UNIT II:

Intermediary Metabolism

Introduction to Carbohydrates

Debdeep Dasgupta, Ph.D
Department of Microbiology
Surendranath College

Overview

- Carbohydrates are the most abundant organic molecules in nature
- Wide range of functions e.g., a significant fraction of the energy in the diet, acting as storage form of energy in body, serving as memb. components that mediate some forms of intercellular communication
- Carbohydrates also serve as structural component of many organisms, including CW of bacteria, exoskeleton of many insects, & fibrous cellulose of plants
- The empiric formula for many of the simpler carbohydrates is $(CH2O)_n$, hence the name “hydrate of carbon”

II. Classification and structure of carbohydrates

- Monosacch (simple sugars) can be classified according to # of C atoms they contain.
- CHO's with an aldehyde as their most oxidized functional group are called aldoses, whereas those with a keto group as their most oxidized functional group are ketoses e.g., glyceraldehyde is an aldose, whereas dihydroxyacetone is a ketose
- CHO's that have a free carbonyl group have the suffix "-ose"

Note: ketoses (with some exceptions e.g., fructose) have an additional 2 letters in their suffix; "-ulose", e.g., xylulose

- Monosacch can be linked by glycosidic bonds to create larger structures
  - Disacch contain 2 monosacch units
  - Oligosacch contain from 3 to about 12 monosacch units
  - Polysacch contain > 12 monosacch units, can be 100's of sugar units

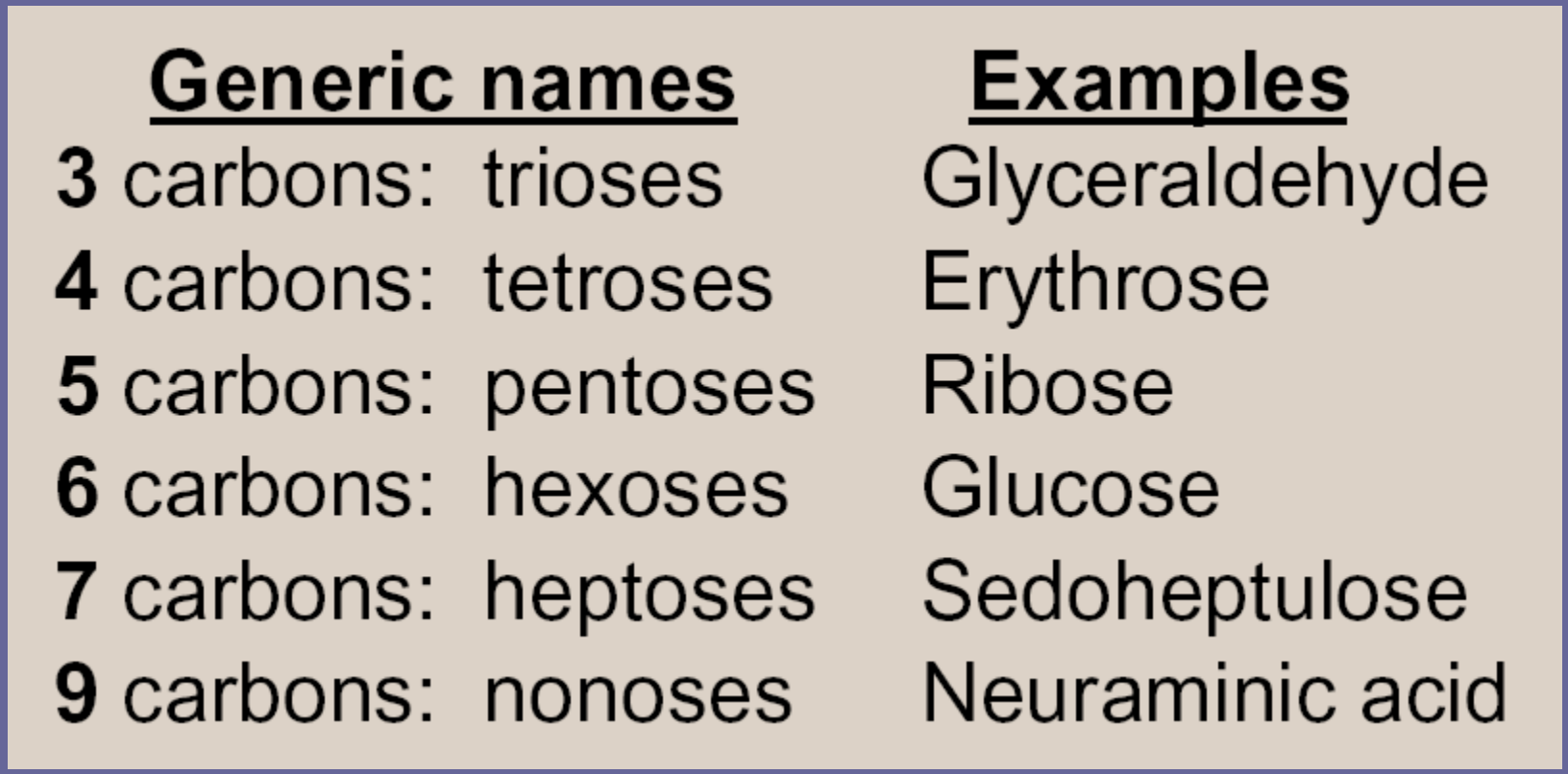


Figure 7.1. Examples of monosaccharides found in humans, classified according to the number of carbons they contain.

