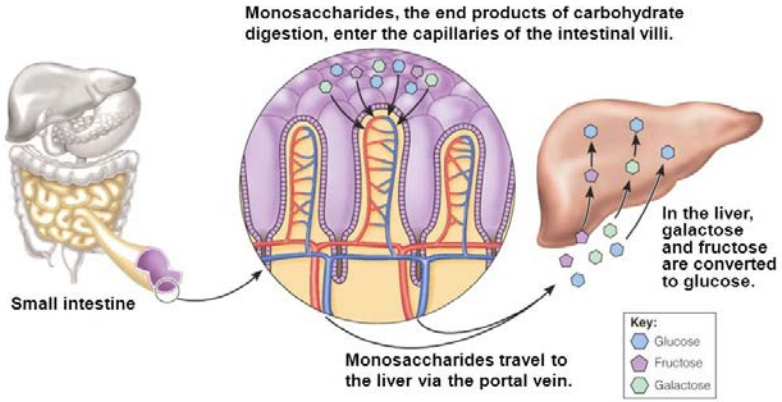
Fructose & Galactose Metabolism



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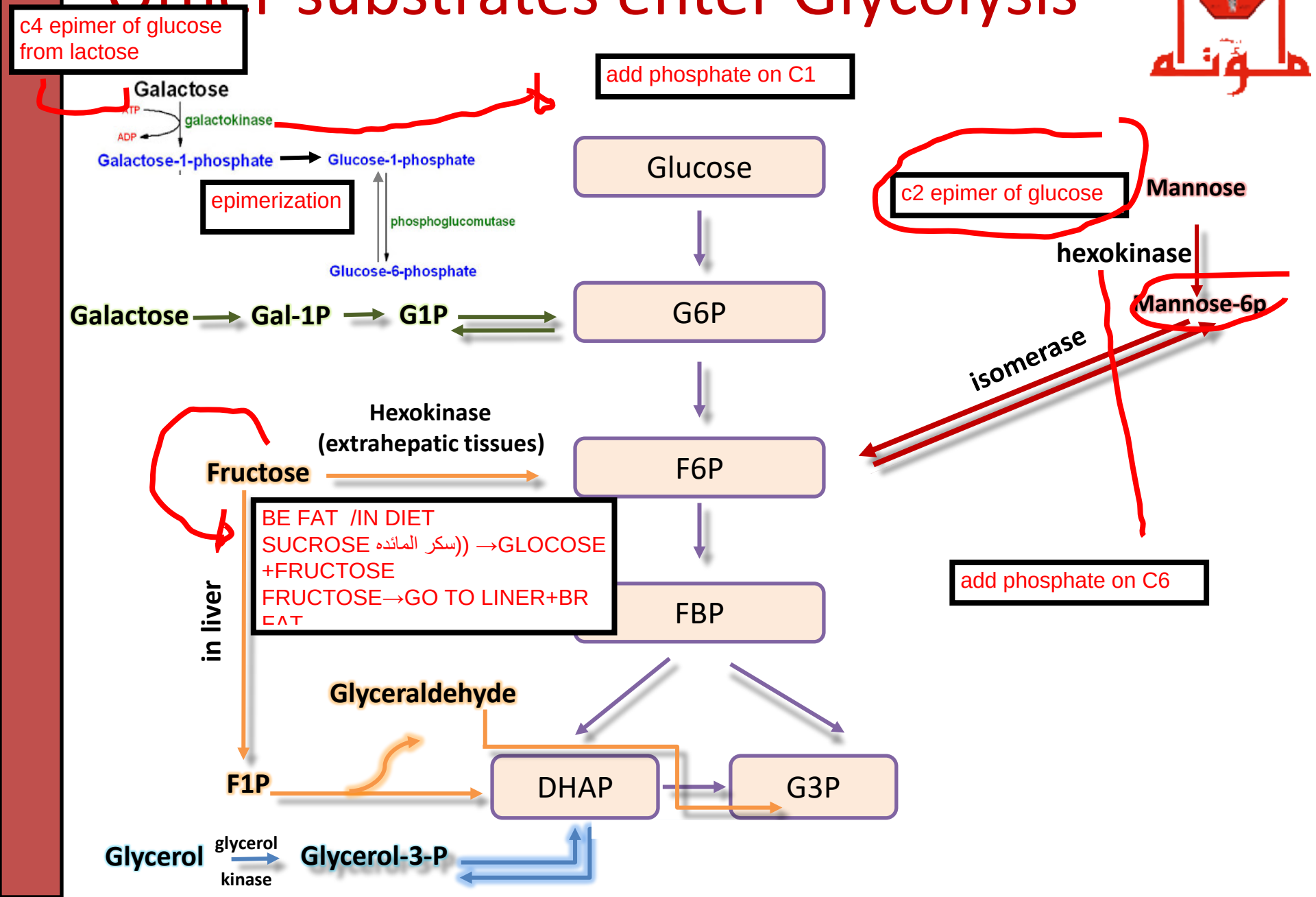
Other substrates enter Glycolysis



Fructose Sources

- **Dietary Sources of Fructose:**
  1. Sucrose (table sugar) consists of glucose and **fructose**
  2. Free fructose: fruits **(fruit sugar)** honey, vegetables
  3. Sweetener: High Fructose Corn Syrup **(HFCS)**

HIGH INTAKE OF FRUCTOSE FROM UN HEATHY SOURCE ASSOASSATION WITH
1-NAFLD /2- DIABTES /3-OBSETY
4-↑BP/5-↑ COLESTROL LEVEL
NEGATIVE IMPACT
3- السكر البديل بزيد كل الي فوق

THERE ARE THREE SOURSE OF FROCTOSE
1- SACROSE>GLOCOSE+ FRCTOSE + UNHEALTHY SOURCE →ALOT OF FRCTOSE SO IT WILL BE FAT
2- FRUTIS / HONEY
A-SMALLER AMOUNT THAN SACROSE
B-HIGH FIBER CONTENT SO ↓FRUCTOSE ABSORBTION
3- CORN FLEX/ SODA /CAKE ....

