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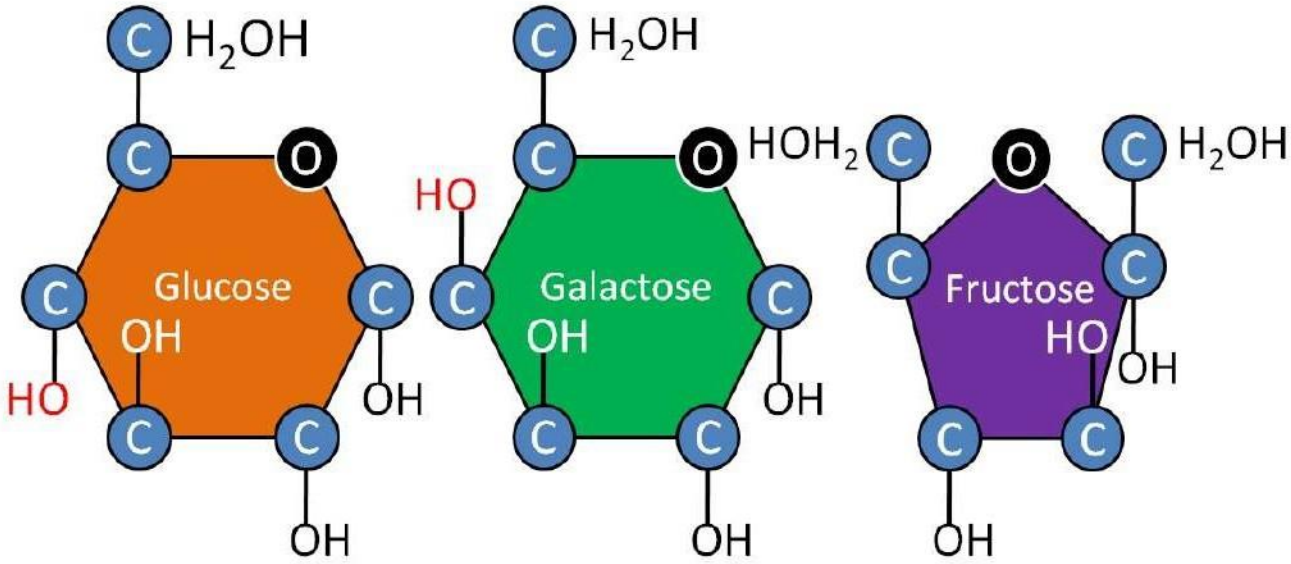
Galactose & Fructose Metabolism



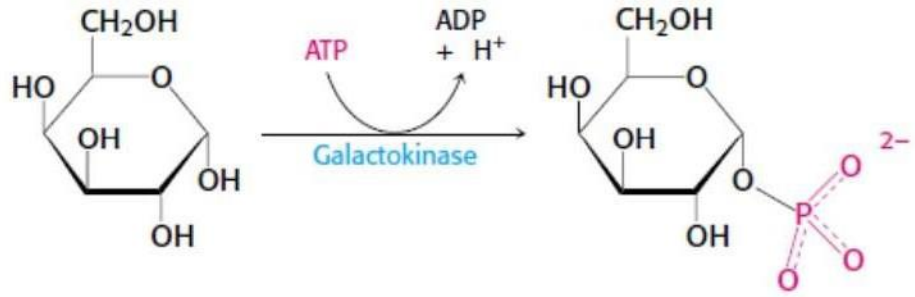
Galactose metabolism

The disaccharide lactose, present in milk and milk products, is the principal dietary source of galactose. Lactase of intestinal mucosal cells hydrolyses lactose to galactose and glucose. Galactose is also produced within the cells from the lysosomal degradation of glycoproteins and glycolipids.

There are no catabolic pathways to metabolize *galactose*, so the strategy is to convert galactose into a metabolite of glucose. galactose entry into the cells is not dependent on insulin.

Galactose is converted into *glucose 6-phosphate* in four steps:

1-The first reaction in the galactose– glucose interconversion pathway is the phosphorylation of galactose to galactose 1-phosphate by galactokinase.