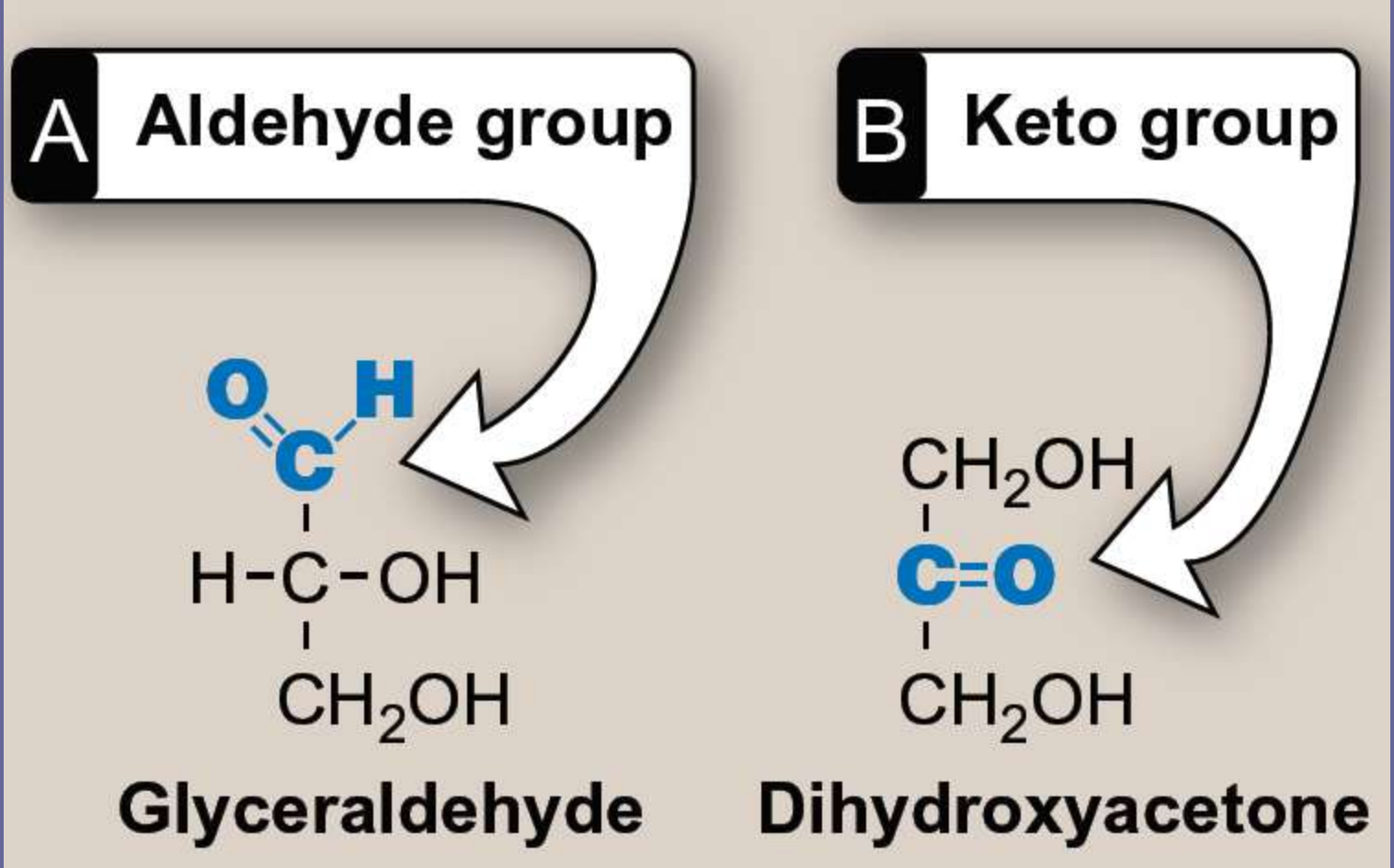


Figure 7.2. Examples of an aldose (A) and a ketose (B) sugar.

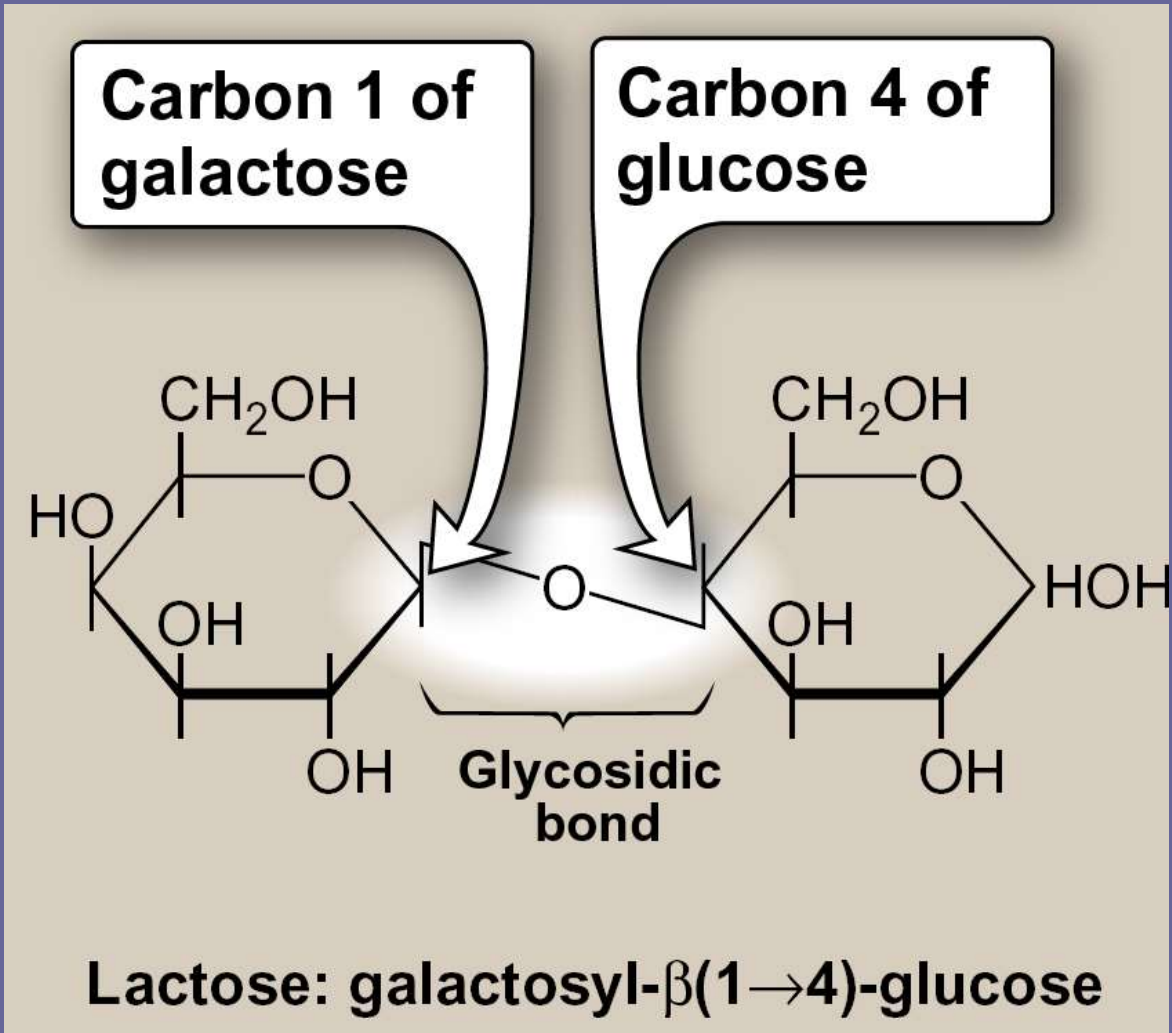


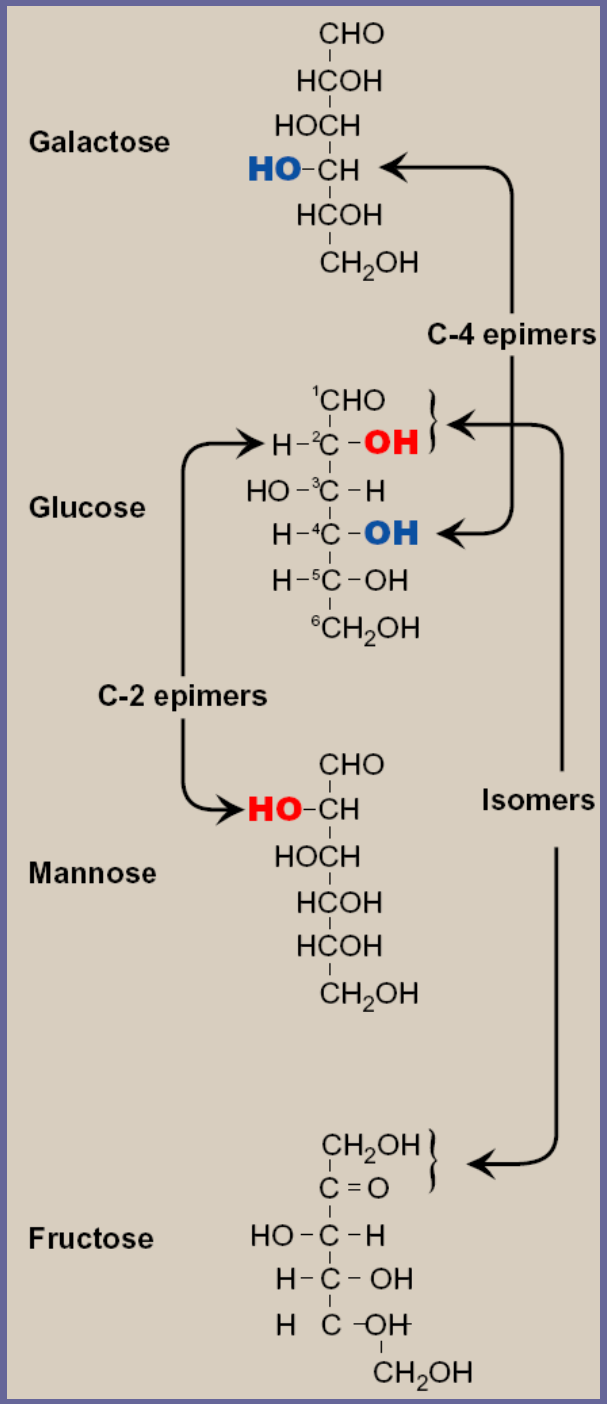
Figure 7.3. A glycosidic bond between two hexoses producing a disaccharide.

