Lecture

6

ISLAMIC UNIVERSITY

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Ph.D. clinical biochemistry

Fructose and Galactose metabolism

Lecture 6

A- Fructose

Fructose is a ketohexose present in fruits, honey and sucrose. Soft drinks have the sweetener, corn syrup, which has a high fructose content and is sweeter than sucrose.

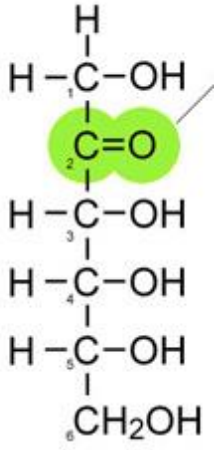


Figure 1: Fructose structure

Metabolism of Fructose

Fructose is mainly metabolized **by liver**, but free fructose is seen in large quantities in **seminal plasma**. The energy for mobility of spermatozoa is mainly derived from fructose.

** Fructose is promptly phosphorylated by **fructokinase in the liver** (which have a high affinity for fructose) for further metabolism.

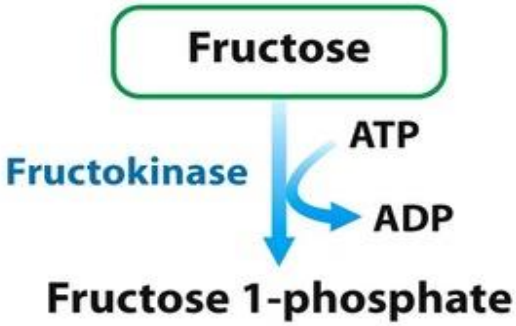


Figure 2: Phosphorylation of Fructose in the

Fructose-1-phosphate-aldolase or **aldolase-B** then cleave the fructose. The products are **glyceraldehyde** and **dihydroxyacetone phosphate**.

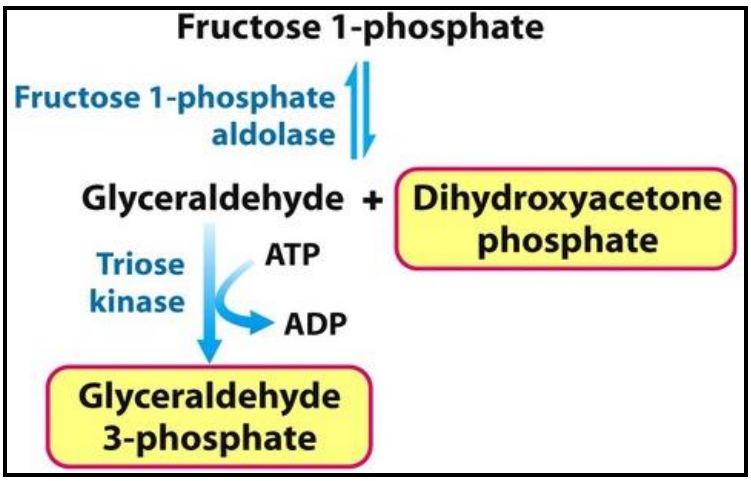
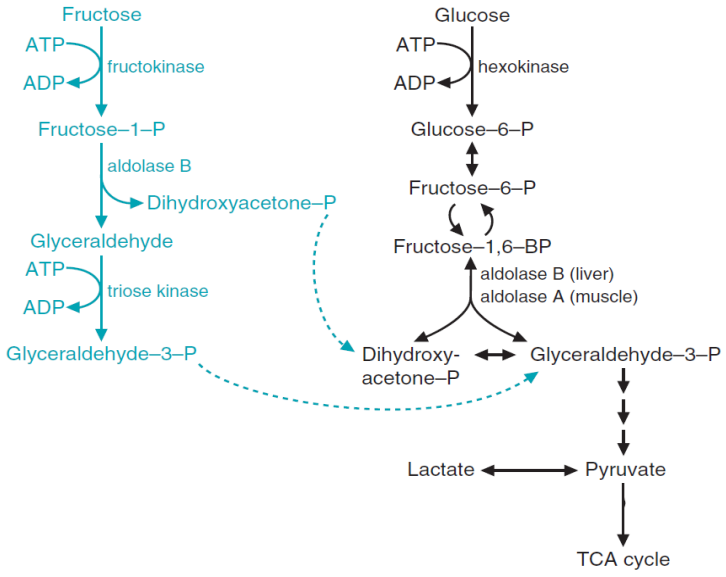


Figure 3: Cleavage of Fructose 1-phosphate



Note: <u>Fructokinase is not dependent on insulin</u>. So, fructose is more rapidly utilized in normal persons.

