11/10/23.

GLYCOLYSIS. (Essay.)

also known as. Embeden meyerhof pathway EM pathway.

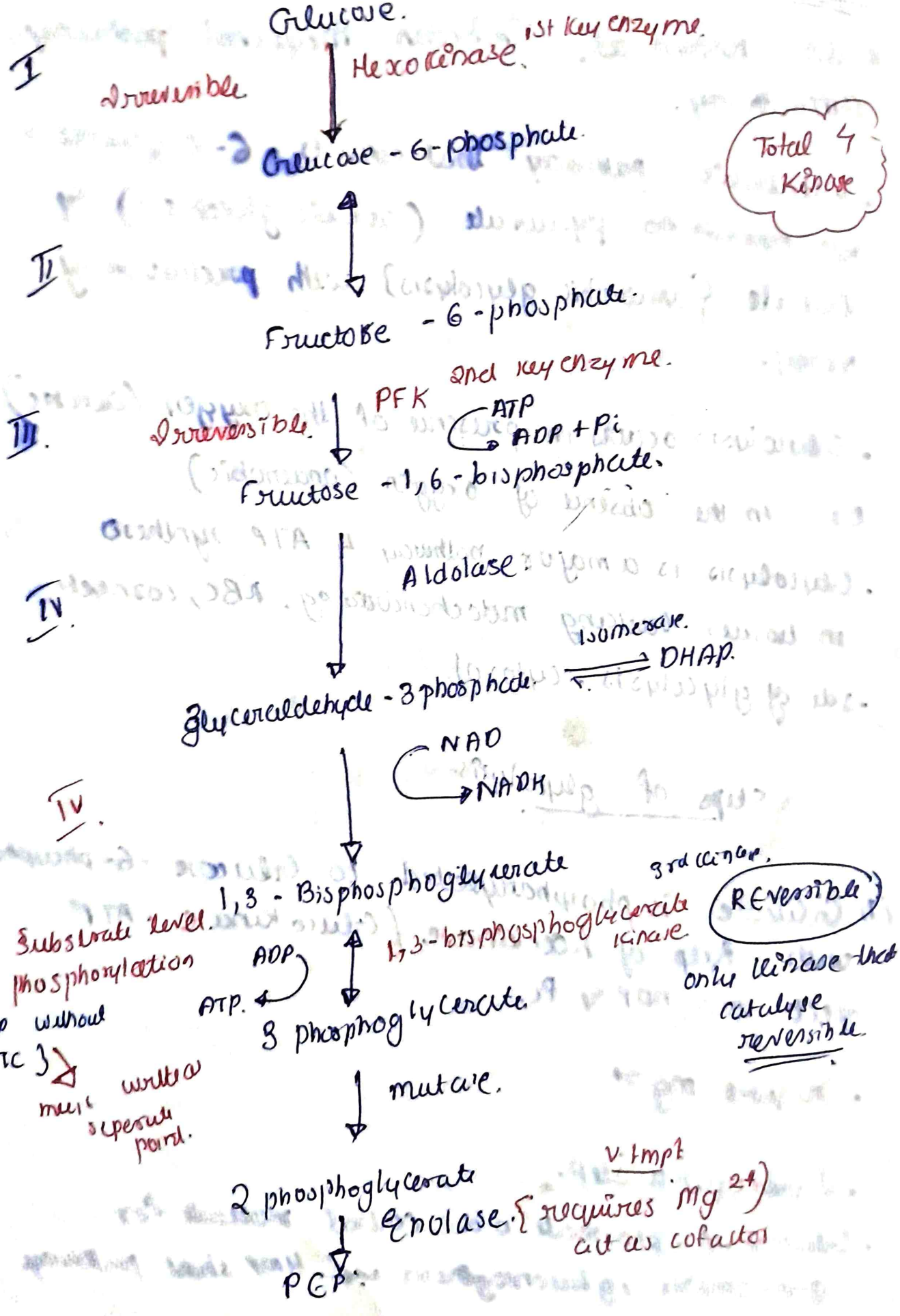
- metabolic pathway that converts 6-C glucose into ~~pyruvic acid~~ pyruvate (aerobic glycolysis) & lactate (anaerobic glycolysis) with production of energy.
- Glycolysis occurs in presence of the oxygen (aerobic) or in the absence of oxygen (anaerobic).
- Glycolysis is a major pathway & ATP synthesis in tissues lacking mitochondria eg: RBC, cornea.
- site of glycolysis: cytosol.

Steps of glycolysis.

(1) Glucose is phosphorylated to Glucose-6-phosphate with help of hexokinase / Gluco kinase. ATP split into ADP & Pi.

- require Mg^{2+}.

