Digestion, Absorption, Transport, and Excretion of Nutrients

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Digestion and Absorption of Specific Types of Nutrients
Carbohydrates and Fiber
Most dietary carbohydrates are consumed in the form of starches, disaccharides, and monosaccharides.

Starches, or polysaccharides, usually make up the greatest proportion of carbohydrates.

Starches are large molecules composed of straight or branched chains of sugar molecules that are joined together, primarily in α-1-4 or α-1-6 linkages.

Most of the dietary starches are amylopectins, the branching polysaccharides, and amylose, the straight chain-type polymers.
Structure of starch: (A) Amylose, showing helical coil structure; (B) Amylopectin, showing 1→6 branch point
Fig. 2.2. Starch is composed of amylose (15% to 20%) and amylopectin (80% to 85%). Amylose is a nonbranching helical chain structure of glucose residues, whereas amylopectin (a portion shown here) has branched chains of 24 to 30 glucose residues (blue) joined by (1→4) glucosidic linkages with (1→6) linkages creating the branching points.
Dietary fiber is also largely made of chains and branches of sugar molecules, but in this case the hydrogens are positioned on the beta (opposite) side of the oxygen in the link instead of the alpha side, resulting in its resistance to enzymatic digestion in human GIT.

That humans have significant ability to digest starch, but not most fiber, exemplifies the "stereospecificity" of enzymes.
Digestible

Amylose: $\alpha-1,4$ glucosidic bonds

Indigestible

Cellulose: $\beta-1,4$ glucosidic bonds

Indigestible

$\beta$-Glucan: mixed $\beta-1,3$ and $\beta-1,4$ glucosidic bonds
In the mouth, salivary amylase (ptyalin) operates at a neutral/slightly alkaline pH and hydrolyzes a small amount of the starch molecules into smaller fragments, and then becomes deactivated after contact with HCl.

The stomach empties before significant carbohydrate digestion can take place; thus, most carbohydrate digestion occurs in the proximal small intestine.
Pancreatic amylase breaks the large starch molecules at α-1-4 linkages to create maltose, maltotriose, and “alpha-limit” dextrins remaining from the amylopectin branches.

Enzymes from the brush border of the enterocytes further break the disaccharides and oligosaccharides into monosaccharides glucose, galactose, and fructose.

The brush border of the enterocytes contain the enzymes maltase, sucrase, lactase, and isomaltase (or α-dextrinase), which act on maltose, sucrose, lactose, and isomaltose, respectively.
Starch and disaccharides

Salivary amylase

Pancreatic amylase

Mouth

Small Intestine

Oligosaccharides and disaccharides

Lactose

Maltose

Sucrose

Galactose

Glucose

Fructose

Brush border enzymes in small intestine (dextrinase, glucoamylase, lactase, maltase, and sucrase)

Small intestine
FIGURE 1-7 The gradual breakdown of large starch molecules into glucose by digestion enzymes.
Glucose, galactose, and fructose pass through the mucosal cells and into the bloodstream via the capillaries of the villi, where they are carried by the portal vein to the liver.

At low concentrations, glucose and galactose are absorbed by active transport, primarily by a sodium-dependent transporter called the glucose (galactose) cotransporter.

At higher luminal concentrations of glucose, glucose transporter (GLUT) 2 becomes a primary facilitative transporter into the intestinal cell.
Fructose is more slowly absorbed and uses GLUT5 and the facilitative transporter from the lumen.

GLUT2 is used to transport glucose, galactose, and fructose across the intestinal cell membranes into the blood.