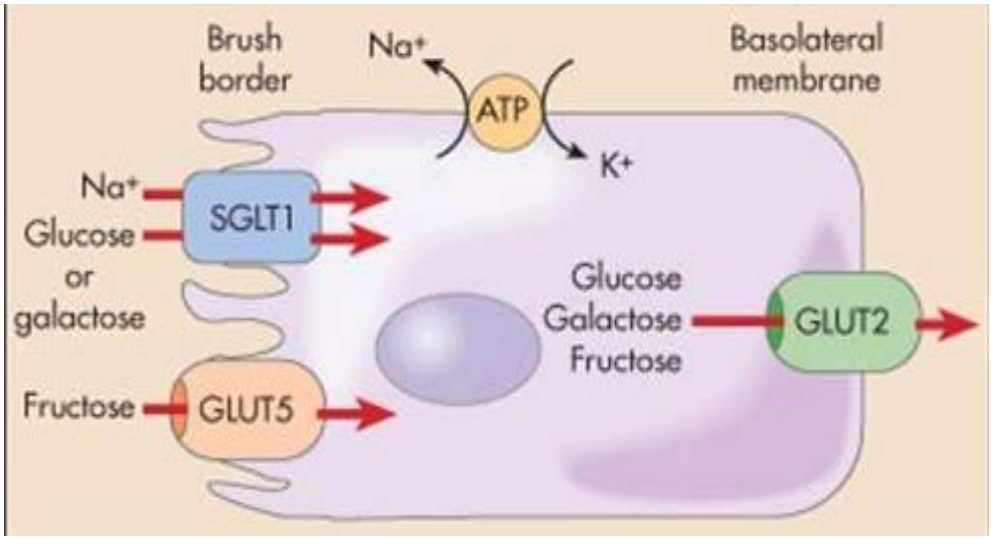
Fructose Absorption

NON INSULIN DEPENTENT

- Free fructose is absorbed from intestinal lumen through GLUT5 found at the apical membrane of the intestinal absorptive cells (enterocytes)
- Fructose then crosses to blood capillaries through GLUT2 at the basolateral membrane

NON INSULIN DEPENTENT

- Fructose absorption and entrance into cells is insulin independent
- Glucose and Galactose are absorbed via SGLT1 at the apical end and then through GLUT2 at the basolateral membrane.

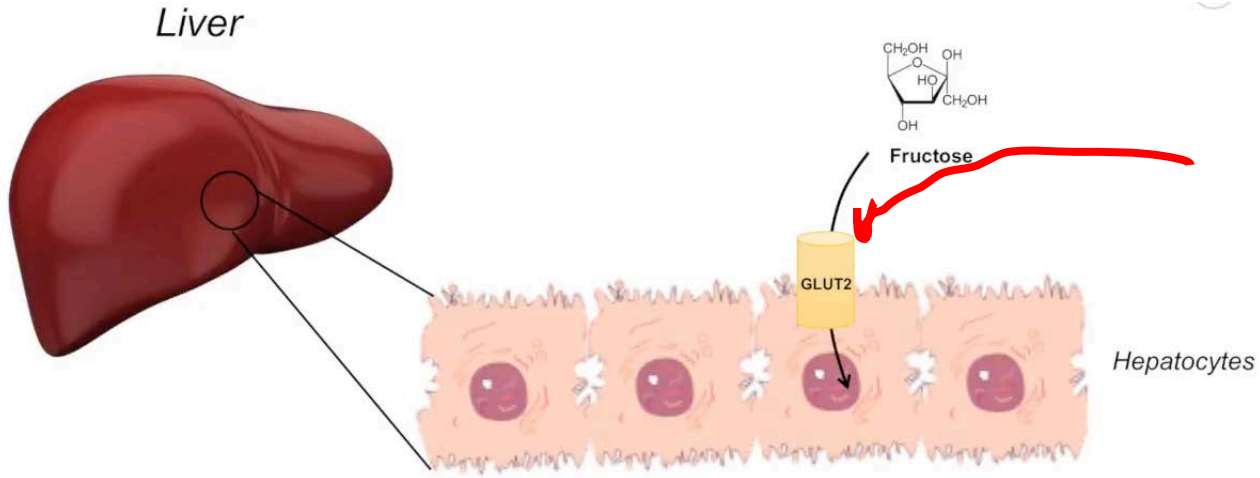


ABSORBTION OF GLUCOSE/GALCTOSE DEPENTENT ON SGLT1

Fructose Metabolic Pathways

- Fructose can be metabolized by one of two metabolic pathways:

1. Major Pathway (called Fructose-1-phosphate) in **Liver**



2. Minor Pathway in other tissues **(Extrahepatic cells like kidney and testis)**

the fructose is phosphorylated by hexokinase and the generated fructose-6-phosphate directly joins the glycolysis

