

Metabolism of mono and disaccharide

Metabolism of fructose

Glucose + Fructose

what are

- The major source of fructose is the disaccharide sucrose, which, when cleaved in the intestine, releases equimolar amounts of fructose and glucose

where

- fructose is also found as a free monosaccharide in high-fructose corn syrup (55 percent fructose/45 percent glucose, which is used to sweeten most cola drinks), in many fruits, and in honey.

- Entry of fructose into cells is not insulin-dependent and, in contrast to glucose, fructose does not promote the secretion of insulin.

Entry of fructose into cells is not insulin-dependent.

يعني دخول fructose إلى الخلايا لا يحتاج insulin.

بعكس glucose في بعض الأنسجة مثل adipose tissue والعضلات، حيث يعتمد دخوله على insulin عبر GLUT4.

كمان:

Fructose does not promote insulin secretion.

يعني fructose لا يحفز إفراز insulin مثل glucose.

لبش هذا مهم؟

فإن glucose لما يرتفع بالدم، pancreatic β -cells تشعر فيه وتفرز insulin.

أما fructose ما يحفز insulin بنفس الطريقة.

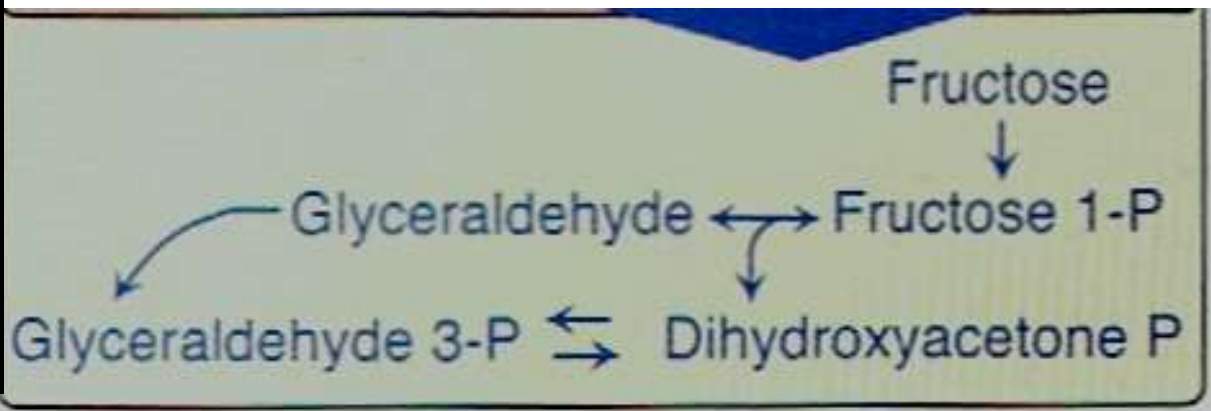
امتحائنا:

لو ساك الدكتور:

Which sugar enters cells independent of insulin and does not stimulate insulin secretion?

الجواب:

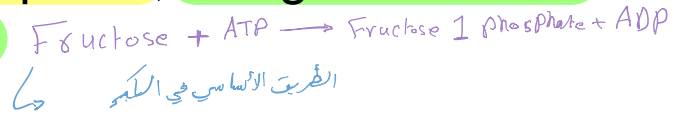
Fructose



① in liver, kidney, small intestinal mucosa
 ② Hexokinase بواسطة

Metabolism of fructose

A. Phosphorylation of fructose: by hexokinase or fructokinase (found in the liver, kidney, and the small intestinal mucosa). and converts fructose to fructose 1-phosphate, using ATP as the phosphate donor