2- galactose 1-phosphate reacts with UDP-glucose in an exchange reaction to form UDP-galactose in presence of the enzyme galactose 1- phosphate uridyltransferase (fig 1).

UDP-galactose is an active donor of galactose for many synthetic reactions involving the formation of compounds like lactose.

3-UDP-galactose can be converted to UDP-glucose by UDP hexose 4-epimerase. In this way, galactose can enter the metabolic pathways of glucose (fig 1).

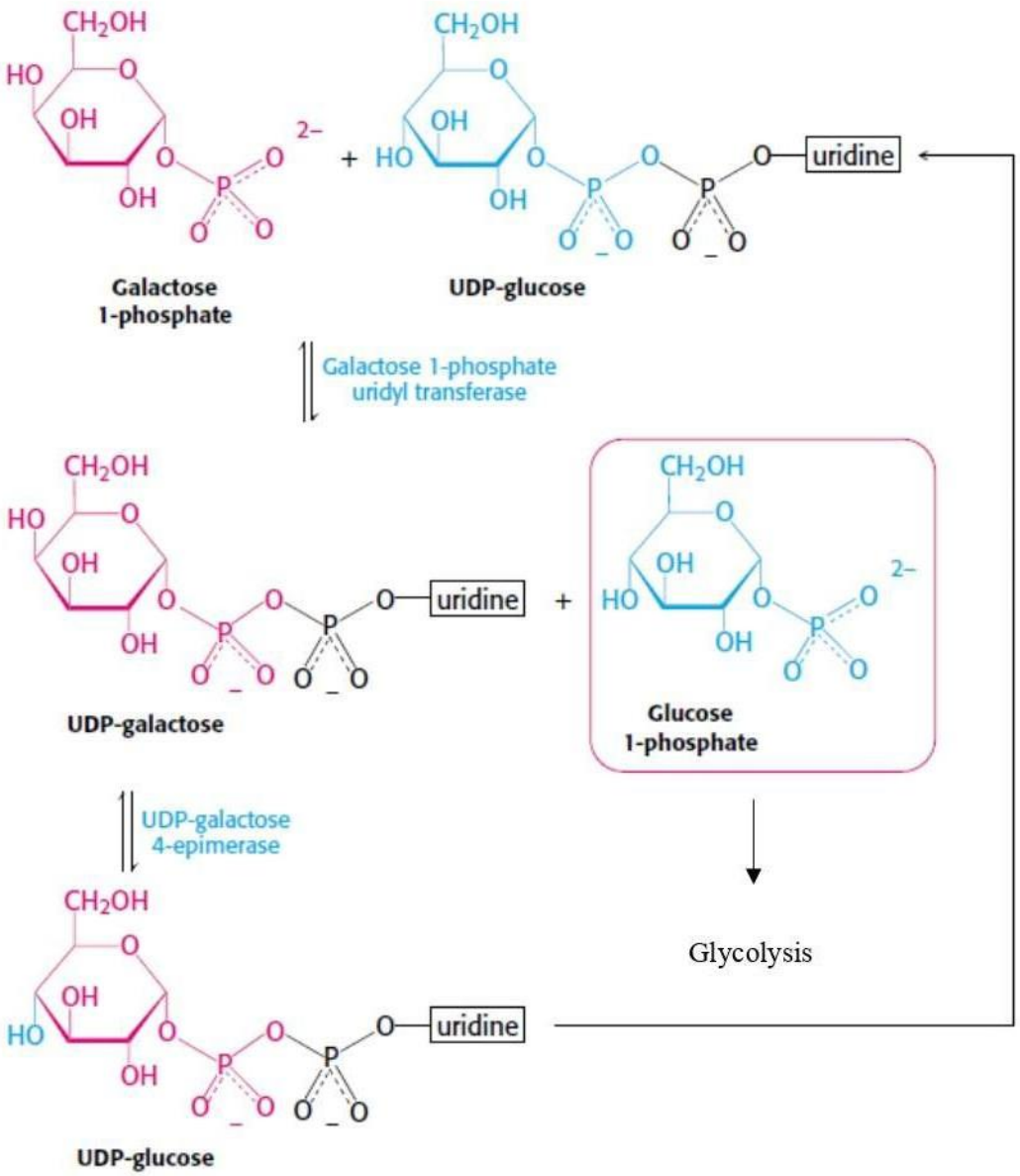


Fig (1) Galactose metabolism pathway

4- glucose 1-phosphate, formed from galactose, is isomerized to glucose 6-phosphate by *phosphoglucomutase*, which in turn enter glycolysis pathway

Disorders of galactose metabolism

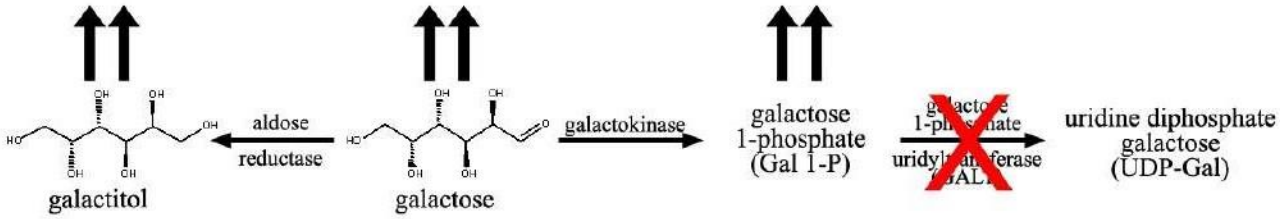
Classical galactosemia

Galactosemia is a rare genetic disease in which the body is unable to convert (metabolize) the simple sugar galactose to glucose due to the deficiency of the enzyme **galactose 1- phosphate uridyltransferase.**

Deficiency of this enzyme results in accumulation of galactose and of galactose-1 phosphate in various tissues like **liver**, nervous tissue, **lens** and **kidney** leads to impairment in their function. which act as cellular toxins.