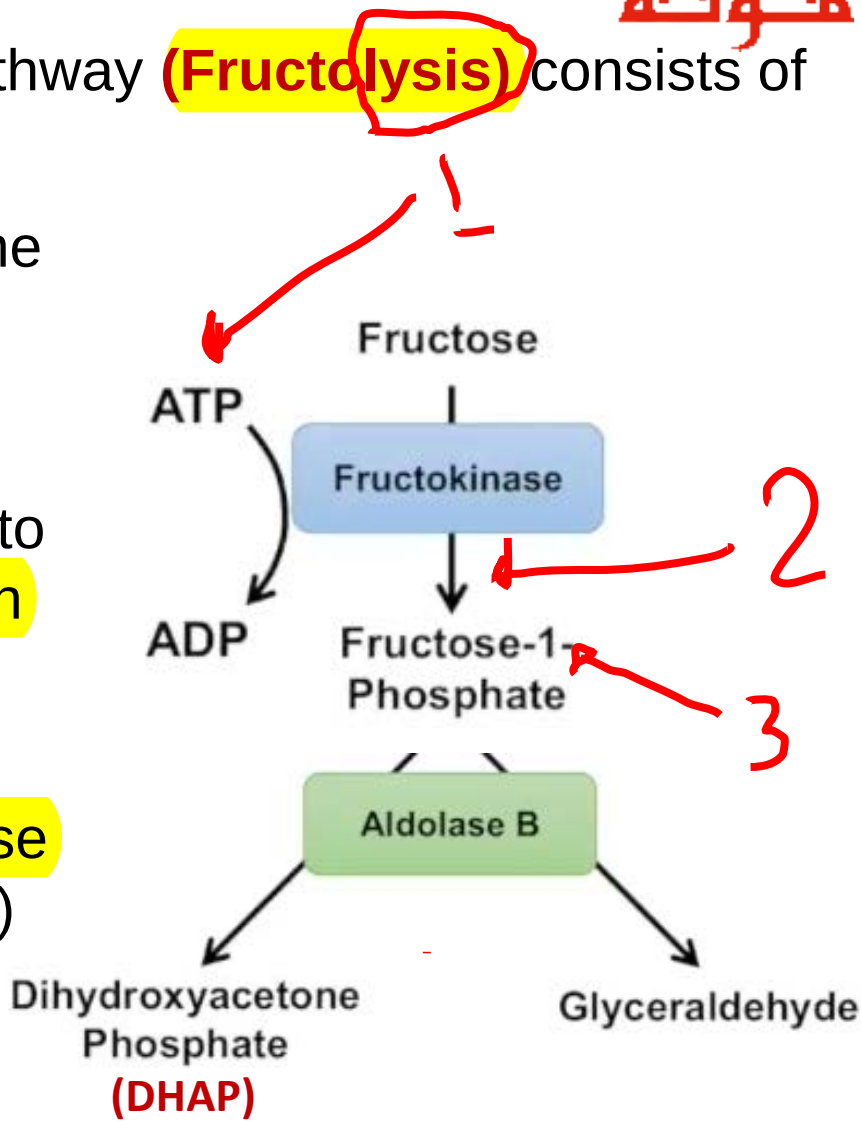
Fructose Metabolism in Liver

- Fructose-1-phosphate (F-1-P) pathway **(Fructolysis)** consists of 3 steps:

MAILY EXPRESSED IN LIVER CELLS

1. Phosphorylation of fructose by the hepatic enzyme **fructokinase** to generate fructose-1-phosphate. This step is important to trap fructose inside hepatocytes and to destabilize fructose (an activation step)

2. The cleavage of F-1-P by aldolase b (also known as F-1-P Aldolase) to produce dihydroxyacetone phosphate **(DHAP)** and glyceraldehyde



ABOUT aldolase

A-ALDOASE B→ MAILY EXPRESSED IN LIVER CELLS
B- ALDOASE HAVE 3 ISOMERS
THEY ARE DIFFERENT IN **THERE SUBSTARTE AND PRODUCT**
1-ISOMTER A
2- ISOMER B >START WITH F-1-P AND GIVE →DHAP + GLCERALDEHYDE
3-ISOMER C
A+C→GLUCOSE METABOLISM
B→FRUCTOSE MEATBOLISM
C+A GIVE →DHAP+GLYCERALDEHYE 3-PHOSPATE