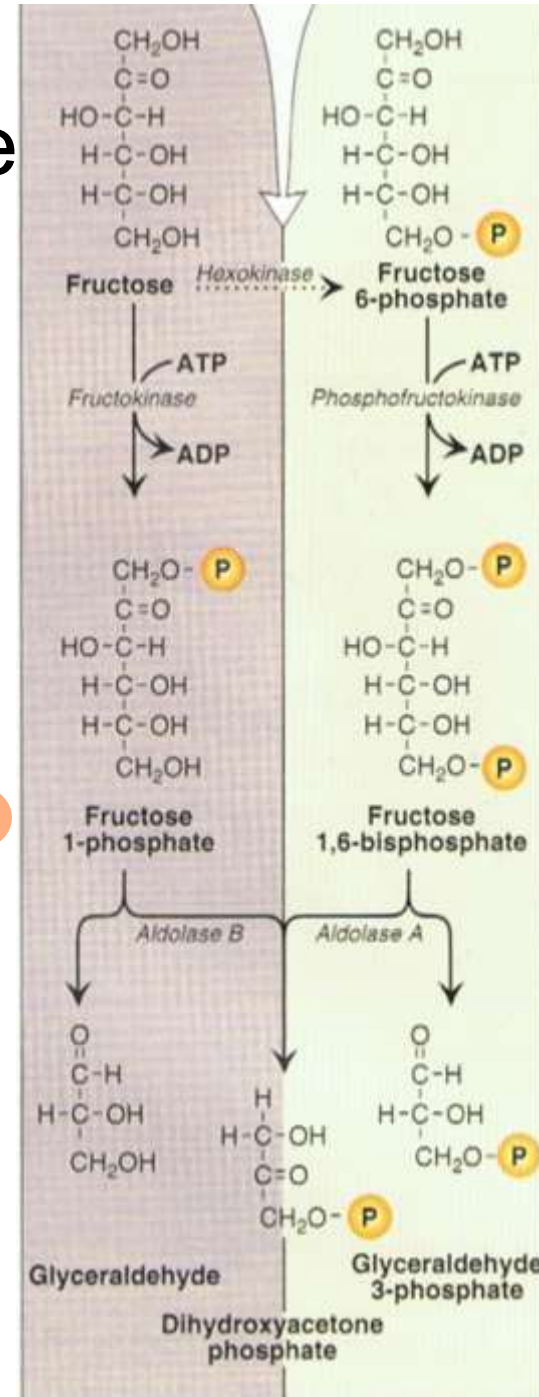


B. Cleavage of fructose 1-phosphate (by aldolase B) to dihydroxyacetone phosphate (DHAP) and glyceralaldehyde. DHAP can directly enter glycolysis or gluconeogenesis, whereas glyceralaldehyde can be metabolized by other pathways

Fructose metabolism in liver = FAT pathway	Letter
Fructokinase	F
Aldolase B	A
Triokinase	T

Fructose 6-phosphate الى hexokinase يحول الى Fructose الـ 6

وهذا يدخل الى glycolysis بشكل اقرب لمسار glucose



Metabolism of fructose

Galactokinase deficiency vs Classic galactosemia مقارنة		
Classic galactosemia	Galactokinase deficiency	Feature
GALT	Galactokinase	Deficient enzyme
Galactose 1-P, galactose, galactitol	Galactose, galactitol	Accumulated substance
Severe	Milder	Severity
Liver damage, jaundice, vomiting, mental retardation, cataracts	Cataracts	Main symptom
Yes	Yes	Galactosuria
Yes	Usually no severe liver disease	Liver damage
Rapid removal of galactose/lactose	Restrict galactose/lactose	Treatment
Galactose 1-P + galactitol	Galactitol	Key toxic metabolite

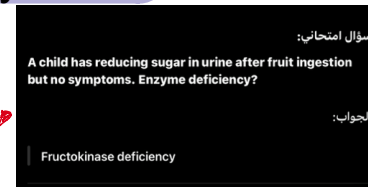
C. Kinetics of fructose metabolism

why?

- The rate of fructose metabolism is more rapid than that of glucose because the trioses formed from fructose 1-phosphate bypass phosphofructokinase (the major rate-limiting step in glycolysis).
- Intravenous infusion of fructose elevate the rate of lipogenesis caused by the enhanced production of acetyl CoA.

D. Disorders of fructose metabolism

- fructokinase deficiency: benign condition
- Hereditary fructose intolerance (HFI): a severe disturbance of liver and kidney metabolism as a result of aldolase B deficiency. Fructose 1-phosphate accumulates, and ATP and inorganic phosphate levels fall significantly, causing hyperuricemia, hypoglycemia, vomiting, jaundice, hemorrhage and hepatomegaly. If fructose was not removed from the diet, liver failure and death can occur.



