HANDWRITTEN NOTES

DAMS

BIOCHEMISTRY

CRISP, CONCISE, CONCEPTUAL

Integrated Edition

Student first @DAMS

DAMS Publications

Published by Delhi Academy of Medical Sciences (P) Ltd.

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New Delhi-110 016
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ISBN : 978-93-89309-74-4

First Published 1999, Delhi Academy of Medical Sciences

Typeset by Delhi Academy of Medical Sciences Pvt. Ltd., New Delhi (India).

HOW TO MAKE BEST USE OF NOTES?

A Message by Mentor Duo Specially for you,

- *Read the notes thoroughly, they are absolutely concise, crisp & conceptual and hence it is best advised not to add a lot of extra information to them as that will dilute the quality.*
- *Images have been provided alongside to aid in better understanding and also help you solve image-based questions, these images have been specially picked by the faculty so have a high probability of being asked in exams.*
- *Notes are handwritten in a way to help make them easier to retain, a lot of tables, graphs and algorithms have been used to simplify the learning.*
- *While reading notes try and use the CFAQ technique —*
    A. *Use the C to denote concept part in the notes and ensure you are clear with this part in the first go if not then it's advisable to listen to this part of the video from your course.*
    B. *Use the F To denotes facts in your notes, it is okay if you can't remember them in first go but will need repeat reading. But these facts are important for exams as they could be integrated to clinical questions.*
    C. *Use A to denote applied parts, this is how concepts and facts are asked indirectly in exams. This will also help you develop MCQ solving skill.*
    D. *Use Q to denote areas where faculty has said it's a direct question or a PYQ or a potential question.*
- *This technique will help you summarize your notes In way that your second reading will become easy and faster.*
- *Active space has been provided with these notes to make your own annotations alongside and this will help you maintain one single notebook for one subject.*
- *Try and solve MCQs with every topic from DQB. Your goal should be to start with at least 30 MCQs every day and then increase to at least 50 MCQs every day. Also, when you do a topic wrong write it alongside the notes that this topic needs to be read again but mark only the specific area that you have done wrong not the whole topic.*
- *After the topic is covered then in the active space try and summarize the topic in the form of mind map. This will help in active recall and make your revision easier.*

Best Wishes & Happy Learning!!!!!

INDEX

BIOCHEMISTRY

Carbohydrate Chemistry & Metabolism

CARBOHYDRATE CHEMISTRY

Carbohydrates are aldehyde/ketone derivatives of polyhydric alcohols. Their general formula is $C_nH_{2n}O_n$.

CLASSIFICATION:

(1) MONOSACCHARIDES ($C_nH_{2n}O_n$): Simplest form of carbohydrates which cannot be further hydrolyzed into simpler carbohydrates.

Carbon Atoms	Aldose	Ketose
C-3	GLYCERALDEHYDE	DIHYDROXYACETONE
C-4	ERYHTROSE	ERYTHRULOSE
C-5	RIBOSE	RIBULOSE
	XYLOSE	XYLULOSE
C-6	GLUCOSE	FRUCTOSE
	MANNOSE	
	GALACTOSE	

(2) DISACCHARIDE: yield two molecules of same/different monosaccharide on hydrolysis.

DISACCHARIDE	UNITS	Enzyme
HOMO-DISACCHARIDES		
MALTOSE	Glu- Glu	Maltase
ISOMALTOSE	Glu- Glu	Isomaltase
CELLOBIOSE	Glu- Glu	
TREHALOSE	Glu- Glu	Trehalase
HETERO-DISACCHARIDES		
LACTOSE	Glu- Gal	Lactase
LACTULOSE	Gal - Fru	
SUCROSE	Gal - Fru	Sucrase