ABOUT DHAP

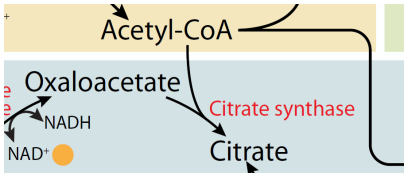
DHAP → BE GLYCERALDEHYE 3-PHOSPATE → SO CONTTUE GLYCOLOSIS

OR

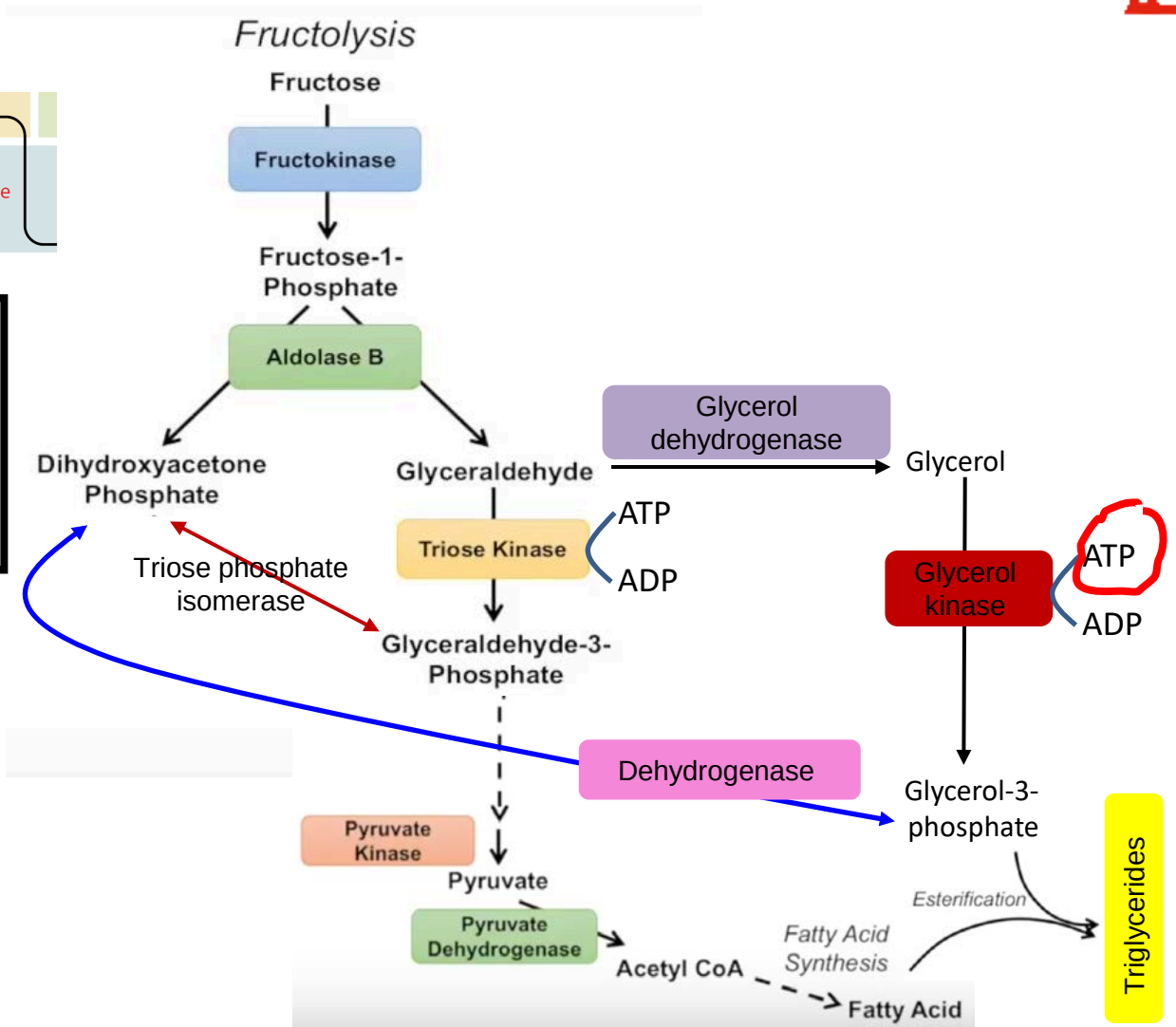
LINK BETWEEN FAT AND CARB METABOLISM → IT IS CONVERT INTO GLYCEROL-3-P→ FAT

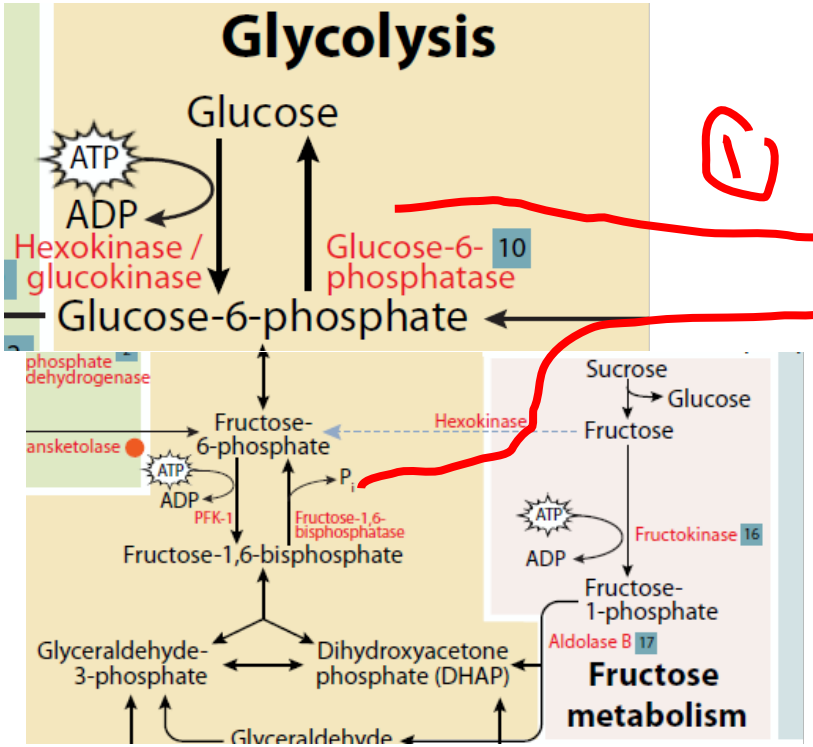
NO PHOSPATE GROUP ON POSTION 3 SO PHOSPOLRATION AT 3 POSITION IT IS ON OF THERE FATES

Fructose Metabolism in Liver



BE ACTEYL-COA→BE CITRATE(IN MITOCHONDREA)→THEN GO TO CYTOPLAM AND SEPRATE TO O.A AND ACETYL-COA WHICH USED IN FA SYNTHESIS





REGUATORY STEP ARE SKIPPED (1+3) IN GLYCOLYLIS
SO THE FRUCTOLYSIS HAVE LITTLE REGULATION COMPARED THE GLYCOLYSIS→ FRUCTOSE→CONVERT TO FAT WITHOUT REGULATION →ACUMALTION OF FA IN LIVER→FATTY LIVER +DIABTES+OBESTY§

Fructose Metabolism in Liver

3. Phosphorylation of glyceraldehyde to form glyceraldehyde-3-phosphate (GAP) by triose kinase. Alternatively, glyceraldehyde is reduced to glycerol by glycerol dehydrogenase then phosphorylated by glycerol kinase to produce glycerol-3-phosphate (reversibly converted to DHAP)

4. DHAP is reversibly converted by isomerase to GAP so can join the glycolysis at this point.

- **Conclusion:** DHAP and glyceraldehyde are very important intermediates which connect carbohydrates with lipid metabolism

DAIBTIC PATIENT
MTEABOLISM OF :
1-GLUCOSE → A LOT OF INSULIN-DEPENTENT STEP
2-FRUCTOSE → NO INSULIN DEPENDENT STEP
SO IT WAS USED FOR DAIBTIC PATIENT AS A alternative OF GLUCOSE BUT, RECENTLY FOUND THAT ITS ASSOASTION WITH SOME HEALTH PROBLRM SUCH WE SAID BEFORE