Diagnosis of HFI can be made on the basis of fructose in the urine

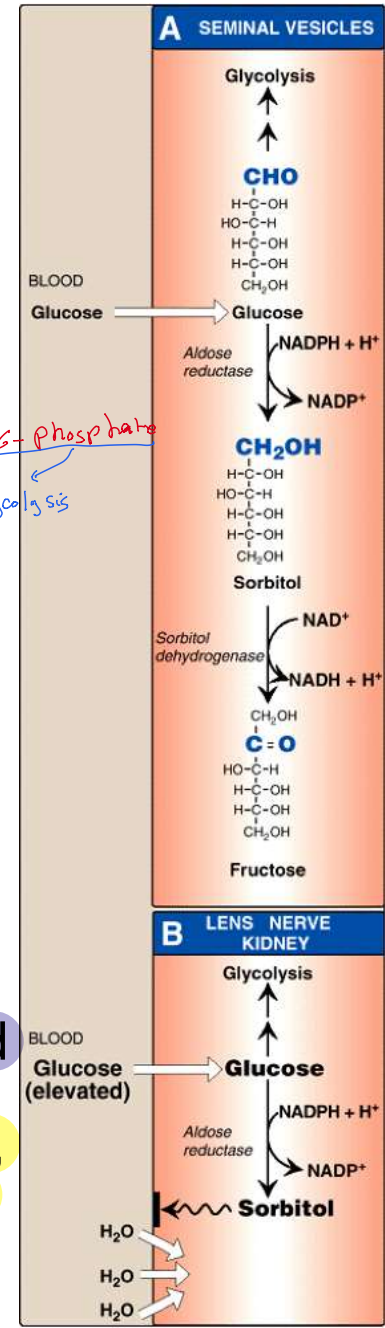
Metabolism of fructose

E. Conversion of mannose to fructose 6-phosphate
 Hexokinase phosphorylates mannose, producing mannose 6-phosphate, which is (reversibly) isomerized to fructose 6-phosphate by phosphomannose isomerase.

F. Conversion of glucose to fructose via sorbitol

A. In seminal vesicles, glucose converts to sorbitol by aldehyde reductase followed by oxidation of sorbitol by sorbitol dehydrogenase to produce fructose. This is necessary in seminal vesicles as fructose is a major carbohydrate energy source.

B. In hyperglycemia as in uncontrolled diabetes glucose enter these cells (retina, lens, kidney, nerve cells) convert to sorbitol which will be trapped inside the cell, leading to water retention due to osmosis. cataract formation, peripheral neuropathy, and vascular problems leading to nephropathy and retinopathy.



Handwritten notes:

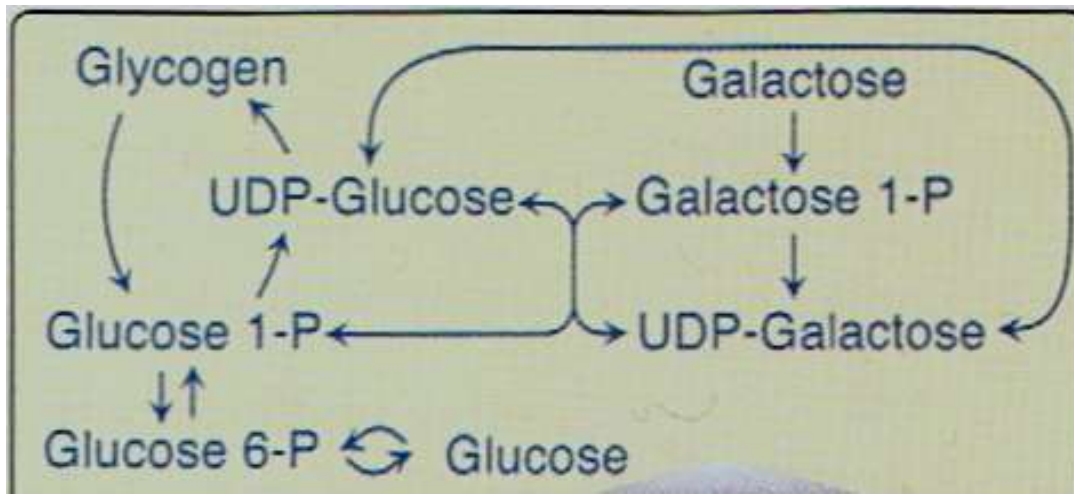
- ① Glucose → Sorbitol
- NADPH + H⁺ + Aldose reductase → NADP⁺
- ② Sorbitol + NAD⁺ → Fructose + NADH + H⁺