Note: Invert Sugar

$C_{12}H_{22}O_{11} + H_2O \rightarrow C_6H_{12}O_6 + C_6H_{12}O_6$

Sucrose → D-Glucose + D Fructose

$[\alpha]_D = +66.5°$ → $[\alpha]_D = +52.5°$ + $[\alpha]_D = -92.6°$

Reducing Substances

Benedict test

Sugars

All Monosaccharides
All Disaccharides

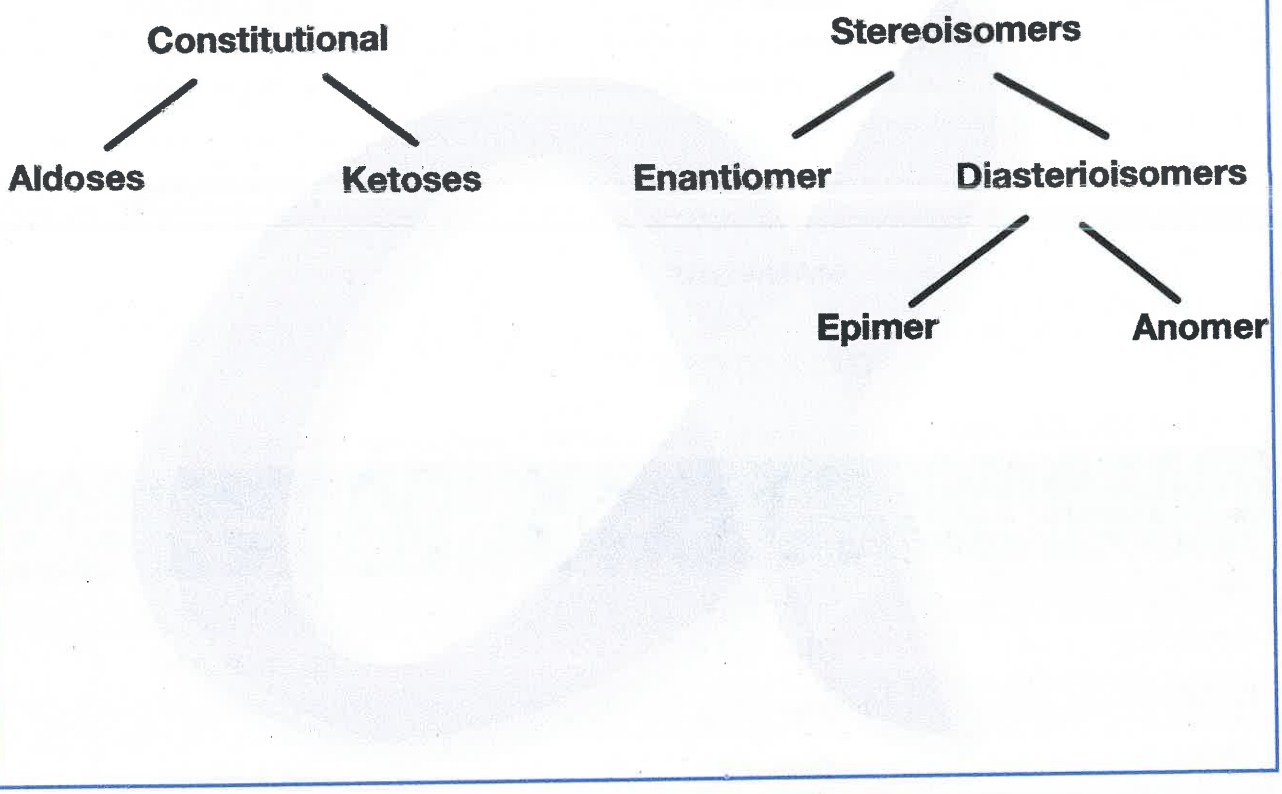
Other substances

- Creatinine
- Glutathione
- Uric acid
- Salicylic acid
- Ascorbic acid
- Homogenetisic acid

Exception

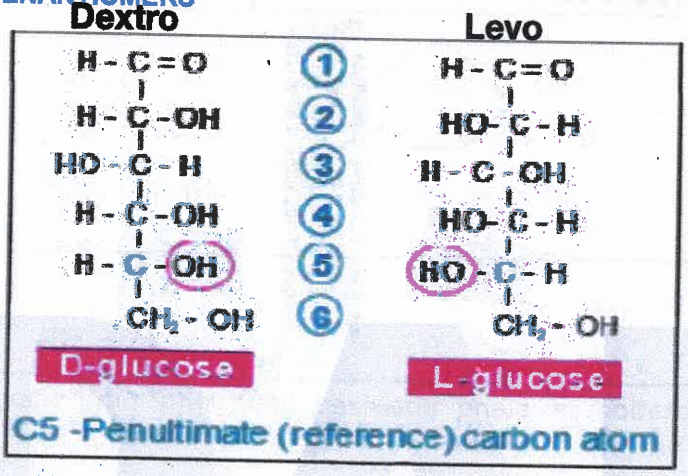
Non-Reducing Sucrose, Lactulose, Trehalose

ISOMERISM



1. **FUNCTIONAL/CONSTITUTIONAL ISOMER:** aldoses & ketose
2. **OPTICAL ISOMERS:** dextrorotatory (d or +sign), & levorotary (l or-sign)
3. **STEREOISOMERS**
   - **ENANTIOMERS:** D& L forms are enantiomers. enantiomers are mirror image of each other.

