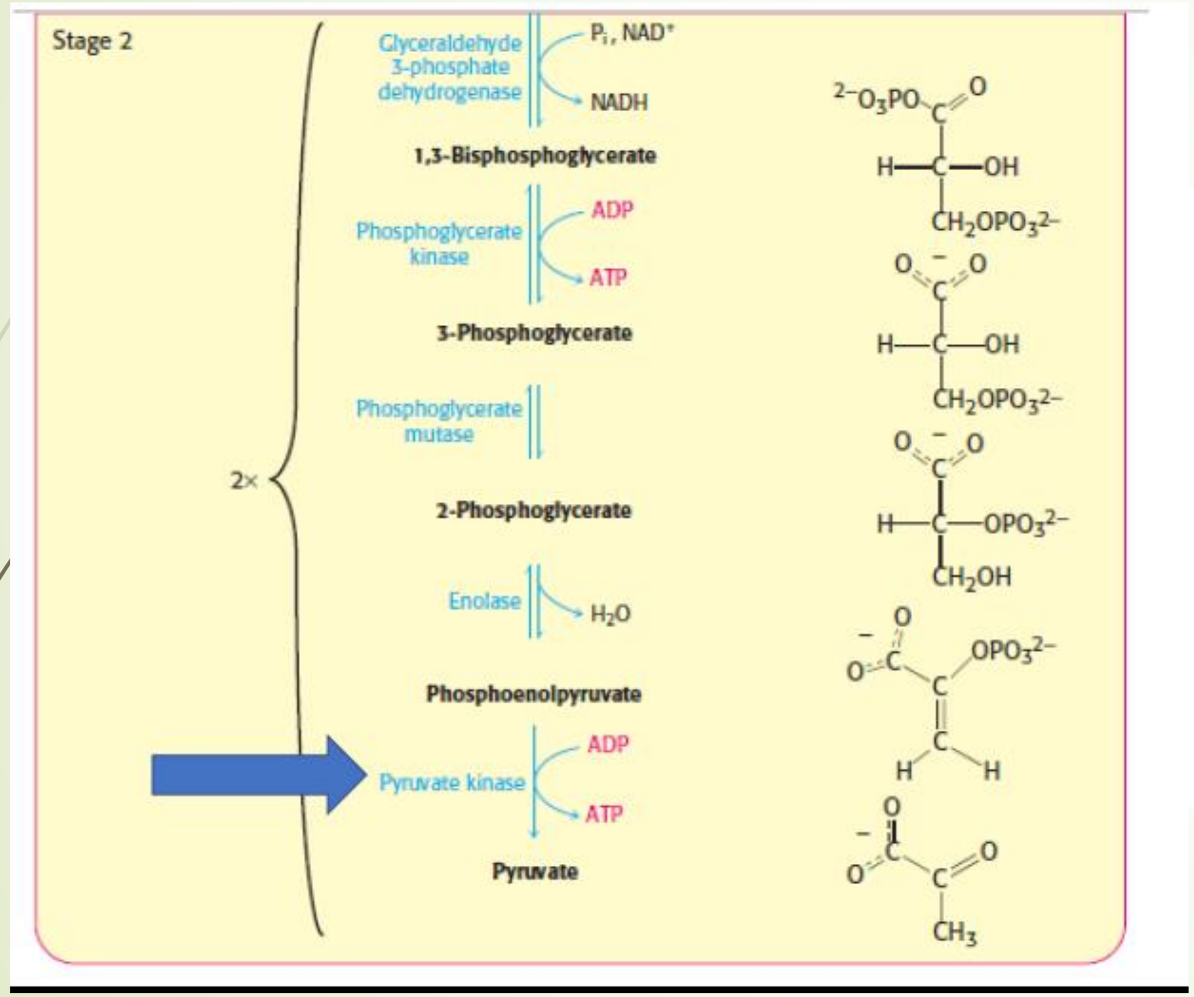


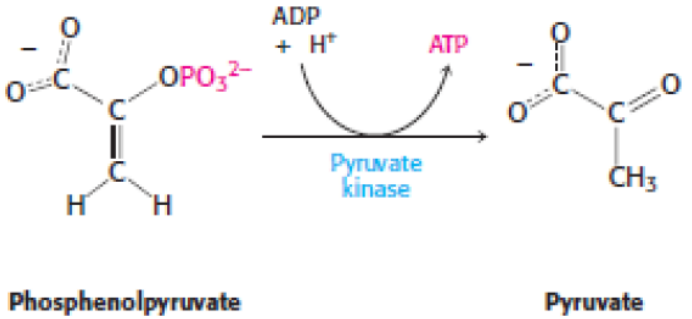
"Mutase", muda o Grupo Fosfato de Posição dentro da Molécula




Stage 2
Glyceraldehyde 3-phosphate dehydrogenase
P_i, NAD^+
NADH
1,3-Bisphosphoglycerate
Phosphoglycerate kinase
ADP
ATP
3-Phosphoglycerate
Phosphoglycerate mutase
2-Phosphoglycerate
2×
Enolase
H_2O
Phosphoenolpyruvate
Pyruvate kinase
ADP
ATP
Pyruvate


