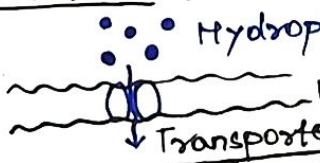
GLUCOSE TRANSPORTERS



SGLT

Sodium dependent Glucose transporters

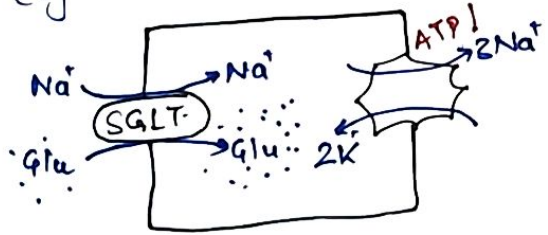
SGLT-1

- Proximal tubule of kidney
- Luminal side of intestine

SGLT-2

- Proximal tubule of kidney

Sec. active transport (Against the conc. gradient)



GLUT

Glucose-transporters

Insulin independent

- GLUT-1
- GLUT-2
- GLUT-3
- GLUT-5
- GLUT-6
- GLUT-7

Insulin dependent

GLUT-4

- Heart;
- Skeletal muscle
- Adipose tissue

Faciliated transport (Along the conc. gradient)

GLUT-1	RBC ; Retina ; Brain Kidney, Placenta ; Colon
GLUT-2	• Beta cells of pancreas • Liver • Intestine (Basolat. surf) • PCT
GLUT-3	Brain, Kidney, Placenta
GLUT-4	Heart, Skeletal muscle ; Adipose tissue
GLUT-5	• Small intestine (Luminal side) • Spermatozoa
GLUT-6	Spleen, Leukocyte
GLUT-7	Liver

Glycolysis :- * aka EMP pathway (Embden - Meyerhof - Parnas)

* Defined as sequence of reactions converting glucose to pyruvate or lactate (anaerobic); with production of ATP.

* Site :- Cytoplasm of cell

* Universal pathway in living cells (takes place both aerobically & anaerobically)

* End product of glycolysis = Pyruvate (in aeorbic condition) ; Lactate (in anaerobic condition)