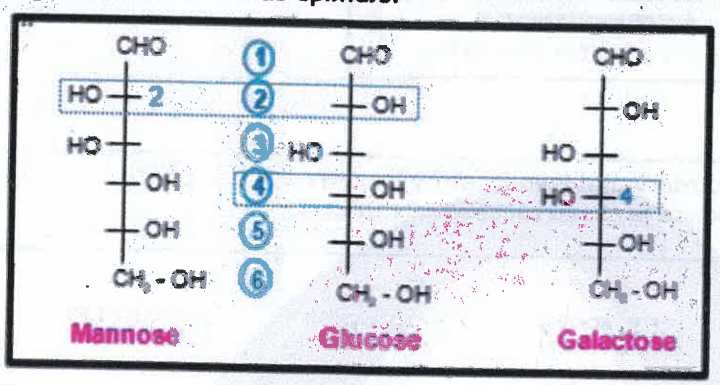
ENANTIOMERS



Glyceraldehyde- Parent/ Principal

EPIMERS:

Isomers differing as a result of variation in configuration of the –OH and –H on carbon atoms 2, 3 & 4 of glucose are known as epimers.

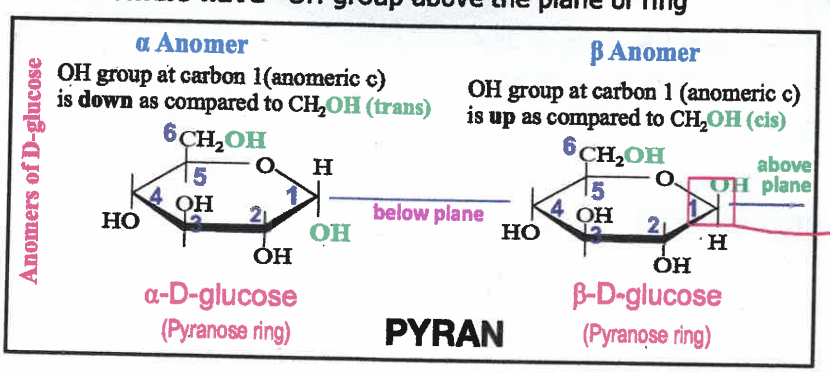


M - 2 - Mannose
A - 3 - Allose
G - 4 - Galactose
I - 5 - Iodose

ANOMERS: they differ in their spatial orientation of –H and –OH atoms with regard to first or anomeric carbon atom. two forms are there –

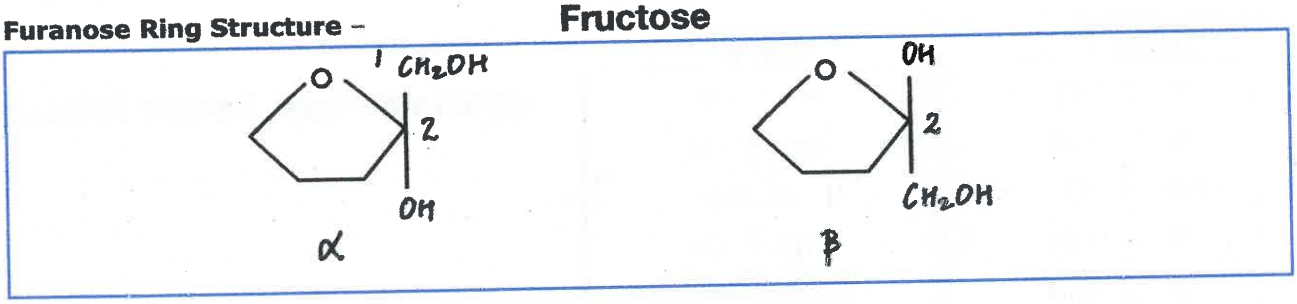
Alpha anomers have –OH group below the plane of ring

Beta anomers have –OH group above the plane of ring



Hemiacetal linkage

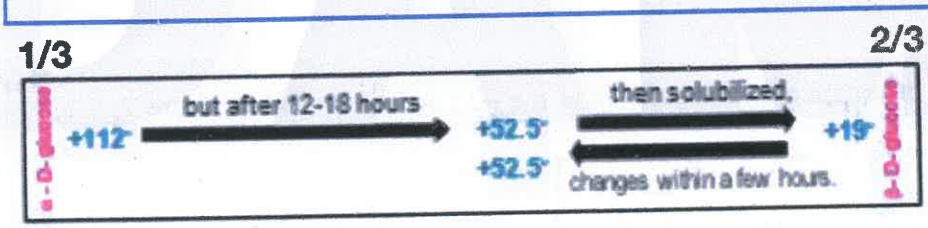
Furanose Ring Structure – **Fructose**



NOTE:

Mutarotation

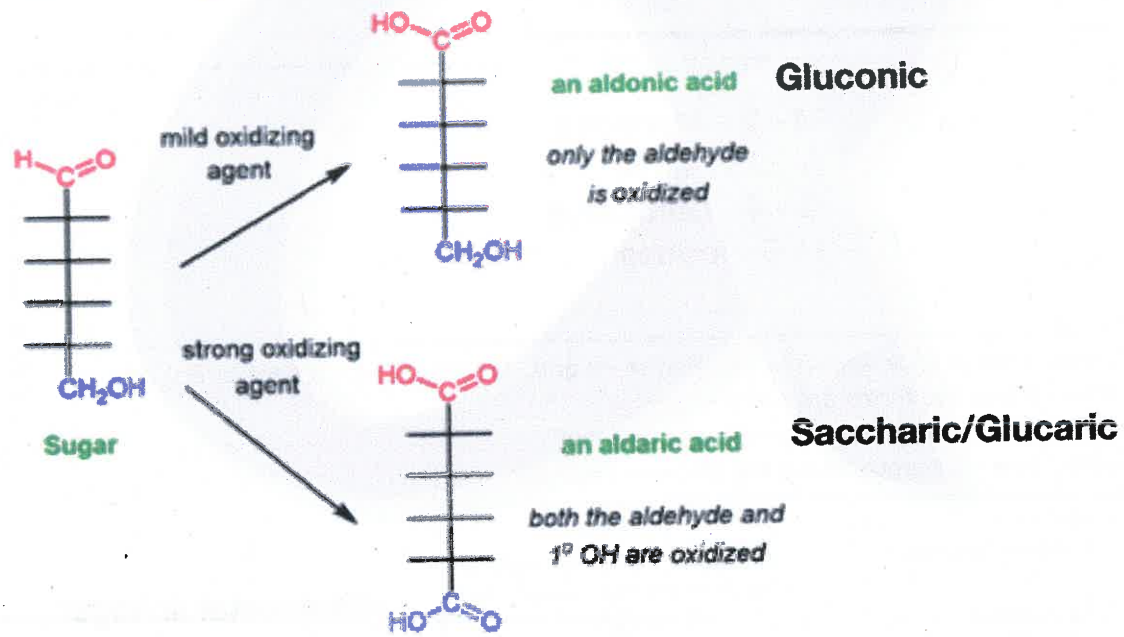
- Mutarotation is change in optical rotation of plane polarized light with time (Only characteristic of glucose solution)



NOTE:

Racemers: When equal amount of dextrorotatory and levo rotatory isomers are present the resulting mixture has not optical activity, such a mixture is called racemic mixture.

Oxidation of sugar:



Glucuronic acid

(3) OLIGOSACCHARIDES: yield 3-10 molecules of monosaccharides units on hydrolysis.
(4) POLYSACCHARIDES: yield more than 10 molecules of monosaccharides on hydrolysis.

HOMOPOLYSACCHARIDES:

STARCH	G-G-G-G- Amylose - Linear Amylopectin - Branched
CELLULOSE	Amylase - α • Salivary • Pancreatic
INULIN	Fructosan F-F-F-F-F β - GFR calculation
DEXTRIN	Partial hydrolysis of starch
DEXTRAN	Non-enzymatic aggregate of of Glucose
CHITIN	$(\beta\text{-N-Acetylglucosamine})_n$

ADD A NOTE ON DIETARY FIBRES -RDA 40g/200-Kcal/day

Soluble	Insoluble
Absorbs H2O	Does not absorb H2O

Beneficial effects of Dietary fibers:
1. Reduces constipation and hemorrhoid formation.
2. Increases bowel motility and reduces exposure of gut to carcinogens.
3. Lowers blood cholesterol.

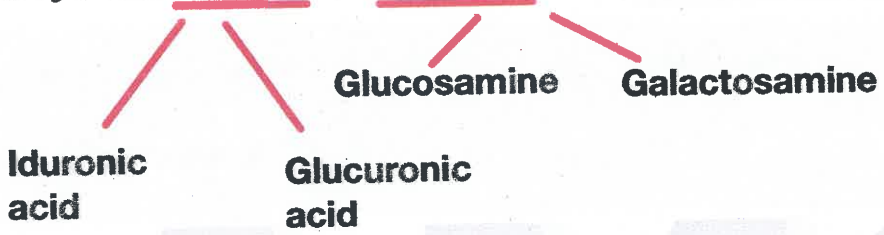
Side effect Interferes with mineral absorption.

QUES: INULIN LIKE FRUCTROSAN USED AS PREBIOTICS AS THEY ARE NON DIGESTIBLE.

a) Presence of α at C-2
b) Presence of β at C-1
c) Presence of β at C-2
d) Absence of digestive enzymes in upper GIT

HETEROPOLYSACCHARIDE/HETEROGLYCANS/ MUCOPOLYSACCHARIDE(MPS)/ GLYCOSAMINOGLYCANS (GAGS):

Polymers of Repeating units of acidic sugar and amino sugar arranged in a linear fashion.



