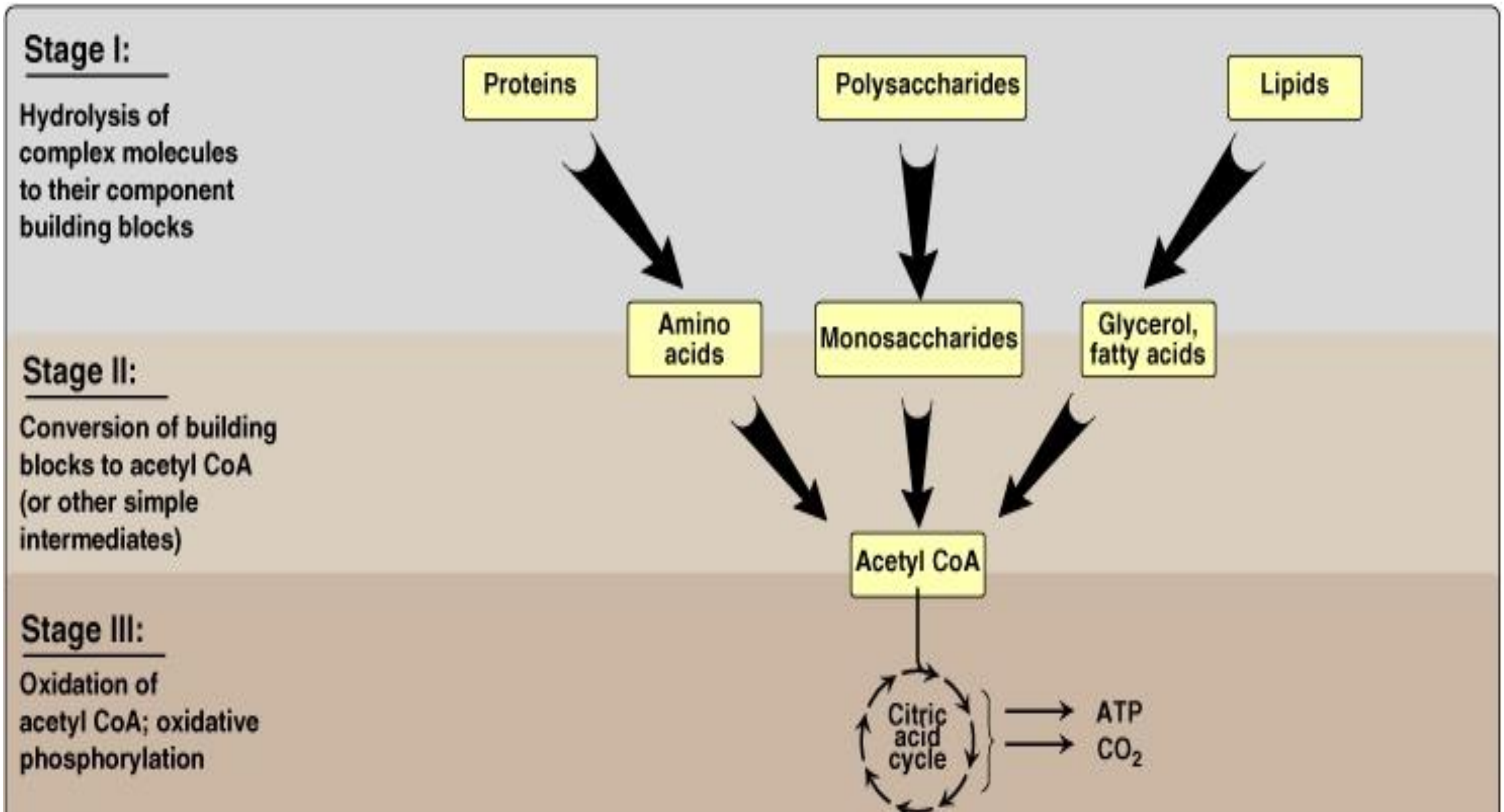
Carbohydrates Metabolism

Review of Carbohydrates
Digestion[1] and absorption[2] of carbohydrates

Suggested Readings:

1: Lippincot's Ilustrated reviews: Biochemistry

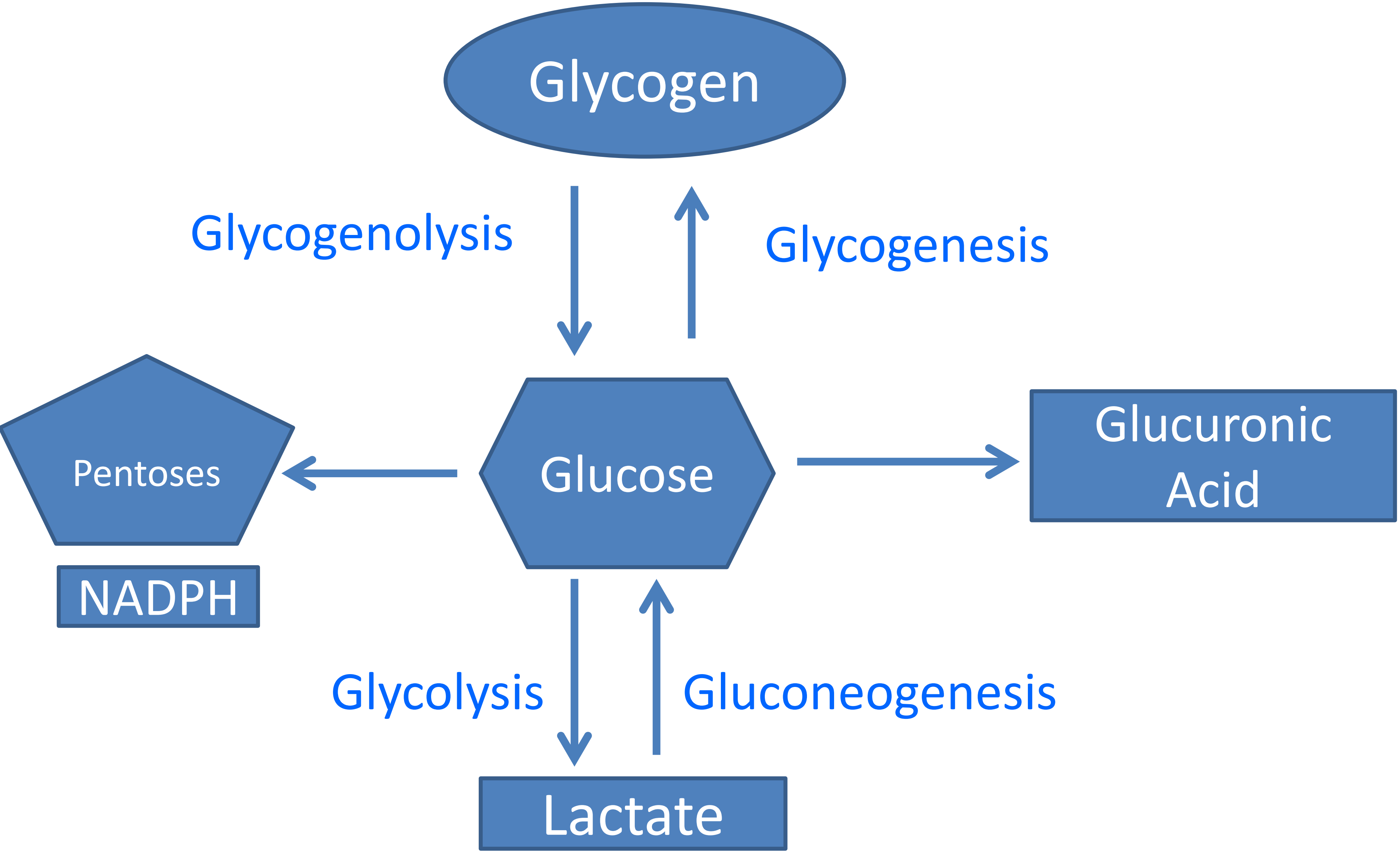
2: Marks' Basic Medical Biochemistry


Stage I:
Hydrolysis of complex molecules to their component building blocks
Stage II:
Conversion of building blocks to acetyl CoA (or other simple intermediates)
Stage III:
Oxidation of acetyl CoA; oxidative phosphorylation
Proteins
Polysaccharides
Lipids
Amino acids
Monosaccharides
Glycerol, fatty acids
Acetyl CoA
Citric acid cycle
ATP
CO2

Carbohydrates Metabolism

- Objectives
  - Utilization of Glucose → Energy
  - Non-Carbohydrates → Glucose
  - Storage of Glucose → Glycogen
  - Release of Glucose from Glycogen
  - Reducing Power NADPH >> GSH
  - Glucuronic acid >> Drug metabolism
  - Interconversion of sugars

An Over-all Picture



Dietary Carbohydrates

40 – 50 % of caloric intact

60% of the carbohydrate $\Rightarrow$ starch

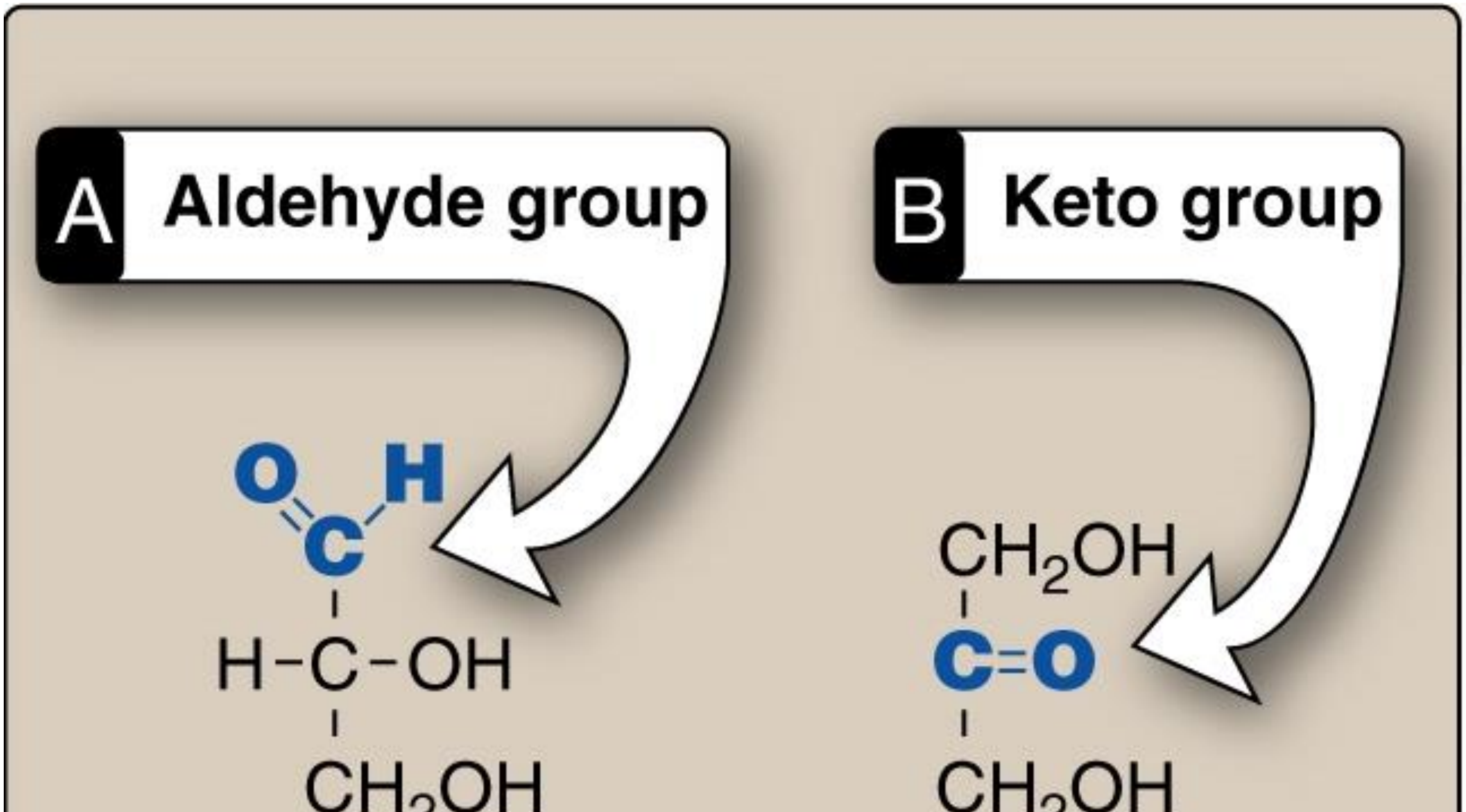
Sucrose
small amount of Fru , Glu , in fruits , honey , Veg.