A. Isomers and epimers

- Cpds that have same chemical formula but have different structures = isomers e.g., fructose, glucose, mannose, & galactose are all isomers of each other, having same formula $C_6H_{12}O_6$
- If 2 monosacch differ in configuration around only one specific C atom (with exception of carbonyl C), they are defined as epimers of each other (of course they are also isomers) e.g.,
  - glucose & galactose are C-4 epimers, their structures differ only in the position of –OH group at C 4.
  - Glucose & mannose are C-2 epimers
  - however, galactose & mannose are not epimers, they differ in position of –OH groups at two carbons, and defined only as isomers

Note: carbons in sugars are numbered beginning at end containing the carbonyl C i.e., aldehyde or keto group

Figure 7.4
C-2 and C-4 epimers and an isomer of glucose.



B. Enantiomers

- A special type of isomerism is found in the pairs of structures that are mirror images of each other. These mirror images = enantiomers, & the 2 members of the pair are designated as D- & L-sugar. Vast majority of sugars in humans are D-sugars

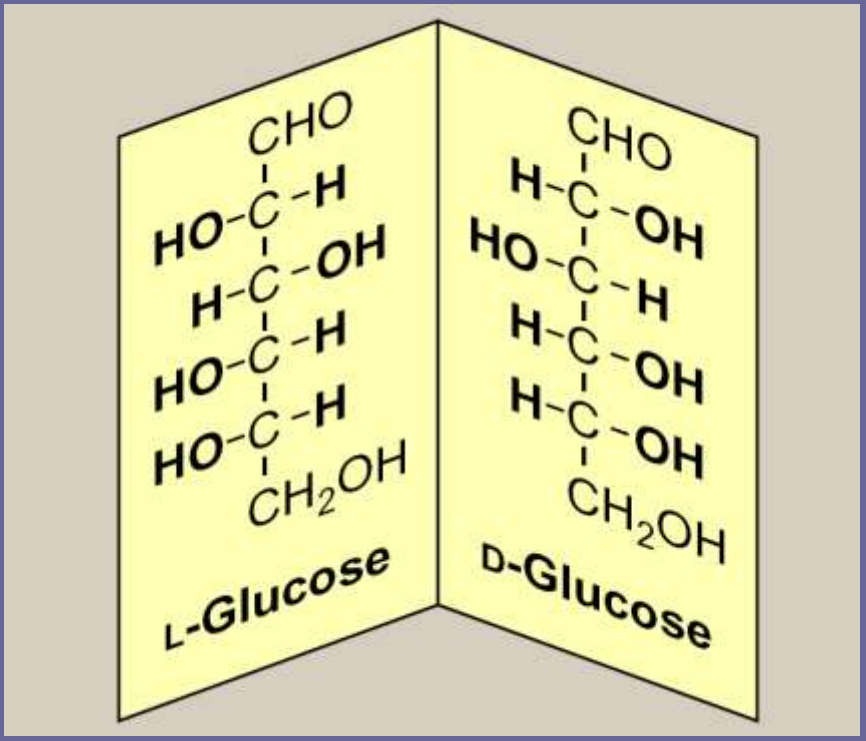


Figure 7.5
Enantiomers (mirror images) of glucose.

C. Cyclization of monosaccharides

- Less than 1% of each of the monosacch with 5 or more C's exist in the open-chain (acyclic) form. Rather, they are predominantly found in ring form, in which aldehyde (or ketone) group has reacted with an alcohol group on the same sugar

1. Anomeric carbon:

- Formation of a ring results in creation of an anomeric C at carbon 1 of an aldose or at carbon 2 of a ketose
- These structures are designated the α or β configurations of the sugar, e.g., α-D-glucose & β-D-glucose. They are both glucose, but are anomers of each other
- Enz's are able to distinguish b/w the 2 structures & use one or the other preferentially e.g., glycogen is synthesized from α-D-glucopyranose.
- The cyclic α & β anomers of a sugar in solution are in equil. with each other, & can be spontaneously interconverted (a process called mutarotation)

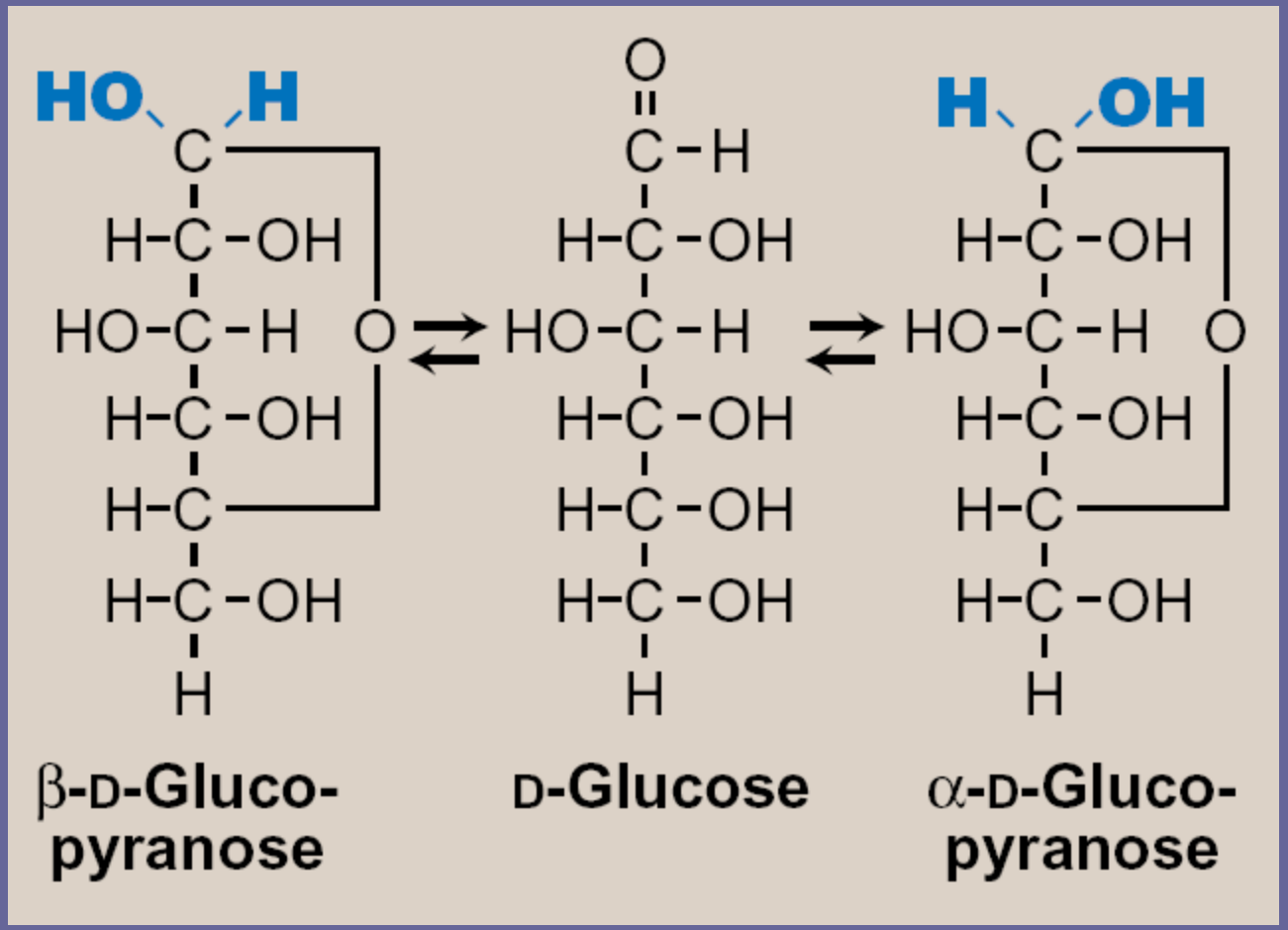


Figure 7.6. The interconversion of the α and β anomeric forms of glucose (mutarotation).