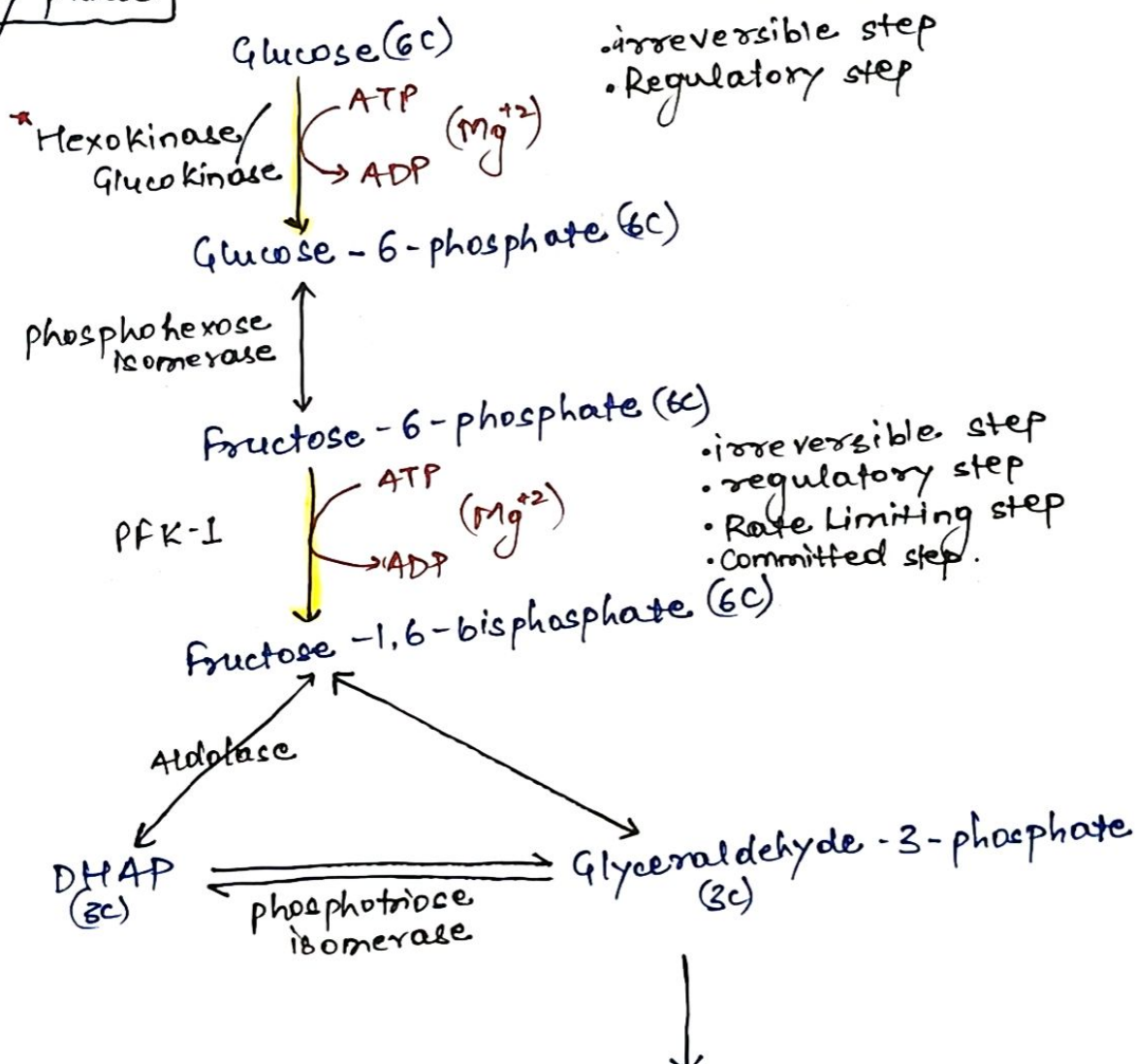
* Steps of glycolysis =

A) Energy investment phase / Preparatory phase
(•ATP is utilised)

B) Splitting phase

C) Energy generation phase / Payoff phase
(ATP is generated)

Preparatory phase



Payoff phase

2× Glyceraldehyde-3-phosphate (3C)

iP → NAD+ → NADH + H+ ×2

Glyceraldehyde-3-phosphate dehydrogenase

2× 1,3-BPG (1,3-Bisphosphoglycerate) (3C)

phosphoglycerate kinase: ADP (Mg+2) → ATP ×2

Substrate Level phosphorylation

2× 3PG (3-Phosphoglycerate) (3C)

phosphoglycerate mutase

2× 2PG (2-phosphoglycerate) (3C)

Enolase: H_2O ← (Mg+2)

2× Phospho Enol Pyruvate (3C) (PEP)

Pyruvate kinase: ADP (Mg+2) → ATP ×2

Substrate Level phosphorylation

- irreversible step
- regulatory step
- Rate Limiting step

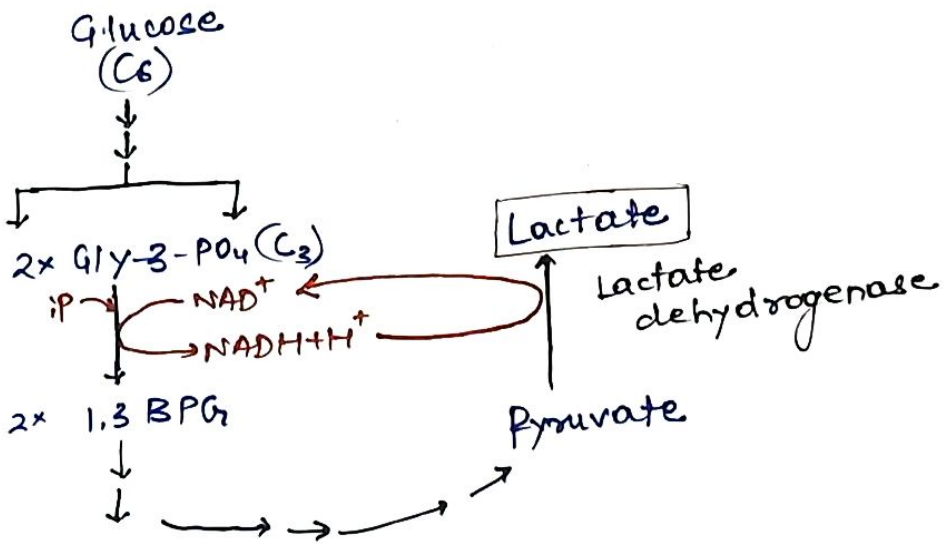
2× Pyruvate (3C)

* Hexokinase & Glucokinase (Isoenzymes)

Hexokinase	Glucokinase
• High affinity ; Low Km (0.1mM)	• Low affinity ; High Km (10mM)
• Catalyses phosphorylation of various hexoses (glucose, fructose, mannose)	• Catalyses phosphorylation of only glucose
• Extra-hepatic tissues	• Site :- Liver, pancreas
• House-keeping enzyme (Always active)	• Inducible enzyme (induced by insulin)
• Inhibited by Glu-6-P	• Not inhibited by Glu-6-P

Anaerobic glycolysis

- No mitochondria (RBC)
- Lack of O_2 {exercising muscle / Heart ischemia}



∴ No net generation of $NADH+H^+$ in RBC (Anaerobic glycolysis)

Energetics

Aerobic glycolysis

Preparatory phase

- Hexokinase = 1 ATP
- PFK-1 = 1 ATP

[(-) 2 ATP]

Payoff phase

- Glyc-3-phos dehydrogenase = 2× NADH
  = 2× 2.5 ATP
  = (+) 5 ATP
- phosphoglycerate kinase = 2× 1 ATP = (+) 2 ATP
- Pyruvate kinase = 2× 1 ATP = (+) 2 ATP

[(+) 9 ATP]

Net ATP generated = **+7 ATP**

Anaerobic glycolysis

Preparatory phase

[(-) 2 ATP]

Pay off phase

[+2 ATP, +2 ATP] = [+4 ATP]