The sodium-dependent transport of monosaccharides is the reason why sodium-glucose drinks are used to rehydrate infants with diarrhea or athletes who have lost too much fluid.
Transport of glucose, fructose, and galactose across the intestinal epithelium. The SGLT 1 transporter is coupled to the Na\(^+\) - K\(^+\) pump, allowing glucose and galactose to be transported against their concentration gradients. The GLUT 5 Na\(^+\) - independent facilitative transporter allows fructose, as well as glucose and galactose, to be transported down their concentration gradients. Exit from the cell for all sugars is via the GLUT 2 facilitative transporter.
Fig. 42.15. Monosaccharide absorption by the enterocyte occurs by active and passive processes. Glucose and galactose are absorbed by a sodium (Na)-dependent glucose/galactose transporter (SGLT1), driven by an Na\(^+\) gradient generated by Na\(^+\)/potassium (K\(^+\))/adenosine triphosphatase (ATPase) at the basolateral membrane of the enterocyte. Fructose is absorbed by facilitated diffusion using a glucose transporter called GLUT5. All monosaccharides exit the enterocyte by facilitated diffusion via a carrier protein called GLUT2. (Reprinted with permission from Chang EB, Sitrin MD, Black DD, eds. Gastrointestinal, Hepatobiliary, and Nutritional Physiology. Philadelphia: Lippincott-Raven, 1996:125.)
<table>
<thead>
<tr>
<th>TYPE</th>
<th>AMINO ACIDS (N)</th>
<th>CHROMOSOME LOCATION</th>
<th>$K_m$ (mmol/L) FOR HEXOSE UPTAKE$^a$</th>
<th>MAJOR EXPRESSION SITES</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLUT1 (red cell)</td>
<td>492</td>
<td>1</td>
<td>1–2 (red blood cells)</td>
<td>Placenta, brain, kidney, colon</td>
</tr>
<tr>
<td>GLUT2 (liver)</td>
<td>524</td>
<td>3</td>
<td>15–20 (hepatocytes)</td>
<td>Liver, β cell, kidney, small intestine</td>
</tr>
<tr>
<td>GLUT3 (brain)</td>
<td>496</td>
<td>12</td>
<td>10 (Xenopus oocytes)</td>
<td>Brain, testis</td>
</tr>
<tr>
<td>GLUT4 (muscle/fat)</td>
<td>509</td>
<td>17</td>
<td>5 (adipocytes)</td>
<td>Skeletal and heart muscle, brown and white fat</td>
</tr>
<tr>
<td>GLUT5 (small intestine)</td>
<td>501</td>
<td>1</td>
<td>6–11 (fructose) (Xenopus oocytes)</td>
<td>Small intestine, sperm</td>
</tr>
</tbody>
</table>

*K_m*, Michaelis-Menten constant.

$^a$The approximate $K_m$ values refer to the uptake of glucose (fructose in the case of GLUT5) in the designated tissue or cells in parentheses and are shown to give an approximate index of the affinity of the transporter for glucose.
Consumption of large amounts of lactose (especially in individuals with a lactase deficiency), fructose, stachyose, raffinose, or alcohol sugars (e.g. sorbitol, mannitol, or xylitol) can result in considerable amounts of these sugars passing unabsorbed into the colon and may cause increased gas and loose stools.
Cellulose, hemicellulose, pectin, gum, and other forms of fiber cannot be digested by humans; thus these carbohydrates pass relatively unchanged into the colon, where they are partially fermented by bacteria in the colon.

Other resistant starches and sugars are also less well digested or absorbed by humans, but are fermented into SCFAs and gases.

It is noteworthy that one form of dietary fiber, lignin, is made of cyclopentane units and is neither readily soluble nor fermentable.
Proteins
Protein digestion begins in the stomach, where some of the proteins are split into polypeptides by the enzyme pepsin.

Inactive pepsinogen is converted into the enzyme pepsin when it contacts HCl and other pepsin molecules.

Unlike any of the other proteolytic enzymes, pepsin digests collagen, the major protein of connective tissue.
Digestion of protein/polypeptide

The peptide bonds between the amino acids are hydrolysed

Pepsin is a protease that hydrolyses the protein into smaller polypeptides

gastric gland in stomach

pepsinogen → pepsin

HCl

pepsin

parietal cell

chief cell

pepsinogen
Contact between chyme and the intestinal mucosa stimulates the release of enterokinase, an enzyme that transforms inactive pancreatic trypsinogen into active trypsin (i.e. the major pancreatic protein-digesting enzyme).

Trypsin in turn activates the other pancreatic proteolytic enzymes.
Pancreatic trypsin, chymotrypsin, and carboxypeptidase break down intact protein to small polypeptides and amino acids.
Trypsin

\[
\text{Polypeptide} + \text{H}_2\text{O} \rightarrow \text{Polypeptide fragments}
\]

\(R = \text{Arg and Lys}\)

Chymotrypsin

\[
\text{Polypeptide} + \text{H}_2\text{O} \rightarrow \text{Polypeptide fragments}
\]

\(R = \text{Phe, Trp, and Tyr}; R' \neq \text{Pro}\)

Carboxypeptidase

\[
\text{Polypeptide (n residues)} + \text{H}_2\text{O} \rightarrow \text{Polypeptide (n-1 residues)} + \text{Amino Acid}
\]

\(R' = \text{Arg, Lys, and ornithine}\)
Proteolytic peptidases located on the brush border also act on polypeptides, breaking them down into amino acids, dipeptides, and tripeptides.

The final phase of protein digestion takes place in the brush border, where some of the dipeptides and tripeptides are hydrolyzed into amino acids by peptide hydrolases.