H_2O
Enolase
2-Phosphoglycerate
Phosphenolpyruvate





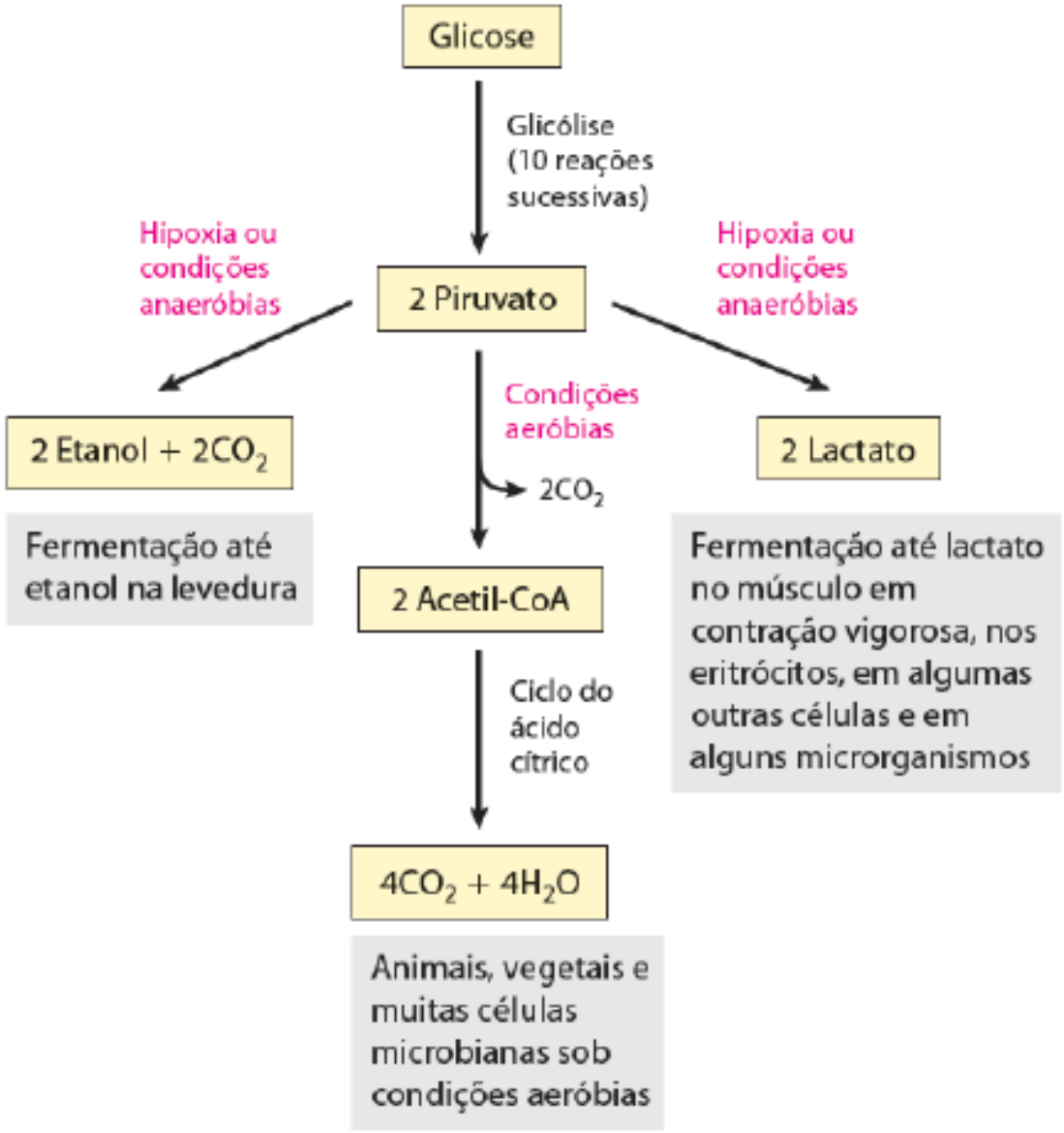
- Reacção Exorgónica Irreversível
- Transferencia do Grupo Fosfato do Fosfoenolpiruvato para o ADP

