Carbohydrate Chemistry

DR PIYUSH TAILOR
Associate Professor
Dept of Biochemistry
Govt. Medical College
Bhavnagar

- **Empiric formula = $C_nH_{2n}O_n$.**
- **n = number of carbon**

Wide range of Functions

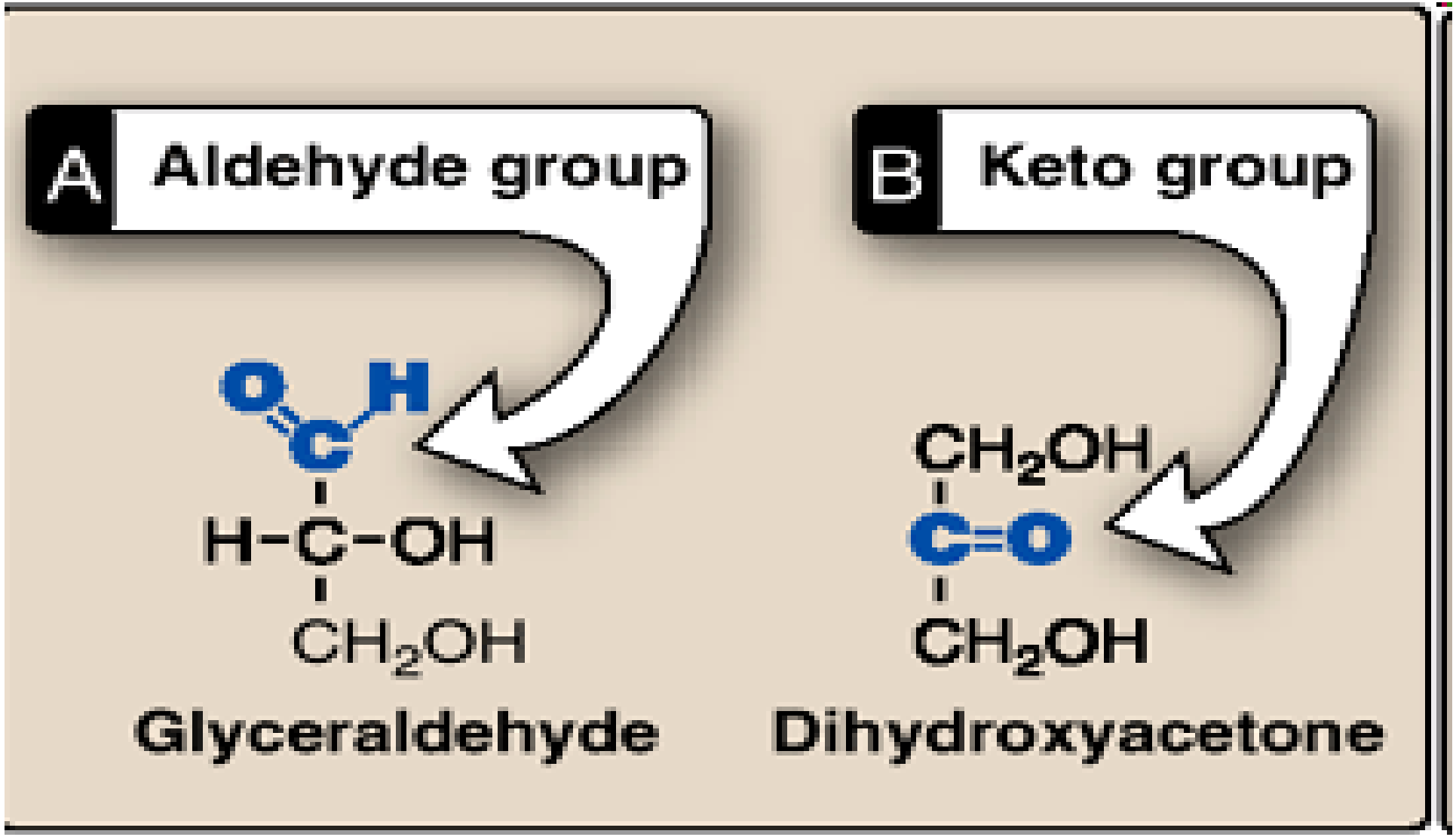
- Significant fraction of the energy.
- Storage form of energy.
- RBC & Brain - Cell membrane components.
- Glycoprotein & Glycolipid
- Excess Carbohydrate convert to fat
- Structural component of many organisms
  - Cell walls of bacteria
  - Exoskeleton of many insects
  - Fibrous cellulose of plants.

Classification and Structure of Carbohydrates

- **According to the number of carbon atoms**
  - **Triose**
  - **Tetrose**
  - **Pentose**
  - **Hexose (Glucose)**
- **Groups**
  - **Aldehyde (called aldoses)**
  - **Keto (called ketoses)**
- **According to number of Monomer**
  - **Monocharride**
  - **Disaccharides = 2 monosaccharide units.**
  - **Oligosaccharides = 3 to 10 monosaccharide units.**
  - **Polysaccharides = more than 10 monosaccharide units.**

Sugar	Number of Carbon	Aldose-sugar	Ketose-sugar
Triose	3	Glyceraldehyde	Dihydroxyacetone
Tetrose	4	Erythrose	Erythrulose
Pentose	5	Ribose	Ribulose
Hexose	6	Glucose Galactose Mannose	Fructose
Heptose	7	Glucoheptose	Sedoheptulose

Type according to Functional Group



According to number of monomer unit

1. **Monosaccharides:**
    1. Glucose
    2. Fructose
    3. Galactose
2. **Disaccharides :**
    1. Heterodisaccharide
        1. Lactose = Glucose + Galactose
        2. Sucrose = Glucose + fructose
        3. Lactulose = Frucose + Galactose (beta 1 – 4 linkage)
    2. Homodisaccharide
        1. Maltose = Glucose + Glucose
        2. Isomaltose = Glucose + Glucose (Alpha 1 – 6 linkage)
        3. Trehalose = Glucose + Glucose (Alpha 1 – 1 linkage)

According to number of monomer unit

3. **Oligosaccharides : No. of monomer 3 – 10**
   a. Trisaccharide = 3 monomer = Raffinose
   b. Tetrasaccharide = 4 monomer = Stachyose
   c. Pentasaccharide = 5 monomer = Verbascose

According to number of monomer unit

4. **Polysaccharides : More than 10 monomer unit**
    1. Homopolysaccharide
        a. Starch, Glycogen,Cellulose,Dextrin ,Dextran, Chitin
        b. Inulin
    2. Heteropolysaccharide
        a. Hyaluronic acid
        b. Heparan sulfate
        c. Chondroitin sulfate
        d. Dermatan sulfate
        e. Keratan sulfate
        f. Blood group polysaccharides

Aminosugar

- Sugar + Amino group
- E.g.
  - Glucosamine = acetylated = N-Acetyl glucosamine
  - Galactosamine = acetylated = N-Acetylgalactosamine
  - Mannosamine = acetylated = N-Acetylmannosamine
- Synthesized by
  - Fructose 6 phosphate
  - Aminotransferase enzyme
- Use in synthesis of
  - Glycolipids, Glycoproteins, Proteoglycans

Properties of Carbohydrate

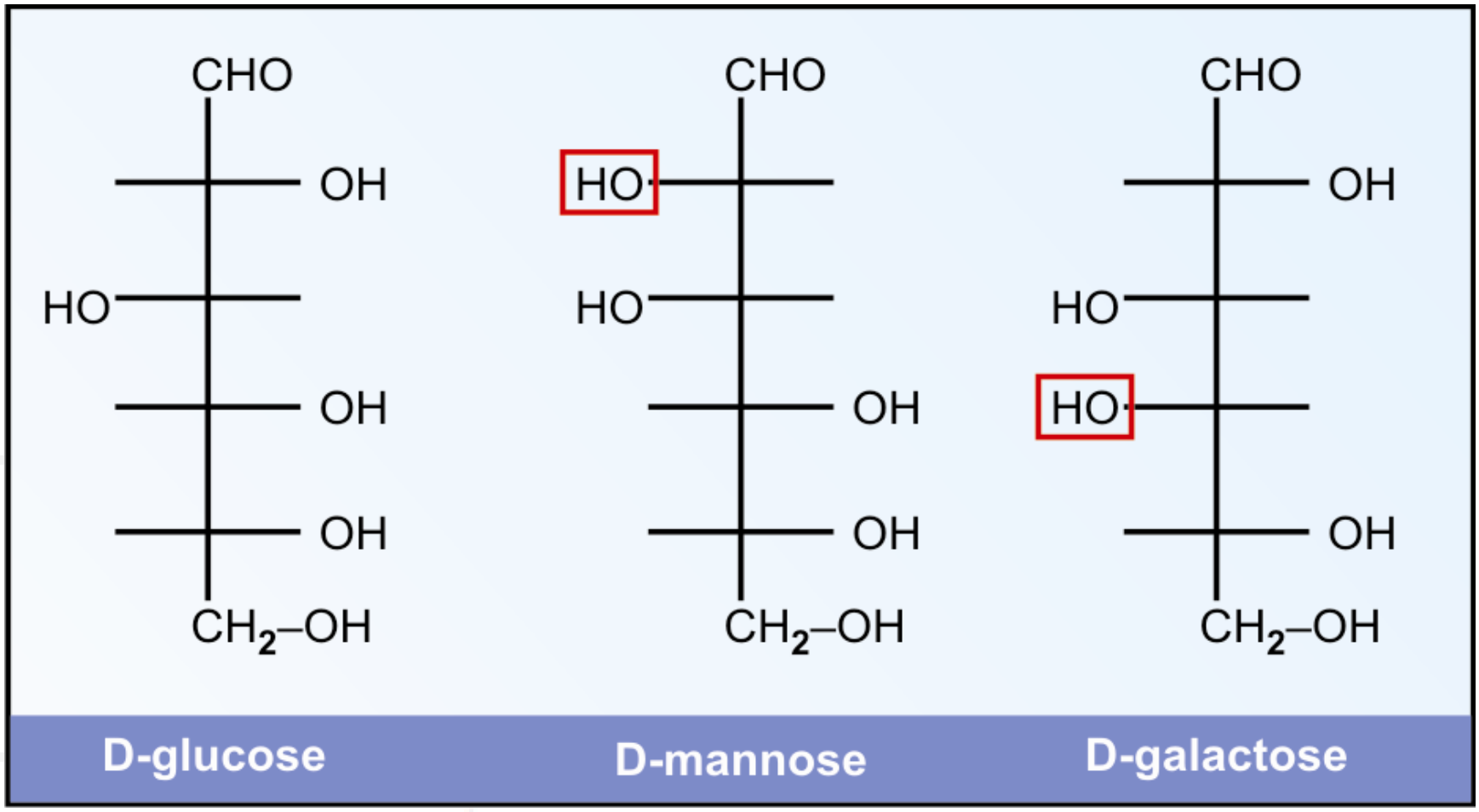
A. Isomers

- Same chemical formula $C_6H_{12}O_6$
- Have different structures are called ISOMERS.
- E.g. Fructose, Glucose, Mannose, and Galactose

B. Epimers

- Differ in configuration around only one specific carbon atom (except on 1st carbon)
- Glucose & Galactose (C-4 epimer)
- Glucose & Mannose (C-2 epimer).