Salient features of GAGS:

- Repeating disaccharides
- Linear in fashion
- H2O soluble
- Negatively physiological pH
- ECM - Extracellular matrix

GAGS of Physiological significance:

HYALURONIC ACID (Glucuronic acid & N-Acetyl Glucosamine)	ECM, Umbilical cord cartilage, synovial fluid, vitreous humor
CHONDROITIN SULFATE (Glucuronic acid & N-Acetyl Galactosamine)	Most prevalent GAG - in cartilage, tendon, ligaments
KERATAN SULFATE (Galactose & N-Acetyl Glucosamine)	No acidic sugar Corneal transparency
HEPARIN (Iduronic Acid & N-Acetyl Glucosamine)	Natural anti coagulant - released by mast cells
HEPARIN SULFATE (Iduronic Acid & N-Acetyl Glucosamine)\	GBM - Glomerular basement membrane
DERMATAN SULFATE (Glucuronic Acid/Iduronic Acid & N-Acetyl Glucosamine)	Widely distributed

Note: 1. KS does not have uronic acid, instead it has got galactose
2. All GAGS are sulfated. Exception is HA which does not have sulfation

TYPE OF MPS	NAME OF THE DISEASE	ENZYME DEFICIENT	URINARY FINDING
MPS I (AR)	HURLER SYNDROME	α- L-Iduronidase	DS+HS
MPS II(XLR)	HUNTER SYNDROME	Iduronate sulfatase	DS+HS
MPS III(AR)	SANFILIPPO	sulfatase	HS
MPS IV A(AR)	MORQUIOA	Galactosamine-6-sulfatase	KS+CS
MPS IV B(AR)	MORQUIO B	β-galactosidase	KS
MPS VI(AR)	MAROTEAUX-LAMY	arylsulfatase B	DS
MPS VII(AR)	SLY SYNDROME	β-Glucoronidase	DS+HS+CS
MPS IX(AR)	NATOWICZ	Hyaluronidase	HA

Disorder	Deficient Enzyme	Inheritance Pattern	High-Yield Associations
Hurler syndrome (mucopolysaccharidosis type I H)	α-L-Iduronidase	Autosomal recessive	Coarse facial features (gargoylism), hepatosplenomegaly, mental retardation, joint and skeletal abnormalities, cardiac disease, corneal clouding
Hunter syndrome (mucopolysaccharidosis type II)	Iduronate sulfatase	X-linked recessive	Same features but with milder mental retardation with aggressive behavior and no corneal clouding

Rate of Absorption of Sugars

Gal > Glu > Fru

Starch

↓

Dextrin

↓

Disaccharide

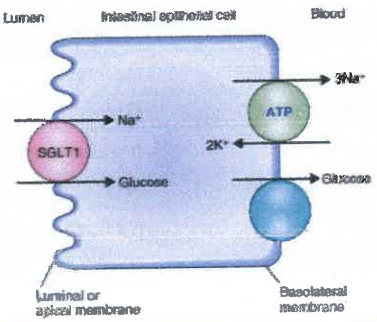
↓

Monosaccharide - Glucose / Galactose / Mannose / Fructose

Glucose Transporters: -

Sodium Dependent Unidirectional Transporter: -

SGLT 1



SGLT 2

Kidney - Renal reabsorption of glucose
Renal glycosuria - SLC5A-2 gene mutation

↓

GGLT-2

SGLT-2 inhibitors
Dapaglifozin
Empagliflozin

Faculitative Bidirectional Transporters: -

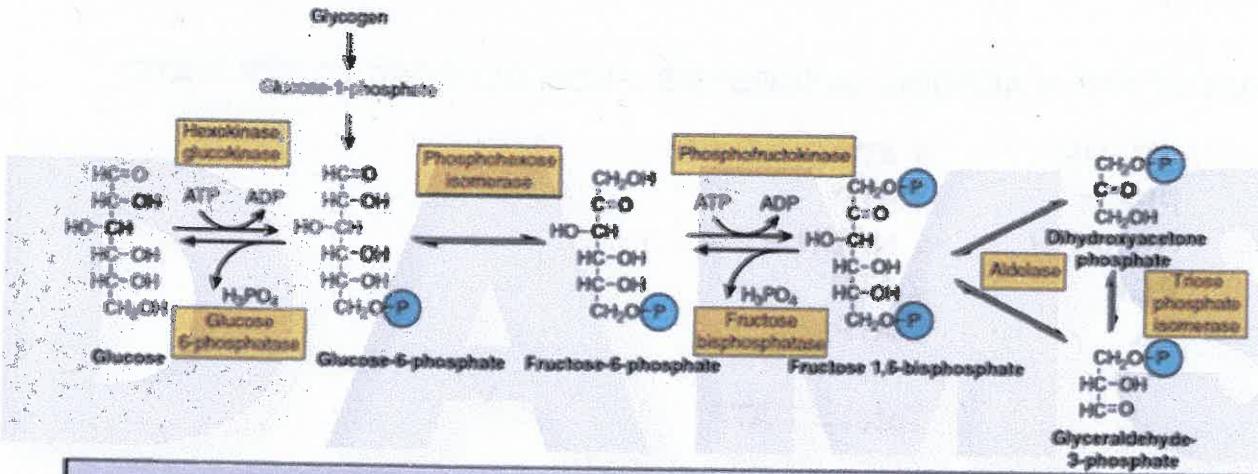
GLUT 1	Brain, RBC, Placenta, Colon, Kidneys
GLUT 3	Neurons, Placenta, Colon, Kidneys
GLUT 5	(Fructose) - Sperms, Small intestine