TABELA 14-2 Variação de energia livre das reações glicolíticas em eritrócitos

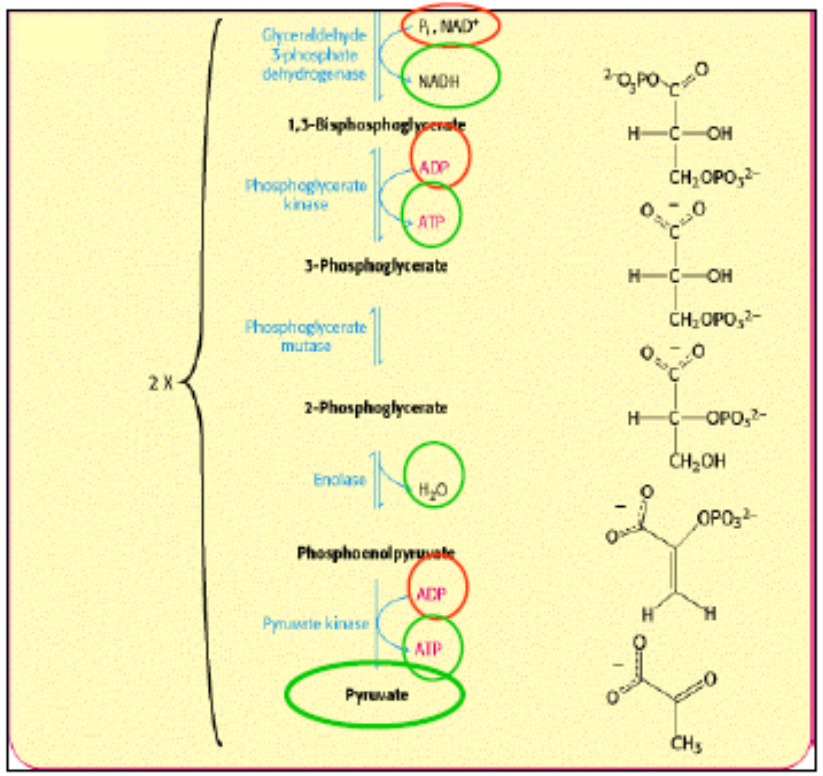
Etapa da reação glicolítica	$\Delta G'^{\circ}$ (kJ/mol)	ΔG (kJ/mol)
❶ Glicose + ATP ⟶ glicose-6-fosfato + ADP	−16,7	−33,4
❷ Glicose-6-fosfato ⇌ frutose-6-fosfato	1,7	0 a 25
❸ Frutose-6-fosfato + ATP ⟶ frutose-1,6-bifosfato + ADP	−14,2	−22,2
❹ Frutose-1,6-bifosfato ⇌ di-hidroxiacetona-fosfato + gliceraldeído-3-fosfato	23,8	−6 a 0
❺ Di-hidroxiacetona-fosfato ⇌ gliceraldeído-3-fosfato	7,5	0 a 4
❻ Gliceraldeído-3-fosfato + P_i + NAD^+ ⇌ 1,3-bifosfoglicerato + NADH + H^+	6,3	−2 a 2
❼ 1,3-Bifosfoglicerato + ADP ⇌ 3-fosfoglicerato + ATP	−18,8	0 a 2
❽ 3-Fosfoglicerato ⇌ 2-fosfoglicerato	4,4	0 a 0,8
❾ 2-Fosfoglicerato ⇌ fosfoenolpiruvato + H_2O	7,5	0 a 3,3
❿ Fosfoenolpiruvato + ADP ⟶ piruvato + ATP	−31,4	−16,7

Nota: $\Delta G'^{\circ}$ é a variação de energia livre padrão, como definido no Capítulo 13 (p. 507-508). ΔG é a variação de energia livre calculada a partir das concentrações reais dos intermediários glicolíticos presentes em condições fisiológicas nos eritrócitos, em pH 7. As reações glicolíticas de contorno da gliconeogênese estão mostradas em vermelho. As equações bioquímicas não são necessariamente equilibradas para H ou carga (p. 517).