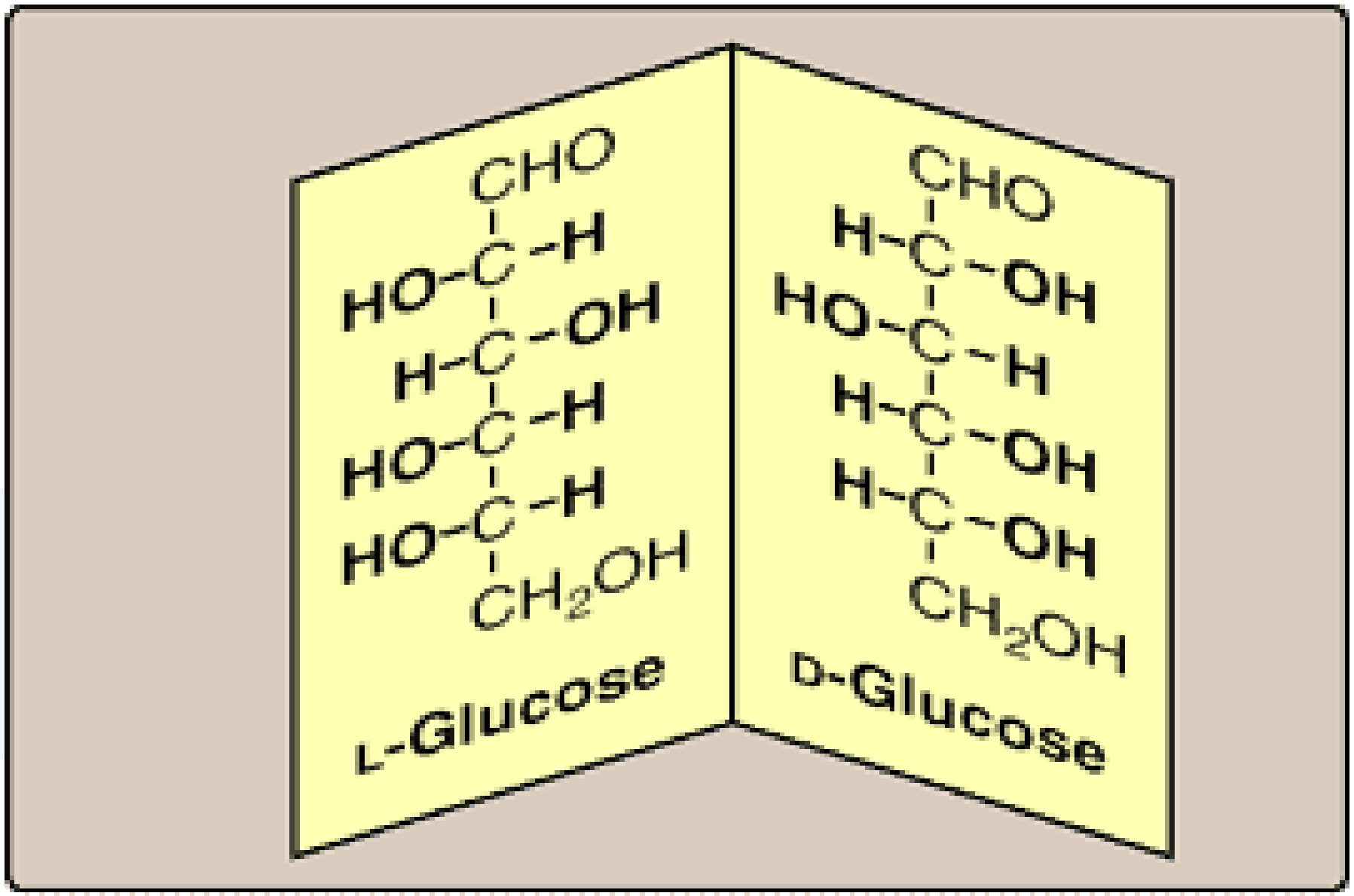
Epimers


CHO
OH
HO
OH
OH
CH2–OH
D-glucose
CHO
HO
HO
OH
OH
CH2–OH
D-mannose
CHO
OH
HO
HO
OH
CH2–OH
D-galactose

C. Enantiomers

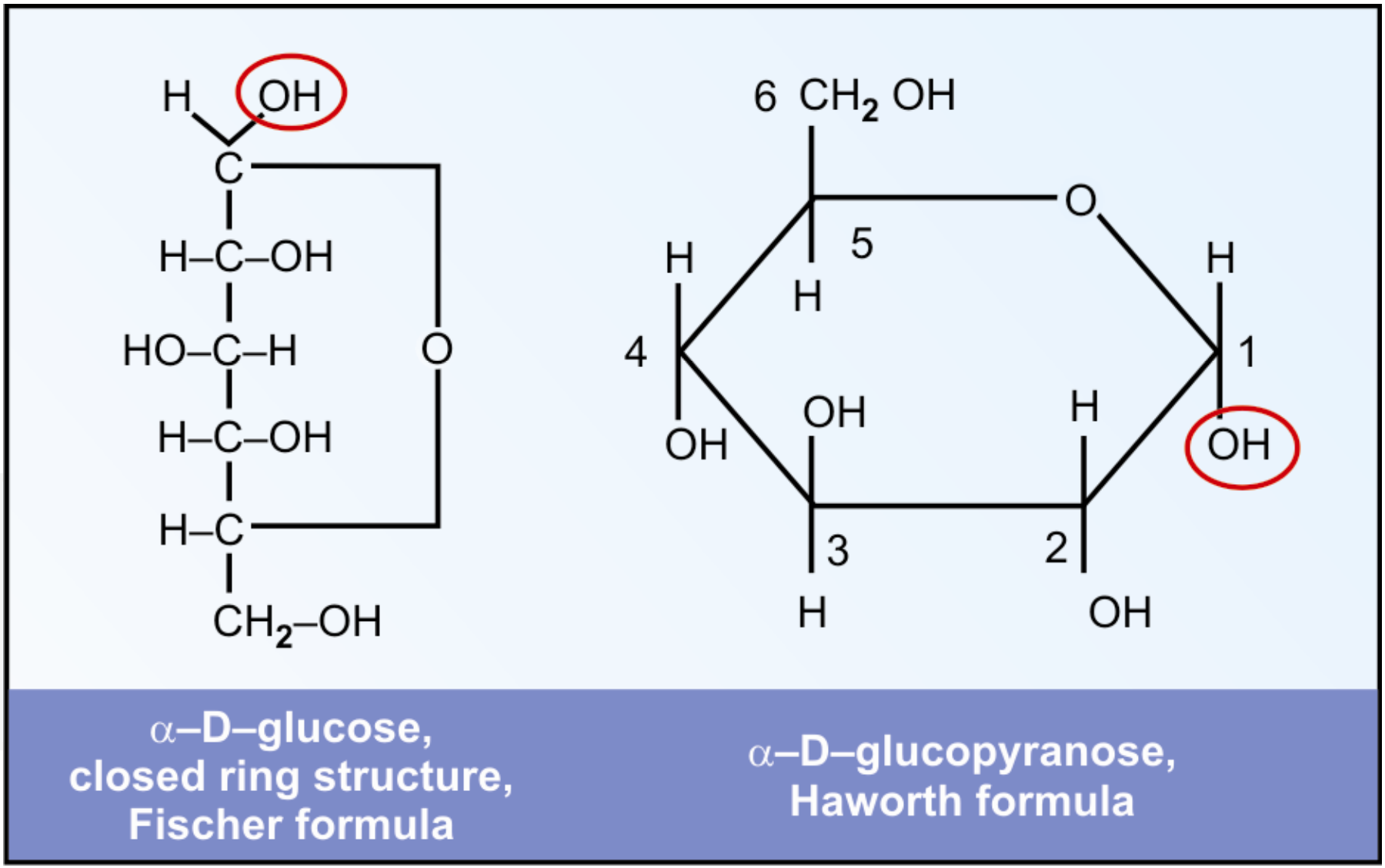
- **Mirror images are called Enantiomers.**
- **Designated as a D- and an L-sugar .**
- **By humans, only D-sugars can be metabolised.**
- D – Glucose & L - Glucose

Enantiomers



D. Cyclization of Monosaccharide :

- Predominantly found in a ring (cyclic) form, for example, glucopyranose.



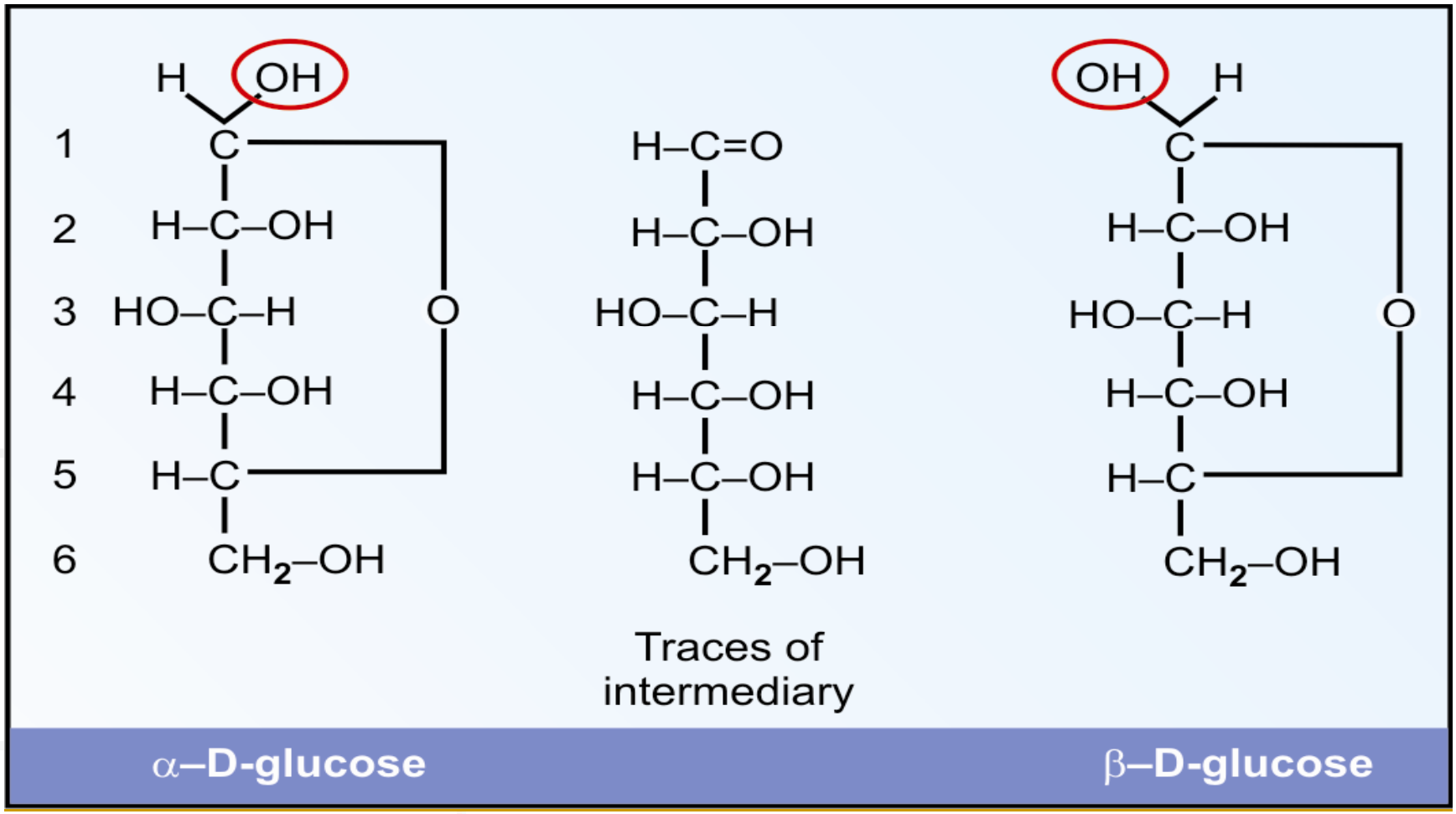
E. Anomerism

- Anomeric carbon – All four group are different
- Generating the α and β configurations of the sugar
- For example,
  - α-D-glucopyranose
  - β-D-glucopryanose
- α = OH on anomeric C (1st) same side as ring.
- β = OH on anomeric C (1st) opposite as ring.
- Enzymes preferentially use only one the configuration.
- Glycogen = α-D-glucopyranose
- Cellulose = β-D-glucopyranose.

Mutarotation

- Spontaneous inter convertion to other anomer, to get equilibrium.
- α and β anomers of a sugar in solution are in equilibrium with each other.