Due to disturbances in the routine metabolism, galactose is diverted to **alternate pathways** through which Galactose is reduced to galacitilol by the enzyme aldose reductase. Galactilol is not metabolized further and is excreted in urine.

Galactilol is osmotically active, and water will diffuse into the lens, leading to cataracts.



The clinical symptoms of galactosemia

- loss of weight
- jaundice (Yellow skin and whites of the eyes)
- mental retardation
- In severe cases, cataract
- Convulsions.
- Vomiting.

The most common treatment is to remove galactose (and lactose) from the diet.

Fructose metabolism

Fructose is a dietary monosaccharide present naturally in fruits and vegetables, either as free fructose or as part of the disaccharide sucrose, and as its polymer inulin. It is also found in free form in honey and many fruits.

Fructose is mostly phosphorylated by fructokinase to fructose 1-phosphate. Fructokinase has been identified in liver, kidney and intestine. Fructose 1-phosphate is cleaved to glyceraldehyde and dihydroxyacetone phosphate (DHAP) by **aldolase B.** Hexokinase, which phosphorylates various monosaccharides, can also act on fructose to produce fructose 6-phosphate which then converted to fructose 1, 6-bisphosphate and split by **aldolase A** fig (2). Glyceraldehyde is phosphorylated by the enzyme triokinase to glyceraldehyde 3- phosphate which enters glycolysis or gluconeogenesis.