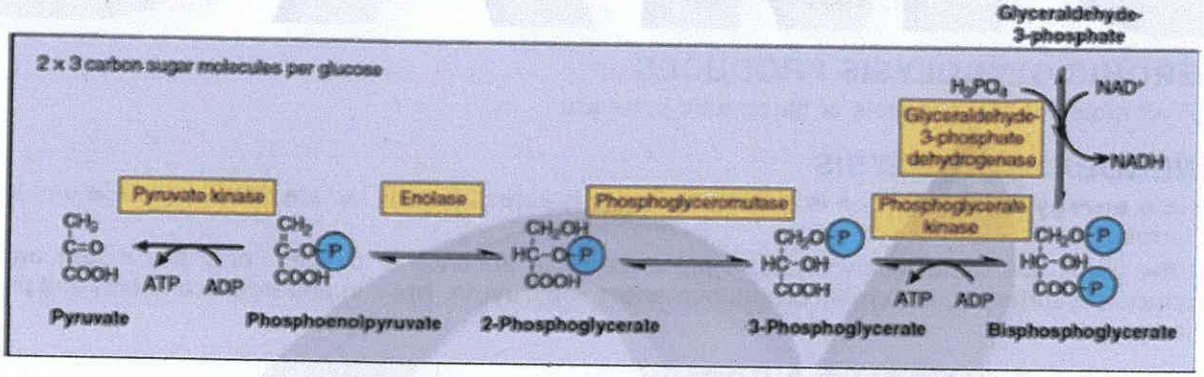
GLUT 2	GLUT 4
Liver, pancreas, small intestine	Heart, Adipose, skeletal muscle
II - Insulin dependent	Insulin dependent
K_m = 15.20 mM	K_m = 5mM

GLYCOLYSIS/ EMBDEN MEYERHOF PATHWAY

DEFINITION: Glycolysis is a process by which glucose molecules are metabolized through a series of enzymatic reactions into 2 molecules of pyruvate.

SITE OF GLYCOLYSIS: Cytosol





3 IRREVERSIBLE STEPS OF GLYCOLYSIS

1) PFK-1(Phosphofructokinase)
2) GK, HK (Glucokinase, Hexokinase)
3) PK (Pyruvate kinase)

Irreversible reactions of glycolysis:

3 reaction of glycolysis are irreversible.

They are:

Hexokinase

1) Glucose----------->Glucose –6-phosphate

Characteristic	Hexokinase	Glucokinase
1. Site	Extrahepatic	Hepatic
2. Substrate	Hexose	Glucose
3. Affinity	Increased	Decreases
4. Km for glucose	1 mM	5 mM
5. Inhibition by glucose-6-phosphate	Happens	Does not happen
6. Effect of feeding and insulin	No role	Induces

Phosphofructokinase-1

2) Fructose – 6- phosphate----------->fructose-1,6-bisphosphate

Pyruvate kinase

3) Phosphoenol pyruvate ----------->pyruvate

SUBSTRATE LEVEL PHOSPHORYLATION:

1) PGK
2) PK
— Glycolysis - Cytosol
3) Succinyl CoA thiokinase - TCA

GAIN OF ATP IN AEROBIC GLYCOSYSIS (FROM GLUCOSE TO PYRUVATE)

GK, HK	1 ATP
PFK-1	1 ATP
Gly3PDH	2 NADH = 2 X 2.5 = 5
PGK	2 ATP
PK	2 ATP
	Total = 7 ATP

AEROBIC GLYCOLYSIS PRODUCES

NET=7 moles of ATP per mole of glucose till pyruvate

ANEROBIC GLYCOLYSIS

At **low energy level** if oxygen is absent, pyruvate is acted upon by lactate dehydrogenase and lactate is formed.

All the steps are same in glycolysis in presence or in absence of oxygen. only the extent and end products are different, in aerobic condition product is pyruvate, while in anaerobic condition end product is lactate.

ANAEROBIC GLYCOLYSIS OCCURS IN

- RBC
- White muscle fiber
- Lens
- Retina
- Renal medulla

Pyruvate to lactate

Pyruvate + NADH $\xrightarrow{\text{Lactate dehydrogyenase}}$ Lactate + NAD

WARBURG EFFECT

Cancer - O2 - Anaerobic

PASTEUR EFFECT

INHIBITORY EFFECT OF O_2 ON GLYCOLYSIS IS CALLED AS PASTEUR EFFECT.