Anomerism

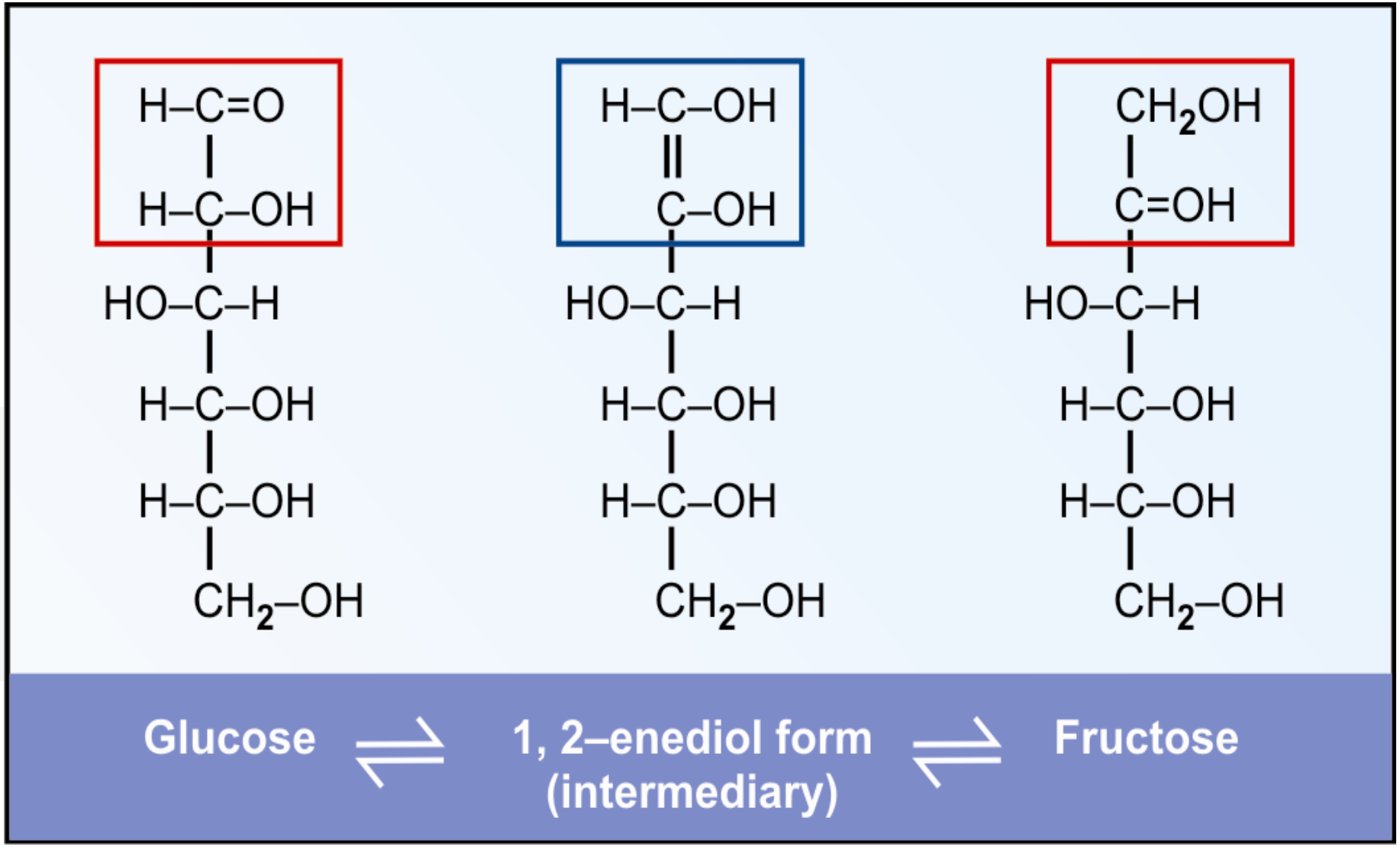

H
OH
1
C
2
H–C–OH
3
HO–C–H
O
4
H–C–OH
5
H–C
6
CH2–OH
H–C=O
H–C–OH
HO–C–H
H–C–OH
H–C–OH
CH2–OH
Traces of intermediary
OH
H
C
H–C–OH
HO–C–H
O
H–C–OH
H–C
CH2–OH
α–D-glucose
β–D-glucose

F. Reducing Sugar

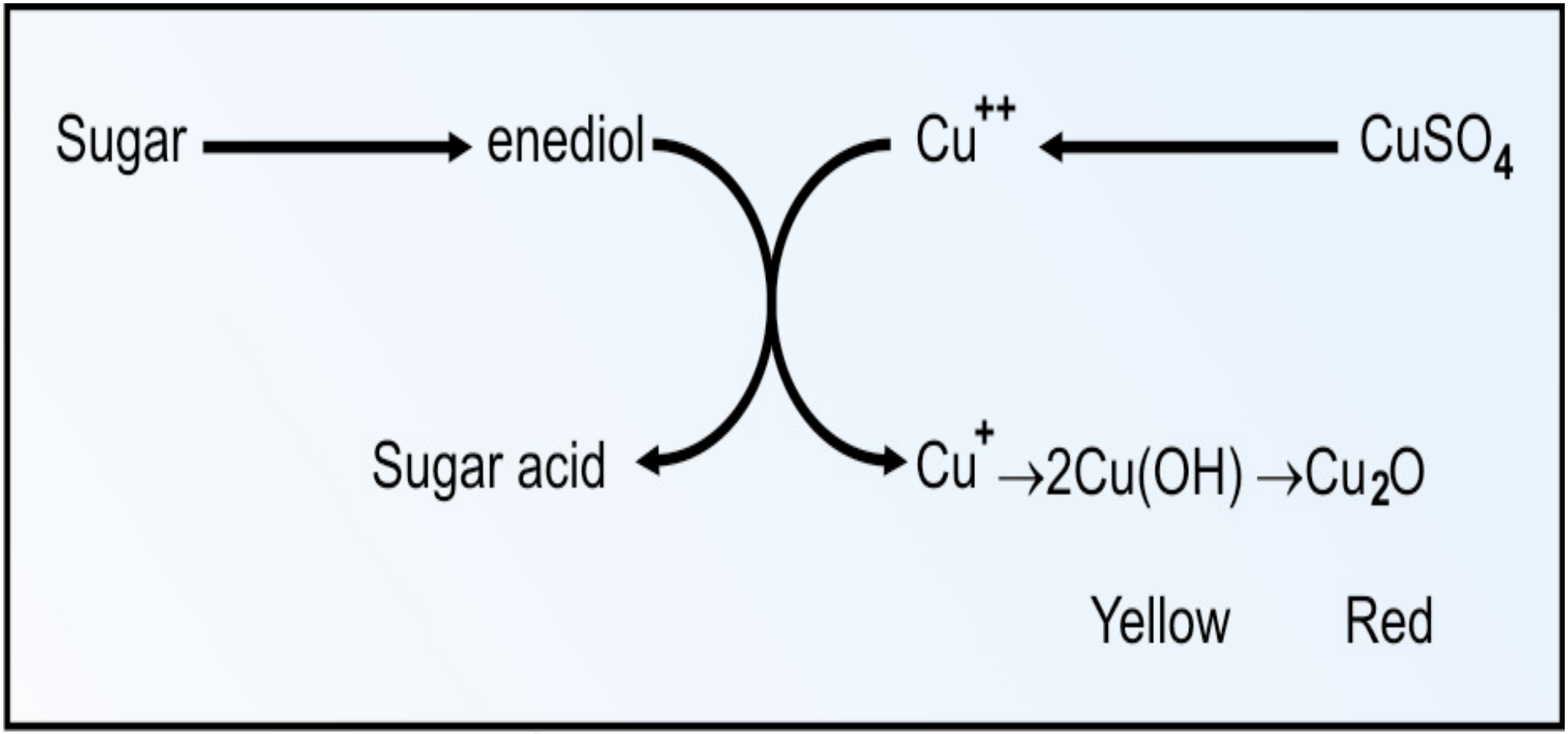
If the oxygen on the anomeric carbon of a sugar is free, that sugar can act as a reducing agent and is termed a reducing sugar. Such sugars can react with chromogenic agents (for example, ***Benedict's reagent*** or Fehling's solution) causing the reagent to be reduced and colored, with the anomeric carbon of the sugar becoming oxidized

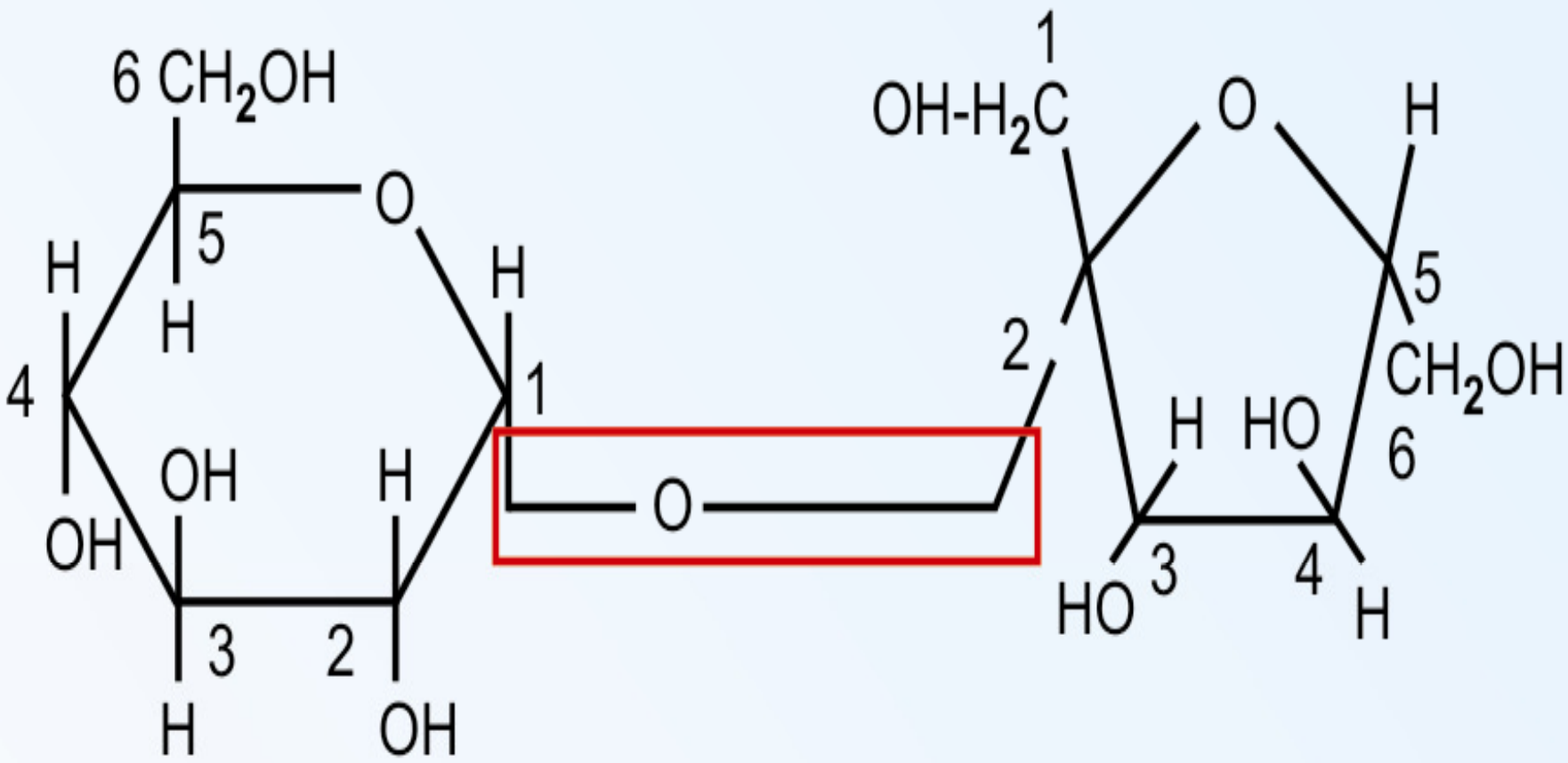
- ✓ ***SUCROSE IS NON-REDUCING SUGAR.***
- ✓ ***SUCROSE IS INVERT SUGAR.***

Enediol formation due to alkalization



Principle of Benedict's test for Reducing Sugar





Glucose component **Fructose component**

Alpha-D-glucosyl-beta-D-fructoside

G. Optical activity

- When beam of plane-polarized light passed through a solution of carbohydrate, it will rotate light either to right or left
- **Dextrorotatory (d) (+)** = right rotation
  - e.g. glucose
- **Levorotatory (l) (-)** = left rotation
  - e.g. fructose