2. Reducing sugars:

- If the oxygen on the anomeric C (the carbonyl group) of a sugar is not attached to any other structure, that sugar is a reducing sugar.
- A reducing sugar can react with chemical reagents e.g., Benedict's soln & reduce the reactive component, with the anomeric C becoming oxidized

Note: only the state of the oxygen on the anomeric C determines if the sugar is reducing or non-reducing, the other hydroxyl groups on the molecule are not involved

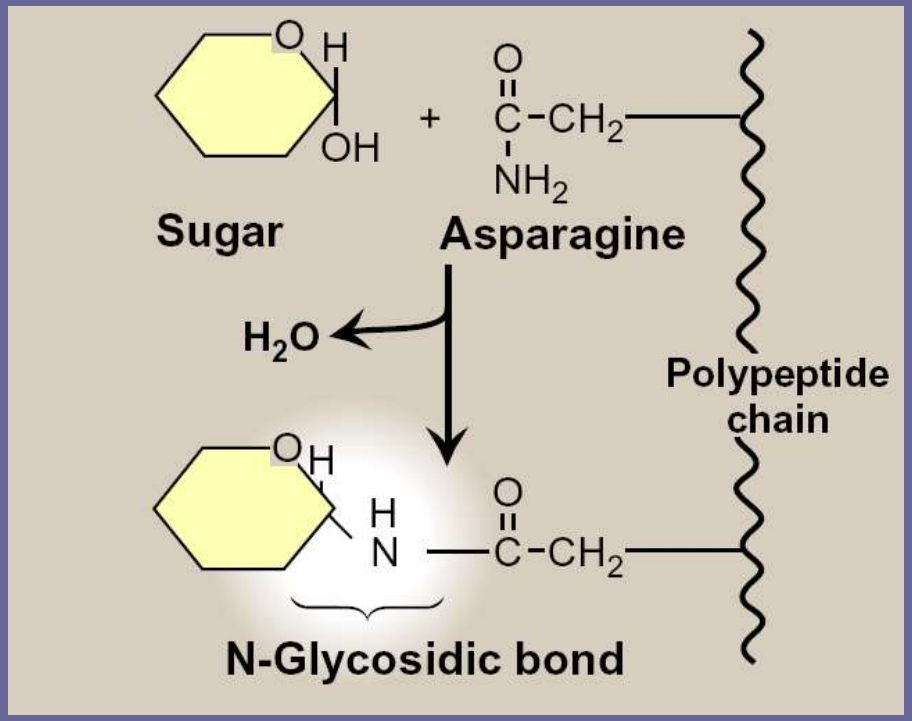
D. Complex carbohydrates

- CHO's can be attached by glycosidic bonds to non-CHO structures e.g., purines & pyrimidines (found in nucleic acids), aromatic rings (such as those found in steroids & bilirubin), proteins (found in glycoproteins & glycosaminoglycans), and lipids (found in glycolipids)
- The aldose (C1) or ketose (C2) participates in the glycosidic link, is called glycosyl residue. E.g., if anomeric C of glucose participates in such a bond, that sugar = glucosyl residue; thus the disacch lactose is galactosyl-glucose

1. O- & N-glycosides:

- If the group of the non-CHO molecule to which sugar is attached is –OH group, the structure is O-glycoside. If the group is –NH2, structure is N-glycoside.

Note: all sugar-sugar glycosidic bonds are O-type



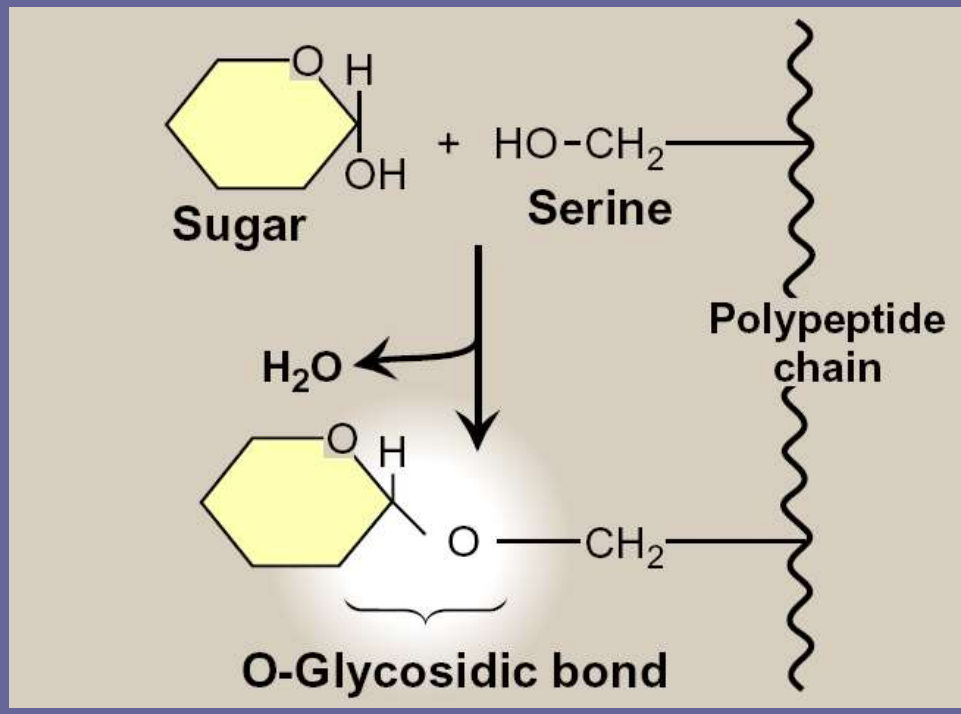


Figure 7.7. Glycosides: examples of N- and O-glycosidic bond

2. Naming glycosidic bonds:

- Glycosidic bonds b/w sugars are named according to numbers of connected C's, & also with regard to position of anomeric hydroxyl group of the sugar involved in the bond
- If anomeric hydroxyl group is in α configuration, the linkage is α-bond. If it is in β → β-bond.
- Lactose e.g., is synthesized by forming a glycosidic bond b/w C-1 of β-galactose & C-4 of glucose. Linkage is = β (1→4) glycosidic bond. [note: anomeric end of glucose is not involved in glycosidic linkage, it (&, therefore lactose) remains a reducing sugar