IT IS DUE TO DECREASED AMP/ATP RATIO. AMP HAS POSITIVE EFFECT ON PFK AND SO DECREASED LEVEL OF AMP CAUSES INHIBITION OFGLYCOLYSIS

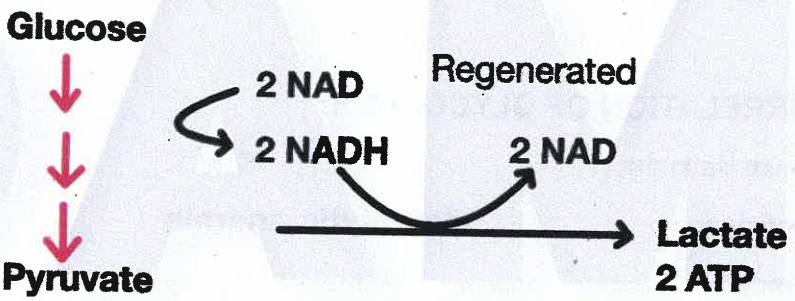
CRABTREE EFFECT

RELATIVE ANAEROBIOSIS PRODUCED WHEN GLUCOSE CONCENTRATION IS INCREASED IN CONSTANT SUPPLY OF OXYGEN

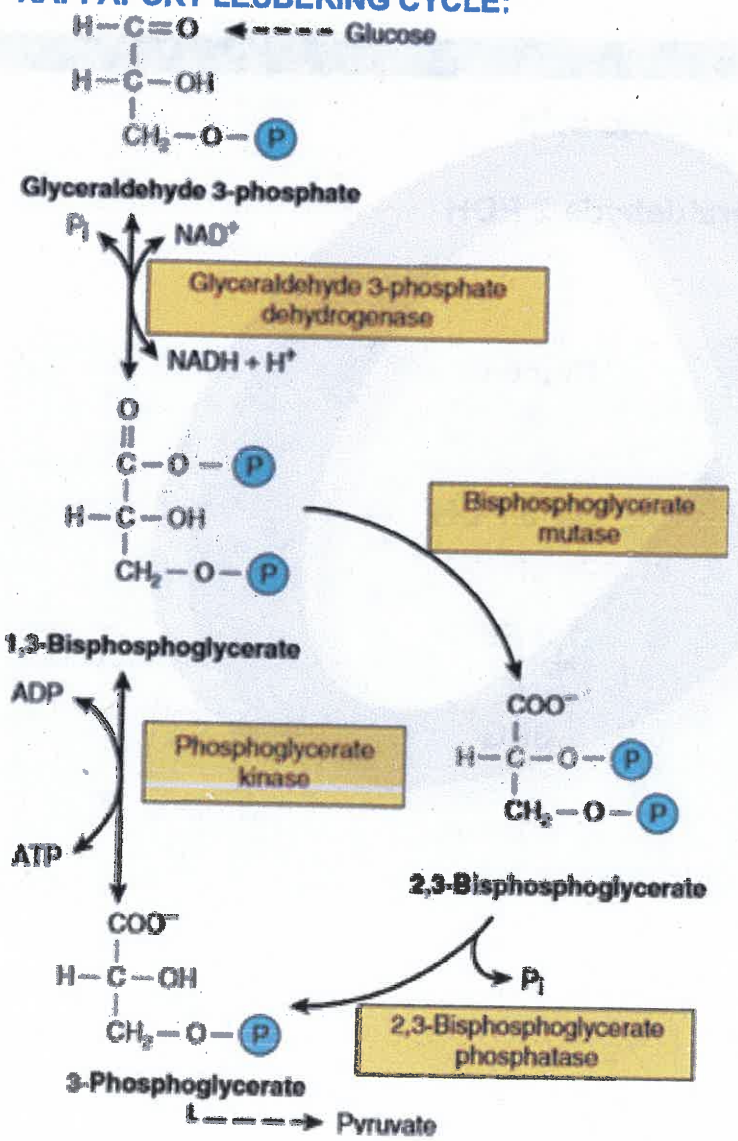
GAIN OF ATP IN ANEROBIC GLYCOSYSIS (FROM GLUCOSE TO LACTATE)

7 ATP - 2 NADH (5 ATP) = 2 ATP

Aerobic glycolysis produces NET=7 moles of ATP per mole of glucose till pyruvate
Anerobic glycolysis produces NET= 2 moles of ATP per mole of glucose.