Lactose in milk

No specific sugar is required

All sugars are interconverted

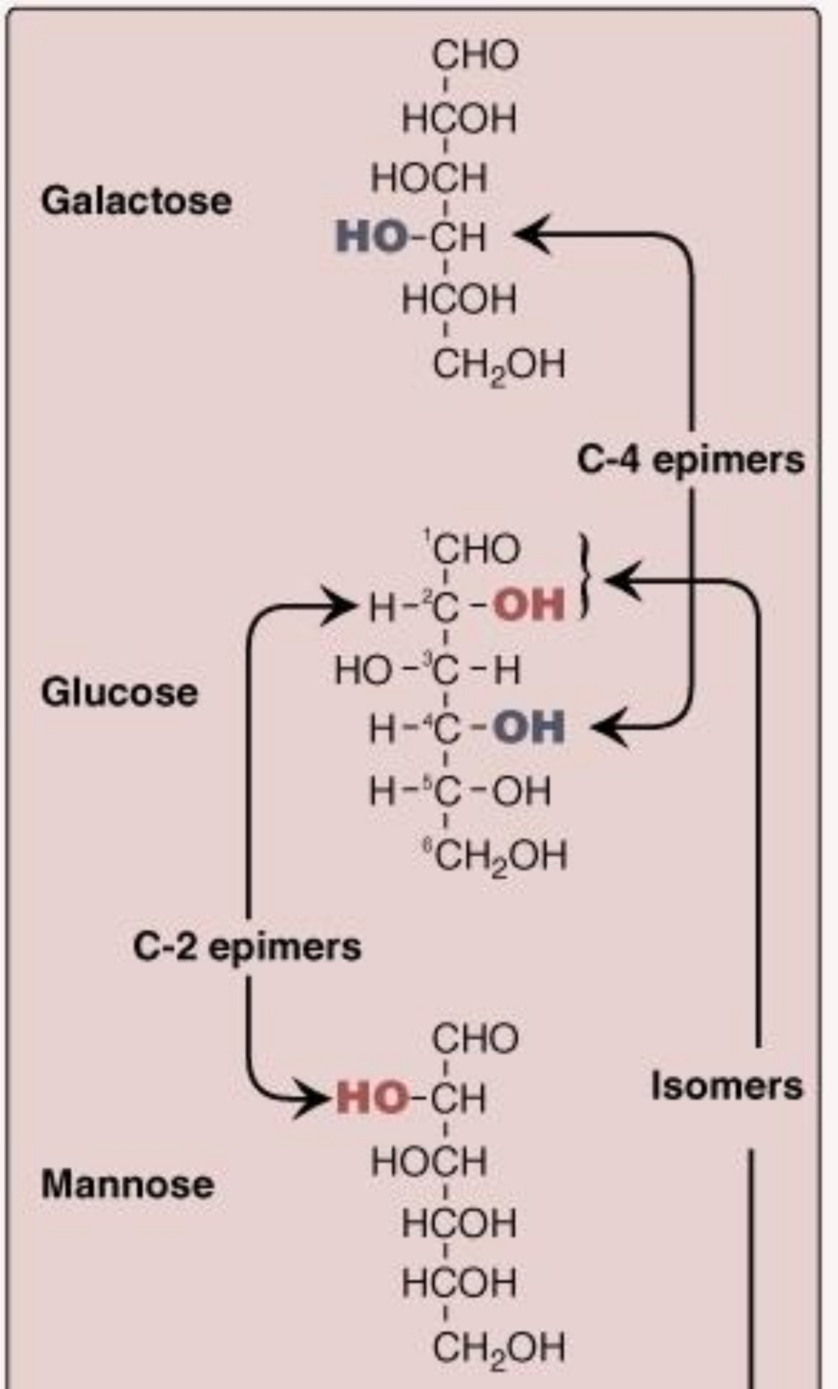
Examples of
an aldose and ketose



Ribose	Ribulose
Glucose	Fructose

Examples of monosaccharides found in human

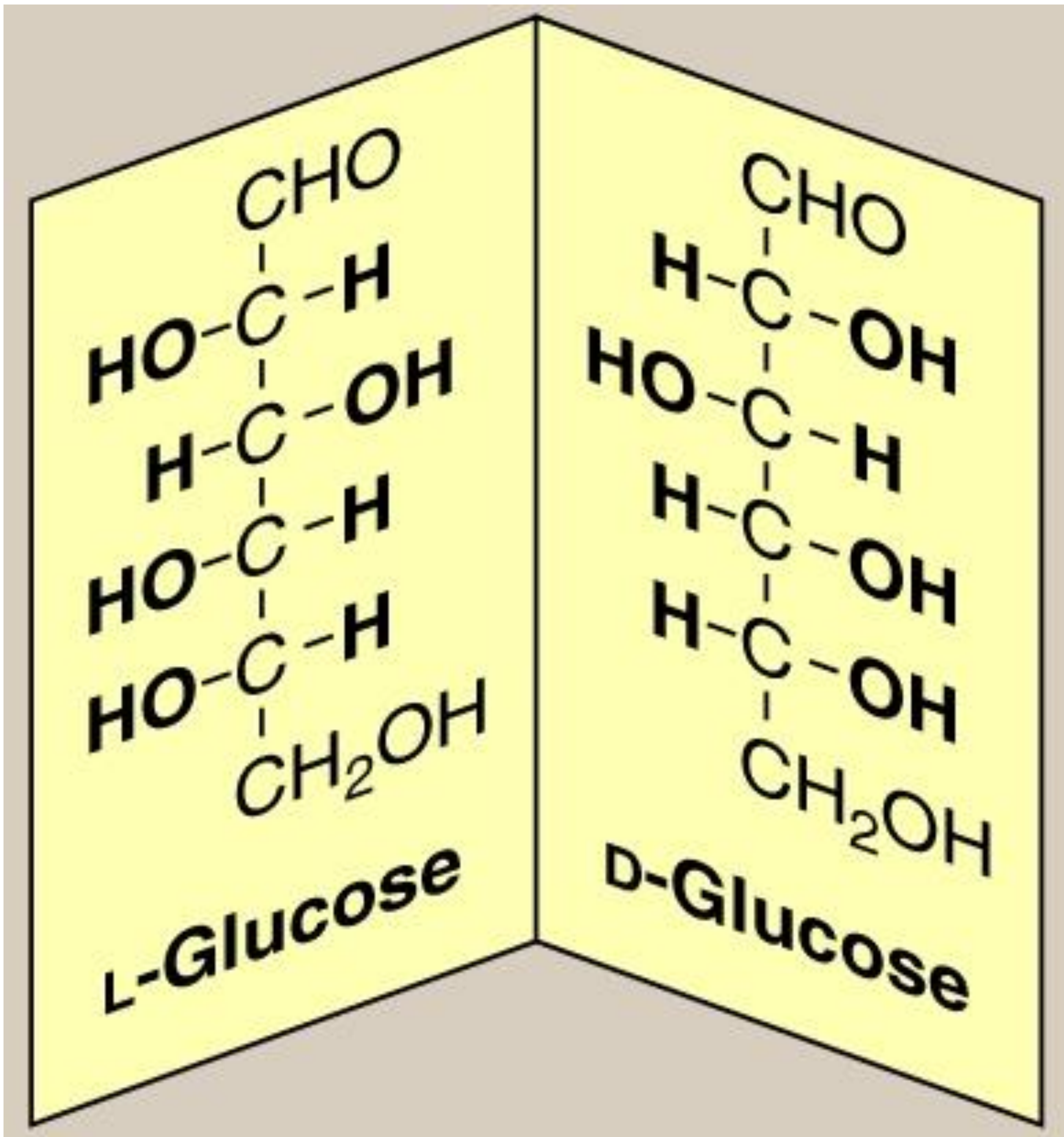
Generic names		Examples
3 carbons:	trioses	Glyceraldehyde
4 carbons:	tetroses	Erythrose
5 carbons:	pentoses	Ribose
6 carbons:	hexoses	Glucose
7 carbons:	heptoses	Sedoheptulose
9 carbons:	nonoses	Neuraminic acid



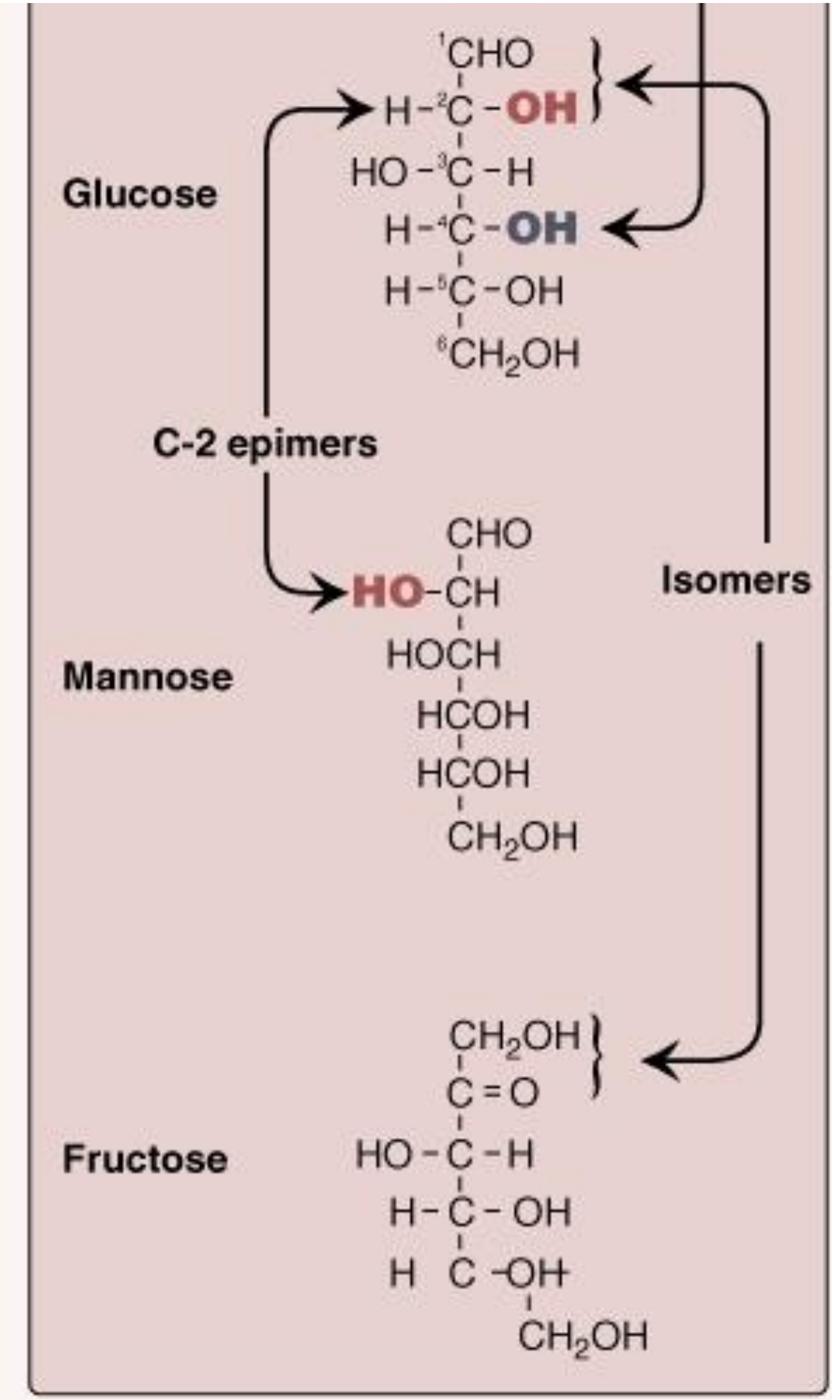
Isomers

Epimers are isomers:

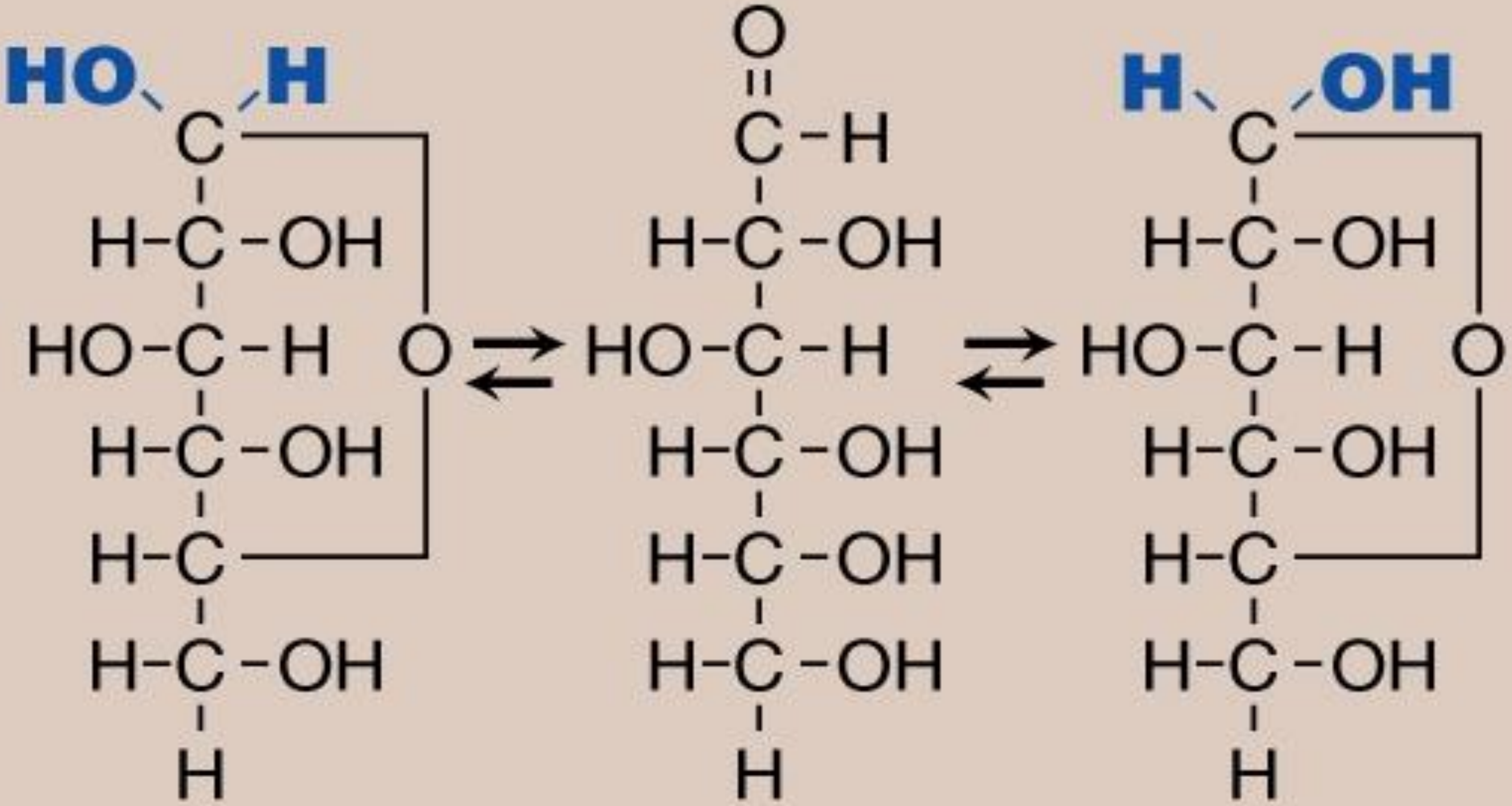
Changing the orientation of one hydroxyl group will produce different sugar



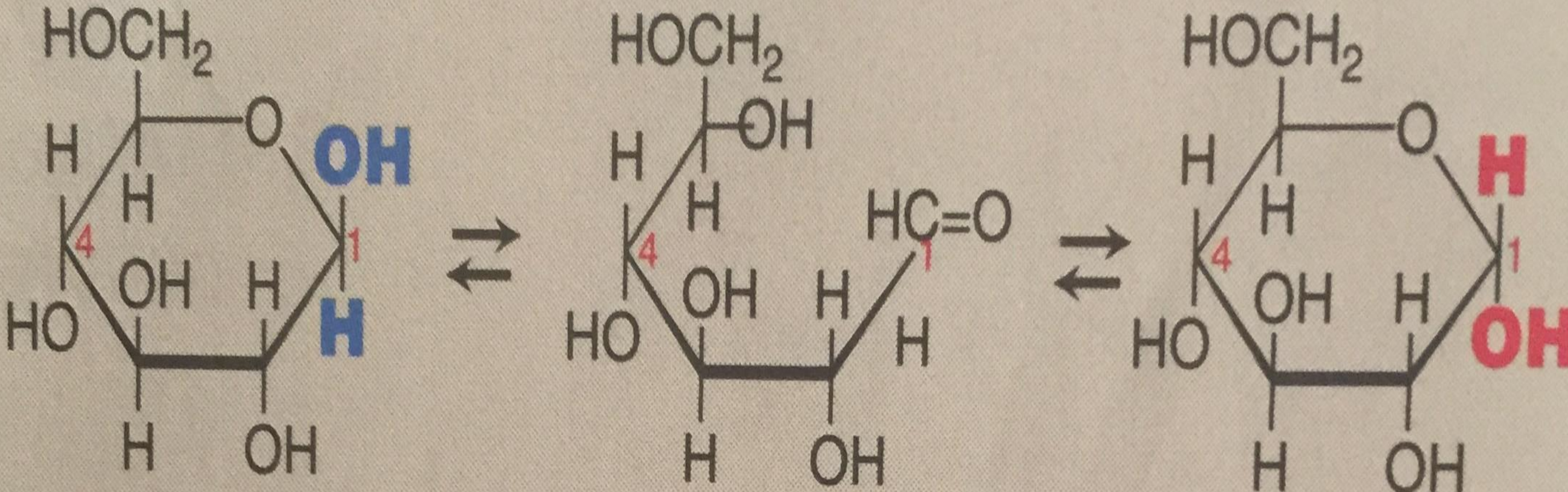
CHO
HO-C-H
H-C-OH
HO-C-H
HO-C-H
CH2OH
L-Glucose
CHO
H-C-OH
HO-C-H
H-C-OH
H-C-OH
CH2OH
D-Glucose