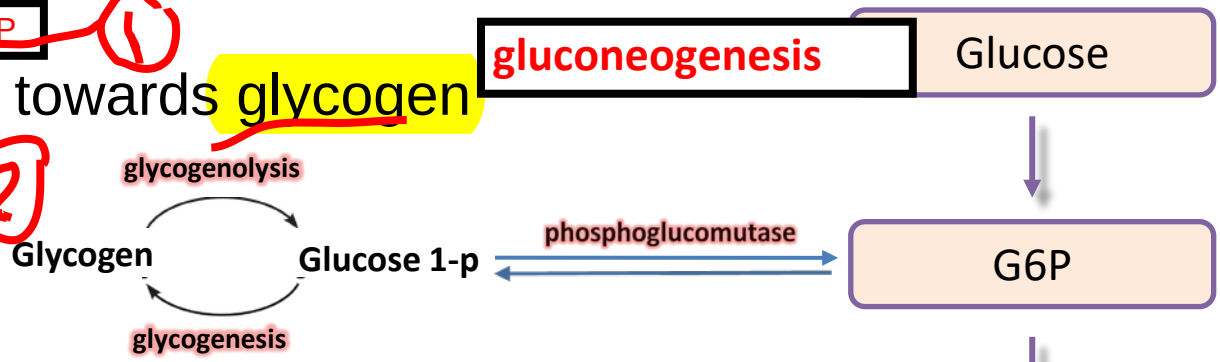
Fructose and Obesity

MOST T.G IN HUMAN IS FROM FRUCTOSE BACKBONE

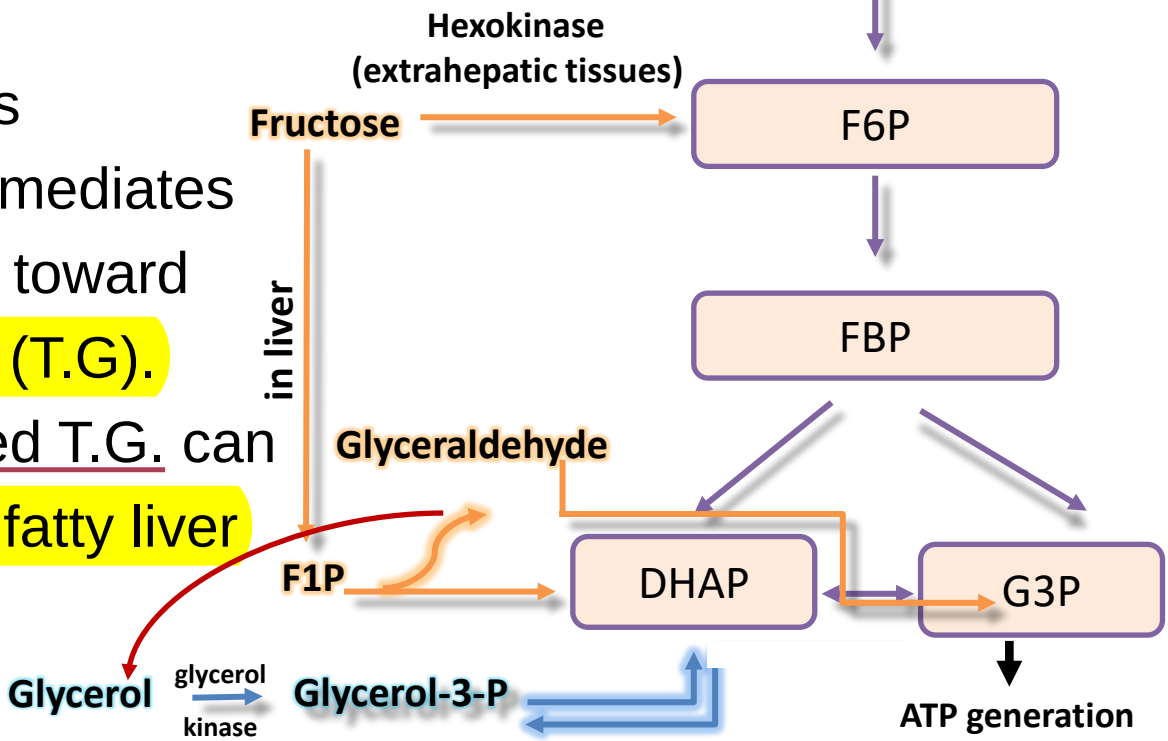
- Fates of fructose metabolism intermediates in liver:

FIRST SYNTHESIS OF ATP

1. Mainly directed towards glycogen replenishment



2. Once liver glycogen is replenished, the intermediates are primarily directed toward triglyceride synthesis (T.G). Prolonged unregulated T.G. can lead to non-alcoholic fatty liver disease and obesity



من العرض

Abnormalities in Fructose Metabolism

INHERTENCRE OF BOTH→A.R

- **Inborn errors in fructose metabolism:**

1. Essential fructosuria: deficiency of the hepatic fructokinase enzyme which results in the incomplete metabolism of fructose in the liver and consequently its excretion in the urine unchanged. It does not require a treatment as it is asymptomatic (benign condition)

2. Hereditary fructose intolerance (HFI): deficiency of the aldolase B enzyme which results in the accumulation of fructose-1-phosphate (severe condition). Symptoms: vomiting, abdominal pain, **hypoglycemia**, **Jaundice**, hemorrhage, **hepatomegaly** and renal failure. It can be treated by limiting fructose intake (fructose, sucrose and sorbitol).