End products of protein digestion are absorbed as both amino acids and small peptides.
Protein digestion

1. Protein
   - Pepsin (stomach glands) in the presence of HCl
     - Stomach

2. Large polypeptides
   - Pancreatic enzymes (trypsin, chymotrypsin, carboxypeptidase)
     - Small Intestine

3. Small polypeptides, small peptides

4. Amino acids (some dipeptides and tripeptides)
   - Brush border enzymes (aminopeptidases, carboxypeptidase, and dipeptidases)
     - Small Intestine
Several transport molecules (sodium- or chloride-dependent, etc.) are required for the absorption of amino acids, probably because of the wide differences in the size, polarity, and configuration of the different amino acids.

Considerable amounts of dipeptides and tripeptides are also absorbed into intestinal cells using a peptide transporter, a form of active transport.
## TABLE 1.5 AMINO ACID TRANSPORTERS

<table>
<thead>
<tr>
<th>SYSTEM</th>
<th>AMINO ACID TRANSPORTED</th>
<th>TISSUE LOCATION</th>
<th>pH DEPENDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium dependent</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Most neutrals (Ala, Ser)</td>
<td>Ubiquitous</td>
<td>Yes</td>
</tr>
<tr>
<td>ASC</td>
<td>Most neutrals</td>
<td>Ubiquitous</td>
<td>No</td>
</tr>
<tr>
<td>B</td>
<td>Most neutrals</td>
<td>Intestinal brush border</td>
<td>Yes</td>
</tr>
<tr>
<td>N</td>
<td>Gln, Asn, His</td>
<td>Hepatocytes</td>
<td>Yes</td>
</tr>
<tr>
<td>N&lt;sup&gt;m&lt;/sup&gt;</td>
<td>Gln, Asn</td>
<td>Muscle</td>
<td>No</td>
</tr>
<tr>
<td>Gly</td>
<td>Gly, sarcosine</td>
<td>Ubiquitous</td>
<td></td>
</tr>
<tr>
<td>X&lt;sub&gt;AG-&lt;/sub&gt;</td>
<td>Glu, Asp</td>
<td>Ubiquitous</td>
<td></td>
</tr>
<tr>
<td>Sodium independent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L</td>
<td>Leu, Ile, Val, Met, Phe, Tyr, Trp, His</td>
<td>Ubiquitous</td>
<td>Yes</td>
</tr>
<tr>
<td>T</td>
<td>Trp, Phe, Tyr</td>
<td>Red blood cells, hepatocytes</td>
<td>No</td>
</tr>
<tr>
<td>y&lt;sup&gt;+&lt;/sup&gt;</td>
<td>Arg, Lys, Orn</td>
<td>Ubiquitous</td>
<td>No</td>
</tr>
<tr>
<td>asc</td>
<td>Ala, Ser, Cys, Thr</td>
<td>Ubiquitous</td>
<td>Yes</td>
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</tbody>
</table>

Data from references 10 to 12, with permission.
<table>
<thead>
<tr>
<th>TRANSPORT SYSTEM</th>
<th>SOLUTE CARRIER (SLC) CLASSIFICATION</th>
<th>AMINO ACIDS</th>
<th>Na-DEPENDENT</th>
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<tr>
<td>Neutral amino acids</td>
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<td></td>
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<tr>
<td>A</td>
<td>SLC38A2</td>
<td>G, P, A, S, C, Q, N, H, M</td>
<td>Yes</td>
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<tr>
<td>L</td>
<td>SLC3A2, SLC7A8</td>
<td>All neutral AAs except P</td>
<td>Yes</td>
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<tr>
<td>B&lt;sup&gt;+&lt;/sup&gt;</td>
<td>SLC6A15</td>
<td>P, L, V, I, M</td>
<td>Yes</td>
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<tr>
<td>T</td>
<td>SLC16A10</td>
<td>F, Y, W</td>
<td>Yes</td>
</tr>
<tr>
<td>IMINO</td>
<td>SLC6A20</td>
<td>P, hydroxyproline</td>
<td>Yes</td>
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<tr>
<td>ASC</td>
<td>SLC1A5</td>
<td>A, S, C, T, Q</td>
<td>Yes</td>
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<tr>
<td>PAT</td>
<td>SLC36A1</td>
<td>P, G, A, β-alanine, taurine</td>
<td>No, H&lt;sup&gt;+&lt;/sup&gt;</td>
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<tr>
<td>Acidic amino acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X&lt;sup&gt;−&lt;/sup&gt;&lt;sub&gt;AG&lt;/sub&gt;</td>
<td>SLC1A1</td>
<td>E, D</td>
<td>Yes, H&lt;sup&gt;+&lt;/sup&gt;</td>
</tr>
<tr>
<td>x&lt;sup&gt;−&lt;/sup&gt;</td>
<td>SLC3A2, SLC7A11</td>
<td>E, cystine</td>
<td></td>
</tr>
<tr>
<td>Basic amino acids</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>B&lt;sup&gt;0+&lt;/sup&gt;</td>
<td>SLC6A14</td>
<td>Neutral and basic amino acids, β-alanine</td>
<td>Yes</td>
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<tr>
<td>Y&lt;sup&gt;+&lt;/sup&gt;</td>
<td>SLC7A1</td>
<td>R, K, H, ornithine</td>
<td></td>
</tr>
<tr>
<td>Y&lt;sup&gt;+&lt;/sup&gt;L</td>
<td>SLC3A2, SLC7A7</td>
<td>K, R, Q, H, M, L</td>
<td>Yes</td>
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<tr>
<td>b&lt;sup&gt;0+&lt;/sup&gt;</td>
<td>SLC3A1, SLC7A9</td>
<td>R, K, ornithine, cystine</td>
<td>No</td>
</tr>
<tr>
<td>Dipeptide/tripeptide</td>
<td>hPept1</td>
<td>Dipeptides and tripeptides</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Amino acids are given in one-letter codes: A, alanine; C, cysteine; D, aspartic acid; E, glutamic acid; F, phenylalanine; G, glycine; H, histidine; I, isoleucine; K, lysine; L, leucine; M, methionine; N, asparagines; P, proline; Q, glutamine; R, arginine; S, serine; T, tyrosine; V, valine; W, tryptophan.