تسلسل احتفاله للسكري:
 Hyperglycemia
 → ↑ glucose entry into insulin-independent tissues
 → ↑ aldose reductase activity
 → ↑ sorbitol
 → osmotic water retention
 → tissue damage
 → cataracts, neuropathy, nephropathy, retinopathy

Galactose metabolism

Glucose + Galactose
↓

- The major dietary source is lactose (in milk)
- ① Phosphorylation of galactose by **galactokinase** to galactose 1P using ATP as phosphate donor
- ② Formation of UDP-galactose by exchange with UDP-glucose. The enzyme that catalyzes this reaction is **galactose 1-phosphate uridyl-transferase**.



مسار Galactose كامل احفظه
Galactose
↓ Galactokinase
Galactose 1-phosphate
↓ Galactose 1-phosphate uridyltransferase / GALT
UDP-galactose + Glucose 1-phosphate
↓ UDP-hexose 4-epimerase
UDP-glucose
↓
Glucose metabolism / glycogen / glycolysis

Galactose metabolism

C. ? Use of UDP-galactose as a carbon source for glycolysis or gluconeogenesis. UDP-galactose is then converted to UDP-glucose by **UDP-hexose 4-epimerase**. 4

D. *What is the* Role of UDP-galactose in biosynthetic reactions? *?* can be utilized in many metabolic pathways as in biosynthesis of lactose, glycoproteins, glycolipids, and glycosaminoglycans.

E. Disorders of galactose metabolism

A. classic galactosemia: **Galactose 1-phosphate uridylyltransferase is missing and so galactose 1P and galactose accumulate in cell causing a problem similar to that in fructose intolerance**

B. Galactokinase deficiency



Galactokinase deficiency vs Classic galactosemia مقارنة

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تسبب Classic galactosemia نقص إنزيم Galactose 1-phosphate uridylyltransferase في الكبد في إنتاج UDP-Glucose من Galactose 1-P. يتم إنتاج Galactose 1-phosphate من Galactose عن طريق إنزيم Galactokinase. إنزيم Galactokinase في الكبد يفتقر في Classic galactosemia. إنزيم Galactose 1-phosphate uridylyltransferase في الكبد يفتقر في Classic galactosemia. إنزيم Galactose 1-phosphate uridylyltransferase في الكبد يفتقر في Classic galactosemia.

Antenatal diagnosis is possible by chorionic villus sampling.

Chorionic villus sampling: أخذ عينة من الخلايا المشيمية.

المرض: قصور الإنزيم.

علاج المرض: Restrict galactose and removal of galactose, therefore lactose, from the diet.

علاج المرض: Restrict galactose/lactose.