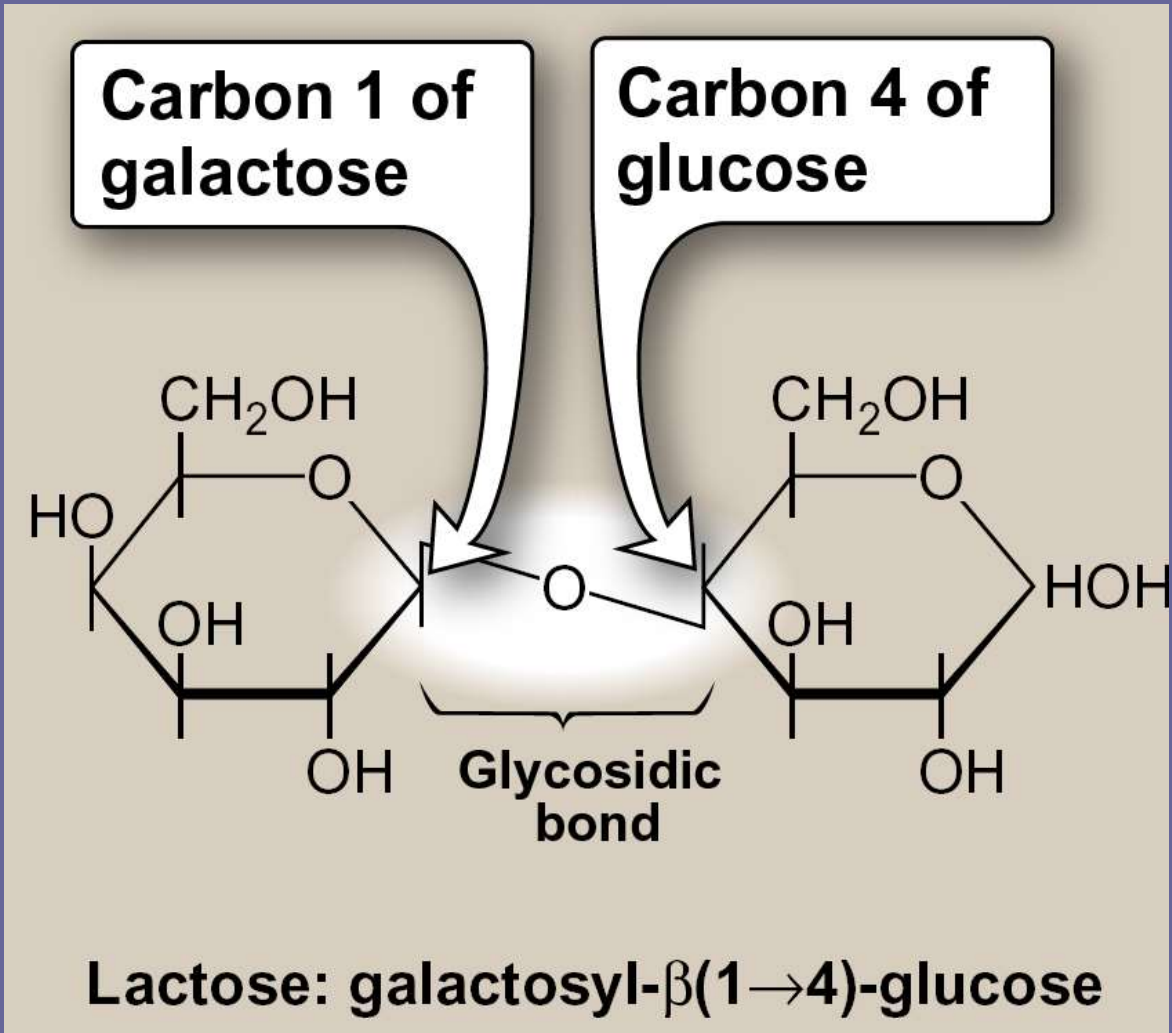


Figure 7.3. A glycosidic bond between two hexoses producing a disaccharide.

Digestion of carbohydrates

- The principal sites of dietary CHO digestion are mouth & intestinal lumen. This digestion is rapid & is generally completed by the time stomach contents reach the junction of duodenum & jejunum
- There is little monosacch present in diets of mixed animal & plant origin. Therefore, enz's needed for degradation of most dietary CHO's are primarily disaccharidases & endoglycosidases (break oligo- & polysacch)
- Hydrolysis of glycosidic bond is catalyzed by a family of glycosidases that degrade CHO's into their reducing sugar components
- These enz's are usually specific for structure & config of glycosyl residue to be removed, as well as type of bond broken