Data from Broer S. Amino acid transport across mammalian intestinal and renal epithelia. Physiol Rev 2008;88:249, with permission.
Almost all protein is absorbed by the time it reaches the distal jejunum, thus only 1% of ingested protein is found in the feces.

Absorbed peptides and amino acids are transported to the liver via the portal vein.

Small amounts of amino acids may remain in the epithelial cells for synthesis of new proteins (e.g. intestinal enzymes).
Lipids
Approximately, 97% of dietary lipids are in the form of triglycerides, and the rest are phospholipids and cholesterol.

Only small amounts of fat are digested in the mouth with lingual lipase and in the stomach with gastric lipase or tributyrinase, which hydrolyzes short-chain triglycerides (such as those found in butter), into fatty acids and glycerol.

Most fat digestion takes place in the small intestine as a result of the emulsifying action of bile salts and hydrolysis by pancreatic lipase.
Lingual lipase
- Hydrolysis of TG present in food
- Perception of fat taste

Gastric Lipase
- Hydrolysis of TG from food

Pancreatic Triglyceride Lipase
- Hydrolysis of TG from food
Entrance of fat and protein into the duodenum stimulates the release of CCK (which stimulates biliary and pancreatic secretions) and enterogastrone, which inhibit gastric secretions and motility, thus slowing the delivery of lipids.

Therefore, a portion of a large, fatty meal may remain in the stomach for 4 hours or longer.
The peristaltic action of the small intestine and the emulsification action of bile reduces the fat globules into tiny droplets, thus making them more accessible to digestion by the pancreatic lipase.

The free fatty acids and monoglycerides produced by digestion form complexes with bile salts called micelles, which facilitate passage of the lipids through the watery environment of the intestinal lumen to the brush border.
Fig. 4.2. Transport hypothesis of fatty acids and 2-monoglycerides through lipase-mediated hydrolysis, micellar transfer, and cellular uptake stages.
Bile is a liver secretion composed of bile acids (primarily conjugates of cholic and chenodeoxycholic acids with glycine or taurine), bile pigments (which color the feces), inorganic salts, some protein, cholesterol, lecithin, and many compounds such as detoxified drugs.

From its storage organ, the gallbladder, approximately 1 L of bile is secreted daily.
Bile is secreted by the liver, stored in the gall bladder and ejected into the small intestine.
Most of the bile salts are actively reabsorbed in the terminal ileum and returned to the liver to reenter the gut in bile secretions through the process of enterohepatic circulation.
1. Secreted bile salts consist of 95% old, recycled bile salts and 5% newly synthesized bile salts.

3. Reabsorbed bile salts are recycled by enterohepatic circulation.

4. 5% of bile salts are lost in feces.
In the mucosal cells the fatty acids and monoglycerides are reassembled into new triglycerides.

These triglycerides, along with cholesterol, fat-soluble vitamins, and phospholipids, are surrounded by a lipoprotein coat, forming chylomicrons.

Chylomicrons pass into the lymphatic system and are transported to the thoracic duct and emptied into the systemic circulation at the junction of the left internal jugular and left subclavian veins.
Fig. 42.13. Chylomicrons are fat droplets that are coated with a monolayer of phospholipid and cholesterol. Dispersed in the monolayer are apoproteins (Apo) A-1, apoA-IV, and Apo B and probably also some Apo C-11 and Apo C-111. These proteins help direct the tissue uptake and catabolism of the chylomicrons. In the circulation, chylomicrons also acquire additional apoproteins. Although triglyceride is the major lipid carried in chylomicrons, they are also carriers of cholesterol, fat-soluble vitamins, and small amounts of many other trace lipophilic molecules. (Reprinted with permission from Patton JS, Hoffman AF. Lipid Digestion. Undergraduate Teaching Project, Unit 19. Bethesda, MD: American Gastroenterological Association, 1986.)
The chylomicrons are then carried through the bloodstream to several tissues, including liver, adipose tissue, and muscle.

In the liver, triglycerides from the chylomicrons are repackaged into very low-density lipoproteins and transported primarily to the adipose tissue for metabolism and storage.
The fat-soluble vitamins A, D, E, and K are also absorbed in a micellar fashion, although water-soluble forms of vitamins A, E, and K supplements and carotene can be absorbed in the absence of bile acids.
Normally, 95% to 97% of ingested fat is absorbed into lymph vessels.

Increased motility, intestinal mucosal changes, pancreatic insufficiency, or the absence of bile can decrease fat absorption.

When undigested fat appears in the feces, the condition is known as steatorrhea.
Because of their shorter length and thus increased solubility, fatty acids of 8 to 12 carbons (i.e. medium-chain fatty acids) can be absorbed directly into mucosal cells without the presence of bile and micelle formation, where they are able to go directly without esterification into the portal vein.

Due to these characteristics, medium-chain triglycerides (MCTs), which have medium-chain fatty acids, are clinically valuable for individuals who lack necessary bile salts for long-chain fatty acid metabolism and transport.
Large lipids such as monoglycerides and long-chain fatty acids first must merge into micelles that move into intestinal cells. Then the intestinal cells assemble the monoglycerides and fatty acids into triglycerides that are incorporated into chylomicrons that can travel through the lymph.

The end products of fat digestion are mostly monoglycerides, some fatty acids, and very little glycerol. Glycerol and short- and medium-chain fatty acids can move directly into the bloodstream.
Summary of fat digestion and absorption

Because fat is not soluble in water, it must undergo a series of transformations in order to be digested and absorbed.

1. Dietary fat in the form of large fat globules composed of triglycerides is emulsified by the detergent action of bile salts into a suspension of smaller fat droplets. This lipid emulsion prevents the fat droplets from coalescing and thereby increases the surface area available for attack by pancreatic lipase.

2. Lipase hydrolyzes triglycerides into monoglycerides and free fatty acids.

3. These water-insoluble products are carried in the interior of water-soluble micelles, which are formed by bile salts and other bile constituents, to the luminal surface of the small intestine epithelial cells.

4. When a micelle approaches the absorptive epithelial surface, the monoglycerides and fatty acids leave the micelle and passively diffuse through the lipid bilayer of the luminal membranes.

5. The monoglycerides and free fatty acids are rehydrolyzed into triglycerides inside the epithelial cells.

6. These triglycerides aggregate and are coated with a layer of lipoprotein to form water-soluble chylomicrons, which are extruded through the basal membrane of the cells by exocytosis.

7. Chylomicrons are unable to cross the basement membrane of blood capillaries, so instead they enter the lymphatic vessels, the central lacteals.
Vitamins and Minerals
Vitamins and minerals from foods are made available as macronutrients and are digested and absorbed primarily in the small intestine.
At least some vitamins pass unchanged from the small intestine into the blood by passive diffusion, but several different mechanisms might be used to transport individual vitamins across the GI mucosa.

Mineral absorption is more complex, especially the absorption of the cation minerals.

These cations, are made available for absorption by the process of chelation, in which a mineral is bound to a ligand, usually an acid, an organic acid, or an amino acid, so that it is in a form absorbable by intestinal cells.
Chelate
Mineral attached in two places by a single ligand.

Not A Chelate
Mineral attached in only one place by a single ligand.

Iron mineral atom nestled between protective glycine molecules.

glycine amino acid
glycine amino acid
neutral charged molecule

Molecules structure of an Iron Bisglycinate Chelate
References:


4- Wikipedia, the free encyclopedia. Available from: URL: http://en.wikipedia.org