Destinos do piruvato

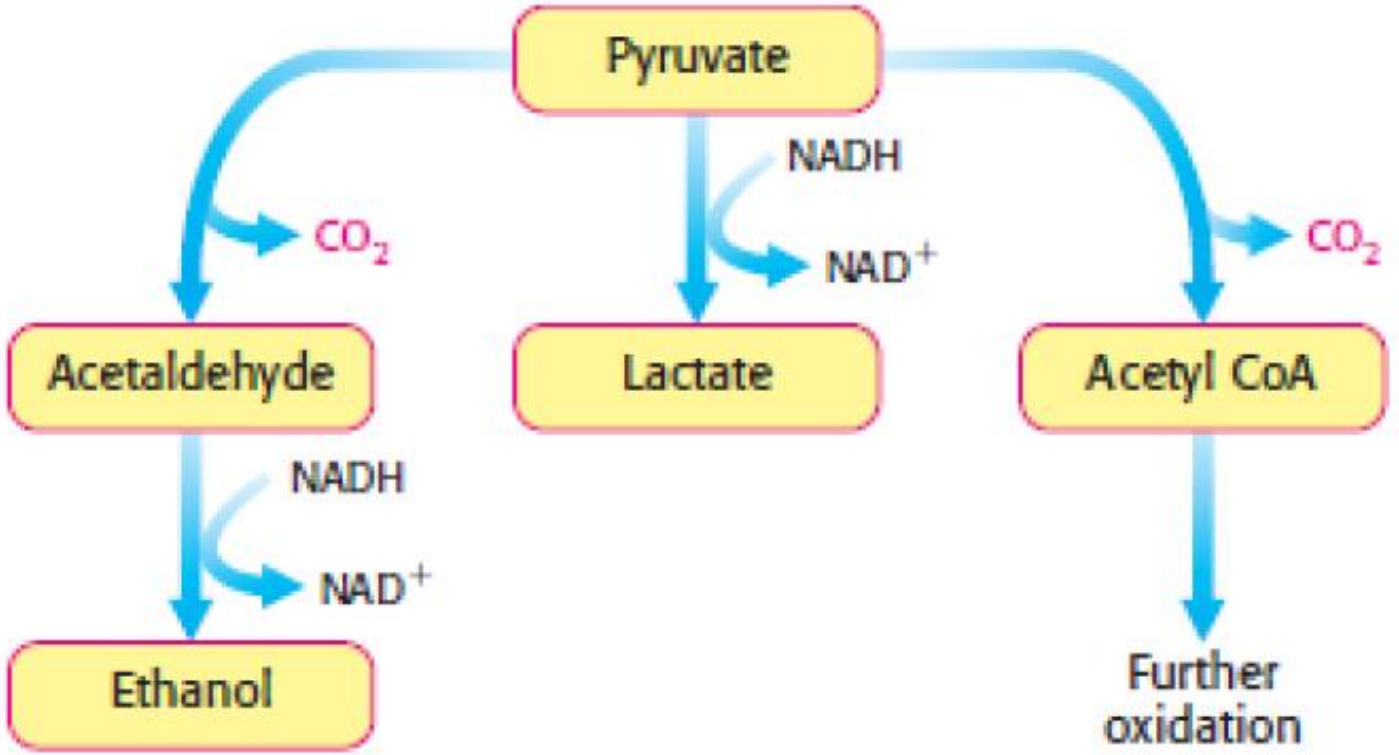


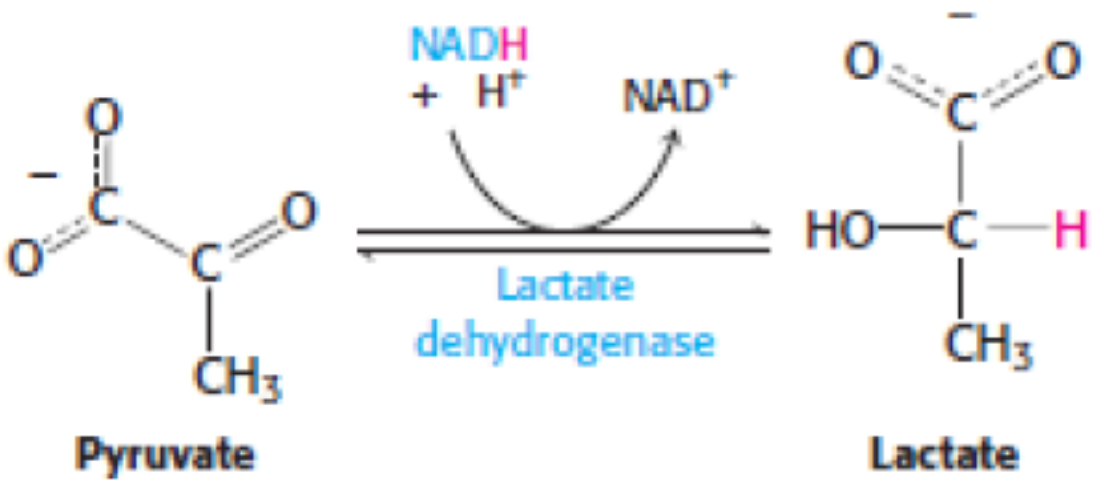
Transformação do Gliceraldeído em Piruvato

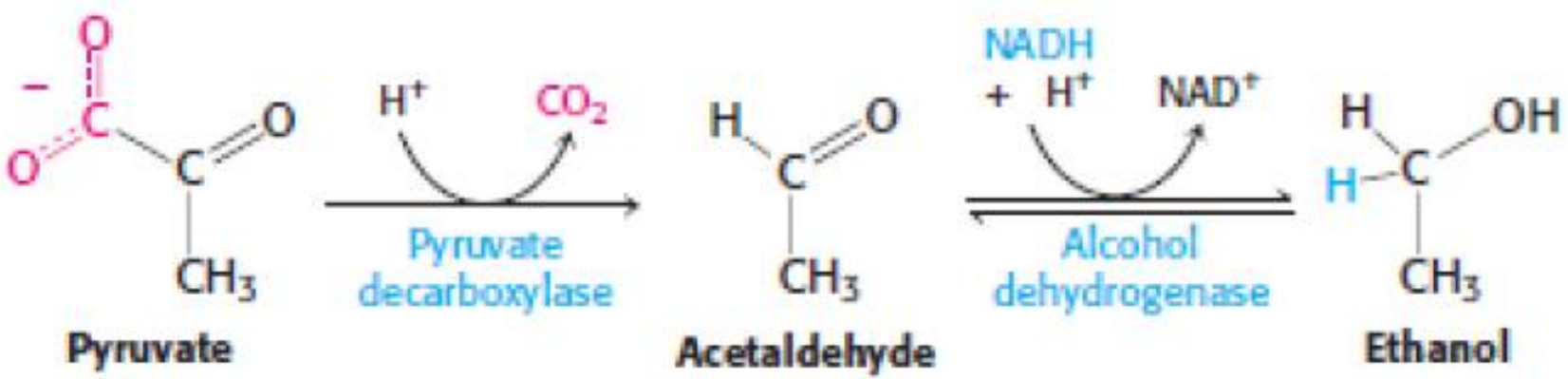


Fase compensatória
Requer NAD+

De onde vem o NAD^+ ?




NADH
+ H+
NAD+
Lactate
dehydrogenase
Pyruvate
Lactate


Pyruvate
H+
CO2
Pyruvate decarboxylase
Acetaldehyde
NADH + H+
NAD+
Alcohol dehydrogenase
Ethanol

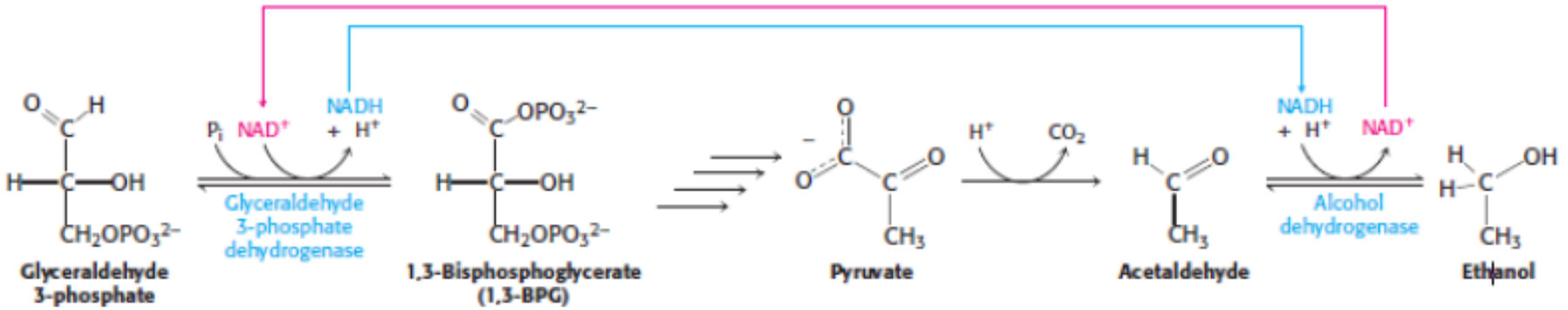
Glicose + 2NAD+ + 2ADP + 2Pi → 2Piruvato + 2NADH + 2H+ + 2ATP + 2H2O