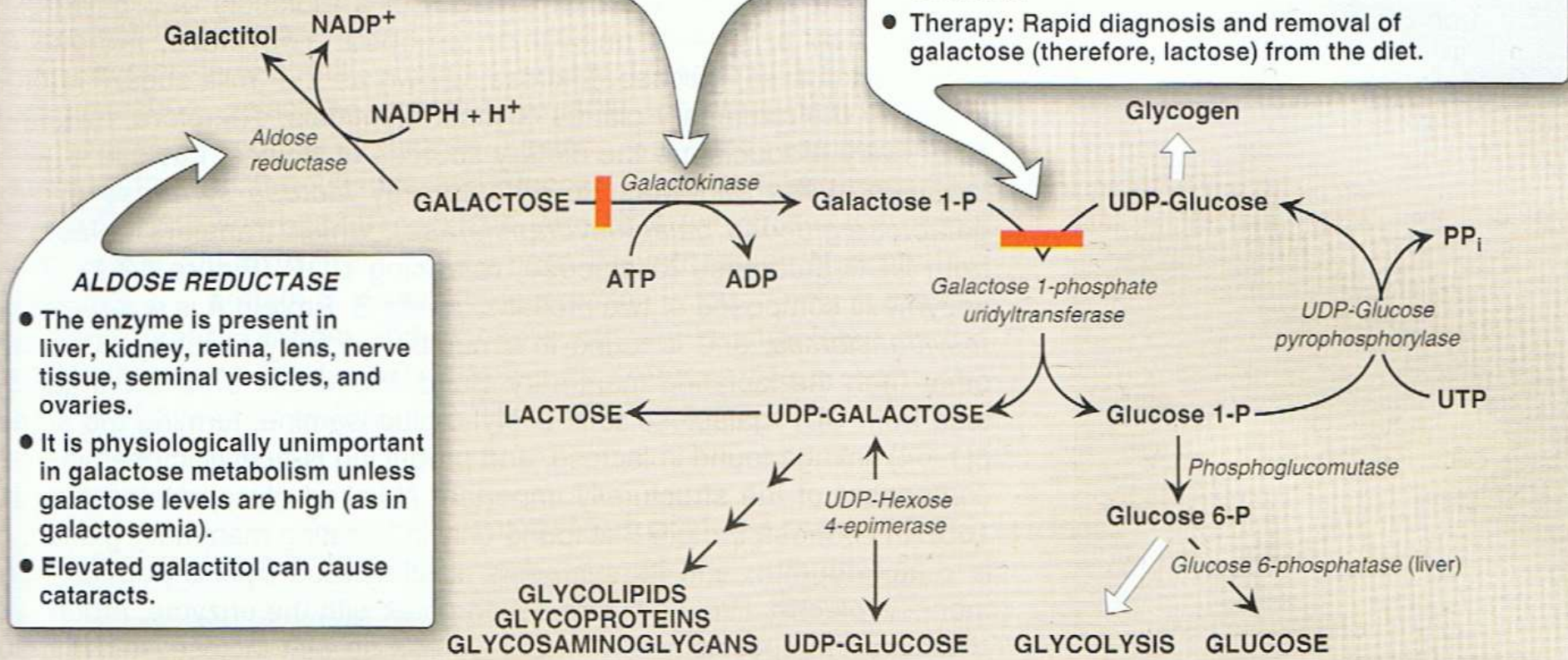
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GALACTOKINASE DEFICIENCY

- This causes galactosemia and galactosuria.
- It causes galactitol accumulation if galactose is present in the diet.

CLASSIC GALACTOSEMIA

- *Uridyltransferase* deficiency.
- Autosomal recessive disorder (1 in 23,000 births).
- It causes galactosemia and galactosuria, vomiting, diarrhea, and jaundice.
- Accumulation of galactose 1-phosphate and galactitol in nerve, lens, liver, and kidney tissue causes liver damage, severe mental retardation, and cataracts.
- Antenatal diagnosis is possible by chorionic villus sampling.
- Therapy: Rapid diagnosis and removal of galactose (therefore, lactose) from the diet.



Lactose synthesis

- ❑ Produced in mammary glands of mammals
- ❑ Lactose is synthesized by lactose transferase which transfers galactose from UDP-galactose to glucose, releasing UDP.
- ❑ This enzyme is composed of two proteins, A and B. Protein A is a β -**o-galactosyltransferase**, and is found in a number of body tissues.
- ❑ In tissues other than the lactating mammary gland, this enzyme transfers galactose from UDP-galactose to N-acetyl-D-glucosamine, forming the same (1-4) linkage found in lactose, and producing N-acetyllactosamine a component of the structurally important N-linked **glycoproteins**.
- ❑ In contrast, protein B is found only in lactating mammary glands. It is **α -lactalbumin**, and its synthesis is stimulated by the peptide hormone, prolactin. Protein B forms a complex with the enzyme, protein A, changing the specificity of that transferase so that lactose, rather than N-acetyllactosamine, is produced.

Protein B

هو:

α -lactalbumin

وهذا موجود فقط في:

Lactating mammary glands

يعني أثناء الرضاعة.

تصنيعه يتحفز بواسطة:

Prolactin

هرمون البرولاكتين المسؤول عن تحفيز إنتاج الحليب = Prolactin.

كيف α -lactalbumin يغير وظيفة الإنزيم؟

تبعث الإنزيم specificity ويغير Protein A يرتبط مع Protein B.

يعني بدل ما α -lactalbumin ينقل galactose إلى N-acetylglucosamine, يصبح ينقل galactose إلى glucose.

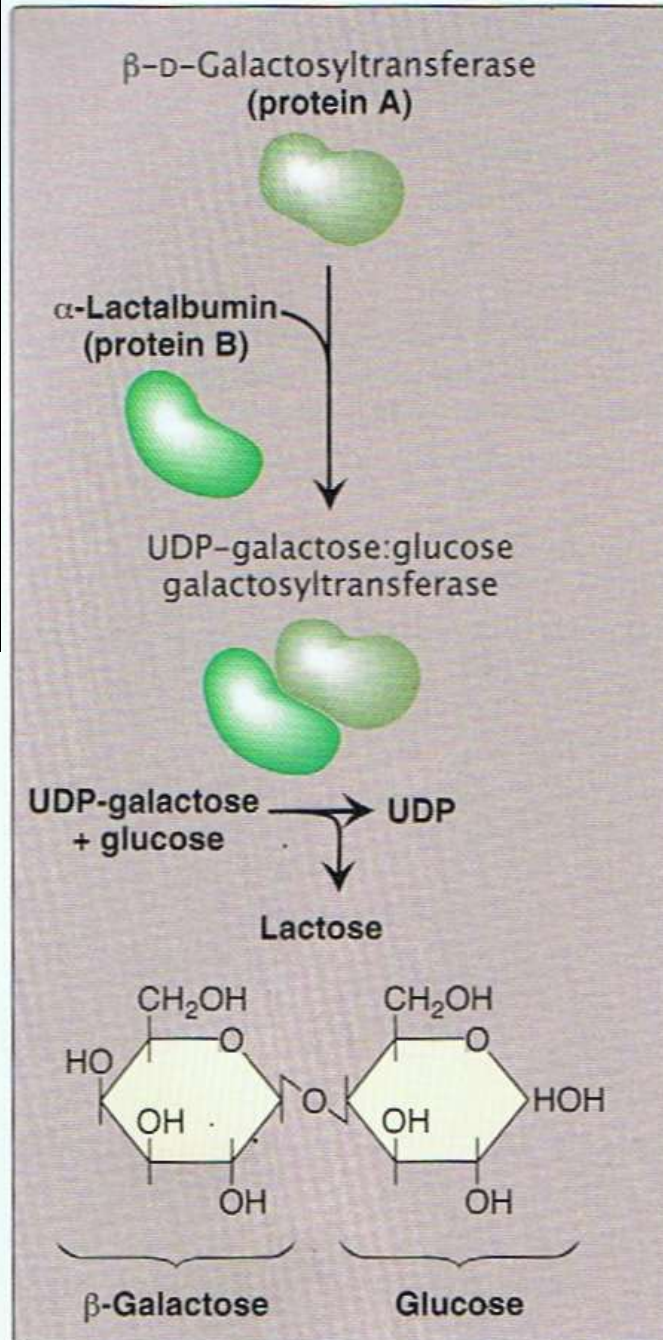
فتكون النتيجة:

Lactose synthesis

الفكرة العبقرية:

موجود في أنسجة كثيرة Protein A.

لكن بوجود α -lactalbumin في mammary gland, يتغير target من N-acetylglucosamine إلى glucose.



Protein A

هو:

β -D-galactosyltransferase

موجود في عدد من أنسجة الجسم.

وظيفته الأصلية في الأنسجة غير الثديية:

ينقل galactose من UDP-galactose إلى:

N-acetyl-D-glucosamine

وينتج:

N-acetylglucosamine

وهذا يدخل في تركيب:

N-linked glycoproteins

يعني Protein A لوحده مش متخصص لصناعة lactose, بل يستخدم في glycoprotein synthesis.

جدول Lactose synthesis

Component	وظيفة
UDP-galactose	galactose يعطي donor
Glucose	galactose يستقبل acceptor
Protein A	β -D-galactosyltransferase
Protein B	α -lactalbumin
Prolactin	يحفز تصنيع α -lactalbumin
Product	Lactose + UDP

أهم مقارنات التشابتر للامتحان

Fructose vs Galactose

Galactose	Fructose	Point
Lactose in milk	Sucrose, fruits, honey, HFCS	Major source
Galactokinase	Fructokinase	First enzyme
Galactose 1-P	Fructose 1-P	First product
Classic galactosemia	HFI	Major dangerous disease
GALT	Aldolase B	Defective enzyme in severe disease
Galactose 1-P	Fructose 1-P	Toxic phosphate metabolite
Remove galactose and lactose	Remove fructose and sucrose	Diet treatment
Yes, due to galactitol	Not classic main feature	Cataracts?