Net ATP gen. = **+2 ATP**

Energy from 1 glucose by Aerobic oxidation =

1. Aerobic glycolysis = 7 ATP
2. PDH = 2× NADH = 2×2.5 = 5 ATP
3. TCA cycle = 2×10 ATP = 20 ATP

Net gain = 32 ATP

Regulation of Glycolysis

Responsible enzymes :-

1. Hexokinase / Glucokinase
2. PFK (Rate Limiting Enzyme)
3. Pyruvate kinase

Hexokinase

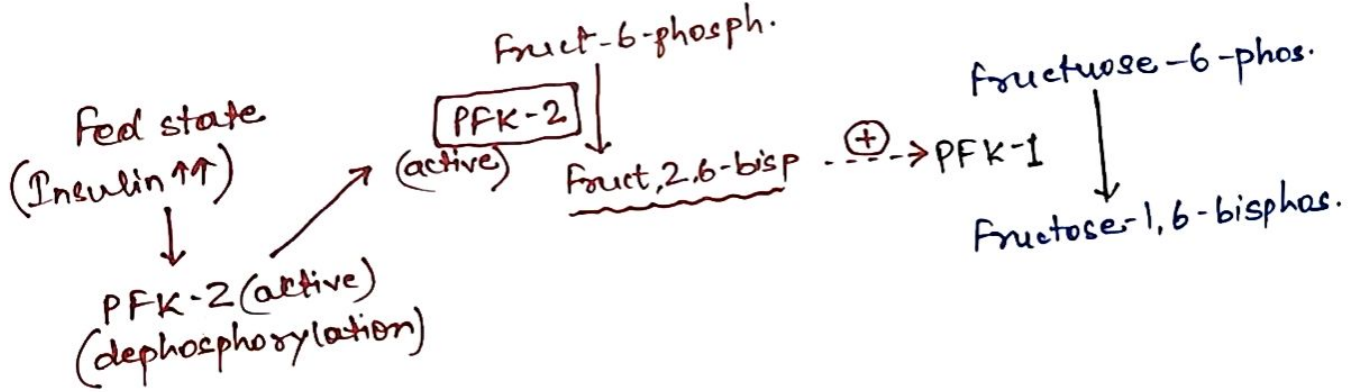
- House keeping enzyme
- Inhibited by Glu-6-P

Glucokinase

- Inducible enzyme
- Induced by Insulin.

PFK (Allosteric enzyme) *

- Allosteric activators = · Fructose 2,6-bisphosphate · ADP · AMP · P_i
- Allosteric inhibitors = · ATP · Citrate · H^+ (low pH)



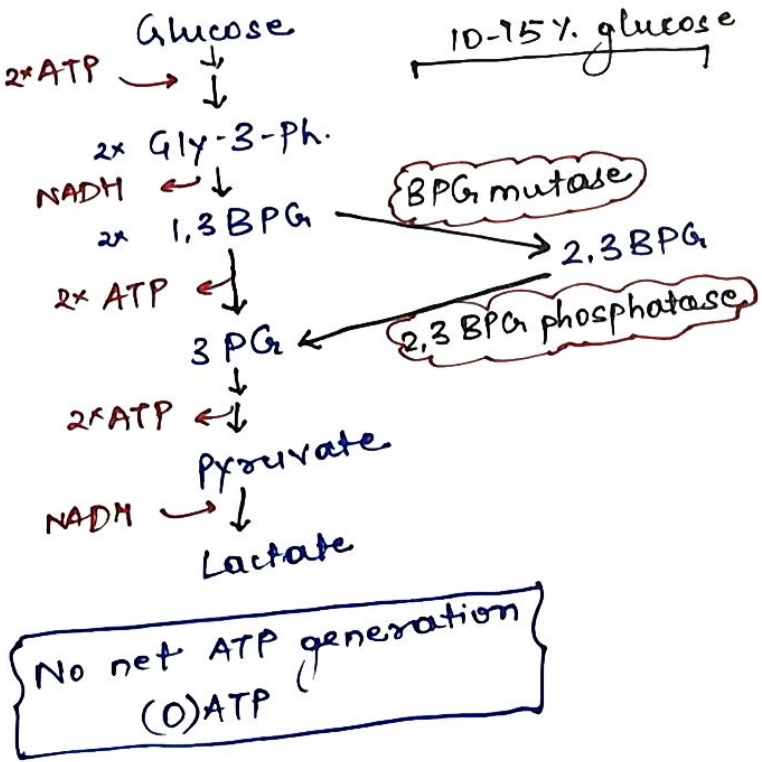
Inhibitors of glycolysis

Arsenate ⊖→ Glyc-3-ph dehydrogenase

Iodoacetate ⊖→

Fluoride ⊖→ Enolase

Rapoport-Leubering cycle (RBC)



No net ATP generation

(0) ATP

- Significance of 2,3 BPG

  - Hypoxia
  - High altitude
  - Fetal tissue
  - Anemic condition

  ⇒ 2,3 BPG binds to hemoglobin

  ⇓

  ↓ affinity of Hb with oxygen

  ⇓

  Oxygen delivered to the tissues ↑