2Piruvato + 2NADH +2H+ → 2NAD + 2CO2 +2Etanol

Glicose + 2ADP + 2Pi +2H+ → Etanol+ 2CO2+ 2ATP + 2H2O

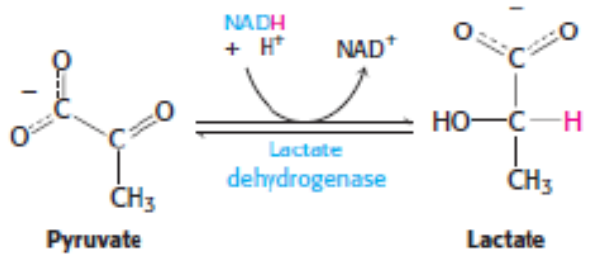
1	Glucose + ATP → glucose 6-phosphate + ADP + H^+
2	Glucose 6-phosphate ⇌ fructose 6-phosphate
3	Fructose 6-phosphate + ATP → fructose 1,6-bisphosphate + ADP + H^+
4	Fructose 1,6-bisphosphate ⇌ dihydroxyacetone phosphate + glyceraldehyde 3-phosphate
5	Dihydroxyacetone phosphate ⇌ glyceraldehyde 3-phosphate
6	Glyceraldehyde 3-phosphate + P_i + NAD^+ ⇌ 1,3-bisphosphoglycerate + NADH + H^+
7	1,3-Bisphosphoglycerate + ADP ⇌ 3-phosphoglycerate + ATP
8	3-Phosphoglycerate ⇌ 2-phosphoglycerate
9	2-Phosphoglycerate ⇌ phosphoenolpyruvate + H_2O
10	Phosphoenolpyruvate + ADP + H^+ → pyruvate + ATP

$$\text{Glucose} + 2\,P_i + 2\,\text{ADP} + 2\,H^+ \longrightarrow 2\,\text{ethanol} + 2\,CO_2 + 2\,\text{ATP} + 2\,H_2O$$



Glicose + 2NAD+ + 2ADP + 2Pi → 2Piruvato + 2NADH + 2H+ + 2ATP + 2H2O

1	Glucose + ATP ⟶ glucose 6-phosphate + ADP + H^+
2	Glucose 6-phosphate ⟷ fructose 6-phosphate
3	Fructose 6-phosphate + ATP ⟶ fructose 1,6-bisphosphate + ADP + H^+
4	Fructose 1,6-bisphosphate ⟷ dihydroxyacetone phosphate + glyceraldehyde 3-phosphate
5	Dihydroxyacetone phosphate ⟷ glyceraldehyde 3-phosphate
6	Glyceraldehyde 3-phosphate + P_i + NAD^+ ⟷ 1,3-bisphosphoglycerate + NADH + H^+
7	1,3-Bisphosphoglycerate + ADP ⟷ 3-phosphoglycerate + ATP
8	3-Phosphoglycerate ⟷ 2-phosphoglycerate
9	2-Phosphoglycerate ⟷ phosphoenolpyruvate + H_2O
10	Phosphoenolpyruvate + ADP + H^+ ⟶ pyruvate + ATP



$$\text{Glucose} + 2\,P_i + 2\,\text{ADP} \longrightarrow 2\,\text{lactate} + 2\,\text{ATP} + 2\,H_2O$$

TABLE 16.2 Examples of pathogenic obligate anaerobes

Bacterium	Result of infection
Clostridium tetani	Tetanus (lockjaw)
Clostridium botulinum	Botulism (an especially severe type of food poisoning)
Clostridium perfringens	Gas gangrene (gas is produced as an end point of the fermentation, distorting and destroying the tissue)
Bartonella hensela	Cat scratch fever (flu-like symptoms)
Bacteroides fragilis	Abdominal, pelvic, pulmonary, and blood infections

TABLE 16.3 Starting and ending points of various fermentations

Glucose	→	Lactate
Lactate	→	Acetate
Glucose	→	Ethanol
Ethanol	→	Acetate
Arginine	→	Carbon Dioxide
Pyrimidines	→	Carbon Dioxide
Purines	→	Formate
Ethylene glycol	→	Acetate
Threonine	→	Propionate
Leucine	→	2-Alkylacetate
Phenylalanine	→	Propionate

Note: The products of some fermentations are the substrates for others.

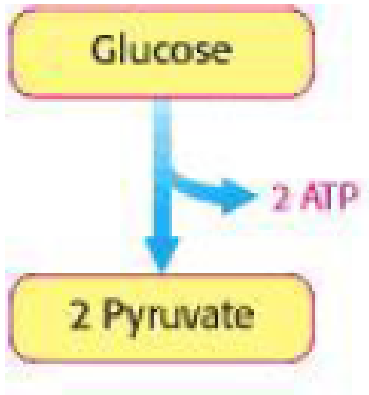
Controle Da Glicólise

A necessidade glicolítica varia de acordo com os diferentes estados fisiológicos

Há uma ativa degradação deste açúcar após uma refeição rica em carboidratos, assim como uma acentuada redução durante o Jejum.