SORBITOL →OXIDATION→FRUCTOSE

- **Reduced phosphorylation potential:**

Intravenous (I.V.) infusion of fructose can lower the phosphorylation potential of liver cells by trapping P_i due to phosphorylation of fructose by fructokinase. Additionally, fructose in high amounts is lipogenic so fructose is contraindicated for total parenteral nutrition (TPN) solutions

Essential fructosuria

1-NO TRAP OF FRUCTOSE IN LIVER BECAUSE NO PHOSPHOLRATION
2-MILD TYPE
3-↓FRUCTOSE IN DIET OR NO THING TO DO
4-AFFECT LIVER ONLY OTHER TISSUE(MINOR PATHWAY) IT WILL BE USED AS NORMAL

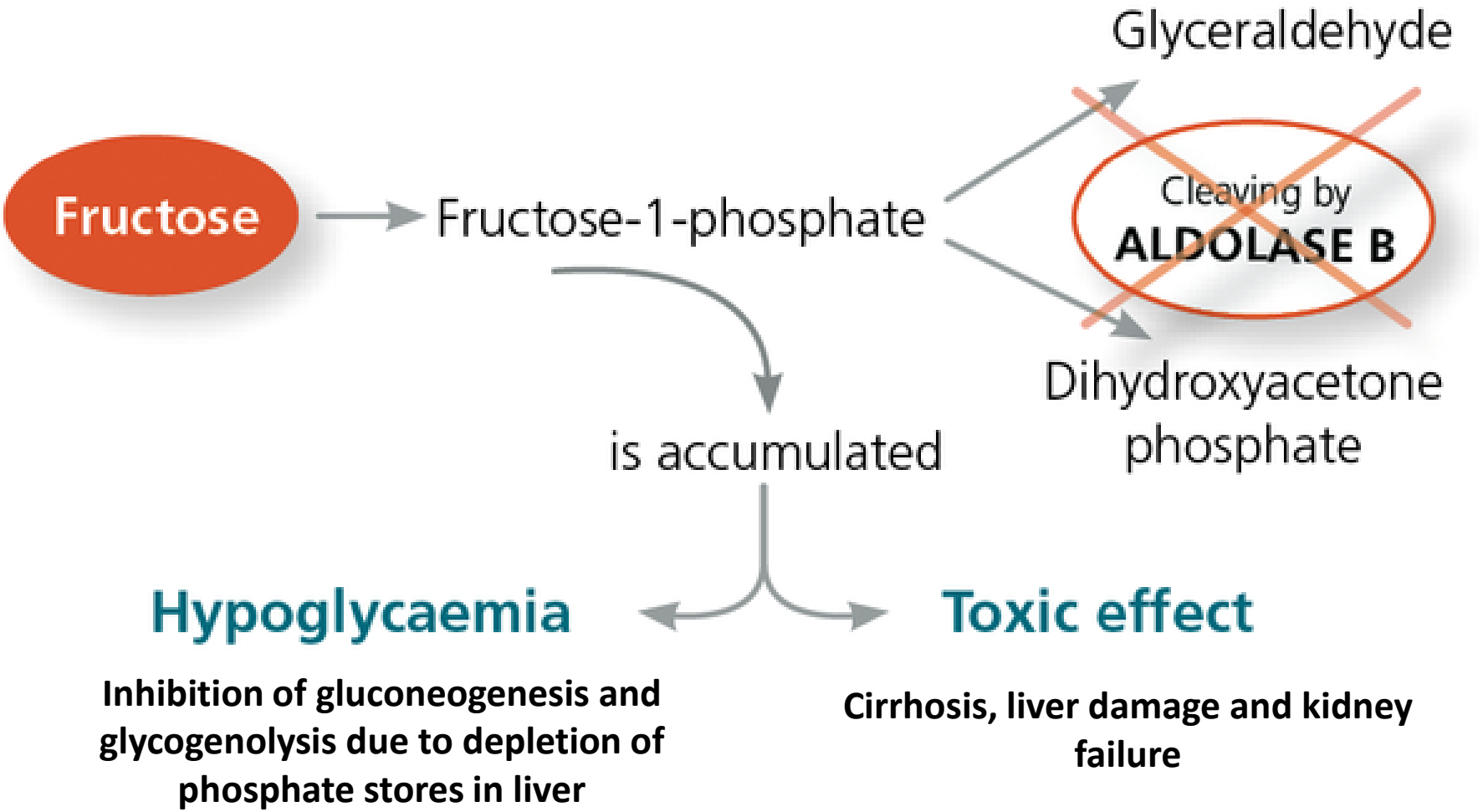
Intravenous (I.V.) infusion of fructose

FRUCTOKINASE IS RAPID PROCESS BUT SPLITTING BY ALDOSE IS SLOW SO GIVE ALOT OF FRUCTOSE IV IN BLOOD →SHOCK TO LIVER LIKE TO HFI
IT IS TRASIET PROBLEM BUT HE WILL HAVE SAME SYPTOMS LIKE HFI
SO WE GIVE paranatally DEXTROSE not fructose

Hereditary fructose intolerance (HFI):

HFI→
1- MORE SEVERE
2-CAUSE OF SYMPTOMS DUE TO→ ↓ INORAGINC PHOSPATE STORED IN LIVER →BECAUSE FRUCTOSE ENTER TO LIVER → CONVERTED TO F-1-P →TRAP INORGANIC PHOSPATE → WE CAN NOT RECYCLE IT (BY ALDOLASE B) FROM F-1-P SO OTHER PATHWAY DEPENDENT ON PHOSPATE↓↓ →HYPOGLYCRMAIA
3-DAMAGE IN LIVER →CAUSE ☻BY↓ PHOSPHATE→↓ELC→↓ATP(ENERGY) FOR LIVER CELL→HEPATIC CELL DEATH
4-TEATMENT →↓↓ FRCTOSE INTAKE

Hereditary Fructose Intolerance (HFI)

