Metabolism of disaccharides: Fructose and Galactose

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Fructose metabolism

- Diets containing large amounts of sucrose (a disaccharide of glucose and fructose) can utilize the fructose as a major source of energy.

- Fructose is found in foods containing sucrose (fruits), high-fructose corn syrups, and honey.

- The pathway to utilization of fructose differs in muscle and liver.
Fructose metabolism

- **In liver**, dietary fructose is converted to Fructose-1-P by fructokinase (also in kidney and intestine).

- Then, by the action of Fructose-1-P adolase (aldolase B), Fructose-1-P is converted to DHAP and glyceraldehyde.

- Glyceraldehyde is converted to glyceraldehyde-3-P by triose kinase which together with DHAP may undergo:
  1. Combine together and converted into glucose (main pathway)
  2. They may be oxidized in glycolysis
Other Substrates for Glycolysis
fructose, mannose and galactose
Fructose metabolism

- The utilization of fructose by fructokinase then aldolase bypass the steps of glucokinase and PFK-1 which are activated by insulin.

  - This explains why fructose disappears from blood more rapidly than glucose in diabetic subjects.
Fructose metabolism

Fructose → fructokinase → Fructose-1-phosphate → fructose-1-P aldolase → Glyceraldehyde and DHAP

Glyceraldehyde → triose kinase → Glyceraldehyde-3-phosphate

DHAP → TIM → Glyceraldehyde-3-phosphate
The affinity of **aldolase B** for fructose-1-P is much poorer than that of fructose-1,6-biphosphate, thus fructose-1-P accumulates in fructokinase-expressing tissues. Thus, **aldolase B is the rate-limiting enzyme for fructose metabolism** (not glucose).

**Muscle** which contains only **hexokinase** can phosphorylate fructose to **F6P** which is a direct glycolytic intermediate.

However, **hexokinase** has a very low affinity to fructose compared to glucose, so it is not a significant pathway for fructose metabolism. Unless it is present in very high concentration in blood.
Fructose-6-P can be converted to **glucosamine-6-P** which is the precursor of all other amino sugars.
Fructose metabolism

- In the testes (seminal vesicles), fructose is converted into glucose through sorbitol formation by aldolase reductase and sorbitol dehydrogenase.

- Deficiency of fructose correlates with male infertility.
Hereditary defects of fructose metabolism

1. Essential fructosuria
   - **Cause:** due to deficiency of fructokinase enzyme
   - **Effect:** not serious condition. The excess accumulated fructose is lost in urine

2. Fructose 1,6 biphosphatase deficiency
   It leads to accumulation of fructose 1,6 biphosphate which inhibits phosphorylase enzyme (glycogenolysis) and fasting hypoglycemia
3. Hereditary fructose intolerance

- **Cause:** due to deficiency of aldolase B. This leads to accumulation of fructose-1-P.

- **Effect:** the accumulation of fructose-1-P leads to:
  - Damage of liver and kidney tissues
  - Inhibition of glycogen phosphorylase leading to inhibition of glycogenolysis and fasting hypoglycemia
Galactose Metabolism

- The major source of galactose is lactose (a disaccharide of glucose and galactose) obtained from milk and milk products.
- Galactose enters glycolysis by its conversion to glucose-1-phosphate (G1P). This occurs through a series of steps.
- **Site:** liver
Galactose metabolism

- First the galactose is phosphorylated by galactokinase to yield galactose-1-p.
- Epimerization of galactose-1-phosphate to G1P requires the transfer of UDP from uridine diphosphoglucose (UDP-glucose) catalyzed by galactose-1-phosphate uridyl transferase.
  - This generates UDP-galactose and G1P. The UDP-galactose is epimerized to UDP-glucose by UDP-galactose-4 epimerase.
  - The UDP portion is exchanged for phosphate generating glucose-1-phosphate which then is converted to G6P by phosphoglucose mutase.
- Glucose can be converted to galactose, thus performed

**galactose is not essential in the diet**
Galactosemias

- **Definition:** it is increase blood galactose concentration due to inability of the body to metabolize galactose

- **Causes:** inherited defects in galactokinase, uridyl-transferase (the most common) or 4-epimerase.

- **Effect:**
  1. **Cataract** (opacity of eye lens): Galactose is reduced in the eye by aldose reductase to form galactitol which accumulates causing cataract
  2. **Liver failure**
  3. **Mental retardation**
  4. **Galactosuria** (excretion of galactose in the urine)
THANK YOU!

Take a break!!
Have a cup of........