Fructose will be better utilized in patients with **<u>diabetes mellitus</u>**. But in experiments, much amounts of fructose were found to be deleterious in diabetic patients. Fructose rapidly enter the tissues, leading to enhanced fatty acid synthesis, raised serum triglycerides and increased LDL cholesterol level in blood; all these are atherogenic and harmful.

<u>Diseases related to Fructose metabolism:</u>

1- Fructosuria

This is a benign metabolic defect due to **deficiency of fructokinase (Figure 6)**. Fructose will not be trapped in the liver and directly arrive to the blood then accumulate and it will be excreted with urine. <u>There is no abnormality other than excretion of fructose in urine</u>. Urine gives positive Benedict's and Seliwanoff's tests as fructose is a reducing sugar. Incidence is 1 in 130,000 births.

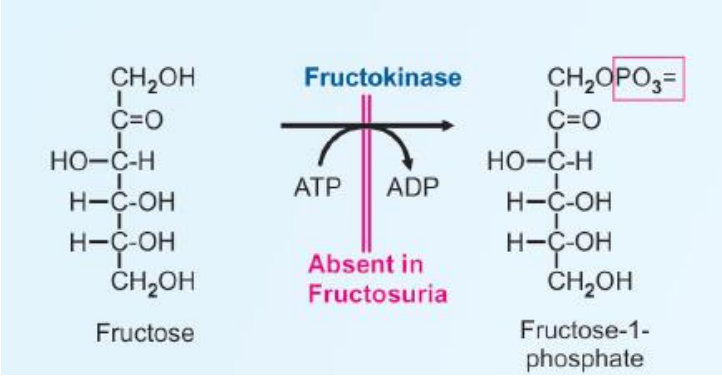


Figure 6: Conversion of fructose to fructose1-phosphate

2- Hereditary Fructose Intolerance (HFI)

It is an autosomal recessive inborn error of metabolism. Incidence of the disease is 1 in 20,000 births, while 1 in 70 persons are carriers of the abnormal gene. The defect is in **aldolase-B;** hence fructose-1- phosphate cannot be metabolized (Figure 7).

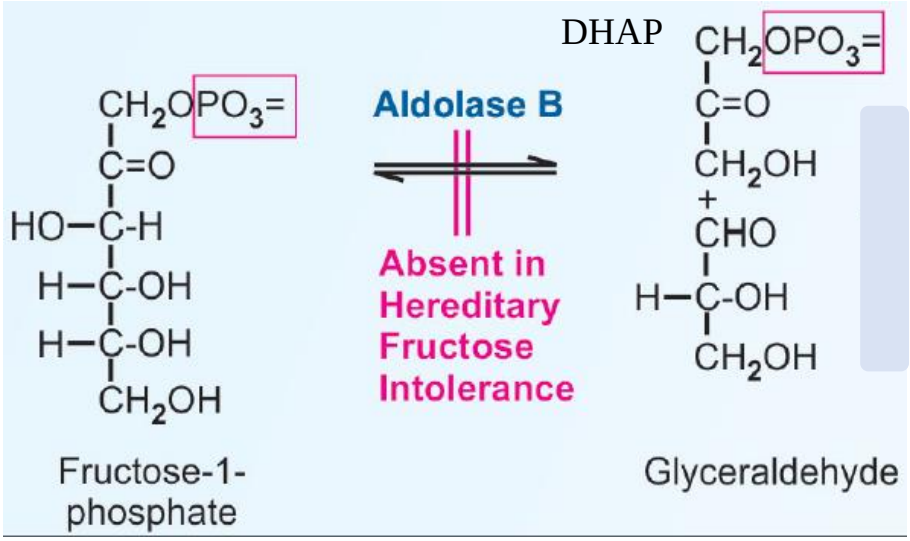


Figure 7: cleavage of fructose1-phosphate

Accumulation of fructose-1-phosphate will inhibit **glycogen phosphorylase**. This leads to accumulation of glycogen in liver and associated **hypoglycemia.**

Symptoms include Vomiting and loss of appetite. The infants often **fail to thrive**. **Hepatomegaly and jaundice** may occur. If liver damage progresses, death will occur. Withdrawal of fructose from the diet will immediately relieve the symptoms.