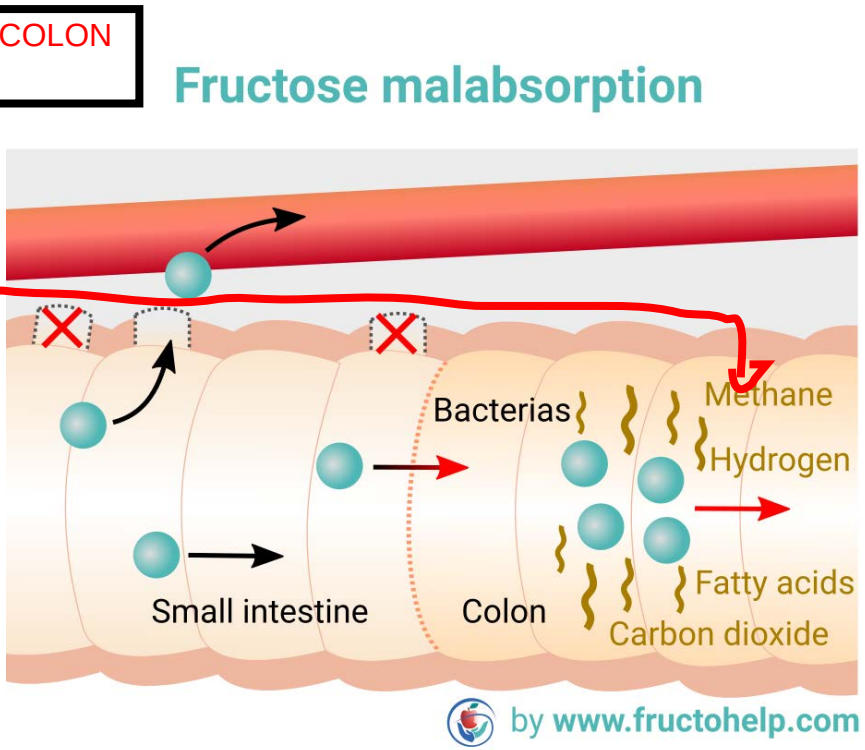


Dietary Fructose Intolerance (DFI)

- Dietary Fructose Intolerance **(DFI):** is also known as **fructose malabsorption** due to impaired absorption of fructose from small intestine as result of deficiency in fructose carriers (GLUT5)
- Symptoms: abdominal pain & cramps, diarrhea, bloating and flatulence, nausea

SORBITOL →OXIDATION→FRUCTOSE

IT WILL REACH COLON GIVE



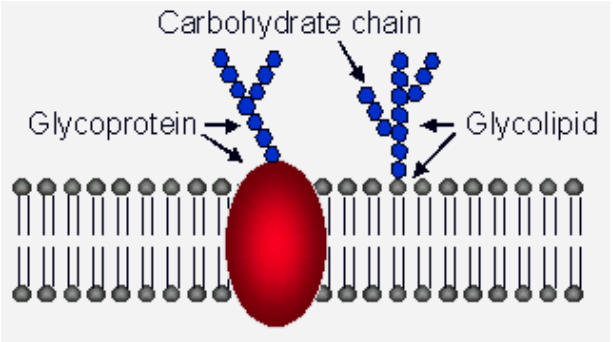
Galactose Sources

- **Dietary Sources of Galactose:**

1. Lactose (milk sugar) consists of glucose and **galactose**

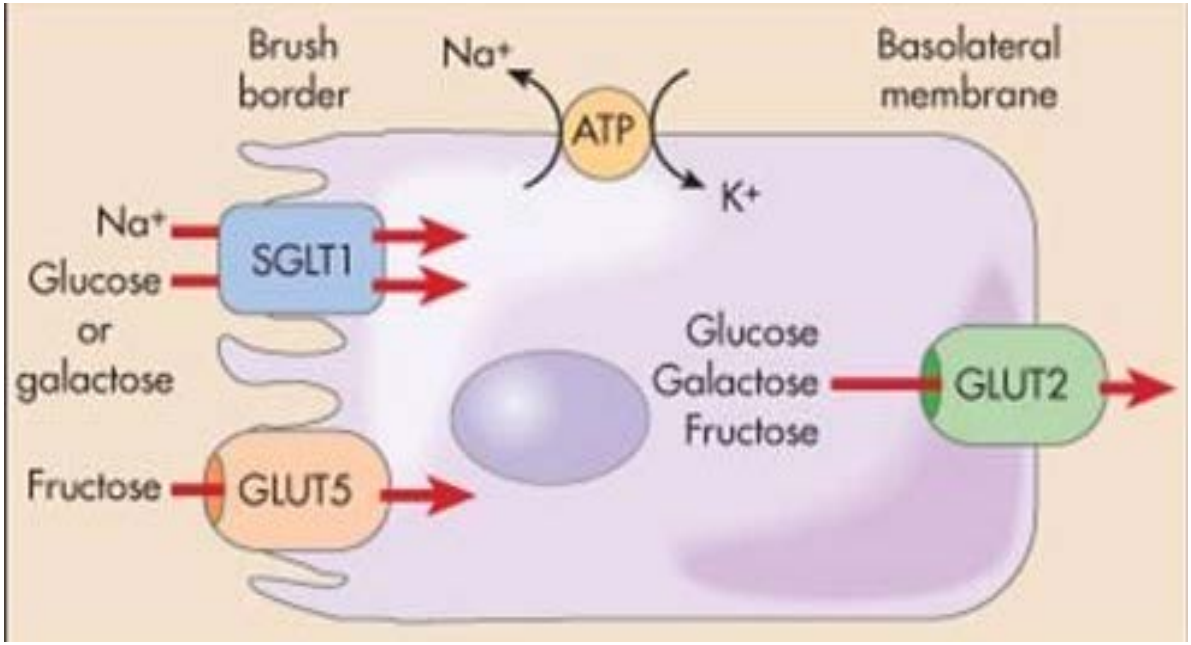
2. Free galactose: fruits & vegetables such as **avocadoes**, papaya, bananas, apples

3. Obtained also from lysosomal degradation of complex CHO (e.g. glycoproteins and glycolipids which are important membrane components)