Deste Modo, o grau de conversão de Glicose para o Piruvato é regulado, por forma a satisfazer as necessidades celulares

Controle Da Glicólise

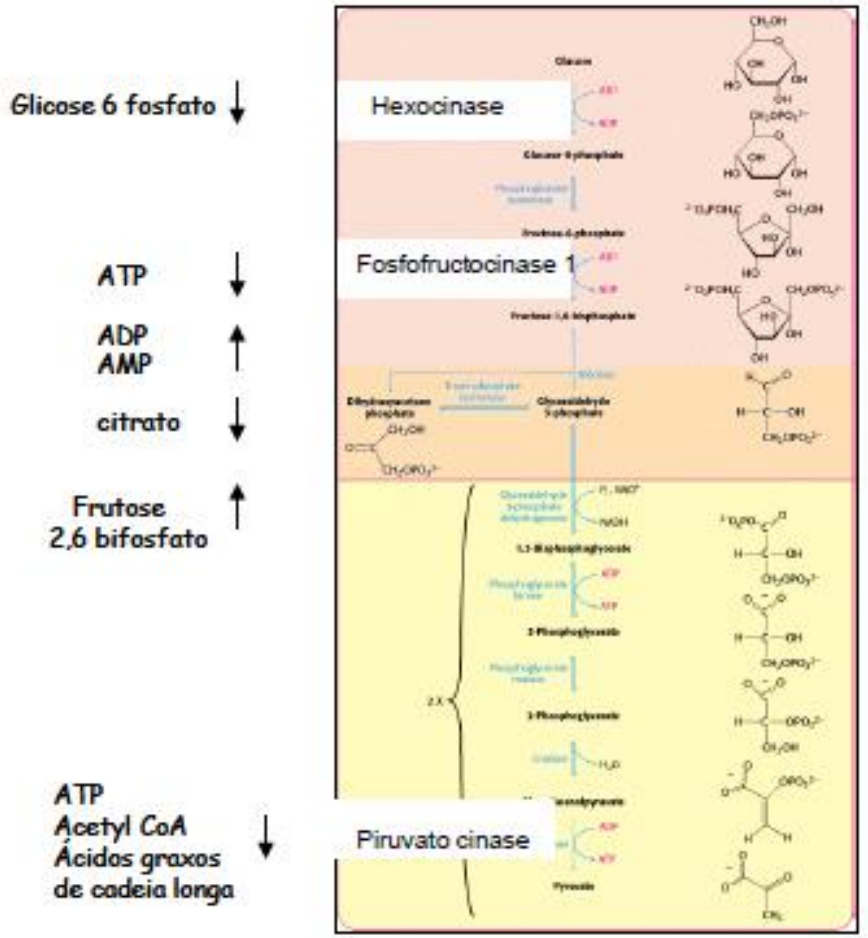


→ O Controle a **Longo Prazo** da Glicólise, particularmente no fígado, é efetuado à partir de alterações na quantidade de enzimas glicolíticas.

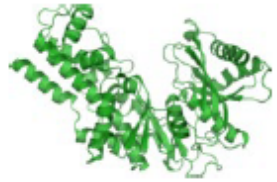
→ O Controlo a **Curto Prazo** é feito por alteração alostérica (concentração de produtos) reversível das enzimas e também pela sua fosforilação.

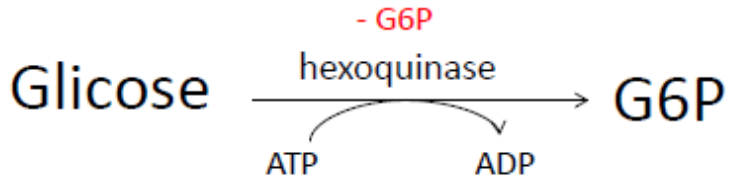
As enzimas mais propensas a serem locais de controle são as que catalisam as reações irreversíveis

Regulação alostérica destas enzimas



Hexoquinase / Glicoquinase



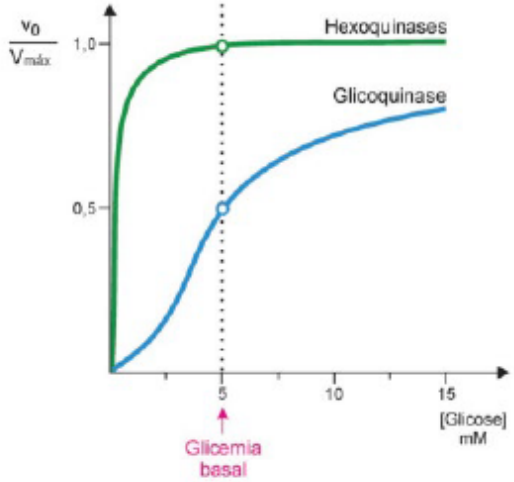


Hexoquinase: Km = 0,1 mM

Hexoquinase IV ou Glicoquinase (fígado): Km = 10 mM

[Glicoquinase] aumenta com insulina

Glicoquinase não é inibida por G6P



Fosfofrutoquinase

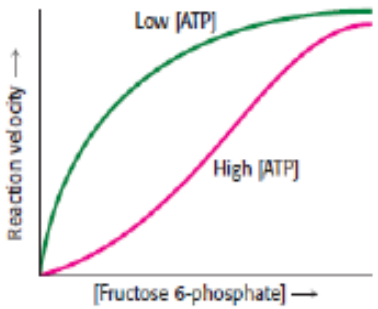
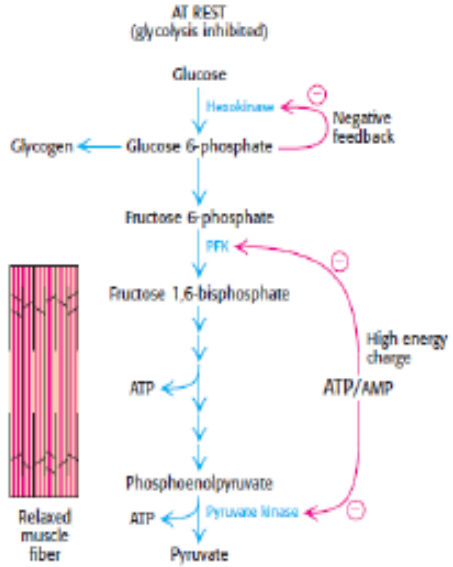
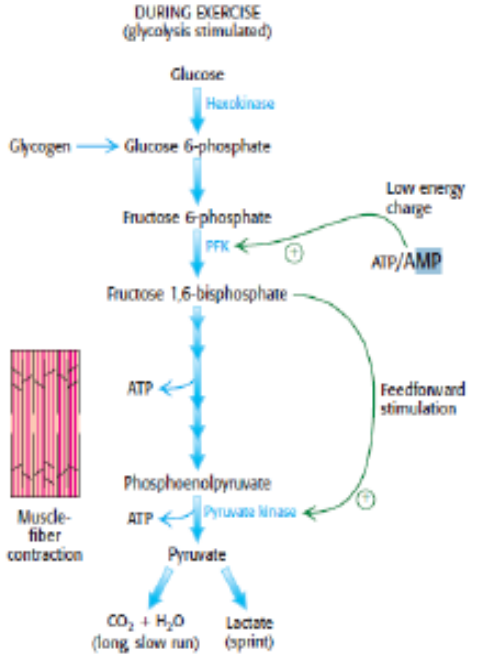
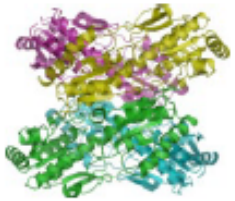


FIGURE 16.16 Allosteric regulation of phosphofructokinase. A high level of ATP inhibits the enzyme by decreasing its affinity for fructose 6-phosphate.