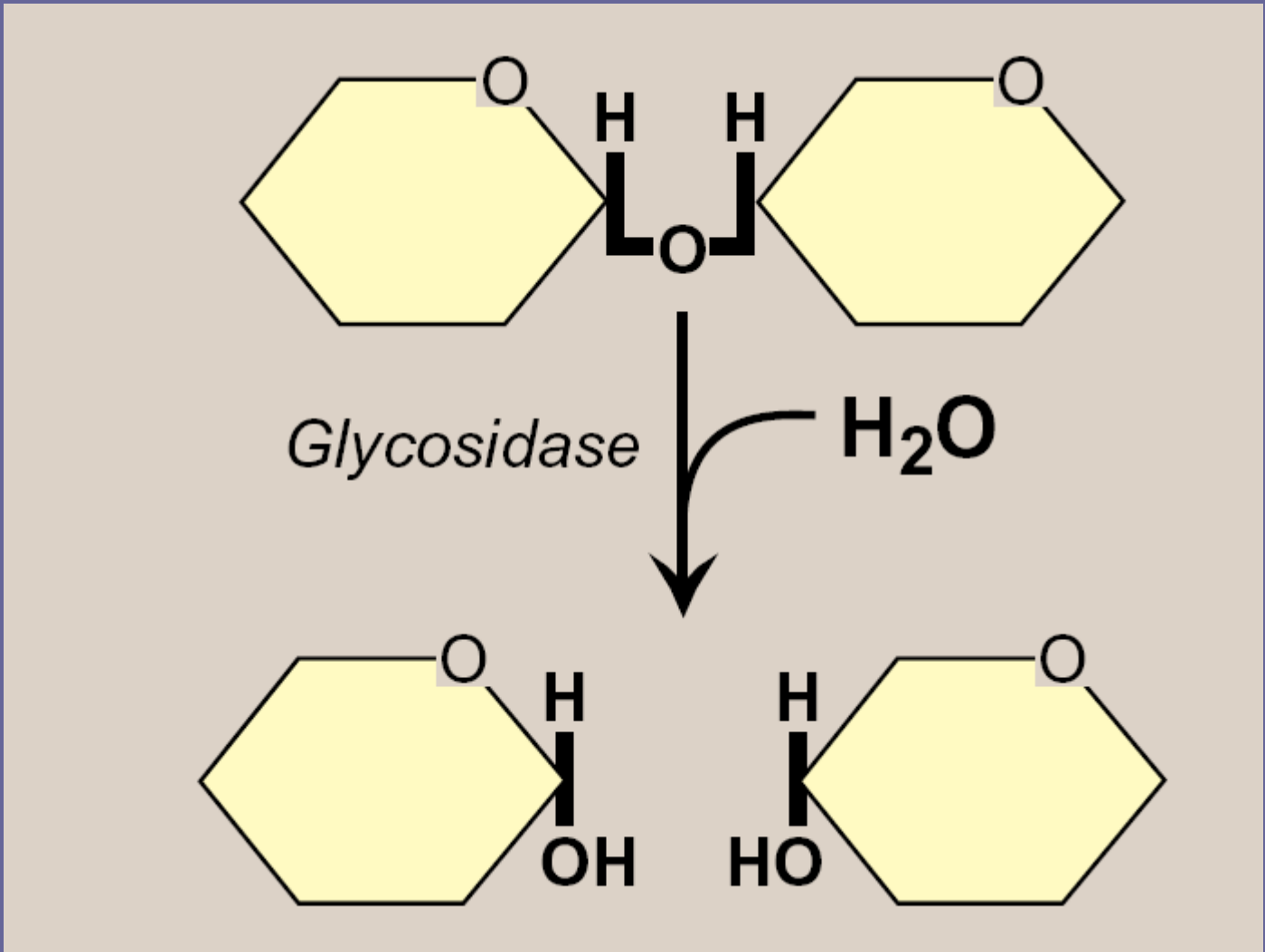


Figure 7.8. Hydrolysis of a glycosidic bond

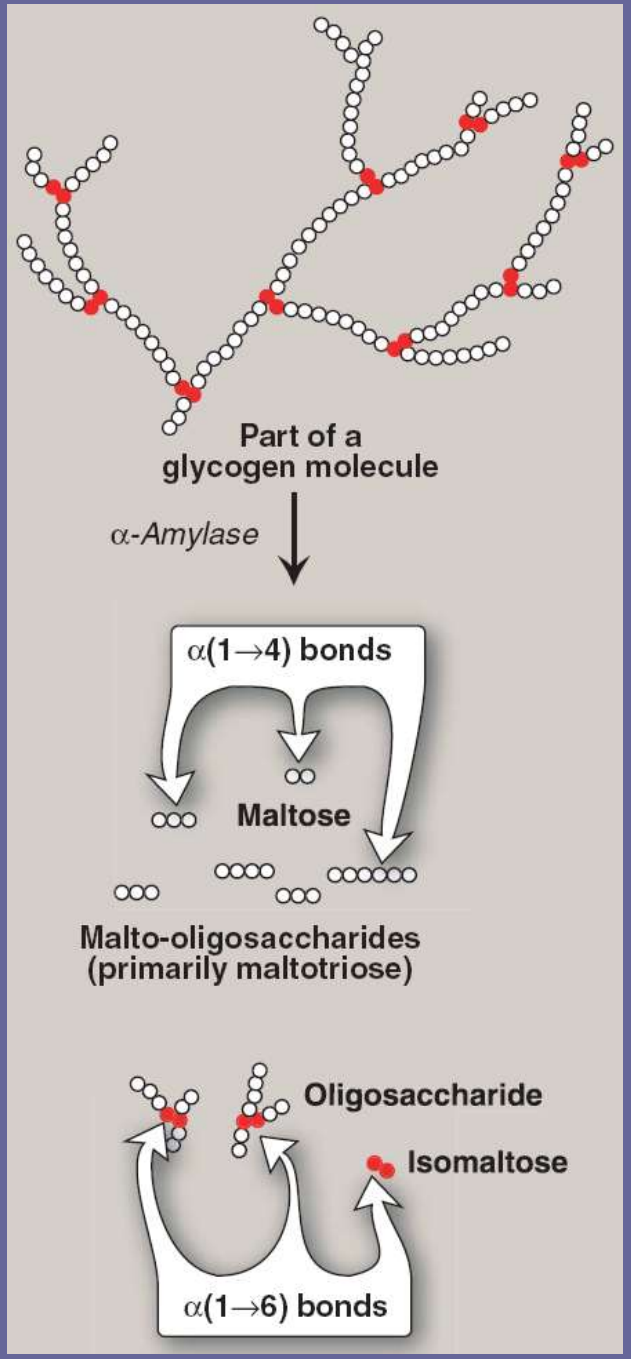
A. Digestion of CHO's begins in the mouth

- Major dietary polysacch are of animal (glycogen) & plant origin (starch, composed of amylose & amylopectin)
- During mastication, salivary amylase acts briefly on dietary starch in a random manner, breaking some α(1→4) bonds

Note: there are both α(1→4) & β(1→4)-endoglucosidases in nature, but human do not produce & secrete the latter in digestive juices, therefore, they are unable to digest cellulose: CHO of plant origin containing β(1→4)-glycosidic bonds b/w glucose residues.

- Because branched amylopectin & glycogen also contain α(1→6) bonds, digest resulting from action of α-amylase contains a mixture of smaller, branched oligosacch molecules
- CHO digestion halts temporarily in stomach, as high acidity inactivates α-amylase

Figure 7.9
Degradation of dietary glycogen by salivary or pancreatic α-amylase.



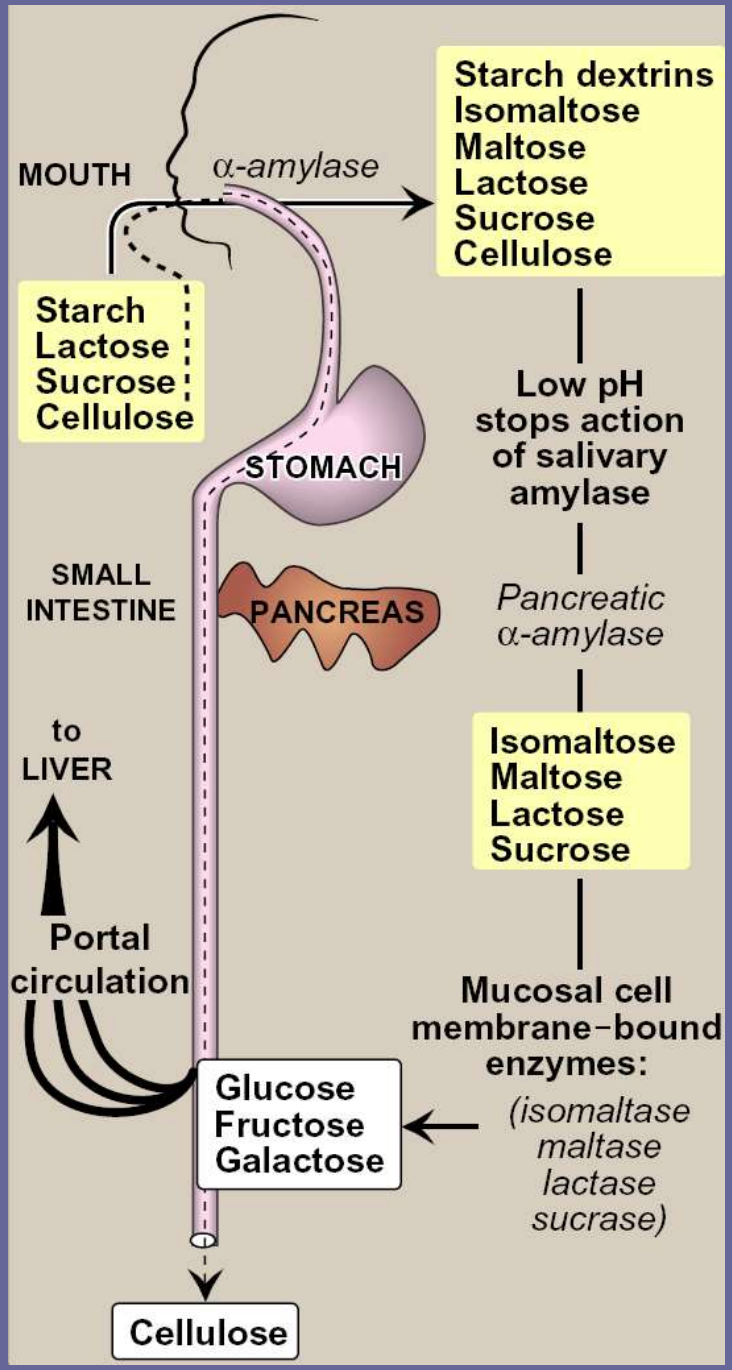
B. Further digestion of CHOs by pancreatic enz's occurs in the small intestine

- When acidic stomach contents reach small intestine, they are neutralized by bicarbonates secreted by pancreas, & pancreatic α-amylase continues process of starch digestion

C. Final carbohydrate digestion by enzymes synthesized from the intestinal mucosal cells

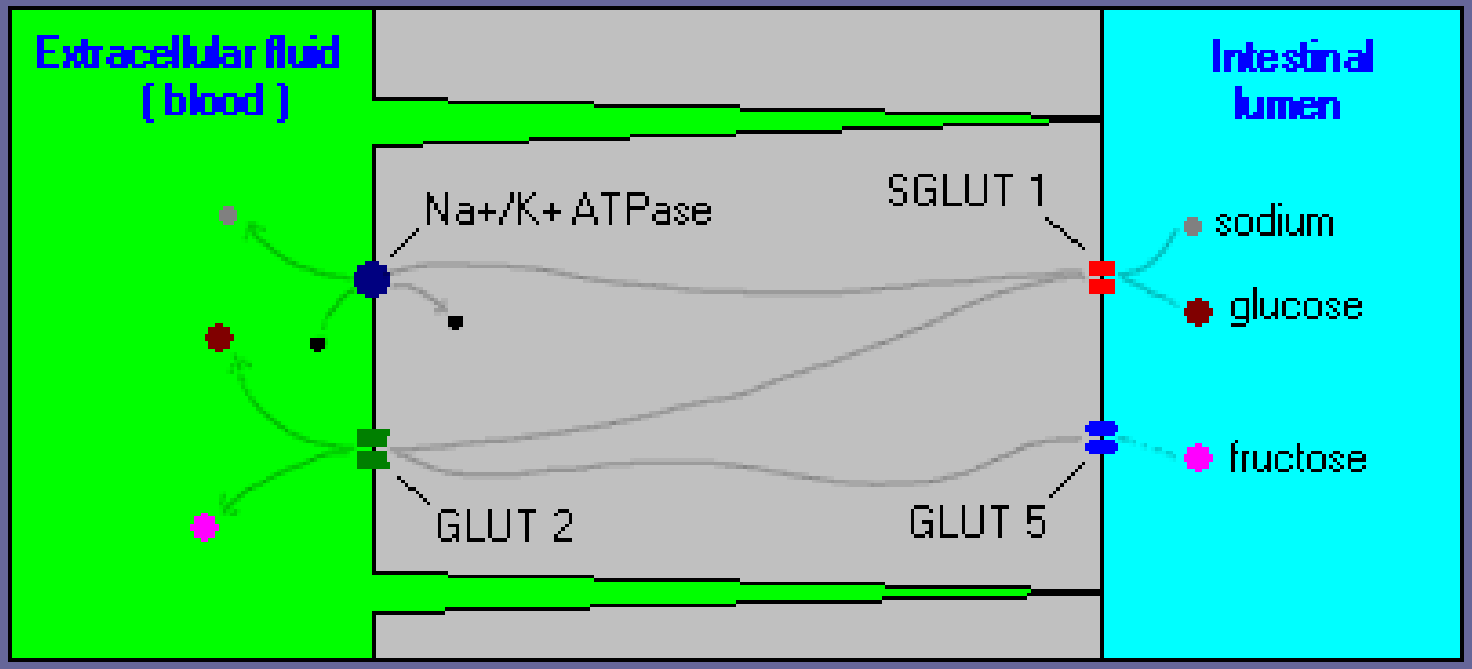
- Final digestion processes occur at mucosal lining of the upper jejunum, declining as they proceed down the small intestine, & include action of several disaccharidases & oligosaccharidases.
- E.g.,
  - isomaltase cleaves the α(1→6) bond in isomaltose and maltase cleaves maltose, both producing: glucose
  - Sucrase cleaves sucrose producing glucose & fructose
  - Lactase (β-galactosidase) cleaves lactose producing galactose & glucose.
- These enz's are secreted through, & remain associated with, luminal side of the brush border memb's of intestinal mucosal cells