RAPPAPORT LEUBERING CYCLE:



C - CO2
A - Acid
D - 2,3 DPG
E - Exercise
T - Temperature

GAIN OF ATP IN ANEROBIC GLYCOSYSIS IF RBC UNDERGOES RAPPAPORT LEUBERING CYCLE:

~~-1 ATP~~ - GK,HK
~~-1 ATP~~ - PFK-1
~~+2 NADH~~
~~+2 ATP~~ - PGK
~~+2 ATP~~
~~-2 NADH~~ LDH

Net ATP gain = 0

CLINICAL CORRELATION OF GLYCOLYSIS:

1. Pyruvate kinase deficiency
2. Aldolase A deficiency — **Hemolytic anemia**
3. PFK 1 deficiency

INHIBITOR OF GLYCOLYSIS:

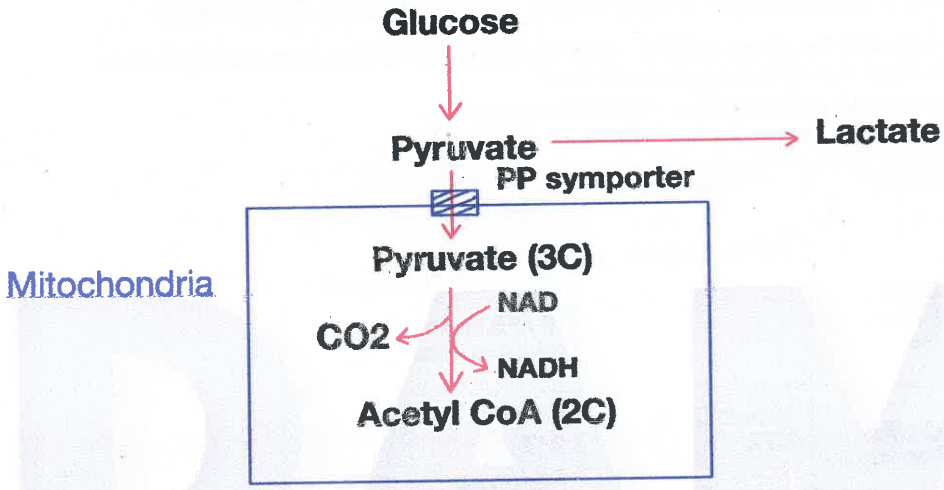
INHIBITOR	ENZYME INHIBITED
• Iodoacetate	**Inhibits lipoic acid** **Glyceraldehyde 3 PDH**
• Arsenite	**Inhibits PGK** **Glucose** ↓ **Gly 3 PDH** ⊖ **Arsenate** $AsO4^{3-}$ **1,3 BPG** *+1 ATP* ↓ **3PG** ↓ **Pyruvate**
• Fluoride	**ENOLASE**

Order of Draw for Evacuated Tube and Syringe Blood Collection

- Verify that you are using a tube with the correct additive. Tube top colors may vary between manufacturers.
- Do not use expired tubes or tubes that have dropped on the floor.
- GENTLY invert all tubes immediately after collection. DO NOT shake tubes.

CONTAINER	ADDITIVE	COMMONLY ORDERED TESTS
 Blood Culture Vials	Culture Medium	Blood Cultures (bacterial and/or fungal) (If AFB specified, call Lab for instructions)
 Light Blue (Plasma)  Partial Draw Top	Sodium Citrate 3.2%	Protime PTT Fibrinogen Coagulation Studies
 Red (serum)	Clot Activator (no gel)	
 Gold with Gel Barrier (serum)	Clot Activator Gel Serum Separator	CMP, Lipid Profile Hepatitis Profiles HIV Thyroid Profiles Therapeutic drugs
 Green (Plasma)  Green w/Gel (Plasma)	Lithium Heparin Lithium Heparin Sep (Gel) Sodium Heparin	**ABG**
 Lavender (plasma/ whole blood)	EDTA K2	CBC ESR (SED Rate) Hemoglobin A1C
 Pink (plasma/ whole blood)	EDTA K2	ABO/Rh
 Gray (plasma)	Sodium Fluoride/ Potassium Oxalate	Glucose Testing Alcohol

FATE OF PYRUVATE



Pyruvate to Acetyl CoA

Pyruvate dehydrogenate complex-
It is a multienzyme complex and contains 3 enzymes and 5 co- enzymes.

Enzymes:

a) Pyruvate dehydrogenase (E1)
b) Dihydrolipoyltransacetylase (E2)
c) Dihydrolipoyl dehydrogenase (E3)

Co-enzymes:

1) Thiamine - *Tender*
2) Lipoic acid - *Love*
3) Coenzyme A - *Care*
4) FAD - *For*
5) NAD - *Nancy*

CLINICAL CORELATION-

Wernicke Korsakoff Psychosis

G - Global confusion
O - Ophthalmoplegia
A - Ataxia

Alcoholism - B1,6,9,12 deficiency

Rx - i.v. Dextrose

Pyruvate to Acetyl CoA Regulation:

NADH = 2.5 ATP