- Irreversible step.
- Glucose-6-phosphate is a central molecule for glycogenesis, gluconeogenesis and HMP shunt pathway


Glucose.
I
Irreversible
Hexokinase.
1st key enzyme.
Glucose - 6 - phosphate.
Total 4 Kinase
II
Fructose - 6 - phosphate.
III.
Irreversible.
PFK
2nd key enzyme.
ATP
ADP + Pi
Fructose - 1,6 - bisphosphate.
IV.
Aldolase.
Isomerase.
DHAP.
Glyceraldehyde - 3 phosphate.
NAD
NADH
IV.
Substrate level phosphorylation
1,3 - Bisphosphoglycerate
3rd reaction.
Reversible
1,3 - bisphosphoglycerate kinase
ADP
ATP.
3 phosphoglycerate.
only kinase that catalyse reversible.
{ATP without ETC}
mein written seperate part.
mutase.
2 phosphoglycerate
V. Imp
Enolase. { requires Mg 2+ act as cofactor
PEP.

PEP.

Irreversible. ADP. ATP ↑ ↓ pyruvate kinase. with kinase.

pyruvate.

lactate dehydrogenase.

lactic acid.

anaerobic process

Na-floride is taken as anticoagulant while taking glucose estimation.
why?

- the 3 irreversible steps are the key steps in glycolysis.

- 4 kinases
- 2 substrate level phosphorylations.

(2) Isomerisation of Glu - 6 - P (an aldose sugar) to fructose - 6 - P (a ketose sugar) catalyzed by phosphohexose Isomerase.

- Reversible

(3) Fructose - 6 - P is phophorylated to fructose - 1,6 - bisphosphate with help of phosphofructokinase (PFK).

- Irreversible step
- Rate limiting

(4) The 6-C fructose 1,6 bisphosphate is split into two 3-C compounds, Glyceraldehyde - 3 - phosphate & Dihydroxy acetone phosphate (DHAP).

- Reversible - ALDOLASE enzyme

- Interconversion -> triose phosphate Isomerase. of DHAP & 3PGAL.

(5) Phospho triose Isomerase catalyze the reversible interconversion of DHAP and glyceraldehyde-3-P.

- two molecules of glyceraldehyde-3-P are obtained from one molecule of glucose.

(6) Glyceraldehyde-3-dehydrogenase converts phosphate glyceraldehyde-3-P to 1,3-bisphosphoglycerate.

- A high energy compound (1,3 bisphospho glycerate) & NADH are formed.

- In anaerobic condition, NADH enters in ETC & generates 5ATP by oxidative phosphorylation.
- In the anaerobic condition this NADH is utilized by LDH.

(7) 1,3-bisphosphoglycerate Kinase act on 1,3-bisphosphoglycerate and convert it to 3-phospho glycerate with production of ATP.

- reversible (only Kinase reaction which is reversible in glycolysis)
- This step is a substrate level phosphorylation.

Substrate Level phosphorylation.

- phosphorylation at the level of substrate or formation of a high energy compound (phosphorylation) without entering into ETC, is coupled with conversion of substrate to product.

(8) 3-phospho glycerate is converted to 2-phospho glycerate by mutase enzyme.

Q. The high energy compound phosphoenol pyruvate is formed from 2-phosphoglycerate by enolase enzyme.

~~Phospho en~~ Flouride inhibit enolase action by removing Mg^{2+} ions

(9) PEP is converted to pyruvate with help of Pyruvate kinase enzyme.

→ substrate level phosphorylation

→ PEP is the high energy compound and generate ATP from ADP.

- This is another Example for Substrate level phosphorylation.
- 2 molecules of ATP are released in this step.

10. In the anaerobic condition pyruvate is converted to lactate in the presence of lactate dehydrogenase enzyme.

- This enzyme utilize NADH generated in glyceraldehyde-3-phosphate dehydrogenase step.

Glucose.

Step 1. Hexokinase. ATP, Mg^{2+}, ADP

ATP, ADP, should be touched.