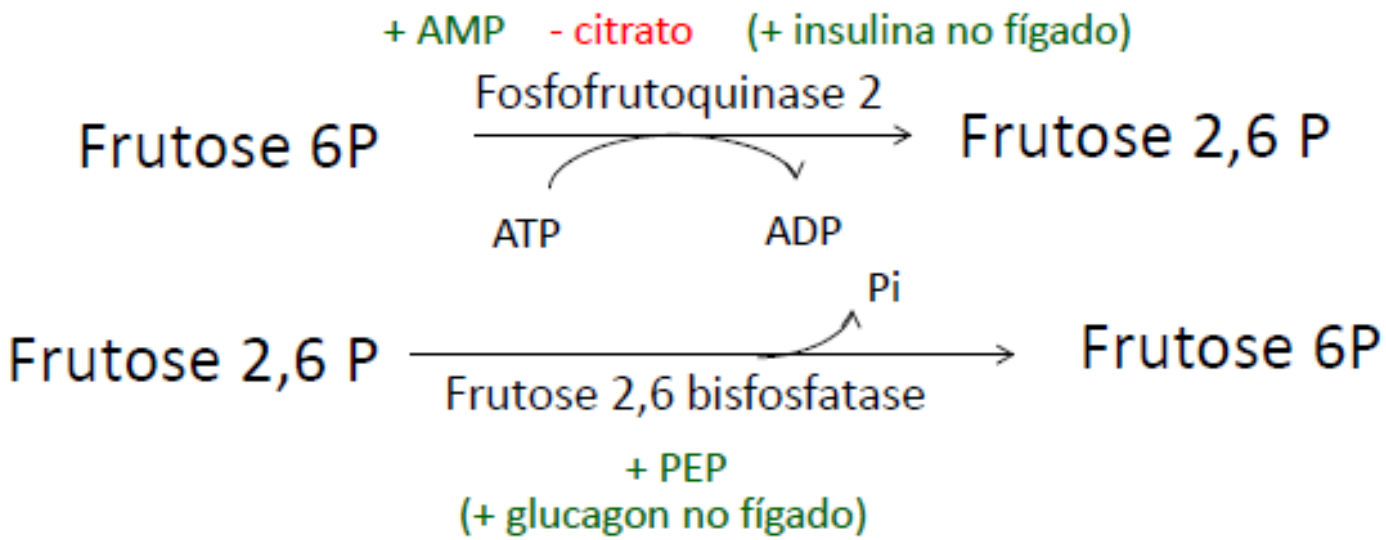
Fosfofrutoquinase 1

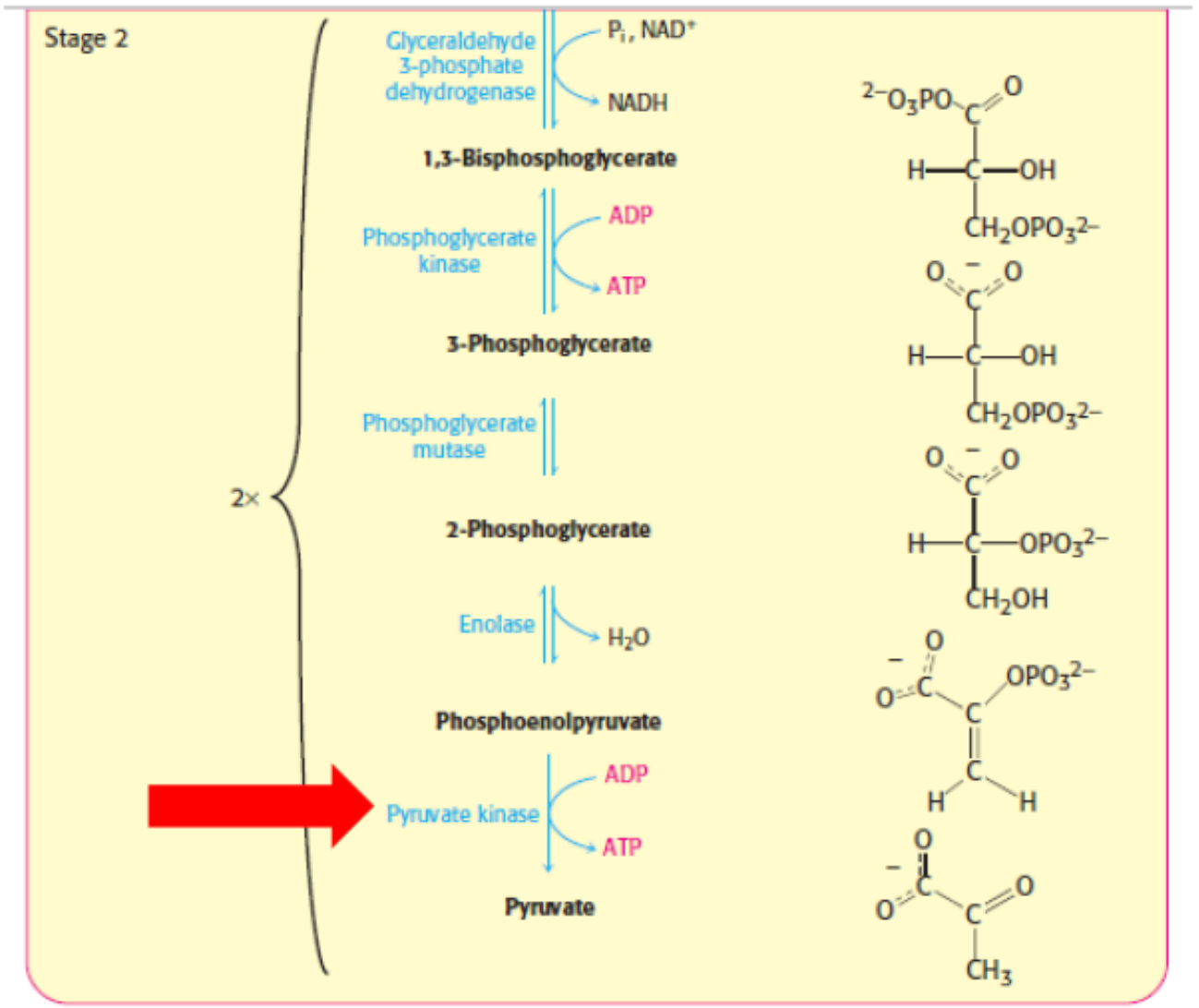


ATP
ADP
AMP
citrato
Frutose 2,6 bifosfato

Frutose 6P → (Fosfofrutoquinase 1; + AMP; **+ Frutose 2,6P**; - ATP; - citrato; ATP; ADP) → Frutose 1,6 P

Fosfofrutoquinase 2





Piruvato Quinase

(+ insulina no fígado) (- glucagon no fígado)
- alanina (no fígado) - ATP
+ Frutose 1,6P

PEP $\xrightarrow[\text{ADP} \quad \text{ATP}]{\text{Piruvato quinase}}$ PYR

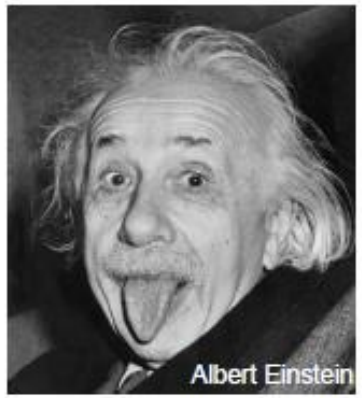
A insulina aumenta a conc. e atividade da piruvato quinase

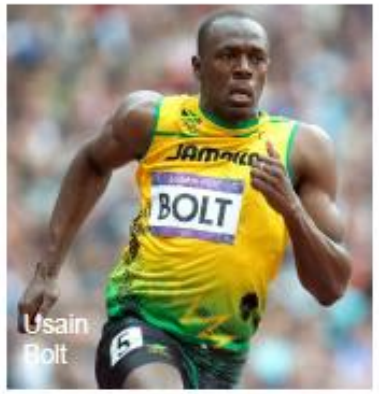
Alguns tecidos dependem da glicose como única fonte de energia

Hemáceas utilizam exclusivamente glicose para a produção de ATP (não tem mitocôndrias).
Produzem lactate constantemente

Músculo utiliza preferencialmente a glicose/glicogênio durante exercício físico intense.

O cerébro utiliza grandes quantidades de glicose.





Intolerância a Lactose