Glucose and Fructose are isomers



β-D-Glucopyranose　　D-Glucose　　α-D-Glucopyranose



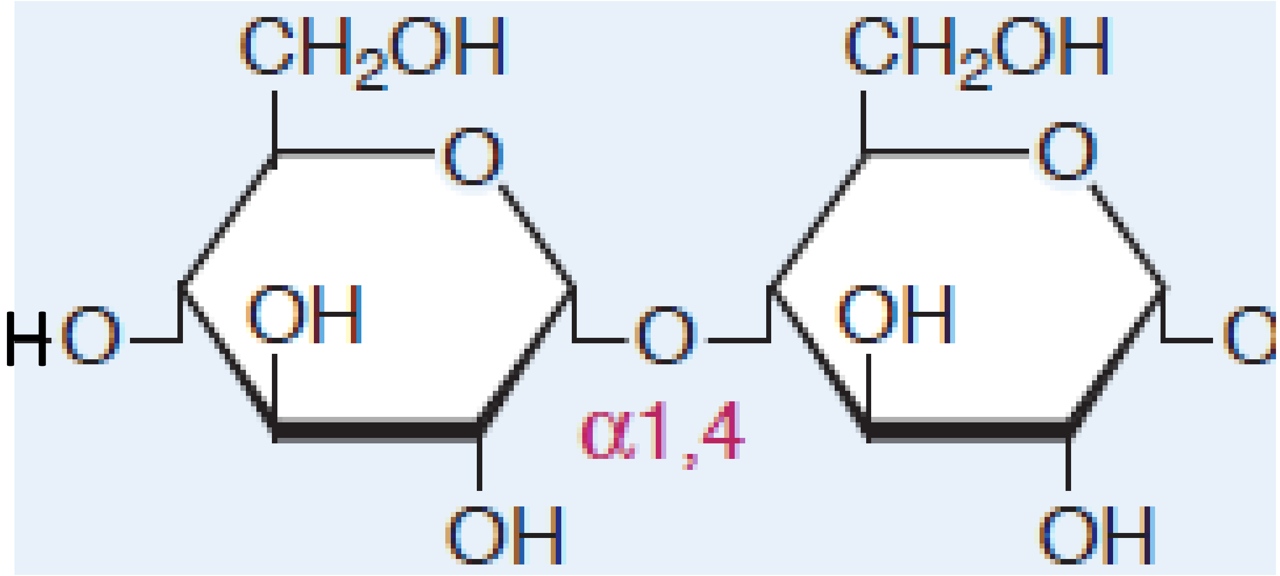
β-D-Gluco-
pyranose

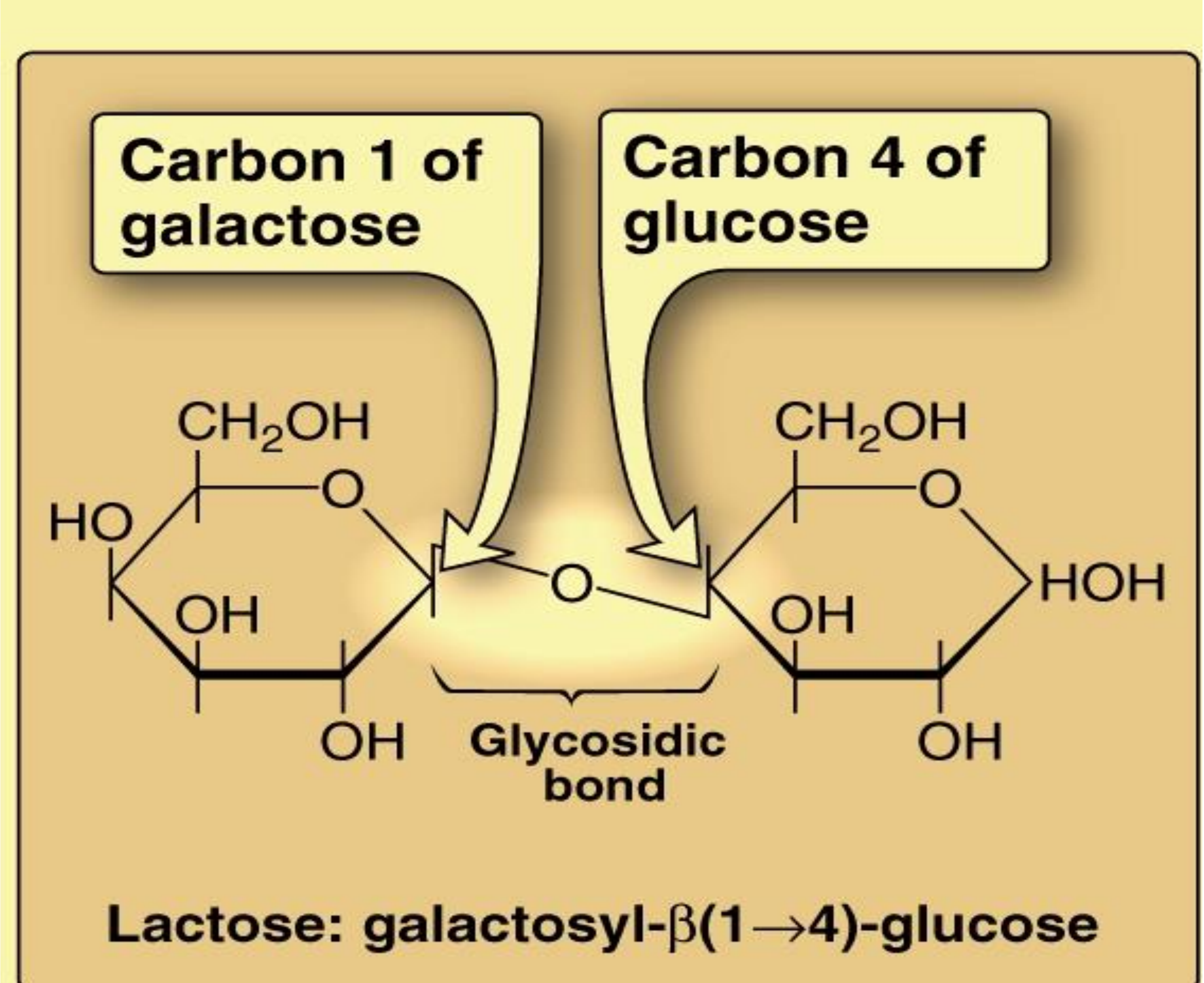
D-Glucose

α-D-Gluco-
pyranose

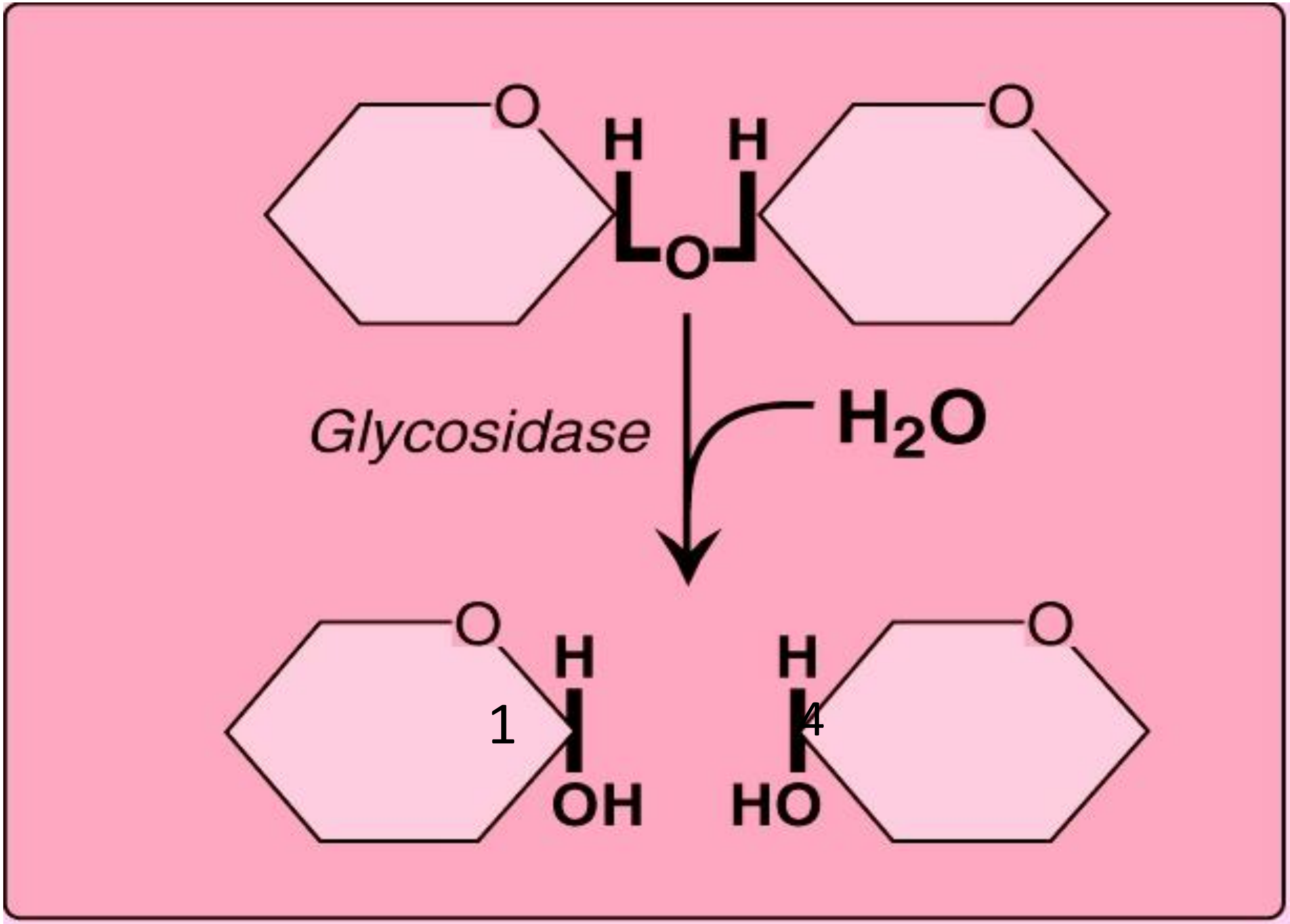
Disaccharide: A sugar made of two sugar units joined by glycosidic bond

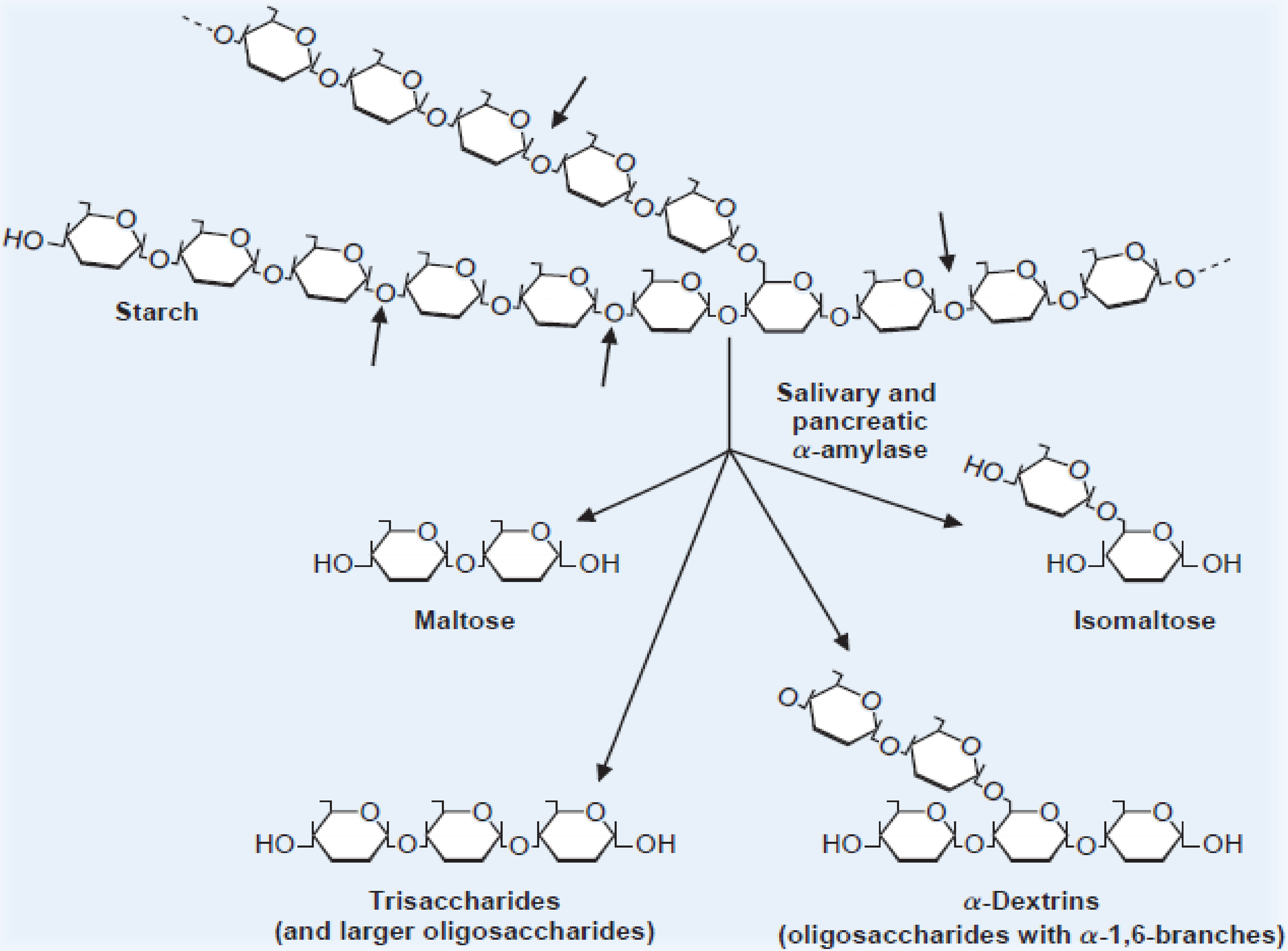
Maltose: a disaccharide made from two glucose units

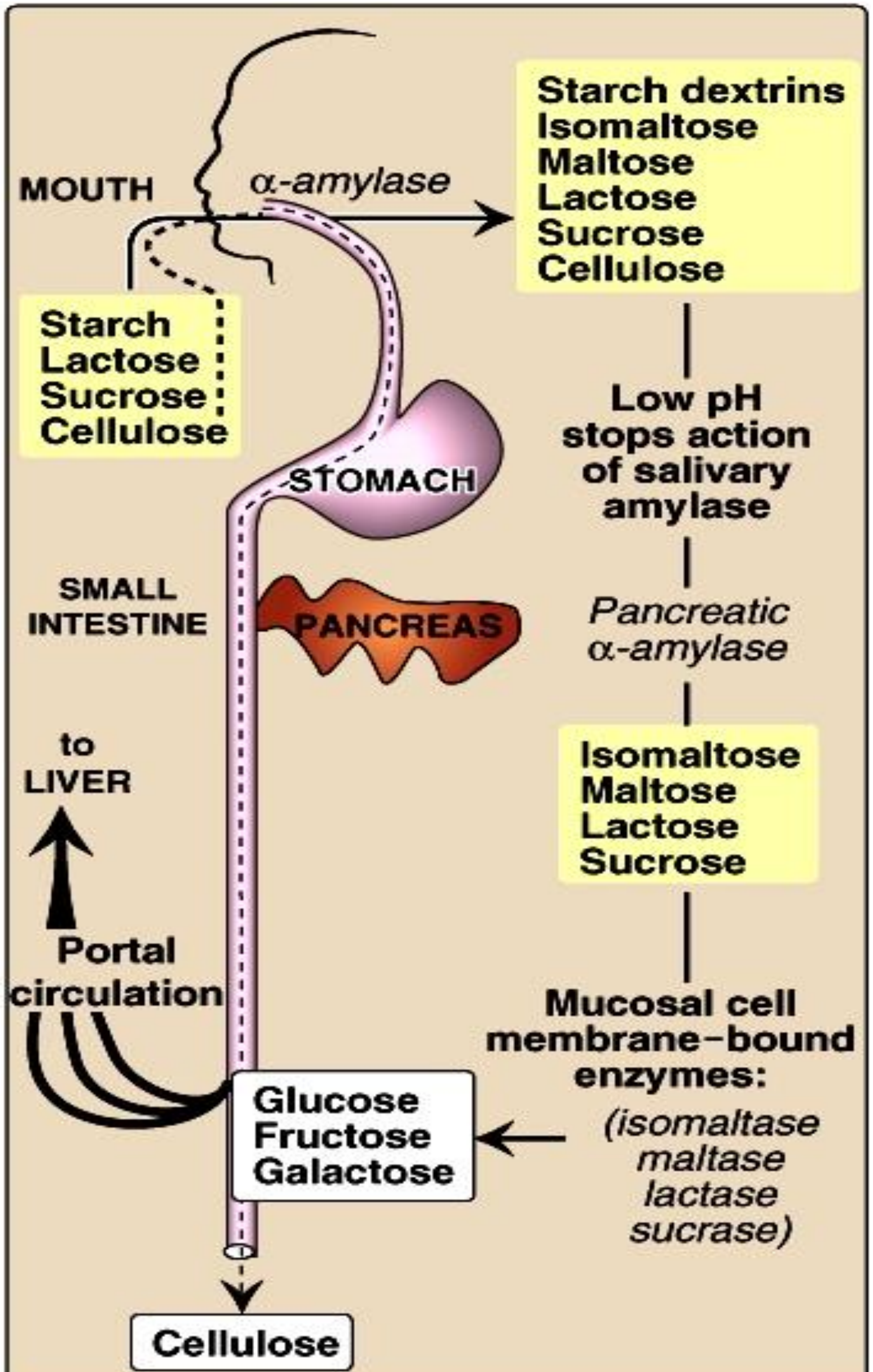



Carbon 1 of galactose
Carbon 4 of glucose
CH2OH
HO
OH
OH
O
O
CH2OH
O
HOH
OH
OH
Glycosidic bond
Lactose: galactosyl-β(1→4)-glucose

Glycosidic bond is cleaved by glycosidase



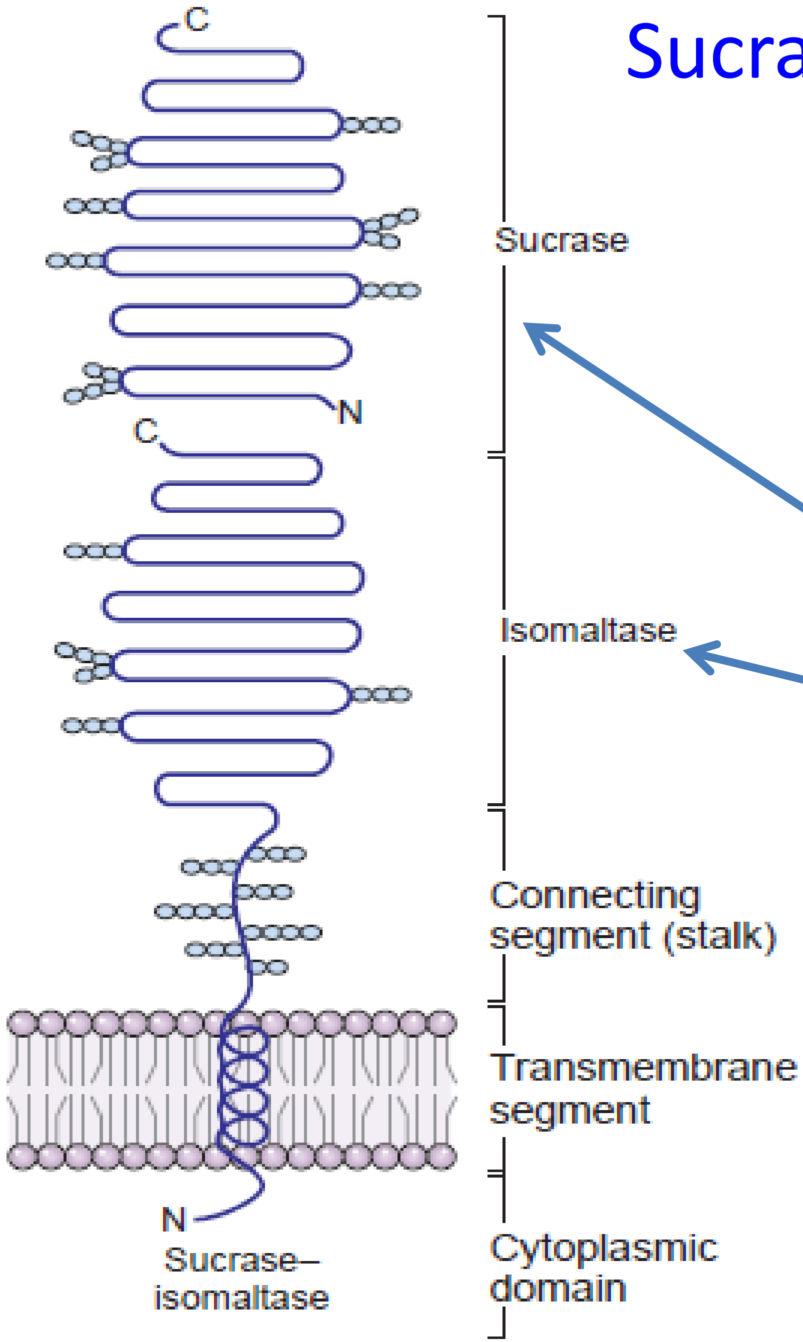

Starch
Salivary and pancreatic α-amylase
Maltose
Isomaltose
Trisaccharides (and larger oligosaccharides)
α-Dextrins (oligosaccharides with α-1,6-branches)


MOUTH
α-amylase
Starch dextrins
Isomaltose
Maltose
Lactose
Sucrose
Cellulose
Starch
Lactose
Sucrose
Cellulose
STOMACH
Low pH stops action of salivary amylase
SMALL INTESTINE
PANCREAS
Pancreatic α-amylase
Isomaltose
Maltose
Lactose
Sucrose
to LIVER
Portal circulation
Mucosal cell membrane-bound enzymes:
(isomaltase maltase lactase sucrase)
Glucose
Fructose
Galactose
Cellulose

Mucosal cell membrane-bound enzymes

ENZYME	Bond Cleaved	Substrates
Isomaltase	α 1→ 6	Isomaltose
Maltase	α 1→ 4	Maltose
Sucrase	α 1→ 2	Sucrose
Lactase	β 1→ 4	Lactose
Trehalase	α 1→ 1	Trehalose
Exoglucosidase	α 1→ 4	Glucoamylose

Sucrase-isomaltase complex and Glucoamylase



* Sucrase + isomaltase
  Single protein → complex of two associated subunits
  -Sucrase-maltase
  - Isomaltasse-maltase
  Together 80% of the maltase activity

* Maltase + exoglucosidase (glucoamylase): no split

Sucrase + isomaltase

FIG. 27.5. The major portion of the sucrase–isomaltase complex, containing the catalytic sites, protrudes from the absorptive cells into the lumen of the intestine. Other domains of the protein form a connecting segment (stalk) and an anchoring segment that extends through the membrane into the cell. The complex is synthesized as a single polypeptide chain that is split into its two enzyme subunits extracellularly. Each subunit is a domain with a catalytic site (distinct sucrase–maltase and isomaltase–maltase sites). In spite of their maltase activity, these catalytic sites are often called just *sucrase* and *isomaltase*.

Maltase + exoglucosidase (glucoamylase , α-1,4 in limit dextrins) ….. No split

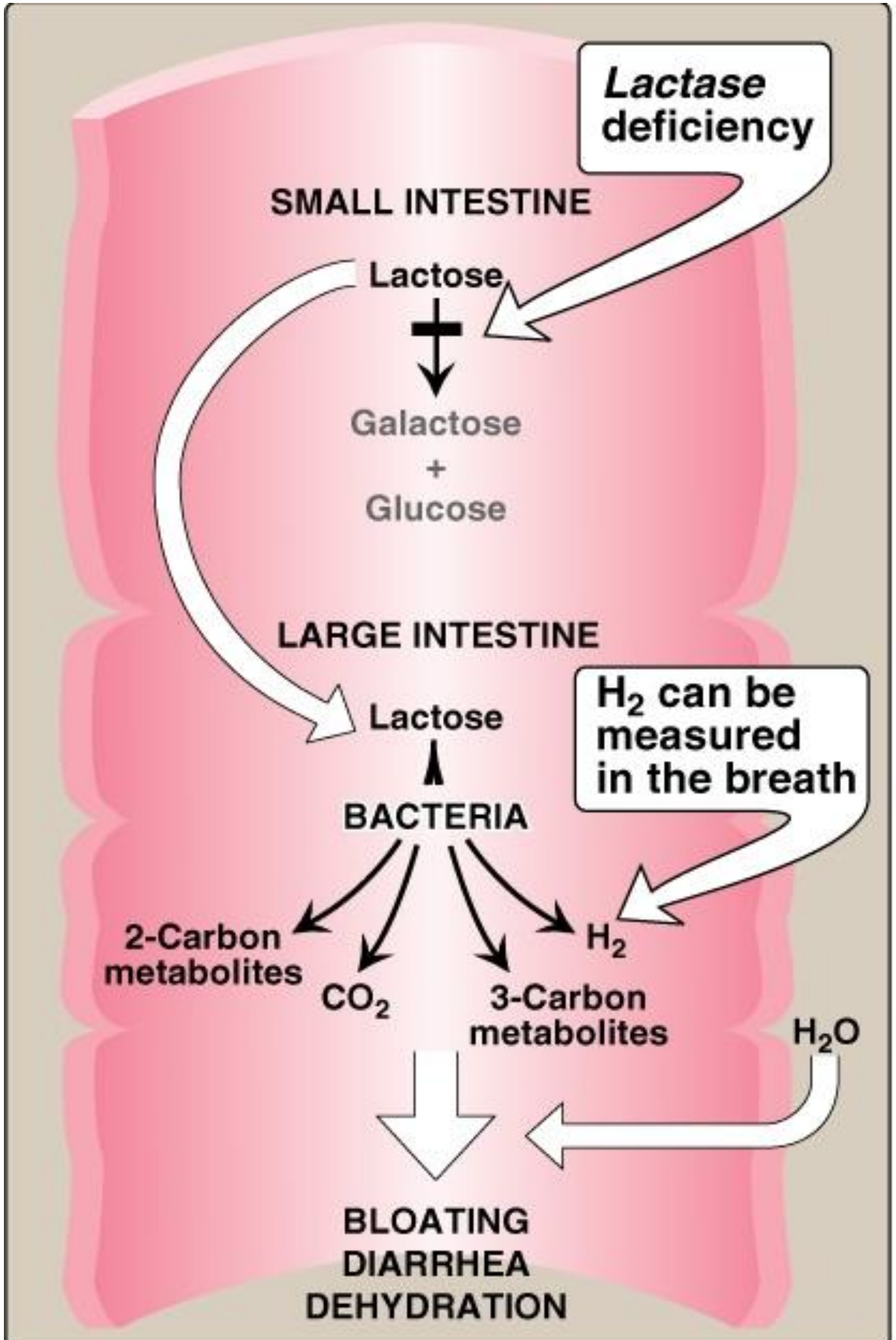
Trehalsae

Abnormal Degradation of disaccharides

- Lactase deficiency:
- ½ world's population
- 90% of African and Asian Adults

- Sucrase isomaltase deficiency:
- 10% of Askimos; 2% NorthEuropean are heterozygotes

- Causes:
  - Genetics
  - Variety of intestinal diseases
  - Malnutrition
  - Injury of mucosa ie by drugs
  - Severe diarrhea



Maximal activity @ 1 month of age

<u>Adult Hypolactasia</u>

(lactase deficiency)

Declines ----- >> adult level at 5 to 7 year of age

10 % of infant level

1 cup of milk (9 grams of lactoses) → loss of 1 liter of extracellular fluid

Absorption of Sugars

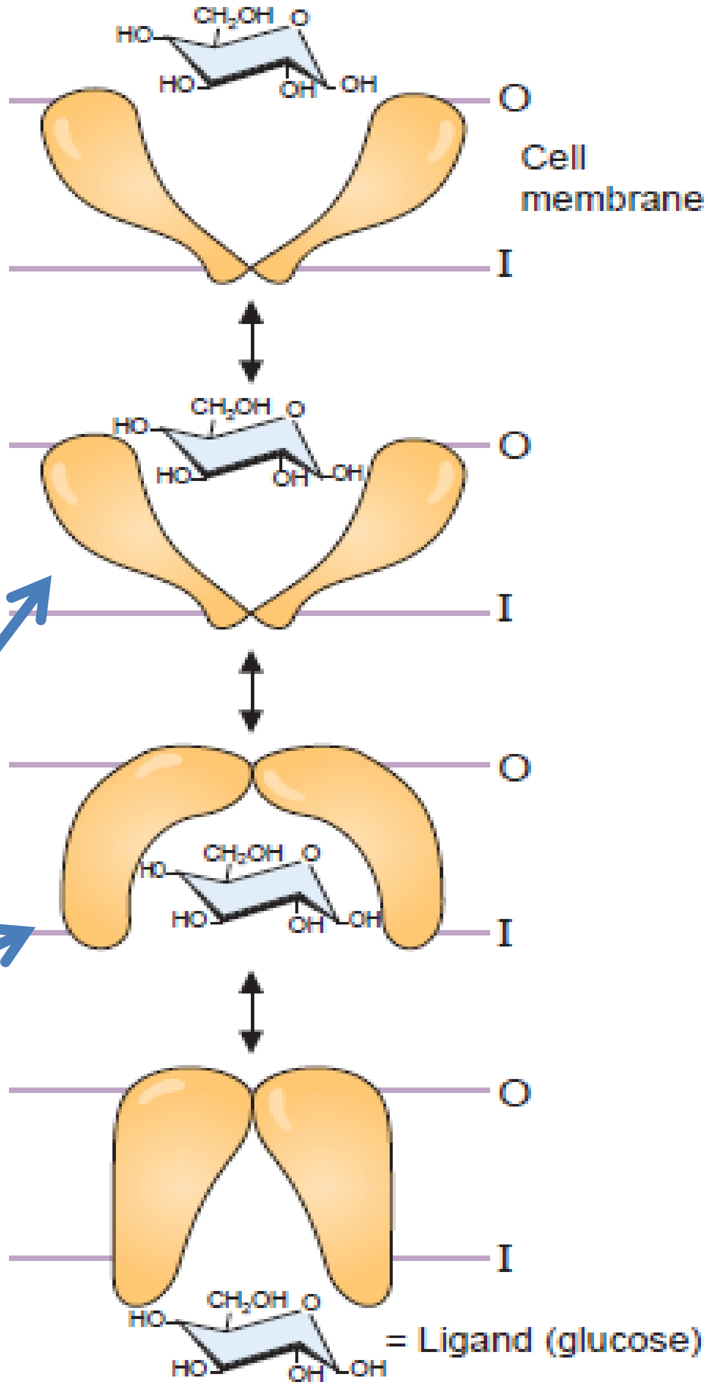
Polar molecules can not diffuse

A: Na^+-independent facilitated diffusion transport

GLUT 1-----GLUT 14

Glc. Movement follows concentration gradient

Two conformation states



Na^+ monosaccharide cotransporter system (SGLT)

* Against concentration gradient.
* Small intestine: Active uptake from lumen of intestine.
* Kidney: reabsorption of glucose in proximal tubule.

Na^+ monosaccharide cotransporter system (SGLT)

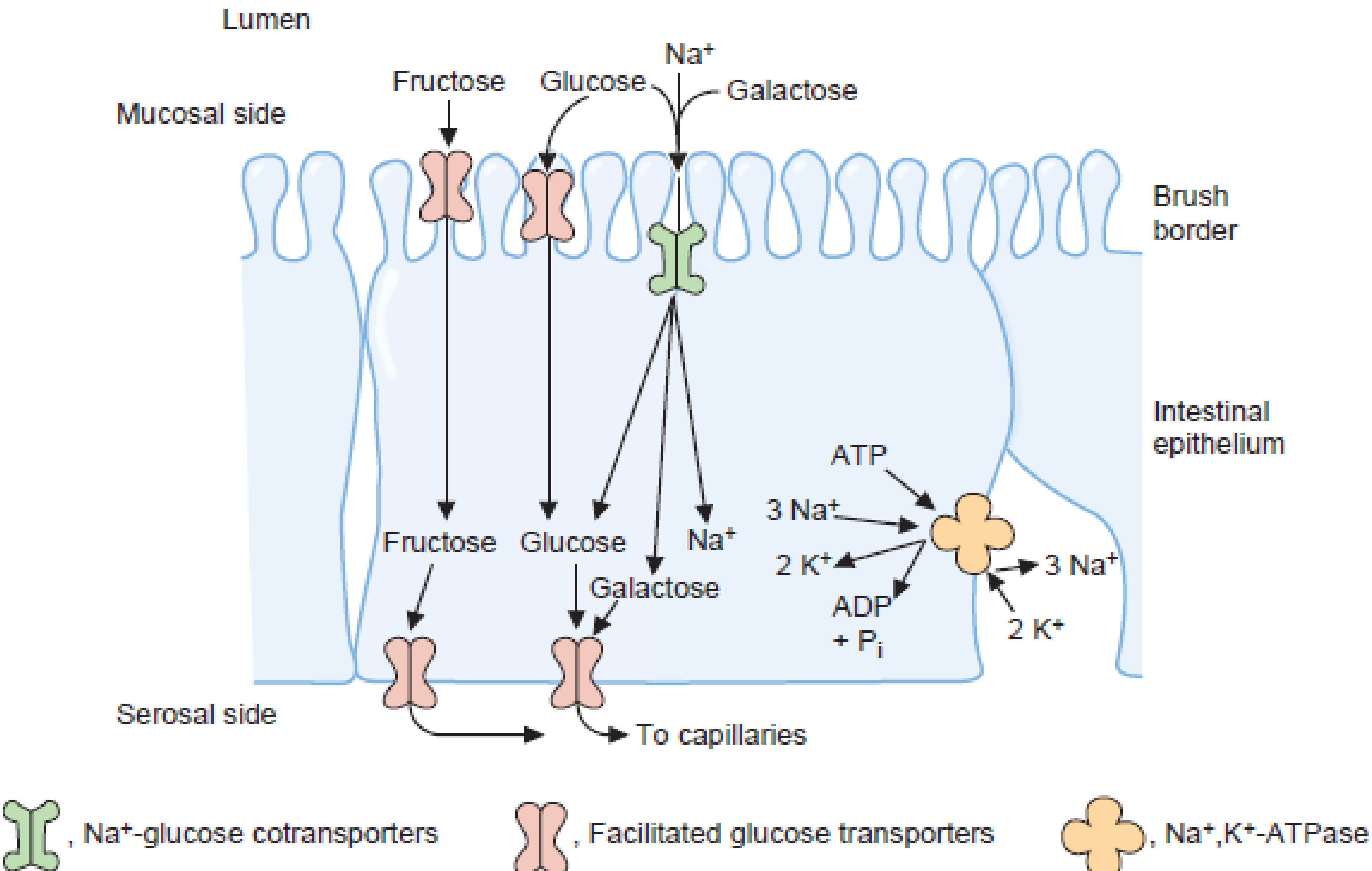
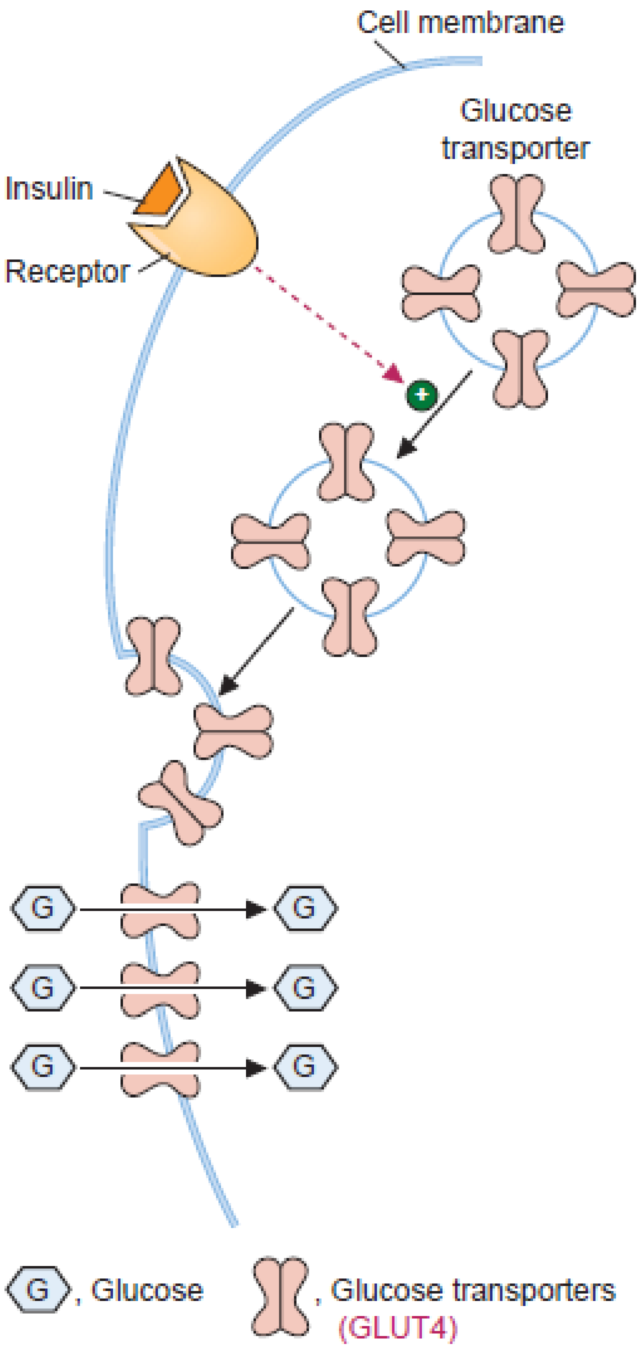
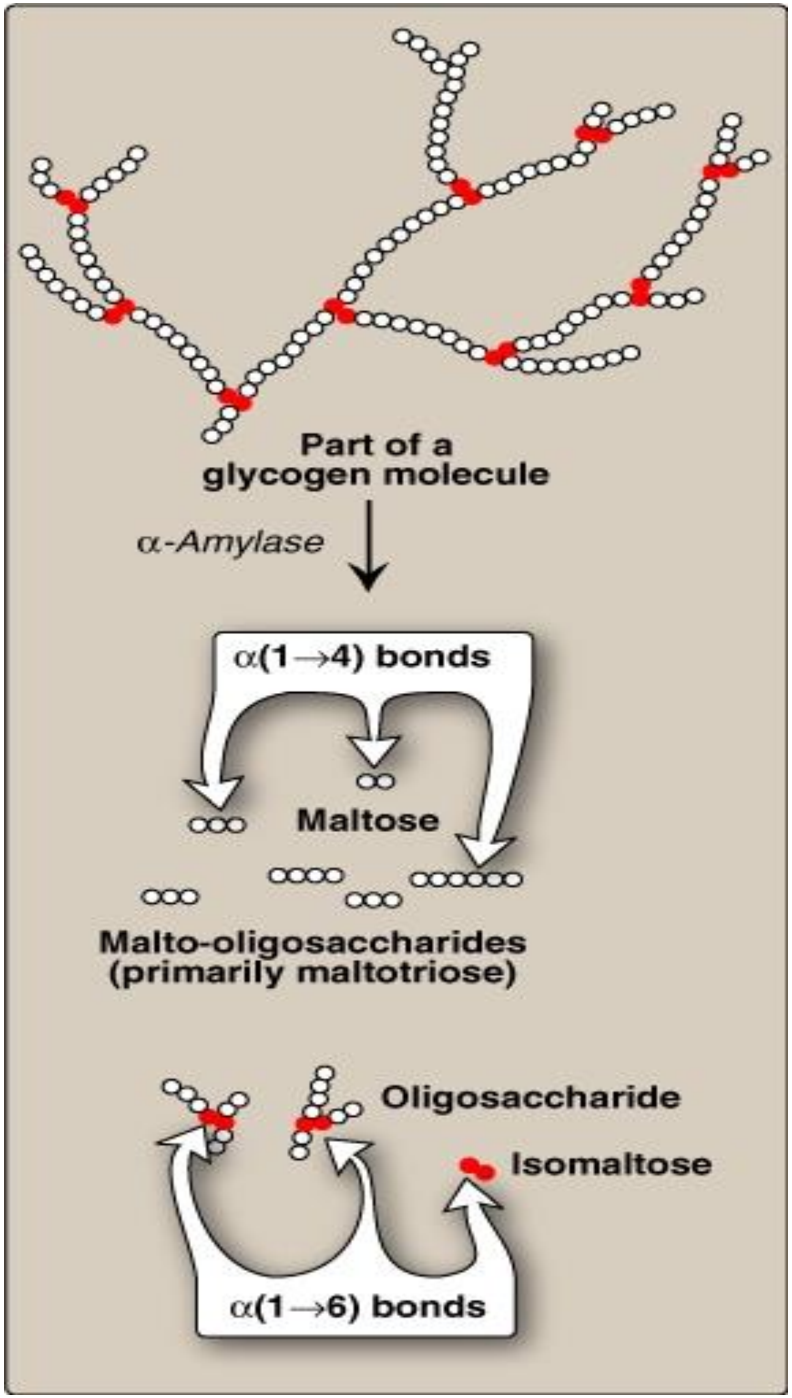


Table 27.5 Properties of the GLUT 1 to GLUT 5 Isoforms of the Glucose Transport Proteins

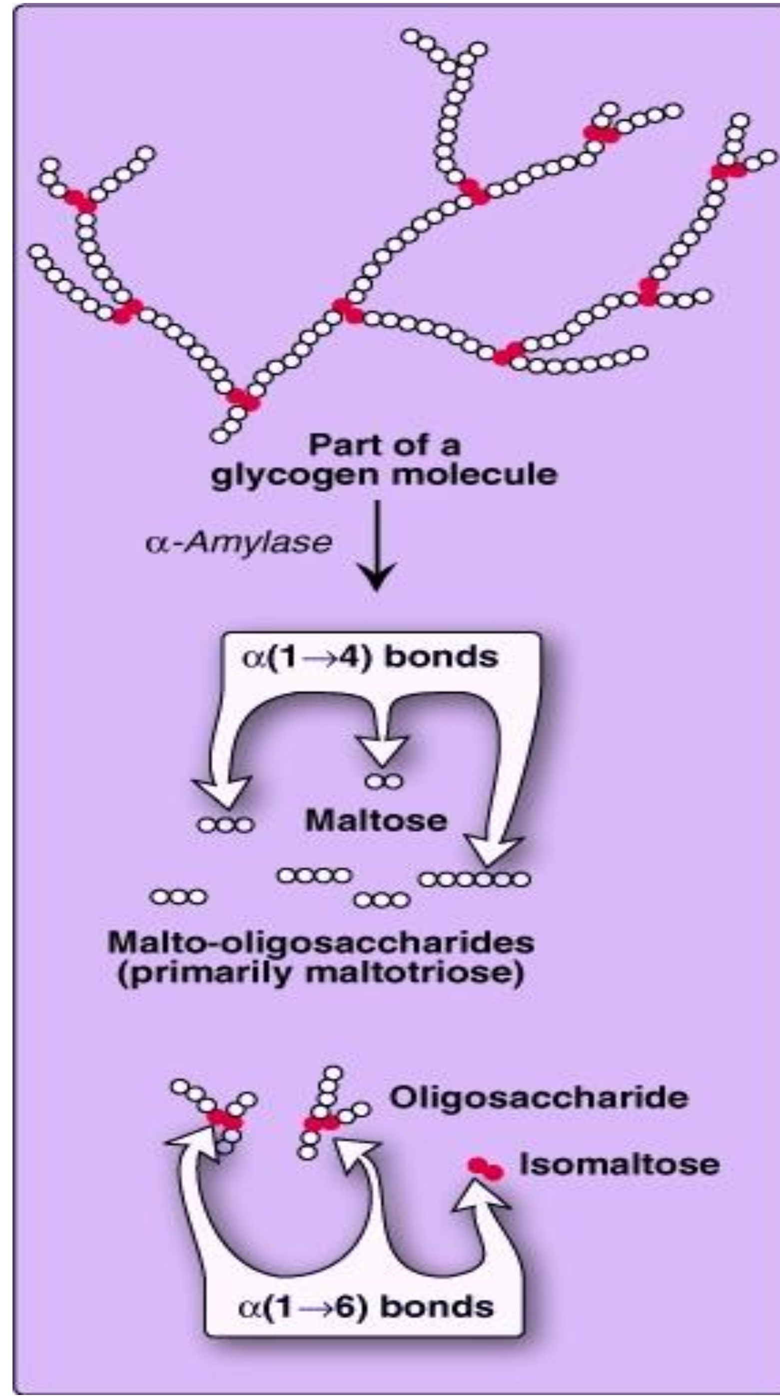
Transporter	*Tissue Distribution*	*Comments*
GLUT 1	Human erythrocyte Blood–brain barrier Blood–retinal barrier Blood–placental barrier Blood–testis barrier	Expressed in cell types with barrier functions; a high-affinity glucose transport system
GLUT 2	Liver Kidney Pancreatic β-cell Serosal surface of intestinal mucosa cells	A high-capacity, low-affinity transporter May be used as the glucose sensor in the pancreas
GLUT 3	Brain (neurons)	Major transporter in the central nervous system; a high-affinity system
GLUT 4	Adipose tissue Skeletal muscle Heart muscle	Insulin-sensitive transporter. In the presence of insulin, the number of GLUT 4 transporters increases on the cell surface; a high-affinity system
GLUT 5	Intestinal epithelium Spermatozoa	This is actually a fructose transporter
GLUT 7	Glucogenic tissues	at endoplasmic reticulum membrane



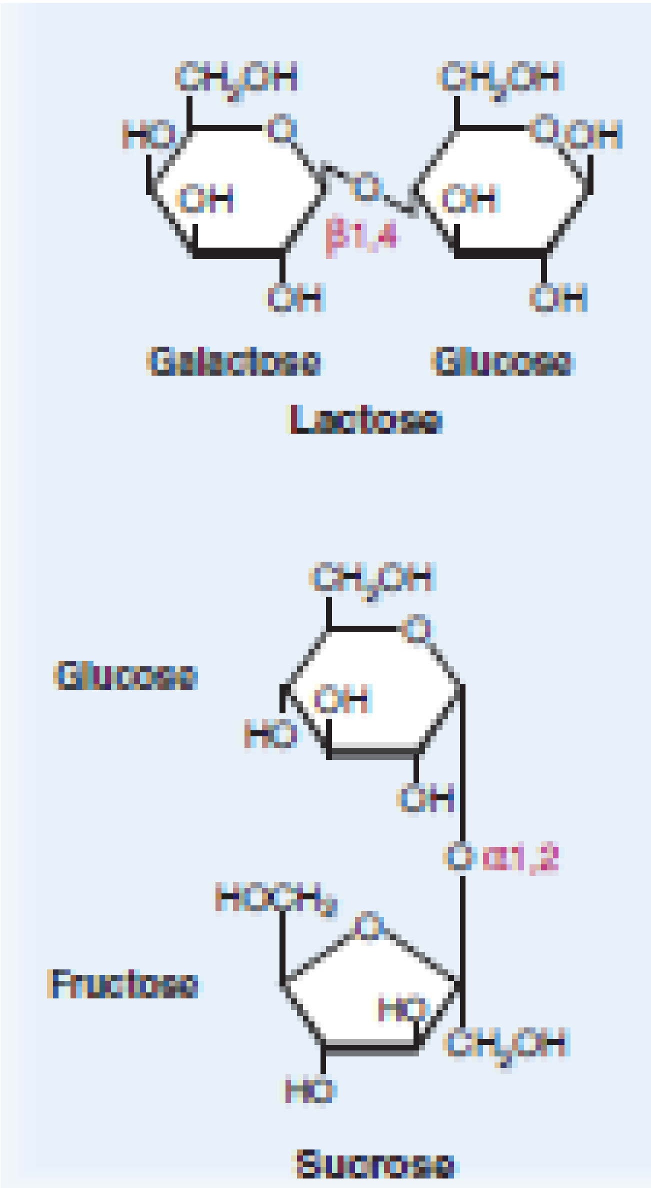
Insulin stimulates transport of glucose into muscle and adipose tissues


Part of a
glycogen molecule
α-Amylase
α(1→4) bonds
Maltose
Malto-oligosaccharides
(primarily maltotriose)
Oligosaccharide
Isomaltose
α(1→6) bonds

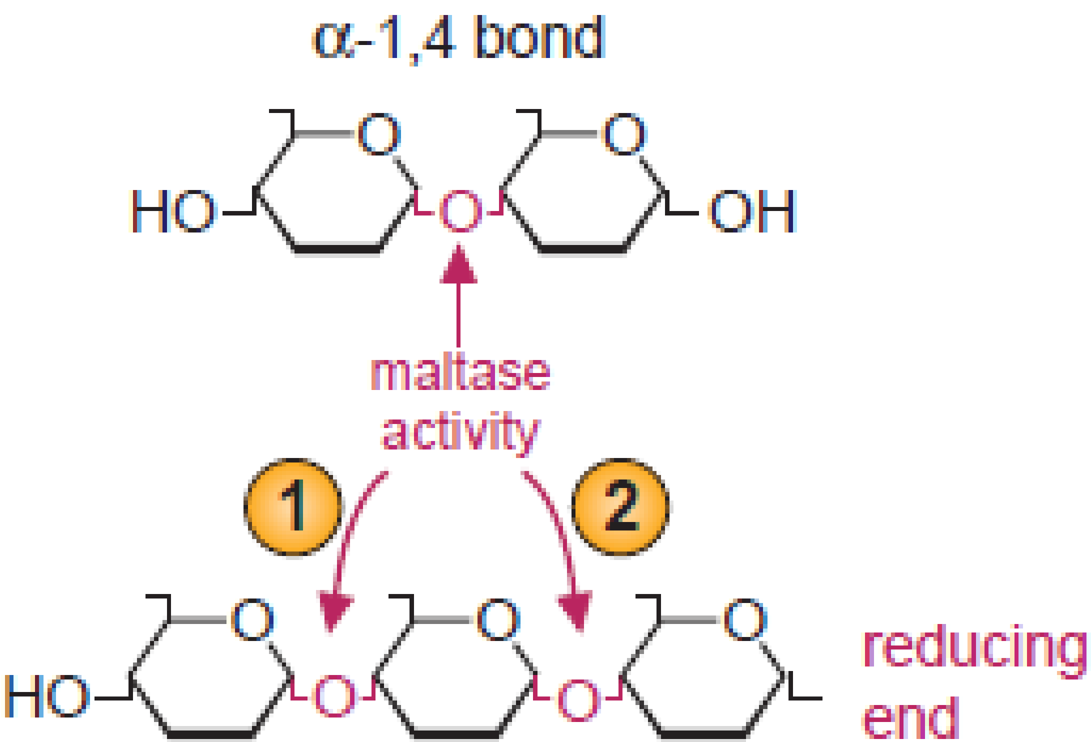
d


Part of a
glycogen molecule
α-Amylase
α(1→4) bonds
Maltose
Malto-oligosaccharides
(primarily maltotriose)
Oligosaccharide
Isomaltose
α(1→6) bonds

e

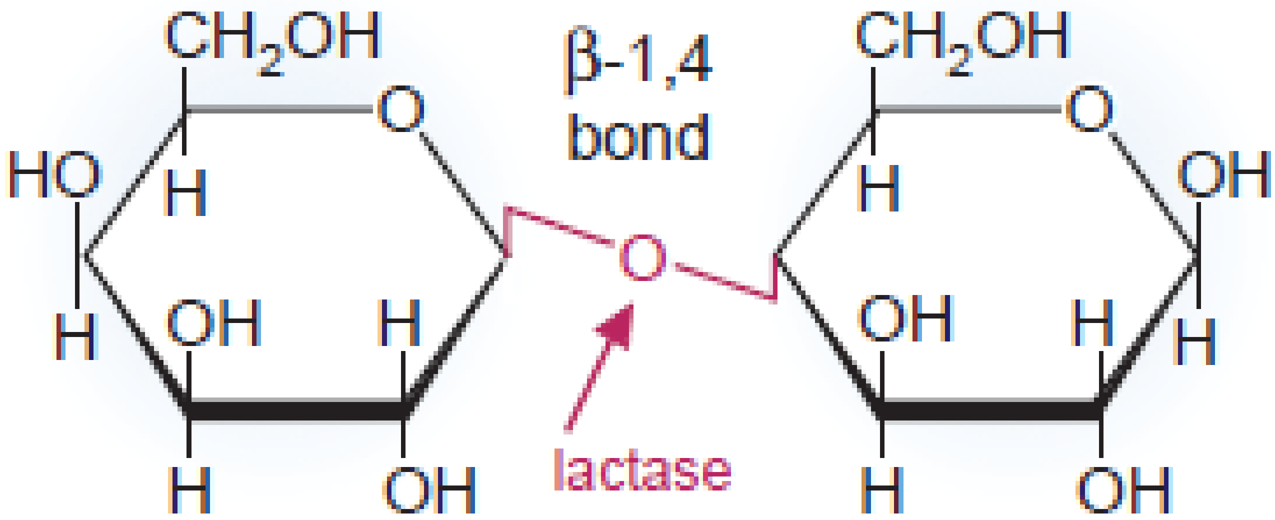

CH2OH
HO
O
OH
OH
β1,4
CH2OH
O
OH
OH
OH
Galactose
Glucose
Lactose
CH2OH
O
Glucose
OH
HO
OH
O α1,2
HOCH2
O
Fructose
HO
CH2OH
HO
Sucrose

Maltose

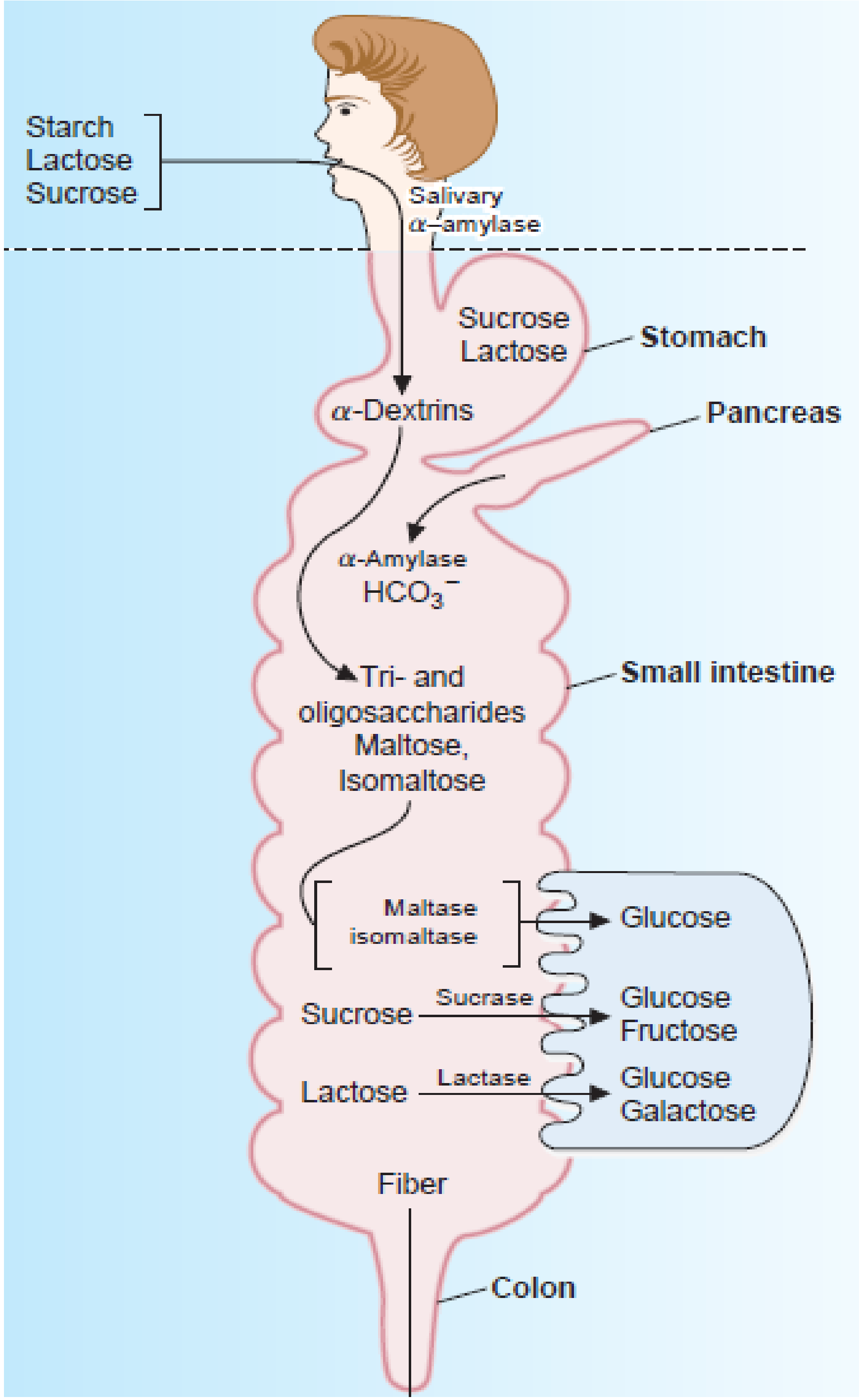


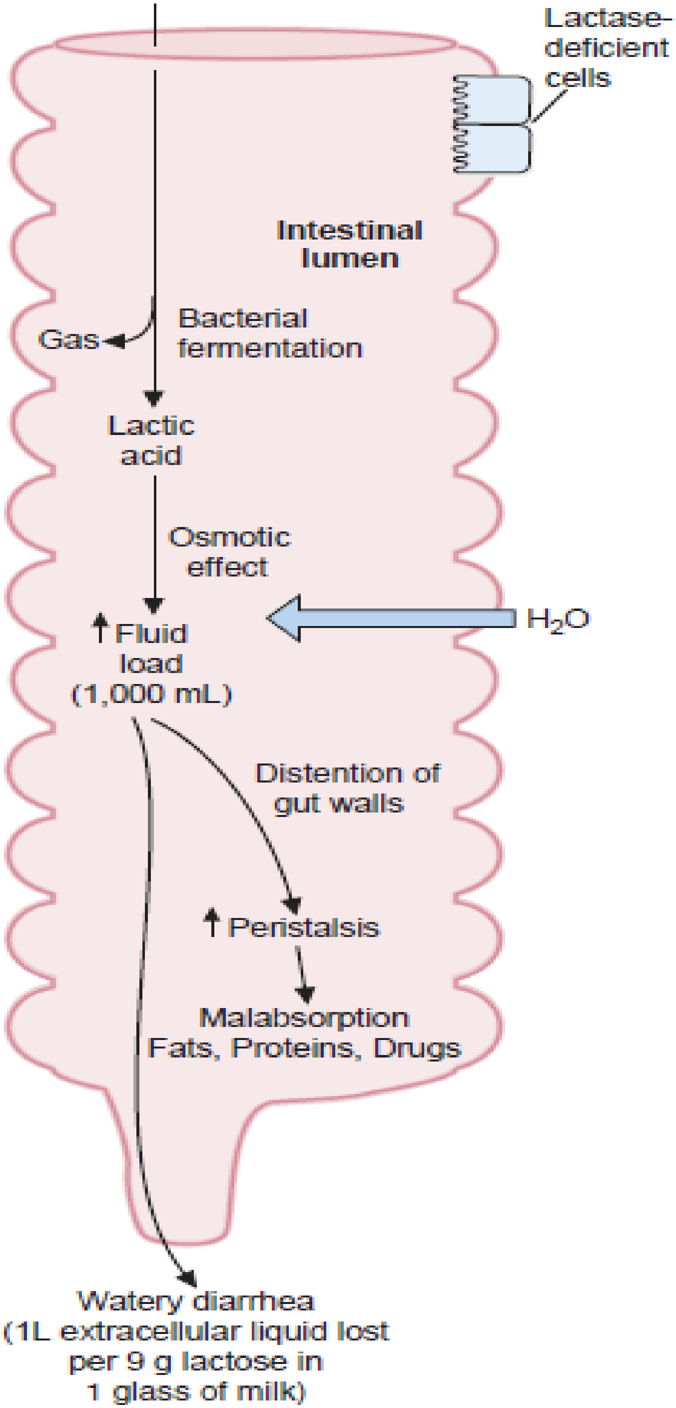
Maltotriose

Lactose



Galactose **Glucose**


Starch
Lactose
Sucrose
Salivary
α-amylase
Sucrose
Lactose
Stomach
α-Dextrins
Pancreas
α-Amylase
HCO_3^-
Small intestine
Tri- and
oligosaccharides
Maltose,
Isomaltose
Maltase
isomaltase
Glucose
Sucrose
Sucrase
Glucose
Fructose
Lactose
Lactase
Glucose
Galactose
Fiber
Colon


Lactase-
deficient
cells
Intestinal
lumen
Gas
Bacterial
fermentation
Lactic
acid
Osmotic
effect
H_2O
↑ Fluid
load
(1,000 mL)
Distention of
gut walls
↑ Peristalsis
Malabsorption
Fats, Proteins, Drugs
Watery diarrhea
(1L extracellular liquid lost
per 9 g lactose in
1 glass of milk)