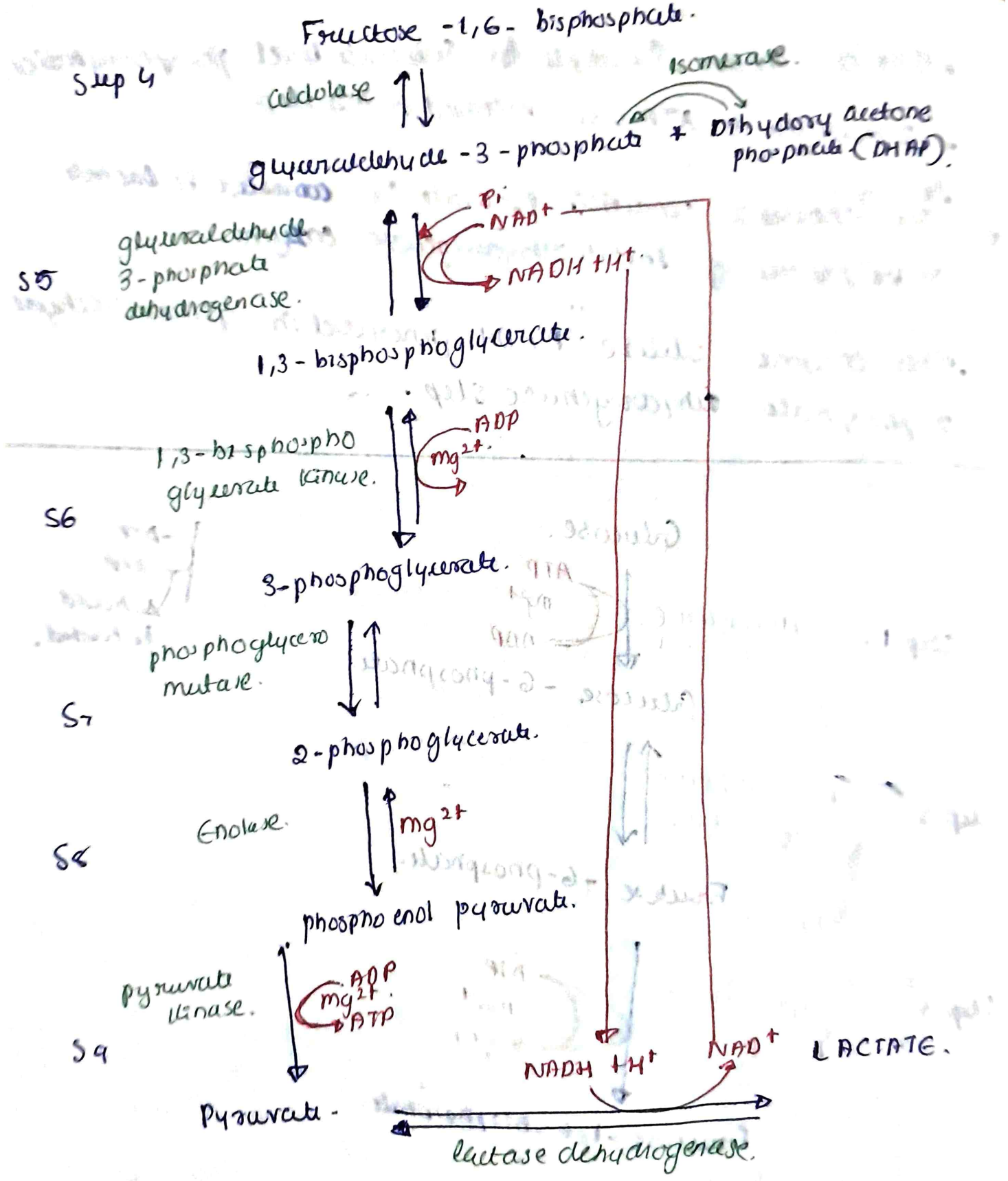
Glucose-6-phosphate.

Step 2 phospho hexose isomerase.

Fructose-6-phosphate.

Step 3 phospho fructo kinase. ATP, Mg^{2+}, ADP

Fructose-1,6-bisphosphate.


Fructose -1,6- bisphosphate.
Step 4
aldolase
Isomerase.
glyceraldehyde -3- phosphate + Dihydroxy acetone phosphate (DHAP).
Pi
NAD+
NADH+H+
S5
glyceraldehyde 3-phosphate dehydrogenase.
1,3 - bisphosphoglycerate.
ADP
Mg2+.
1,3-bisphospho glycerate kinase.
S6
3-phosphoglycerate.
phosphoglycero mutase.
S7
2-phosphoglycerate.
Enolase.
Mg2+
S8
phospho enol pyruvate.
pyruvate kinase.
ADP
Mg2+.
ATP
S9
NADH+H+
NAD+
LACTATE.
Pyruvate -
lactase dehydrogenase.

Sco.

12/10/23.

Glyceraldehyde -3 -phosphate.

↓ NAD → NADH +H+

1,3 - Biphosphoglycerate.

↓

pyruvate. → lactate.

pyruvate ⇏ can be blocked in absence of oxygen.

↓

acetyl CoA.

Regulation of Glycolysis.

Irreversible steps in Glycolysis.

Steps catalysed by.

Hexokinase or Glucokinase.

phosphofructokinase. (PFK)

pyruvate kinase.

Regulatory enzymes of glycolysis.

Enzyme	activation	Inhibition
HK	Insulin	G-6-P, Glucagon
PFK	Insulin, AMP, F-6-P, PFK-2, F-2-6-BP.	glucagon, ATP, Citrate, Low pH, Cyclic AMP.
PK	Insulin, F-1,6-BP.	Glucagon, ATP, cyclic AMP.

product inhibition

covalent modification

product inhibition

PFK 2 & F-2,6-BP activate PFK1

#Insulin → hypoglycemic. ↓ reduce. ↓ glucose in blood.

activator: F 26 BP.