Figure 7.10
Digestion of carbohydrates.

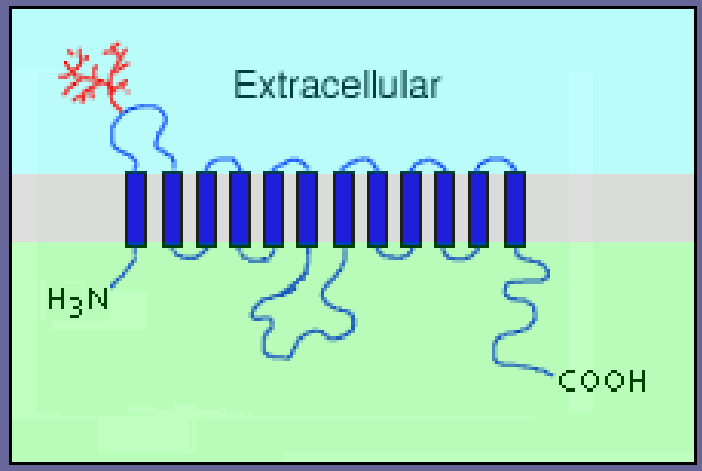


D. Absorption of monosaccharides by intestinal mucosal cells

- Duodenum & upper jejunum absorb the bulk of dietary sugars.
- Insulin is not required for uptake of glucose by intestinal cells.
- Different sugars have different mechanisms of absorption e.g.,
  - galactose & glucose are transported into mucosal cells by an active, energy requiring process that involves a specific transport protein & requires a concurrent uptake of sodium ions.
  - Fructose uptake requires a sodium-independent monosaccharide transporter (GLUT-5) for its absorption
  - All 3 monosacch's are transported from intestinal mucosal cell into the portal circulation by yet another transporter, GLUT-2



The hexose transporters are large integral membrane proteins. They have 12 membrane-spanning regions with cytoplasmic C-terminal and N-terminal tails. Also, they all appear to be glycosylated on one of the extracellular loops.



E. Abnormal degradation of disaccharides

- Overall process of CHO digestion & absorption is efficient in healthy individuals. Ordinarily all digestible dietary CHO is absorbed by time the ingested material reaches lower jejunum
- Because predominantly monosacch's are absorbed, any defect in a specific disacch activity of intestinal mucosa causes the passage of undigested CHO into large intestine
- As a consequence of presence of this osmotically active material, water is drawn from the mucosa into large intestine → osmotic diarrhea. This is reinforced by the bacterial fermentation of remaining CHO to 2- & 3-C cpds (which are also osmotically active) plus large volumes of CO_2 & H_2 gas, causing abdominal cramps, diarrhea and flatulence

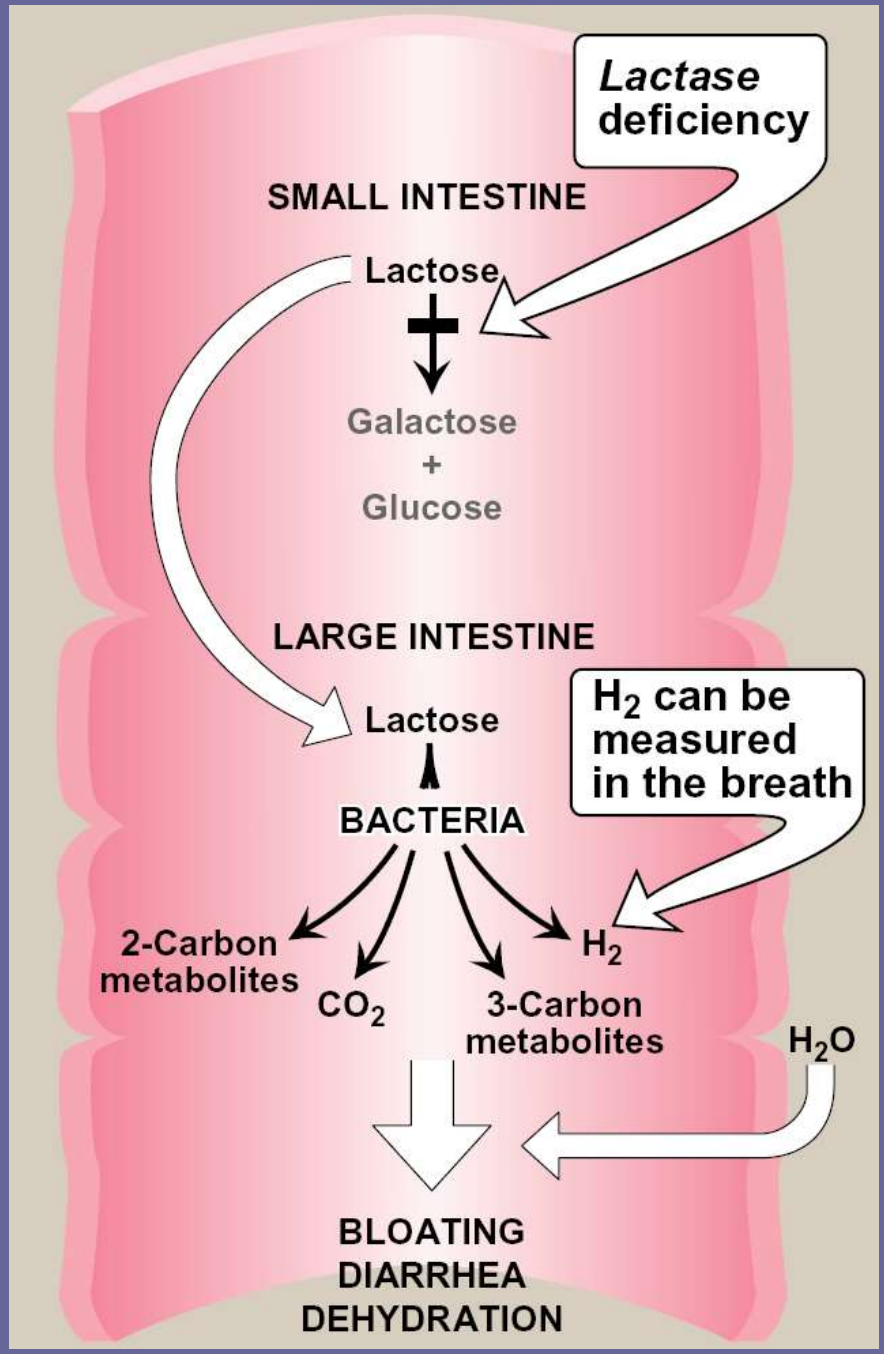
1. Digestive enzyme deficiencies:

- Hereditary deficiencies of the individual disaccharidases have been reported in infants & children with disaccharide intolerance
- Alterations in disaccharide degradation can also be caused by a variety of intestinal diseases, malnutrition, or drugs the injure mucosa of small intestine
- E.g., brush border enz's are rapidly lost in normal individuals with severe diarrhea causing a temporary acquired enz deficiency.
- Thus, patients suffering or recovering from such a disorder cannot drink or eat significant amount of dairy products or sucrose without exacerbating diarrhea

2. Lactose intolerance:

- More than ½ of the world's adults are lactose intolerant. This is particularly manifested in certain races e.g., up to 90% of adults of African or Asian descent are lactase-deficient &, are less able to metabolize lactose than individuals of northern European origin
- The mechanism by which enz is lost is not clear, but it is determined genetically and represents a reduction in amount of enz protein rather than a modified inactive enz.
- Treatment for this disorder is simply to remove lactose from diet, or to take lactase in pill form prior to eating

Figure 7.11
Abnormal lactose metabolism.



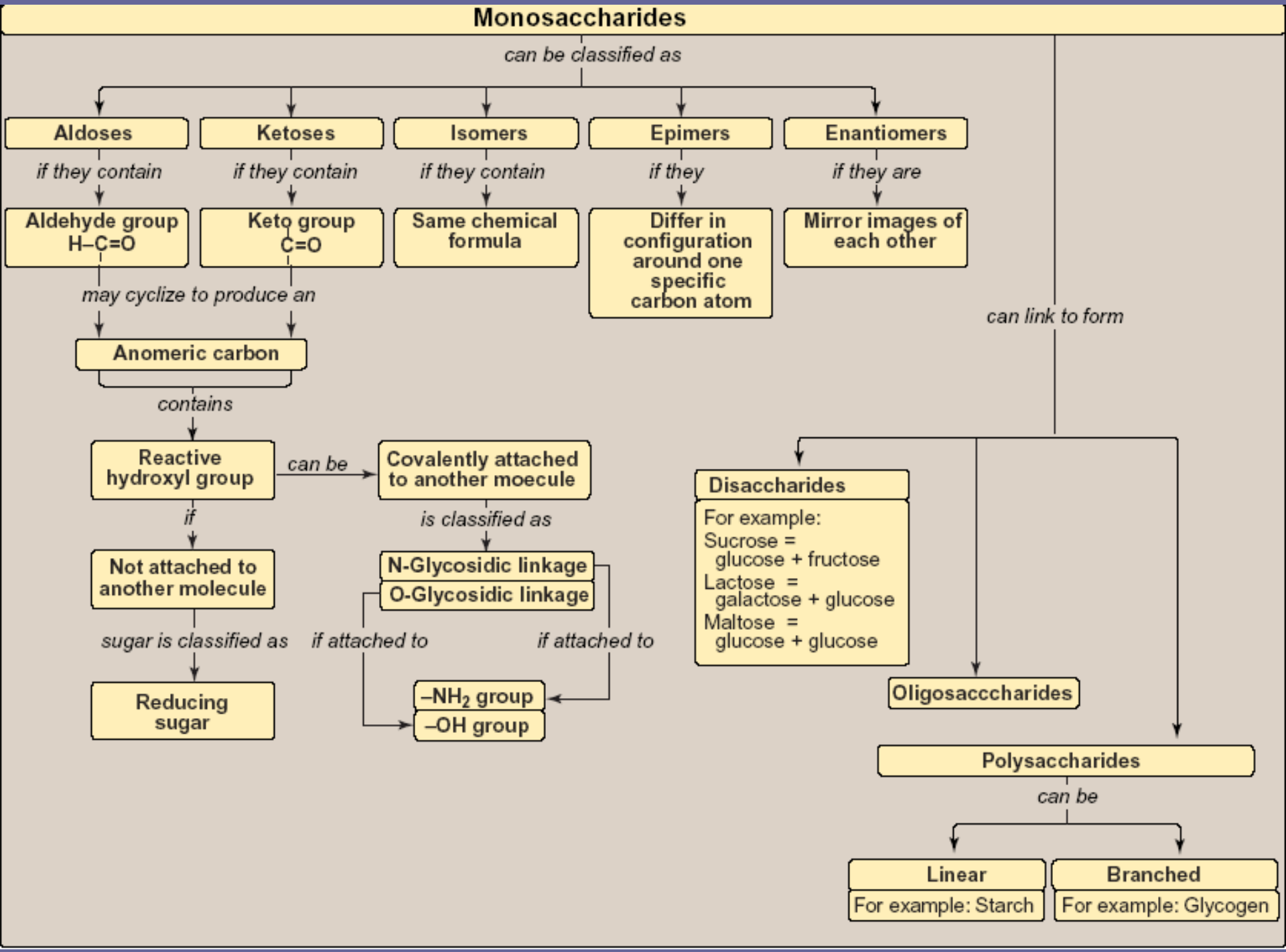
4. diagnosis:

- Identification of specific enz deficiency can be obtained by performing oral tolerance with individual disaccharides
- Measurement of hydrogen gas in breath is a reliable test for determining the amount of ingested CHO not absorbed by the body, but which is metabolized instead by intestinal flora.

Summary

- Monosacch (simple sugars) containing aldehyde group = aldoses, those with keto = ketoses
- Disacch, oligosacch, & polysacch cosist of monosacch's linked by glycosidic bonds
- Compounds with same chemical formula = isomers. If 2 monosacch isomers differ in config around one specific C atom (with the exception of carbonyl C) are defined as epimers of each other
- If a pair of sugars are mirror images (= enantiomers) the 2 members of a pair are D- & L-sugars
- When a sugar cyclizes, an anomeric C is created from the aldehyde group of an ladose or keto group of a ketose. This C can have 2 configs α or β. If the oxygen on anomeric C is not attached to any other structure, the sugar is a reducing sugar
- A sugar with its anomeric C linked to another structure is called a glycosyl residue
- Sugars can be attached either to –NH2 or –OH group → N- & O-glycosides

- Salivary α-amylase acts on dietary starch (glycogen, amylose, amylopectin) → oligosacch's
- Pancreatic α-amylase continues the process of starch digestion
- The final digestive processes occur at mucosal lining of small intestine. Several disaccharidases [e.g., lactas (β-galactosidase), sucrase, maltase, & isomaltase] → monosacch's (glucose, galactose & fructose)
- These enz's secreted by & remain associated with luminal side of brush border memb's of intestinal mucosal cells
- Absorption of monosacch's requires specific transporters
- If CHO degradation is deficient (as result of heredity, intestinal disease, malnutrition, or drugs that injure mucosa of small intestine), undigested CHO will pass into large intestine → osmotic diarrhea
- Bacterial fermentation of the cpds → large volumes of CO_2 & H_2 gas → abdominal cramps, diarrhea & flatulence
- Lactose intolerance, caused by lack of lactase, most common of these deficiencies


Monosaccharides
can be classified as
Aldoses
Ketoses
Isomers
Epimers
Enantiomers
if they contain
if they contain
if they contain
if they
if they are
Aldehyde group H–C=O
Keto group C=O
Same chemical formula
Differ in configuration around one specific carbon atom
Mirror images of each other
may cyclize to produce an
Anomeric carbon
contains
Reactive hydroxyl group
can be
Covalently attached to another moecule
if
is classified as
Not attached to another molecule
N-Glycosidic linkage
O-Glycosidic linkage
sugar is classified as
if attached to
if attached to
Reducing sugar
–NH2 group
–OH group
can link to form
Disaccharides
For example:
Sucrose = glucose + fructose
Lactose = galactose + glucose
Maltose = glucose + glucose
Oligosacccharides
Polysaccharides
can be
Linear
For example: Starch
Branched
For example: Glycogen