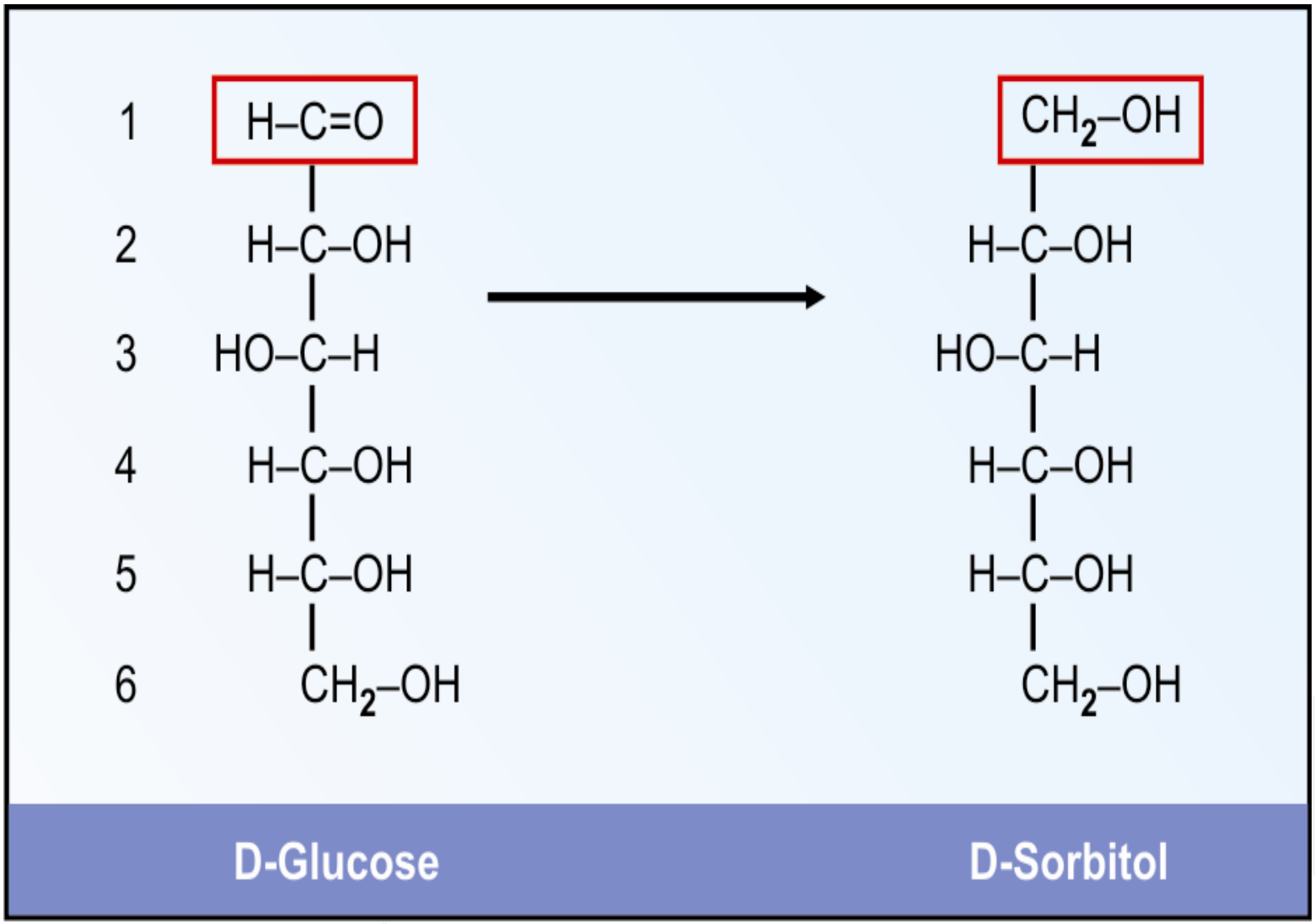
Reaction of Carbohydrate

1. **Reduction**

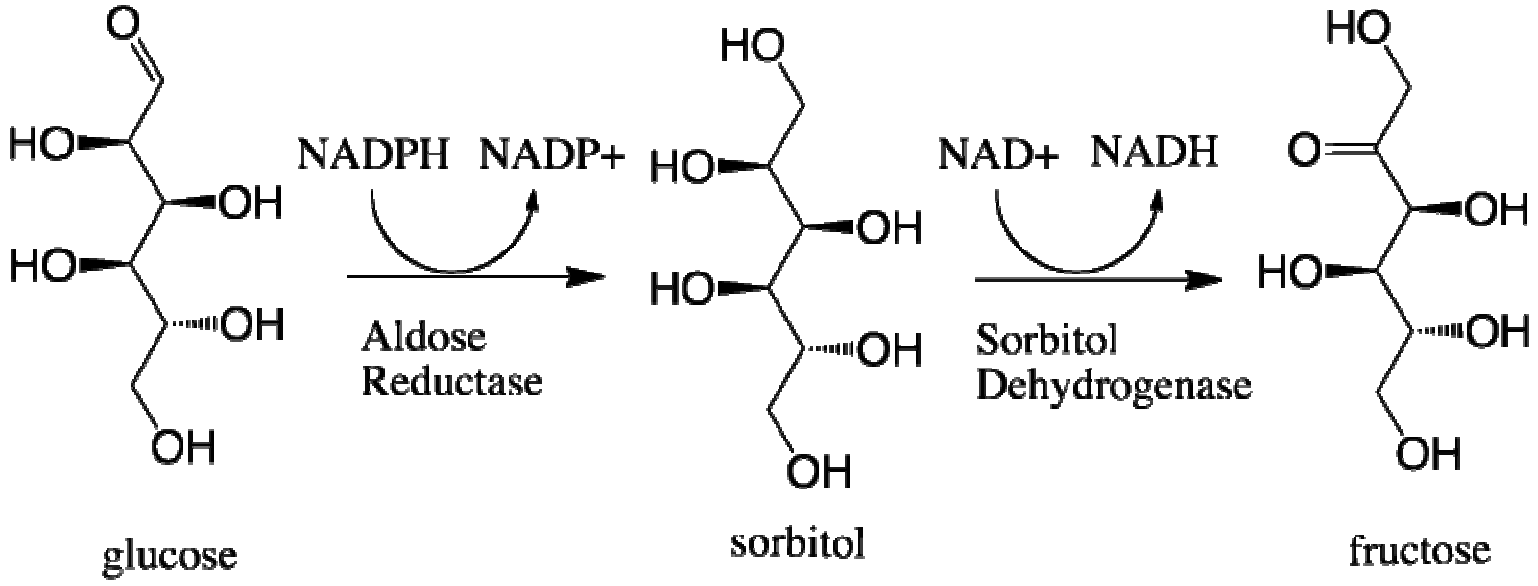
- Aldose / Ketose yields corresponding Alcohol
- Ketose forms two alcohols
  - Glucose --- Sorbitol
  - Fructose --- Sorbitol /// Mannitol
  - Galactose --- Dulcitol
  - Ribose --- Ribitol

Significant of Reduction

- Bacteria use alcohol as energy sources.
- Alcohol added in Culture media
- So it is use to identify bacteria.
- **Mannitol**
- To reduce intracranial pressure.
  - In Haemorrage,SOL
- Diuresis – Hypotension
- **Sorbitol & Dulcitol**
- Cataract


1 H–C=O
2 H–C–OH
3 HO–C–H
4 H–C–OH
5 H–C–OH
6 CH2–OH
CH2–OH
H–C–OH
HO–C–H
H–C–OH
H–C–OH
CH2–OH
D-Glucose
D-Sorbitol

Polyol Pathway

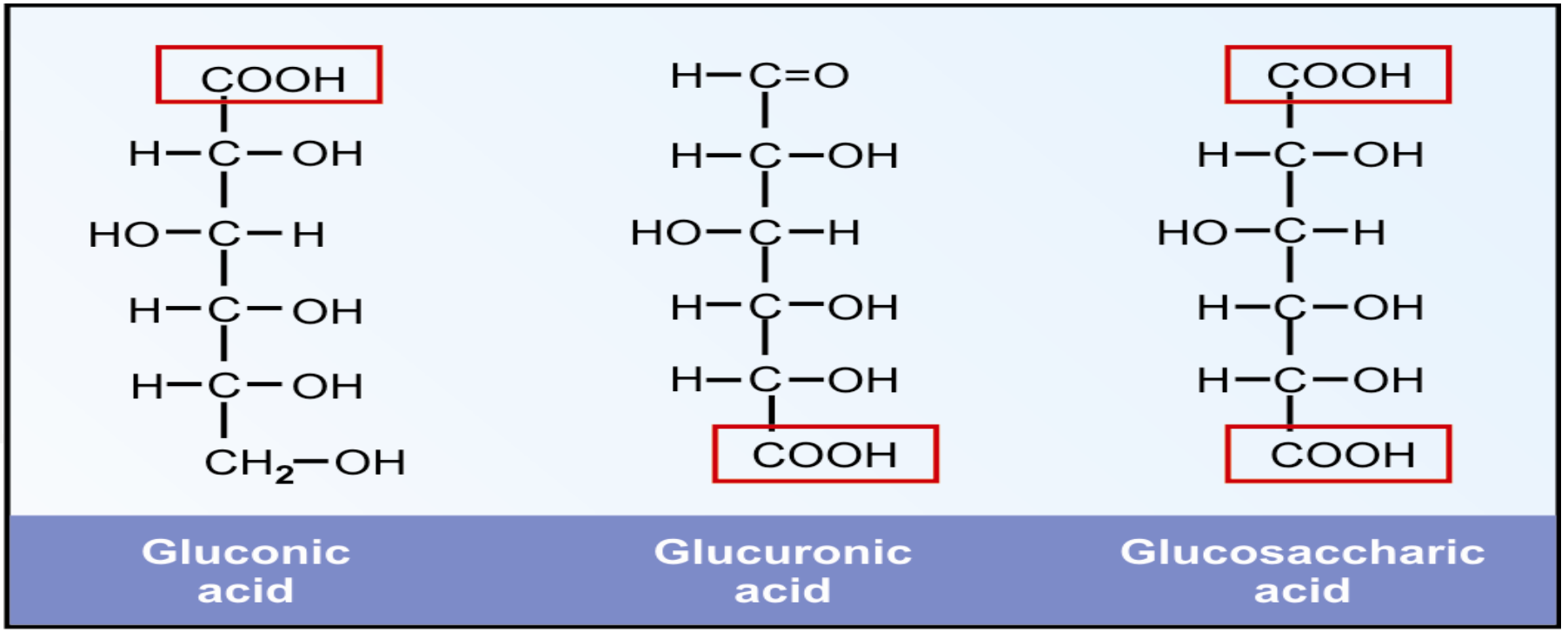


Aldose Reductase inhibitor use to prevent Diabetic Complication

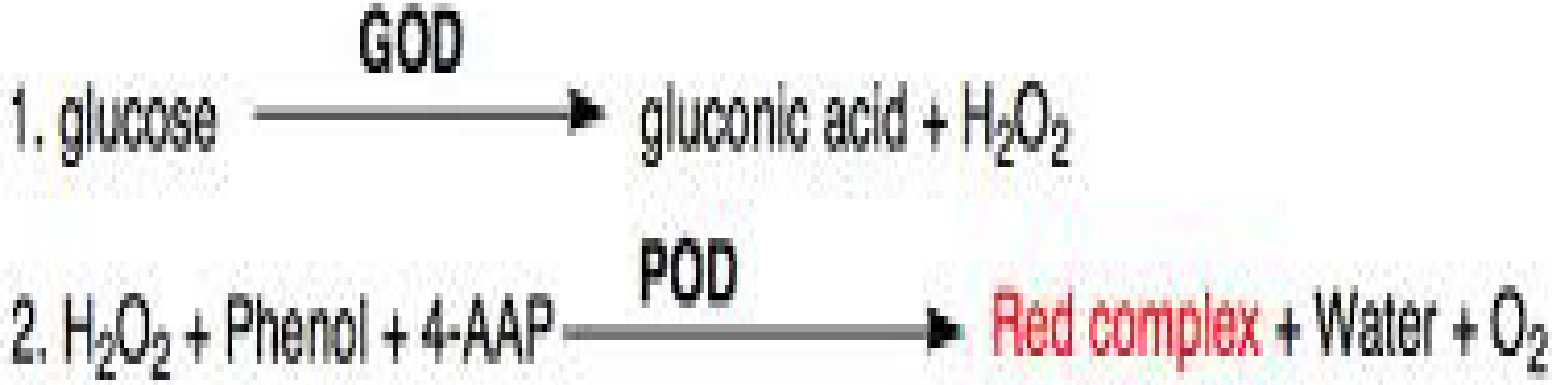
2. Oxidation : = - COOH

- **Mild**
  - 1st carbon oxidized = Aldonic acid
  - E.g. Gluconic acid,mannonic acid
- **Moderate**
  - Last carbone = Uronic acid.
  - E.g Glucuronic acid, mannuronic acid
  - **Glucuronic acid**
  - **Used for conjugation of Billirubin & Toxin**
  - **to convert insoluble water to water soluble water**
  - **Synthesis of Mucopolysaccharide.**

- Under strong oxidative condition
  - First & last both carbon oxidized = Dicarboxylic acid (Saccharic acid)
  - E.g. Glucosaccharic acid, mannaric acid
  - Galactose is converted to mucic acid ,which form insoluble crystals, is the basis for identification of galactose.



GOD – POD Reaction

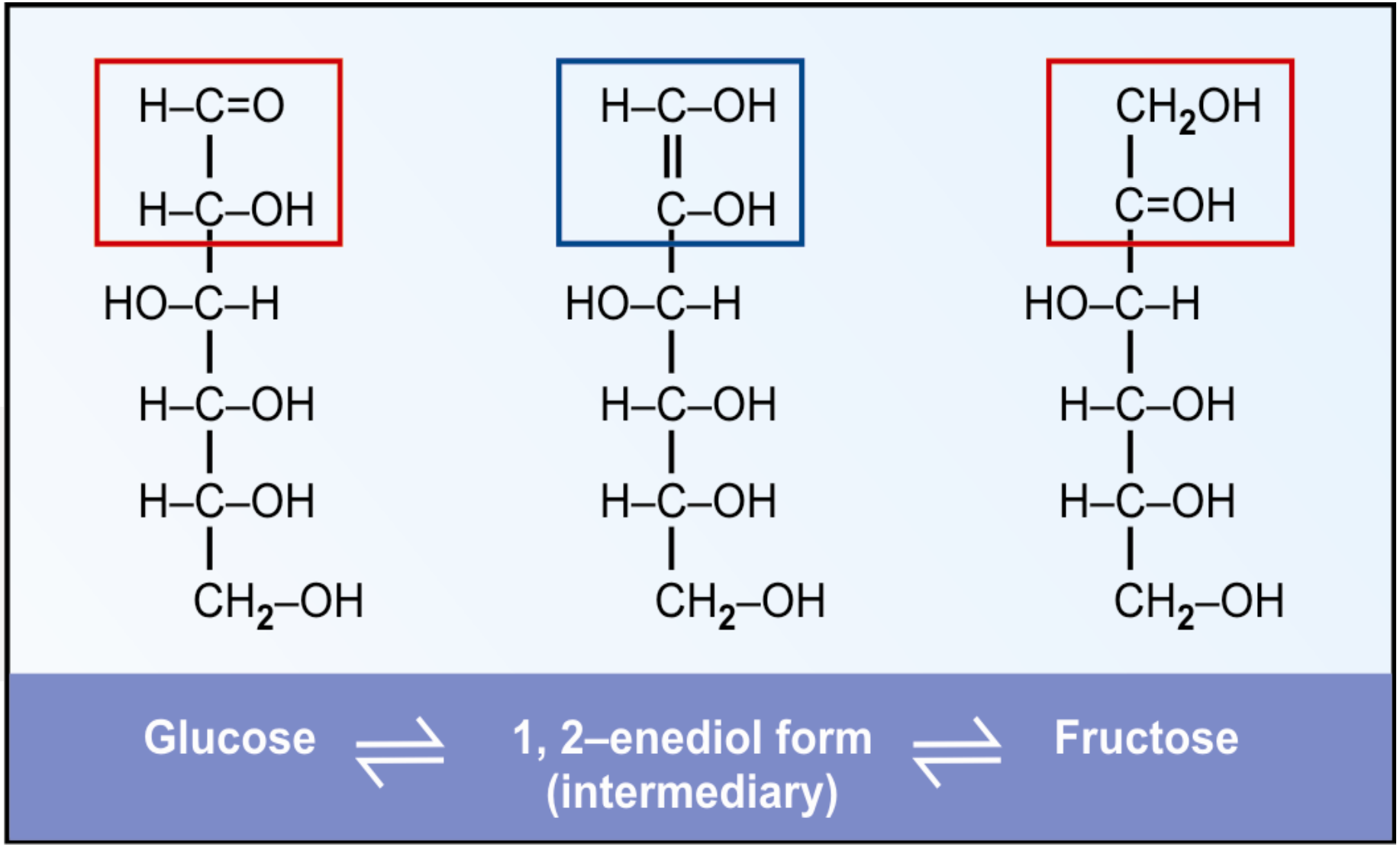


GOD = Glucose Oxidase
POD = Peroxidase

3. Alkalization

- Free group will tautomerise to form enediol.
- In alkaline medium, glucose is converted into enediol, then it can be converted to fructose or mannose.
- Enediol is highly reactive molecule in alkaline medium

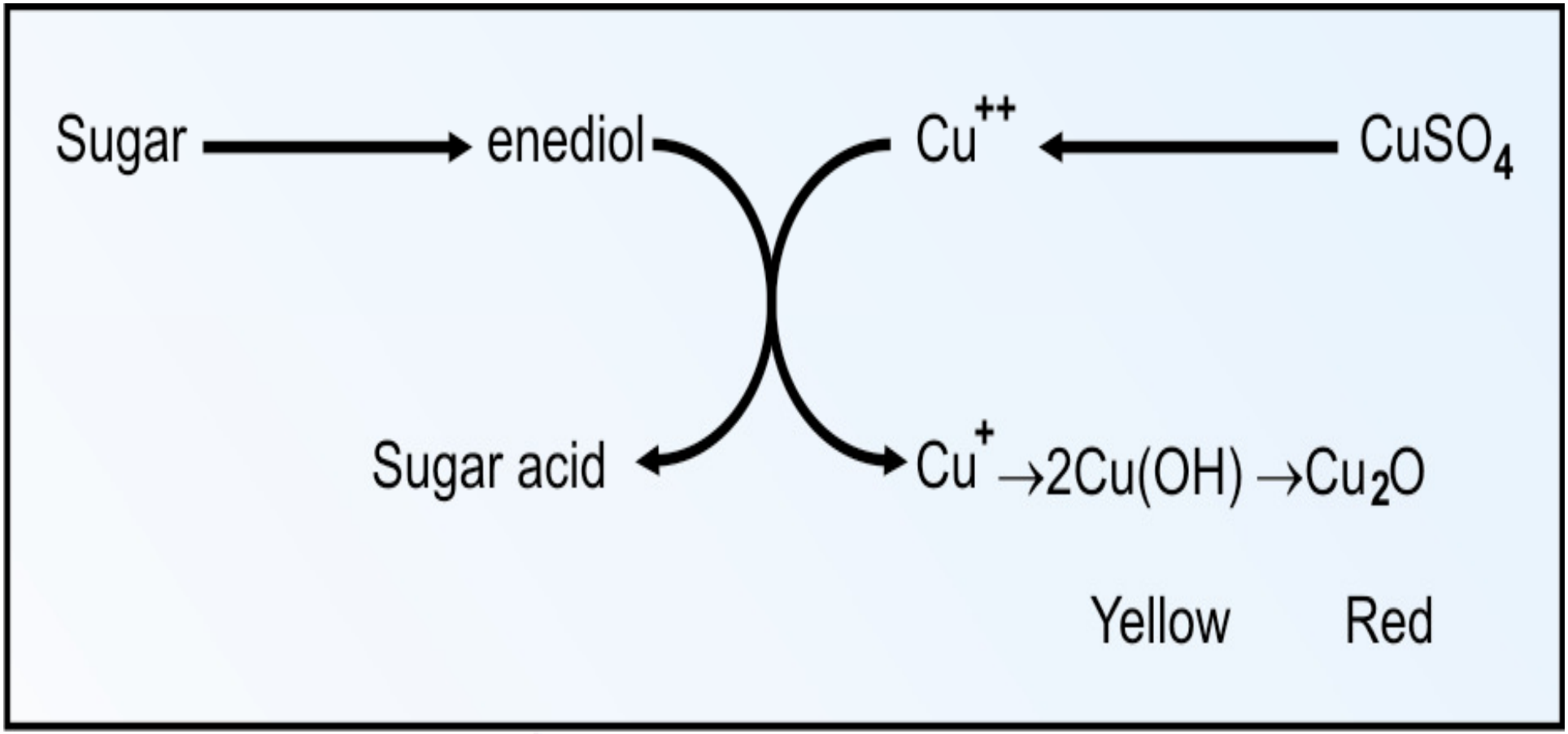
Enediol formation due to alkalization



Benedict's Reaction

- It is semiqualitative test
- to detect the reducing sugar in urine.
- Benedict's reagent contain
  - Sodium carbonate – alkaline medium
  - Copper sulfate -
  - Sodium citrate – stabilizing agent
- Copper is reduce to produce precepitation
- Green = 0.5 gm %
- Yellow = 1.0 gm %
- Orange = 1.5 gm %
- Red = 2.0 gm %

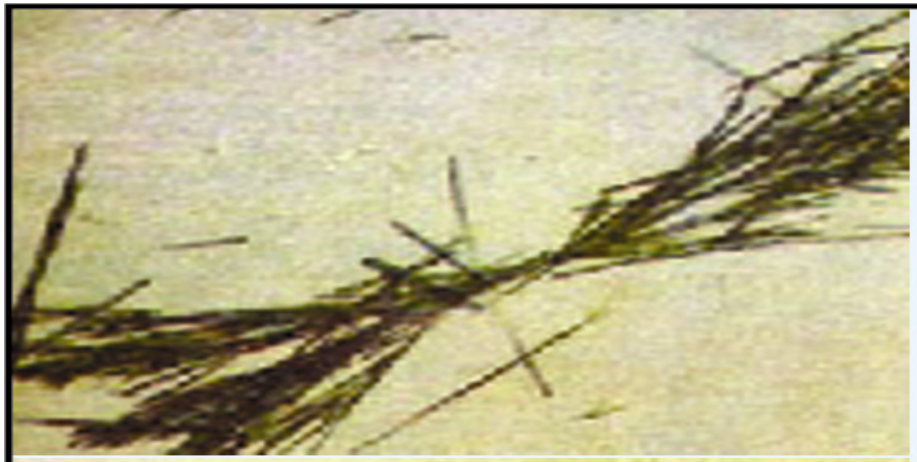
Principle of Benedict's test for Reducing Sugar



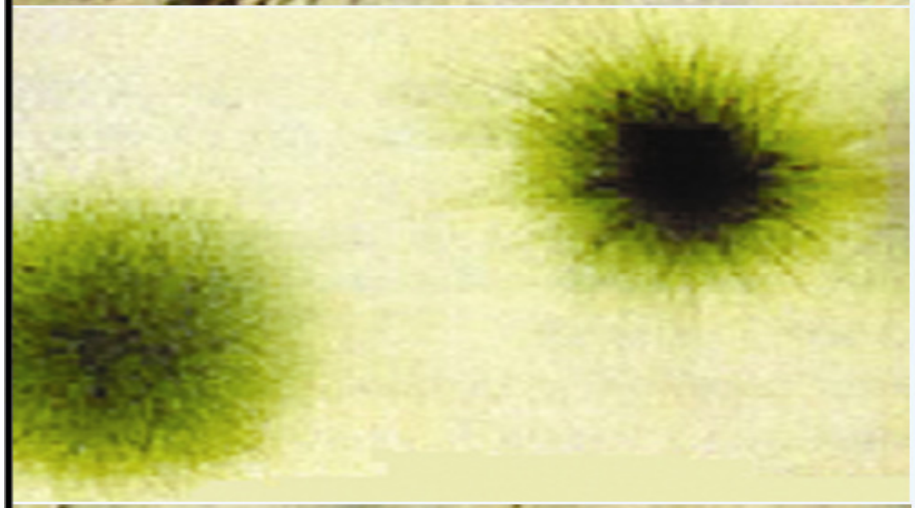
Benedict Test

4. Osazone formation

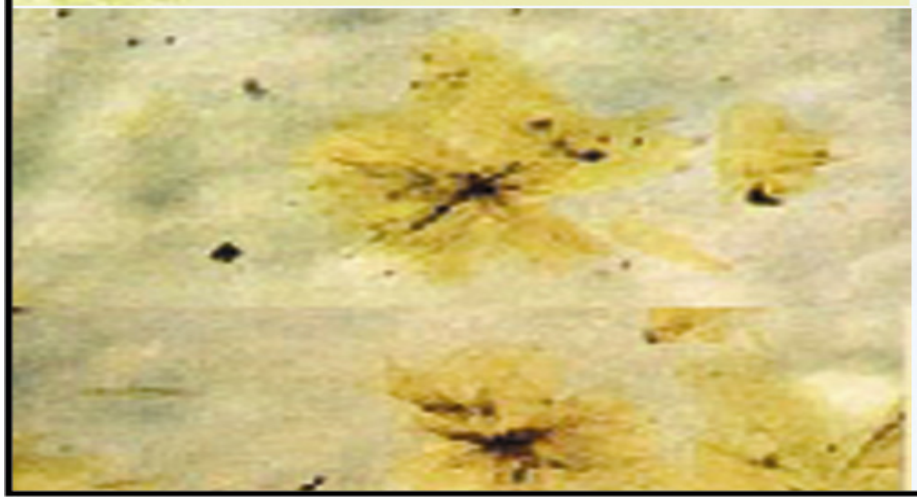
- All reducing sugar is reacted with phenyl hydrazine
- Useful to differentiate Disaccharides.
  - Glucose --- needle shape
  - Lactose --- pincushion shape
  - Mannose --- sunflower shape
- *Glucose, fructose & maltose form same type osazone ???*



Needle shaped crystals arranged like a broom
Glucososazone
Glucose, fructose and mannose will give same osazone.



Hedgehog or "pincushion with pins" or flower of "touch-me-not-plant"
Lactososazone



Sunflower shaped or petal shaped crytals of
Maltosazone

5.Furfural formation

- Monosaccharides, when treated with concentrated acid,undergo dehydration with removal of 3 molecule of water.
- Hexoses – hydroxymethyl furfural
- Pentoses – furfural
- Furfural react with phenolic compounds to give coloured product.
- This forms basis for Molisch test.

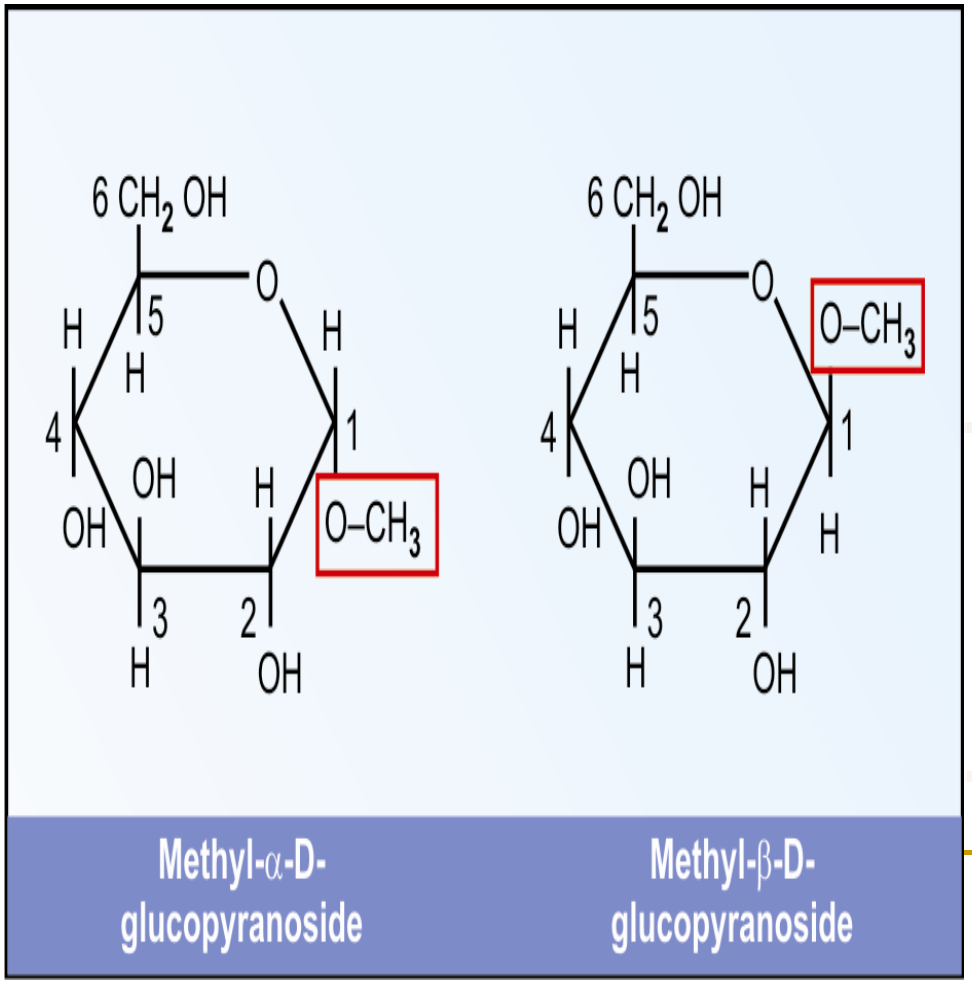
6. Glycosides

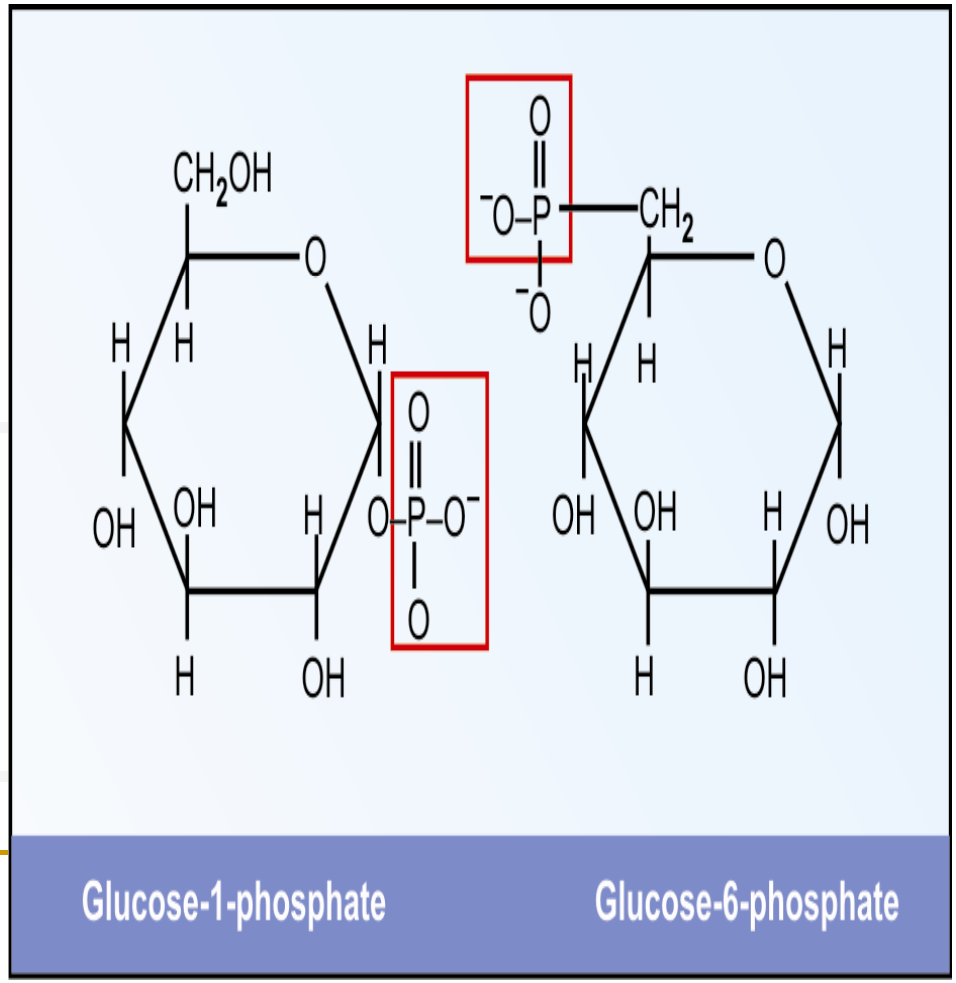
- When the semi-acetal group is condensed with an alcohol or phenol group, it is called a glycoside.
- Glucose + phloretin = Phlorhizin
  (renal damage)
- Galactose / xylose + digitogenin = Digitonin
  (cardiac stimulant)
- Glucose + indoxyl = Plant indican
  (Stain)

7. Formation of Esters

Hydroxyl group of sugar can be esterified to form

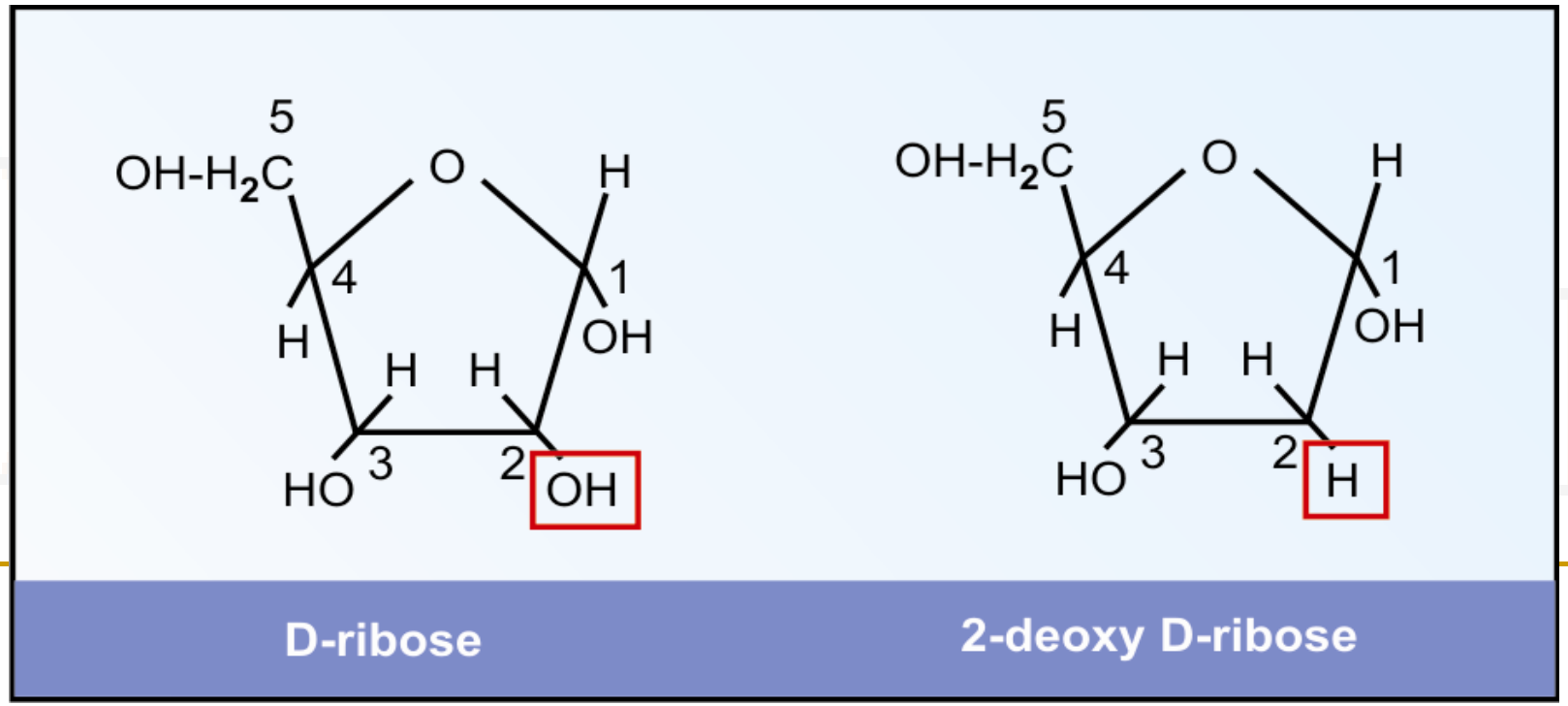
e.g. Methylation, phosphorylation, amination





Deoxy Sugars

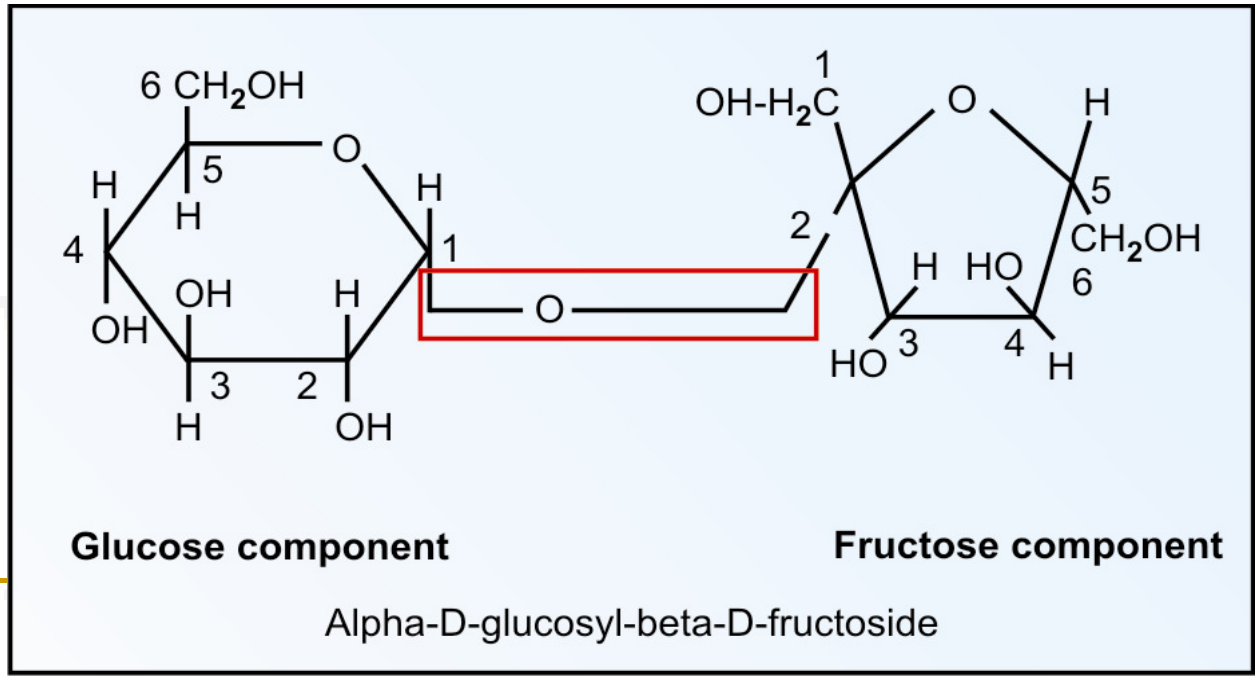
- 6-deoxy-L-galactose (L-fucose) = Present in blood group antigens.
- 6-deoxy-L-mannose (L-rhamnose) = Present in many glycosides.
- Deoxy ribose = ???.....



SUCROSE

Sucrose (+ 66.5º) = Glucose (+52.5º) + Fructose (- 92º)

- Sweetening agent known as cane sugar.
- Sucrase = Invertase
- Non – reducing sugar
- Invert sugar



Starch

- Abundant in Potatoes,Rice, Wheat
- Hydrolysis of Starch, with boiling
  - Amylose (10-20 %) – soluble form
    - Unbranch molecule
    - Alpha 1 – 4 likage only
    - M.W. > 4,00,000
  - Amylopectine (80-90 %) – Unsoluble,gel for
    - Branched molecule
    - alpha 1 – 4 & alpha 1 – 6 likage
    - M.W. > 10,00,000

Starch

- Iodine test with Starch & it's hydrolysed product
  - Starch – blue colour, Non reducing
  - Amylodextrin – violet colour, Non reducing
  - Erythrodextrin – red colour, Mild reducing
  - Achrodextrine – No colour, Reducing
  - Maltose – No colour, Powerful reducing

- Salivary & Pancreatic amylase split alpha 1 – 4 likage of starch.

Glycogen

- Reserve carbohydrate
- Store in muscle & liver
- Glucose unit with alpha 1- 4 & 1 – 6 likage.
- M.W. 5,00,000
- Primer protein = Glycogenin.
- More branches (at each 3-4 unit) compare to starch (at each 8 – 9 unit)

Cellulose

- Chief carbohydrate in plant
- Beta 1 – 4 likage (cellobiose bridge)
- Cellobiose enzyme require for digetion
- Straight line structure, no branch point.
- Commercial application – synthetic fibers,plastics

Inulin

- Homoglycan of D - fructose
- Beta 1 – 2 linkage
- Present in chicory, onion, garlic
- Clinical utility to find out
  - Renal clearance value
  - Glomerular filtration rate

Dextran

- Highly Branched homopolymer of glucose
- Alpha 1-4,1-6 & 1-3 likages
- *PLASMA EXPANDER*

Chitin

- Unit of N-acetyl glucosamine
- Beta 1 - 4 likages
- Form Exoskeleton of crustacea & insects.

Heteroglycans

- More than one type of sugar residue

AGAR

- Contain glucose , galactose & other sugars.
- Dissolve in water at 100ºc, after cooling it form gel
- Can not be digested by bacteria, so it is use as supporting media to culture bacterial colonies.
- immuno diffusion & immuno electrophoresis.

AGAROSE

- Galactose + anhydrogalactose

Mucopolysaccharides

- Glucosaminoglycans(GAG)
- Uronic acid + amino sugars
- Charged molecule.
- Attrach water molecule.
- Produce viscous solution.
  1. Hyaluronic acid
  2. Heparan sulfate
  3. Chondroitin sulphate
  4. Keratan sulphate
  5. Dermatan sulphate

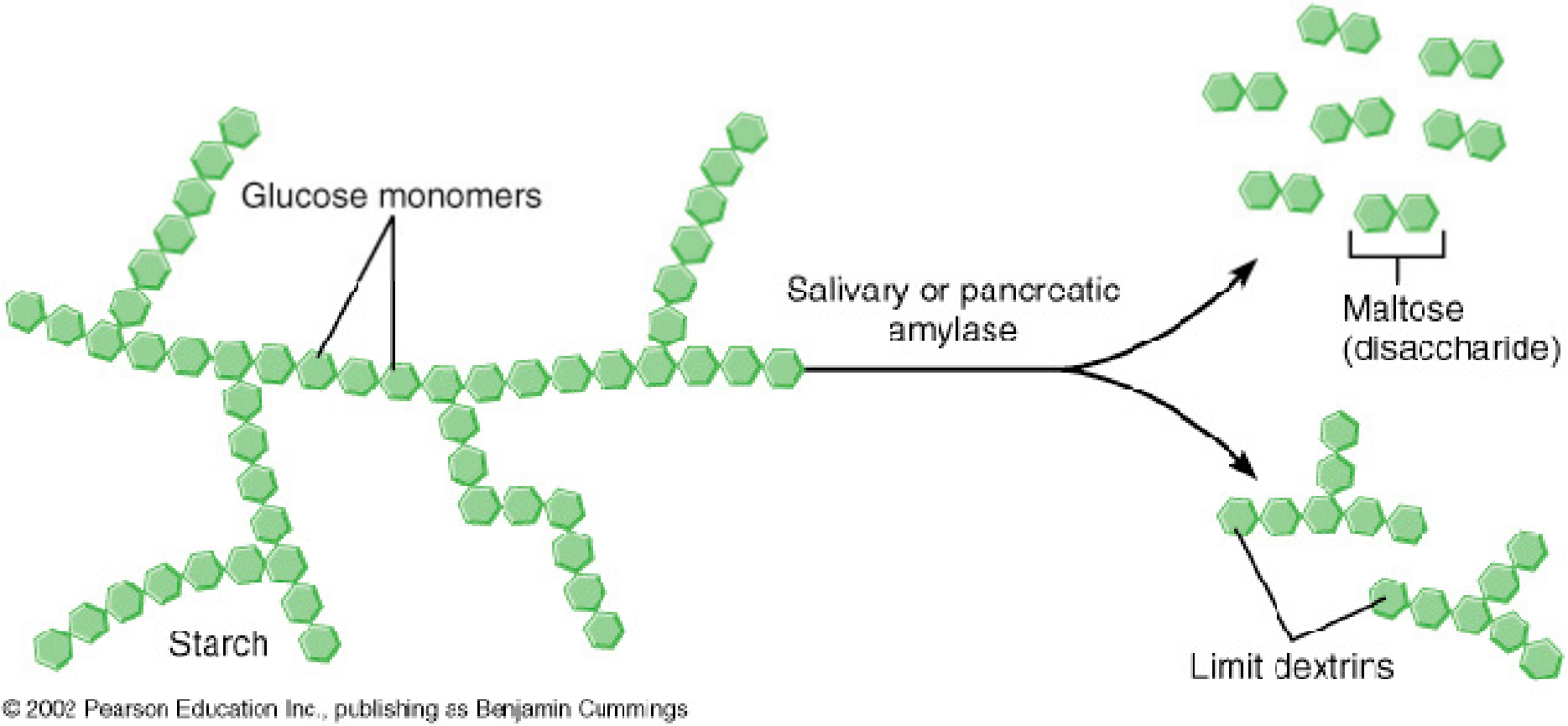
1. Hyaluronic acid
   - Connective tissue, tendon , synovial fluid, vitreous humor
   - N-acetyl glucosamine + glucuronic acid
2. Heparan sulphate
   - Anticoagulant
   - Activate anti-thrombin iii , which inactivates thrombin, factor x & factor ix
   - Present in liver, lungs,spleen & monocytes
   - Sulphated glucosamine + iduronic acid

3. Chondroitin sulphate
   - Cartilage , bone tendon
   - N –acetyl galactosamine sulphate + glucuronic acid
4. Keratan sulphate
   - Does not contain any uronic acid
   - Cornea & tendons
   - N-acetyl glucosamine + galactose
5. Dermatan sulphate
   - Skin , blood vessels , heart valves
   - N-acetyl galactosamine + iduronic acid

Digestion & Absorption

- The major dietary polysaccharides
  - Plant (starch, composed of amylose and amylopectin)
  - Animal (glycogen) origin.
- During mastication, salivary α-amylase acts on starch and glycogen.
- Hydrolyzing some α(1→4) bonds.
- They are unable to digest cellulose— a carbohydrate of plant origin containing β(1→4) glycosidic bonds between glucose residues.
- Branched amylopectin and glycogen also contain α(1→6) bonds, which α-amylase cannot hydrolyze.
- In the stomach, the highly acidic pH inactivates the salivary α-amylase, hense digestion remains incomplete.

Carbohydrate (CHO) Digestion



Digestion by pancreatic enzyme

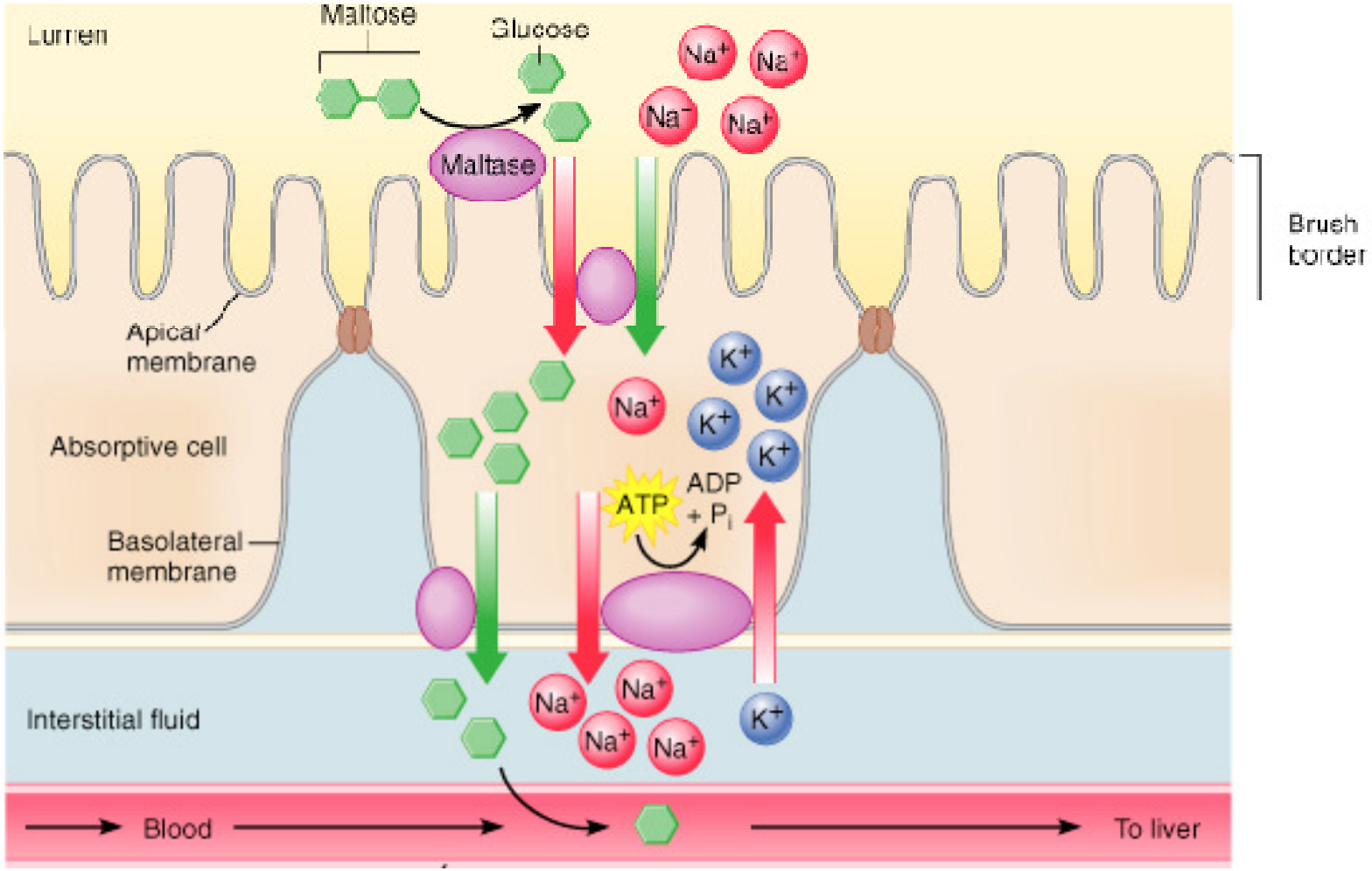
- When the acidic stomach contents reach the small intestine, they are neutralized by bicarbonate secreted by the pancreas, and pancreatic α-amylase continues the process of starch digestion

- The final digestive processes occur at the mucosal lining of the upper jejunum
- and include the action of several disaccharidases and oligosaccharidases (Figure 7.10).
- For example, isomaltase cleaves the α(1→6) bond in isomaltose and maltase cleaves maltose, both producing glucose,
- sucrase cleaves sucrose producing glucose and fructose,
- and lactase (β-galactosidase) cleaves lactose producing galactose and glucose.
- These enzymes are secreted through, and remain associated with, the luminal side of the brush border membranes of the intestinal mucosal cells.

Digestion by enzyme from intestinal mucousa

- The final digestive processes occur at the mucosal lining of the upper jejunum
- Include the action disaccharidases and oligosaccharidases.
- For example,
  - Isomaltase cleaves the α(1→6) bond in isomaltose
  - Maltase – maltose = glucose,
  - Sucrase - sucrose = glucose and fructose,
  - Lactase (β-galactosidase) - lactose = galactose +glucose.
- These enzymes are secreted through, and remain associated with, the luminal side of the brush border membranes of the intestinal mucosal cells.

Carbohydrate (CHO) Digestion



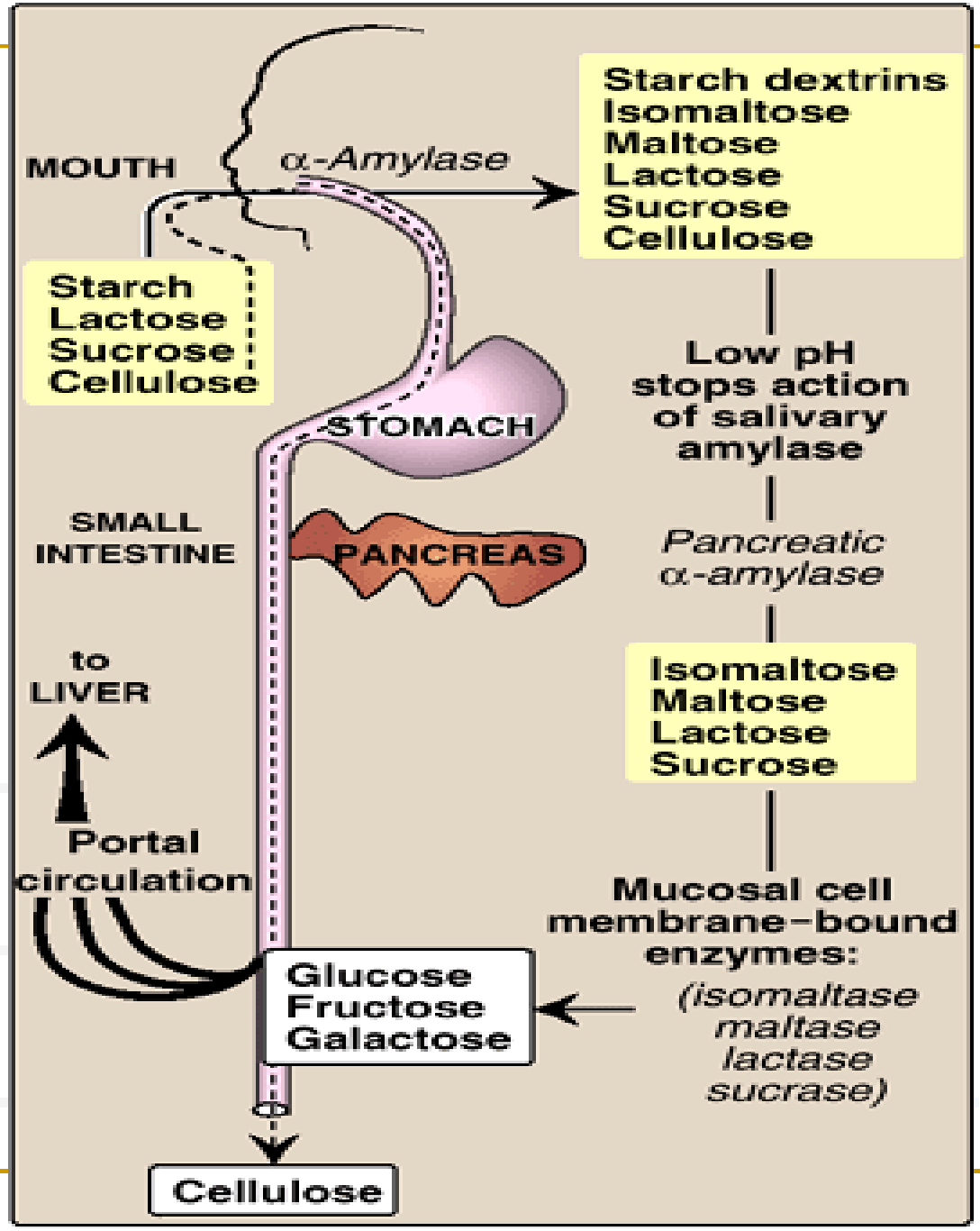

MOUTH
α-Amylase
Starch dextrins
Isomaltose
Maltose
Lactose
Sucrose
Cellulose
Starch
Lactose
Sucrose
Cellulose
STOMACH
Low pH
stops action
of salivary
amylase
SMALL
INTESTINE
PANCREAS
Pancreatic
α-amylase
to
LIVER
Isomaltose
Maltose
Lactose
Sucrose
Portal
circulation
Mucosal cell
membrane-bound
enzymes: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

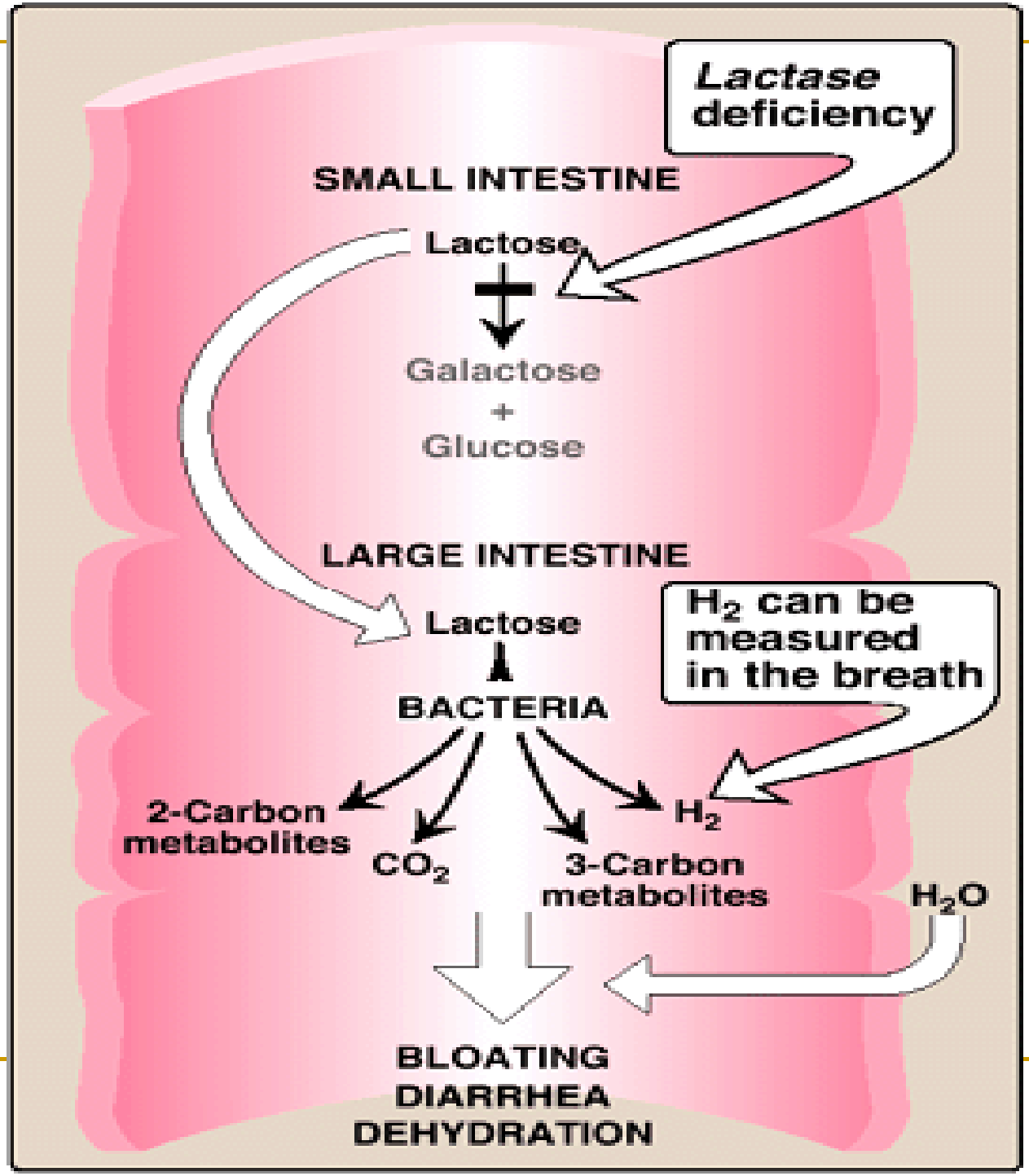
Figure 7.10

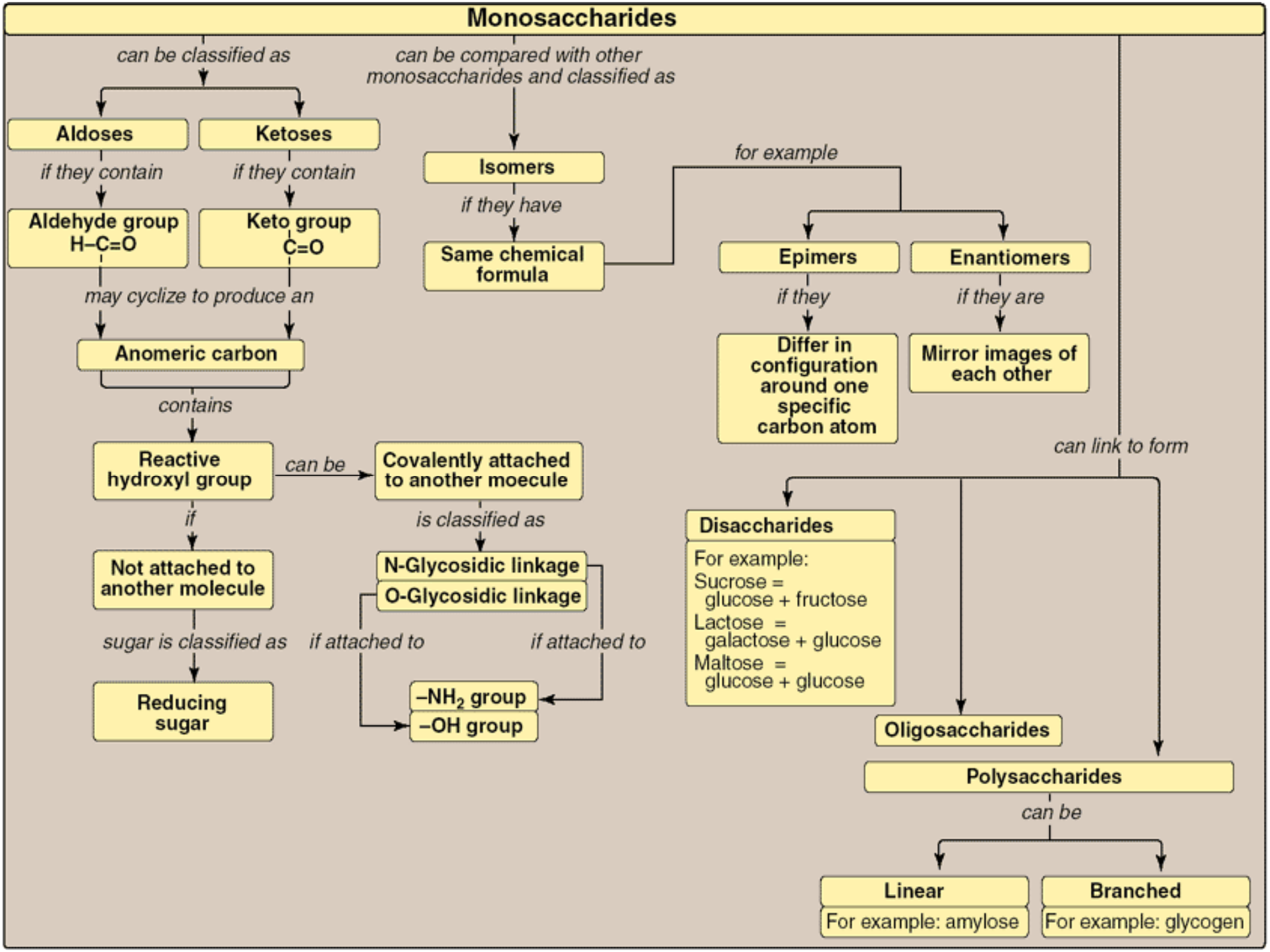
Abnormal degradation of disaccharides

- Carbohydrate digestion and absorption is so efficient in healthy individuals
- All digestible dietary carbohydrate is absorbed as it reaches the lower jejunum.
- Predominantly monosaccharides are absorbed.
- Any ***defect in a specific disaccharidase*** activity of the intestinal mucosa causes the passage of undigested carbohydrate into the large intestine.
- As a consequence of the presence of this ***osmotically active*** material, water is drawn from the mucosa into the large intestine, causing ***osmotic diarrhea***.
- This is reinforced by the ***bacterial fermentation*** of the remaining carbohydrate to two- and three-carbon compounds (which are also osmotically active) plus large volumes of CO2 and H2 gas,
- Causing ***abdominal cramps, diarrhea, and flatulence***.

Lactose intolerance

- More than three quarters of the world's adults are lactose intolerant .
- They are less able to metabolize lactose.
- The mechanism by which this age-dependent loss of the enzyme occurs is not clear,
- but it is determined genetically and represents a reduction in the amount of enzyme protein rather than a modified inactive enzyme.
- Treatment = to reduce consumption of milk while eating yogurts and cheeses, as well as green vegetables.


Lactase deficiency
SMALL INTESTINE
Lactose
Galactose
+
Glucose
LARGE INTESTINE
Lactose
BACTERIA
H2 can be measured in the breath
2-Carbon metabolites
CO2
3-Carbon metabolites
H2
H2O
BLOATING
DIARRHEA
DEHYDRATION


Monosaccharides
can be classified as
can be compared with other monosaccharides and classified as
Aldoses
Ketoses
if they contain
if they contain
Aldehyde group H–C=O
Keto group C=O
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
Isomers
if they have
Same chemical formula
for example
Epimers
Enantiomers
if they
if they are
Differ in configuration around one specific carbon atom
Mirror images of each other
can link to form
Disaccharides
For example:
Sucrose = glucose + fructose
Lactose = galactose + glucose
Maltose = glucose + glucose
Oligosaccharides
Polysaccharides
can be
Linear
For example: amylose
Branched
For example: glycogen