F-2,6-BP

F-6-P → PFK1 → F-1,6-BP

F-6-P → PFK(2) → F-2,6-BP → Fructose 2-6 bis phosphatase → Hydrolyse.

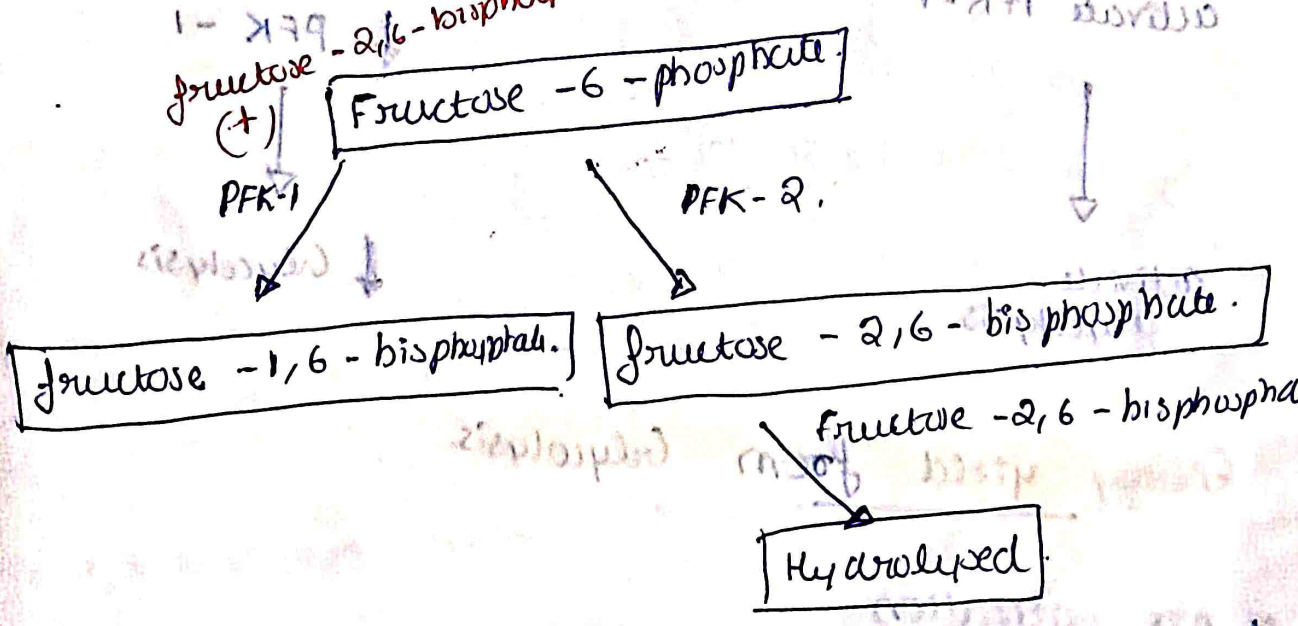
Short note.

Tandem enzyme / Bifunctional enzyme.

- phospho fructo kinase - 2 (PFK-2).
  and.
  fructose - 2,6 - Bis phosphate.

- these two enzymes are components of a single polypeptide; so called as bifunction enzyme / tandem enzyme.

- The activity of both enzymes are reciprocally regulated



↑ Glucose

↓

dephosphorylate.
PFK2

↓

PFK-2 is active

↓

Fructose - 2,6-BP.

↓

activate PFK-1

↓

activate glycolysis.

↓ Glucose.

↓

phosphorylated Fru 2,6 bisphosphatase

↓

Fruc-2,6-bisphosphatase is active

↓

↓ fructose, 26 BP

↓

↓ PFK-1

↓

↓ Glycolysis

Energy yield from Glycolysis.

1. ATP utilization

- 2 molecules of ATP per molecule of glucose.

II. ATP production (under aerobic condition)

A. Substrate level phosphorylation.

1. 1,3 - bisphosphoglycerate Kinase reaction - 2ATP

2. pyruvate Kinase reaction - 2ATP.

Total 4 ATP molecules

B. Oxidative phosphorylation.

- glyceraldehyde - 3 - P - dehydrogenase

2.5 × 2 = 5ATP

Net yield = 4+5 = 9 ~~- 2~~

9 - 2

= 7ATP

ATP production (under anaerobic condition).

1. 1,3 bisphosphoglycerate Kinase reaction - 2ATP.

2. pyruvate Kinase reaction - 2ATP.

Total 4ATP

Net yield : 4 - 2 = 2ATP.