B- Galactose

Galactose is an **aldohexose** and is the epimer of glucose (Figure 4) **.** Galactose is a constituent of lactose of milk sugar, and

is taken in the diet. Galactose is <u>not an essential nutrient</u>, because **UDP glucose** can form **UDP galactose.**

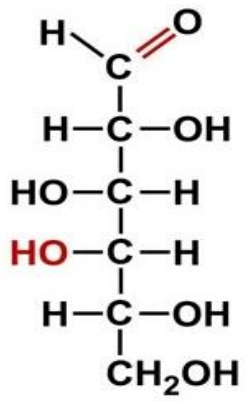


Figure 4: Structure of galactose

Metabolism of galactose

Galactose is metabolized almost exclusively by the liver**.**

1- Galactokinase reaction: Galactose is first phosphorylated by galactokinase to galactose-1- phosphate **(step1, Figure 5)**.

2- Galactose-1-phosphate uridyl transferase (GALT): This is the **rate-limiting** enzyme in galactose metabolism. UDP-galactose may be used as such for synthesis of compounds containing galactose (e.g. lactose) **(step2, Figure 5)**.

3- **Epimerase reaction:** By this reaction, galactose is channeled to the metabolism of glucose **(Step 3, Figure 5)**. Since the reaction is freely reversible, even if the dietary supply of galactose is deficient, UDP-glucose can be epimerized to UDP-galactose.

4- **Alternate pathway**: The galactose-1-phosphate pyro-phosphorylase in liver becomes active only after 4 or 5 year of life. The enzyme will produce UDP-galactose directly, which can be epimerized to UDP-glucose **(Step 4, Figure 5)**.

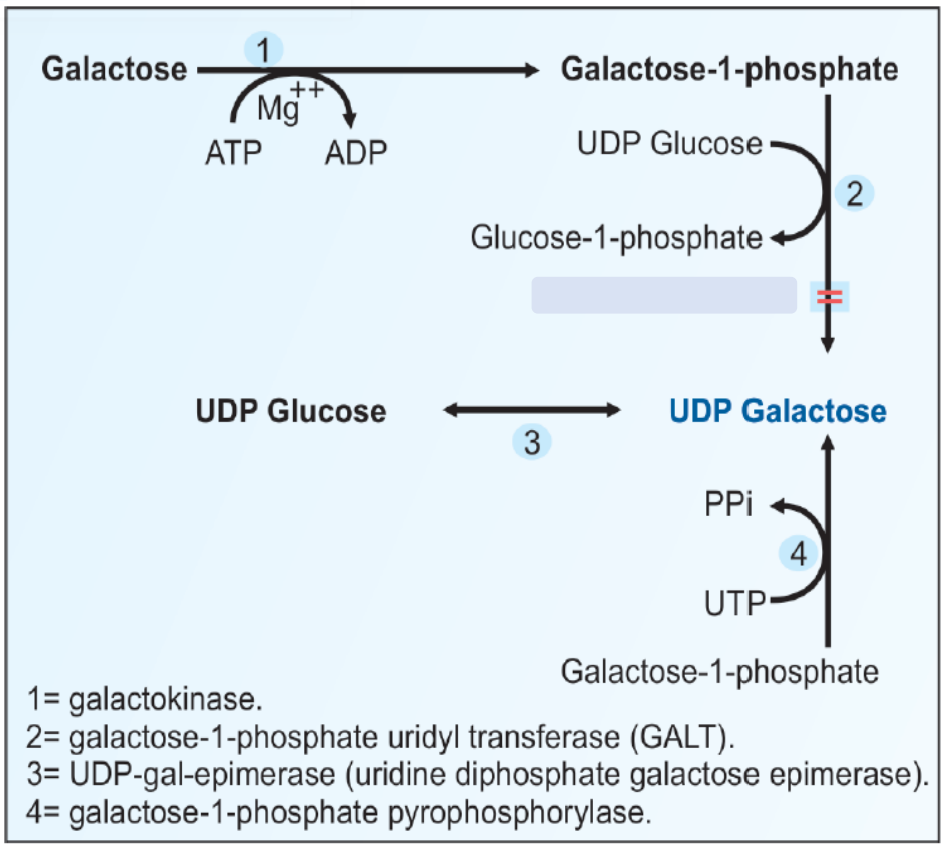


Figure 5: Summary of galactose metabolism

Galactose is necessary for synthesis of the following:

a- **Lactose Synthesis:** In mammary gland during lactation

$$\text{UDP glucose} \xrightarrow{\text{Epimerase}} \text{UDP galactose}$$

$$\text{UDPgalactose} + \text{glucose} \xrightarrow{\text{Lactose synthase}} \text{Lactose}$$

Diseases related to Galactose metabolism:

1- Galactosemia: It is an inborn error of metabolism, which causes a deficiency of enzyme **galactose-1-phosphate uridyl transferase.**

Due to the block in this enzyme, **galactose-1- phosphate** will accumulate in liver. This will inhibit galactokinase as well as glycogen phosphorylase, **Hypoglycemia** is the result.

Bilirubin uptake is less and bilirubin conjugation is reduced; so **unconjugated bilirubin** level is increased in blood. Also There is enlargement of liver, jaundice and severe **mental retardation.** Free galactose accumulates, leading to **galactosemia**. It is partly excreted in urine **(galactosuria).**

Galactose is reduced **to dulcitol or galacticol**. The accumulation of dulcitol in the lens results in **cataract** due to its osmotic effect. This is called **congenital cataract** and is a very characteristic feature of **galactosemia.**

Galactose-1-phosphate may get deposited in renal tubules, producing **tubular damage** leading to generalized **amino aciduria.**

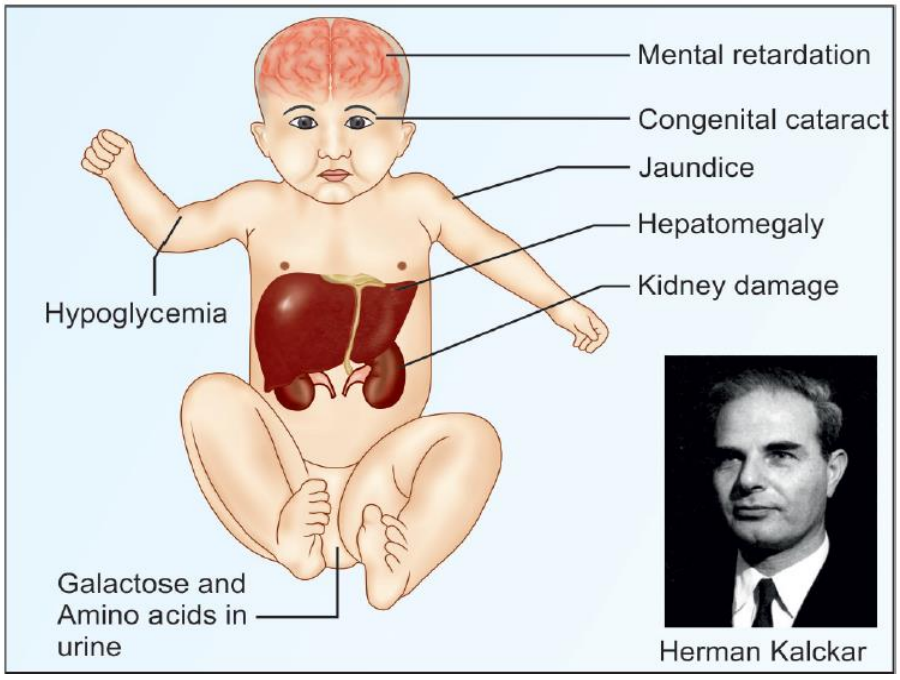


Figure 8: Clinical features of galactosemia

2- **Galactokinase Deficiency**

A variant of the disease occurs due to the deficiency of **galactokinase**. But here the symptoms are milder. This is because galactose-1-phosphate is not formed and hence no toxic effects of this compound are manifested. **However, cataract is seen**.