Carbohydrates Metabolism

Review of Carbohydrates
Digestion\textsuperscript{1} and absorption\textsuperscript{2} of carbohydrates

Suggested Readings:
1: Lippincot’s Illustrated reviews: Biochemistry
2: Marks’ Basic Medical Biochemistry
Stage I:
Hydrolysis of complex molecules to their component building blocks

Proteins → Amino acids
Polysaccharides → Monosaccharides
Lipids → Glycerol, fatty acids

Stage II:
Conversion of building blocks to acetyl CoA (or other simple intermediates)

Amino acids → Monosaccharides → Acetyl CoA

Stage III:
Oxidation of acetyl CoA; oxidative phosphorylation

Acetyl CoA → Citric acid cycle → ATP, CO₂
Carbohydrates Metabolism

• Objectives
  – Utilization of Glucose $\rightarrow$ Energy
  – Non-Carbohydrates $\rightarrow$ Glucose
  – Storage of Glucose $\rightarrow$ Glycogen
  – Release of Glucose from Glycogen
  – Reducing Power NADPH $\rightarrow$ GSH
  – Glucuronic acid $\rightarrow$ Drug metabolism
  – Interconversion of sugars
An Over-all Picture

Glycogen

Glycogenolysis

Glycogenesis

Pentoses

Glycolysis

NADPH

Gluconeogenesis

Glucuronic Acid

Glycogenesis

Glucose

Lactate
Dietary Carbohydrates

40 – 50 % of caloric intact

60% of the carbohydrate → 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.
Examples of monosaccharides found in human

<table>
<thead>
<tr>
<th>Generic names</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 carbons:</td>
<td>trioses</td>
</tr>
<tr>
<td>4 carbons:</td>
<td>tetrooses</td>
</tr>
<tr>
<td>5 carbons:</td>
<td>pentoses</td>
</tr>
<tr>
<td>6 carbons:</td>
<td>hexoses</td>
</tr>
<tr>
<td>7 carbons:</td>
<td>heptoses</td>
</tr>
<tr>
<td>9 carbons:</td>
<td>nonoses</td>
</tr>
<tr>
<td></td>
<td>Glyceraldehyde</td>
</tr>
<tr>
<td></td>
<td>Erythrose</td>
</tr>
<tr>
<td></td>
<td>Ribose</td>
</tr>
<tr>
<td></td>
<td>Glucose</td>
</tr>
<tr>
<td></td>
<td>Sedoheptulose</td>
</tr>
<tr>
<td></td>
<td>Neuraminic acid</td>
</tr>
</tbody>
</table>
Epimers are isomers:

Changing the orientation of one hydroxyl group will produce different sugar.
Glucose and Fructose are isomers
Disaccharide: A sugar made of two sugar units joined by glycosidic bond

Maltose: a disaccharide made from two glucose units
Lactose: galactosyl-β(1→4)-glucose
Glycosidic bond is cleaved by glycosidase
Starch

Salivary and pancreatic \(\alpha\)-amylase

Maltose

Isomaltose

Trisaccharides (and larger oligosaccharides)

\(\alpha\)-Dextrins (oligosaccharides with \(\alpha\)-1,6-branches)
### Mucosal cell membrane-bound enzymes

<table>
<thead>
<tr>
<th>ENZYME</th>
<th>Bond Cleaved</th>
<th>Substrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isomaltase</td>
<td>α 1→ 6</td>
<td>Isomaltose</td>
</tr>
<tr>
<td>Maltase</td>
<td>α 1→ 4</td>
<td>Maltose</td>
</tr>
<tr>
<td>Sucrase</td>
<td>α 1→ 2</td>
<td>Sucrose</td>
</tr>
<tr>
<td>Lactase</td>
<td>β 1→ 4</td>
<td>Lactose</td>
</tr>
<tr>
<td>Trehalase</td>
<td>α 1→ 1</td>
<td>Trehalose</td>
</tr>
<tr>
<td>Exoglucoamylose</td>
<td>α 1→ 4</td>
<td>Glucoamylose</td>
</tr>
</tbody>
</table>
Sucrase-isomaltase complex and Glucoamylase

- Sucrase + isomaltase
  Single protein → complex of two associated subunits
  - Sucrase-maltase
  - Isomaltase-maltase

Together 80% of the maltase activity

- Maltase + exoglucoamylase (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 + exoglucoamylase (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

**Adult Hypolactasia** (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. $\text{Na}^+$-independent facilitated diffusion transport

GLUT 1-----GLUT 14

Glc. Movement follows concentration gradient

Two conformation states
Na\textsuperscript{+} 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

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

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

\[ \alpha(1 \rightarrow 4) \text{ bonds} \]

Maltose

Malto-oligosaccharides (primarily maltotriose)

\[ \alpha(1 \rightarrow 6) \text{ bonds} \]

Oligosaccharide

Isomaltose

\[ \alpha(1 \rightarrow 6) \text{ bonds} \]

Oligosaccharide

Isomaltose
Maltose

\( \alpha-1,4 \text{ bond} \)

\[
\begin{array}{c}
\text{HO-} \\
\text{O-} \\
\text{HO-}
\end{array}
\begin{array}{c}
\text{O-} \\
\text{HO-}
\end{array}
\]

\text{maltase activity}

\[
\begin{array}{c}
\text{HO-} \\
\text{O-} \\
\text{HO-}
\end{array}
\begin{array}{c}
\text{O-} \\
\text{HO-}
\end{array}
\]

\text{Maltotriose}

\text{reducing end}
Intestinal lumen

Gas

Bacterial fermentation

Lactic acid

Osmotic effect

Fluid load (1,000 mL)

H₂O

Distention of gut walls

↑ Peristalsis

Malabsorption
Fats, Proteins, Drugs

Watery diarrhea
(1L extracellular liquid lost per 9 g lactose in 1 glass of milk)