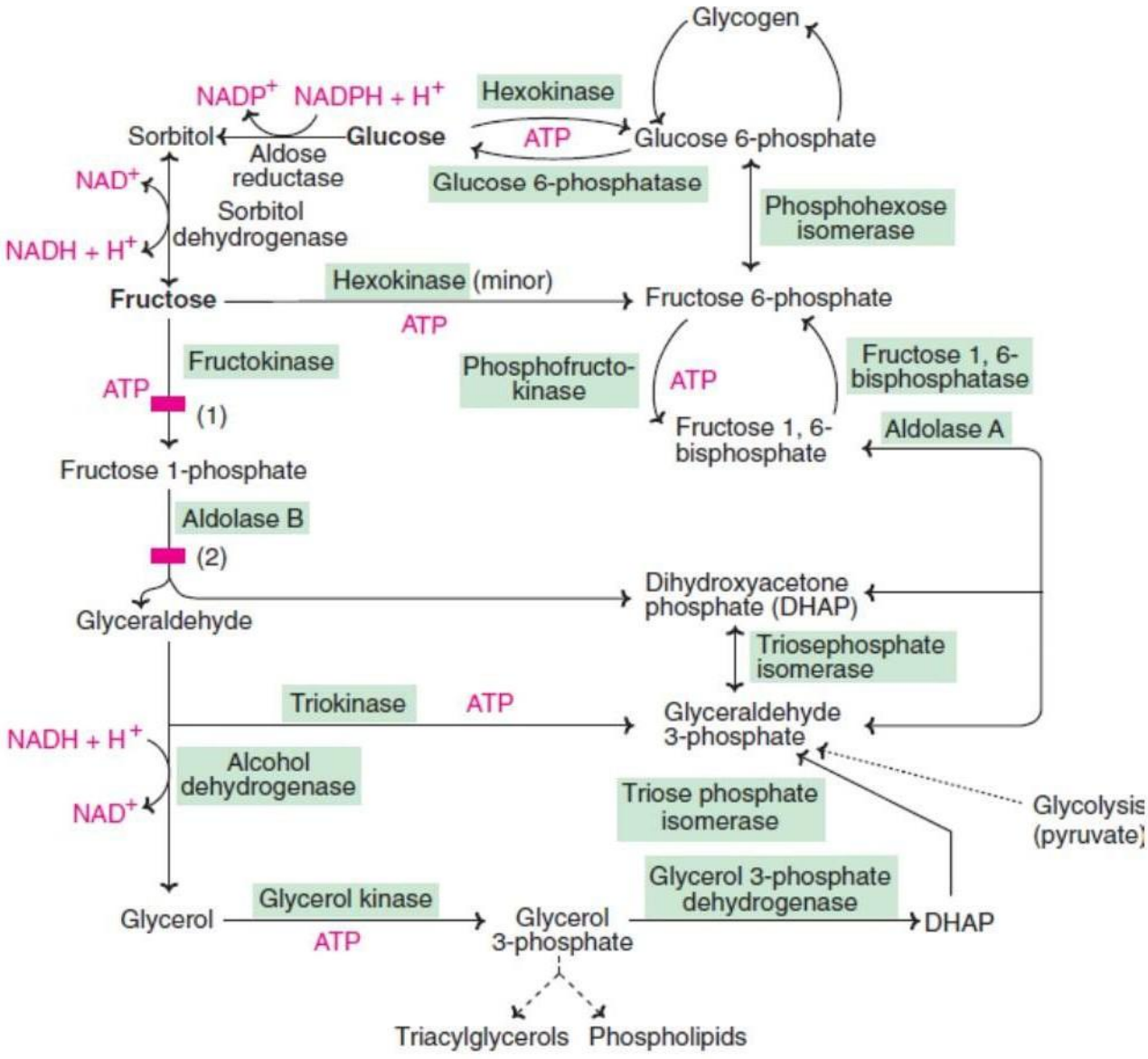


Fig (2) Fructose metabolism pathway

Defects in fructose metabolism

Essential fructosuria

Due to the deficiency of the enzyme hepatic **fructokinase** fructose is not converted to fructose 1-phosphate. This is an asymptomatic condition with excretion of fructose in urine. Treatment involves the restriction of dietary fructose.

Hereditary fructose intolerance:

This is due to the absence of the enzyme **aldolase B.** Hereditary fructose intolerance causes intracellular accumulation of fructose 1-phosphate, severe hypoglycemia, vomiting, hepatic failure and jaundice. Early detection and intake of diet free from fructose and sucrose, are advised to overcome fructose intolerance.