Galactose Absorption

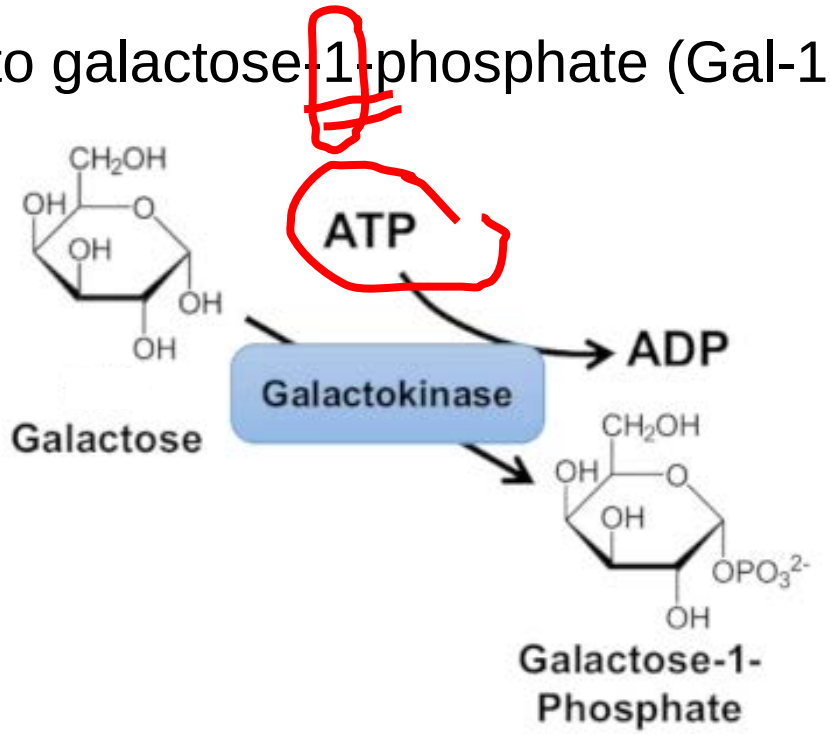
- Free galactose is absorbed from intestinal lumen through SGLT1 (sodium dependent) found at the apical membrane of the intestinal absorptive cells (enterocytes)
- Galactose then crosses to blood capillaries through GLUT2 at the basolateral membrane
- Galactose absorption and entrance into cells is **insulin independent**



Galactose Metabolism

- Unlike glucose, galactose as well as fructose do not have their own catabolic pathways and should be metabolized into molecules which are part of the glycolysis
- Galactose is metabolized to glucose-6-phosphate in 3 steps:

1. Phosphorylation of galactose to galactose-1-phosphate (Gal-1-p) by galactokinase (trapping and destabilization)

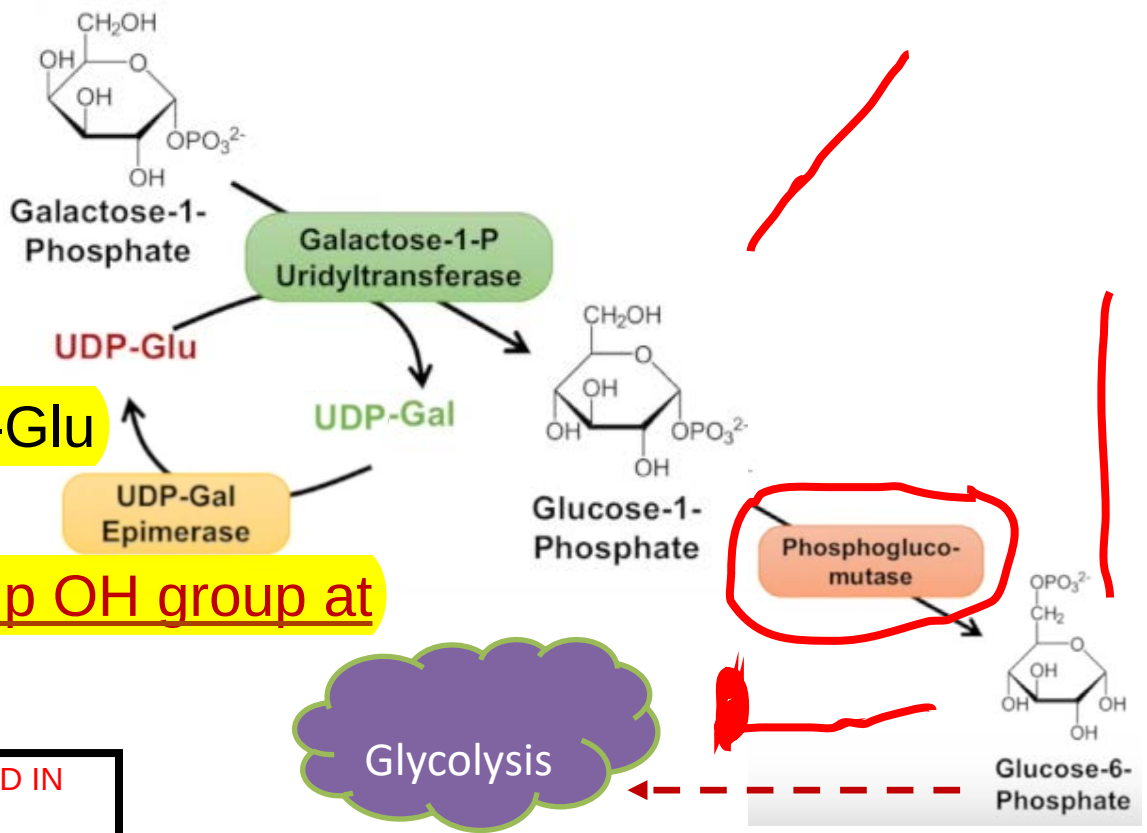


Galactose Metabolism

2. Gal-1-p Uridyltransferase enzyme transfers uridine monophosphate (UMP) group to Gal-1-p forming UDP galactose and glucose-1-phospate

3. Glu1-p is converted to glu6-p by the enzyme phosphoglucomutase (reversible)

4. Regeneration of UDP-Glu from UDP-Gal using epimerase enzyme (flip OH group at C4 from up to down)



UDP-GALACTOSE→ BE USED IN LACTOSE SYNTHESIS

Galactosemia

- Galactosemia: is a rare genetic disorder characterized by the inability to metabolize galactose due to deficiency in one of the three enzymes involved in galactose metabolism: