CASE 25

A 38-year-old female presents to the clinic with complaints of alternating diarrhea and constipation. She reports some abdominal discomfort and bloating that are relieved with her bowel movement. She states that her episodes are worse in times of stress. She denies any blood in her diarrhea. She denies any weight loss or anorexia. Her physical exam is all within normal limits. She has been prescribed a cellulose-containing dietary supplement, which her doctor says will increase the bulk of her stools.

- **What is the most likely diagnosis?**

- **What is the biochemical mechanism of the dietary supplement's effect on the intestines?**

ANSWERS TO CASE 25: IRRITABLE BOWEL SYNDROME

Summary: A 38-year-old female complains of alternating constipation and diarrhea associated with times of stress and abdominal cramping and bloating relieved with bowel movements. She is prescribed a cellulose dietary supplement.

- **Diagnosis:** Irritable bowel syndrome.
- **Biochemical mechanism:** Cellulose-containing foods are not digestible but swell up by absorbing water and correlate with larger softer stools. The increase in dietary fiber also increases the intestinal transit time and decreases the intracolic pressure, thereby decreasing the symptoms of irritable bowel.

CLINICAL CORRELATION

Irritable bowel syndrome affects many individuals in Western countries, and it manifests as abdominal cramping and bloating in the absence of disease. It is thought to be caused by increased spasms of the intestines. Constipation with or without episodes of diarrhea may be seen. Weight loss, fever, vomiting, bloody stools, or anemia would be worrisome and should not be attributed to irritable bowel syndrome. Typically, affected patients are anxious and may be under stress. After ruling out other disease processes, a trial of fiber-containing foods, stress reduction, and avoidance of aggravating foods are effective therapies. Patients should be advised to avoid laxative use. Rarely antispasmodic or antiperistaltic agents can be used. Notably, increased fiber in the diet may also decrease the absorption of fats and may lower the risk of colon cancer.

APPROACH TO INDIGESTIBLE POLYSACCHARIDES

Objectives

1. Know about the indigestible polysaccharides.
2. Be aware of β-1,4 cellulose bonds.
3. Know about the major types of fiber.

Definitions

Cellulose: A polysaccharide composed of β-D-glucopyranose units joined by a β(1→4) glycosidic bond, which is not hydrolyzed by enzymes in the digestive tracts of humans.

Gums: Complex polysaccharides composed of arabinose, fucose, galactose, mannose, rhamnose, and xylose. Gums are soluble in water and, because of their mucilaginous nature, slowly digestible.

Hemicellulose: Polysaccharides with a random, amorphous structure that are components of plant cell walls. Unrelated to cellulose structurally, they are composed of a variety of monosaccharides, including some acidic sugars, with xylose being the most prevalent.

Insoluble fibers: Components of plant cell walls that are insoluble in water and not broken down by the body's digestive enzymes.

Lignins: Aromatic polymers formed by the irreversible dehydration of sugars. Because of their structure, they cannot be broken down by the digestive enzymes and make up part of the stool bulk.

Mucilaginous: Having a characteristic that is like the viscous and sticky nature of glue.

Pectins: One of the soluble fibers in the diet composed primarily of polymers of galacturonic acid with varying amounts of other hexose and pentose residues.

Soluble fibers: Mucilaginous fibers such as pectin and true plant gums that are soluble in water and digestible by the enzymes of the intestinal tract. By absorbing water and forming viscous gels, they decrease the rate of gastric emptying.

DISCUSSION

Simply stated, dietary fiber is that part of food that remains intact and not absorbed following the digestive process in humans. It consists of all of the components of the cell walls of plants that are not broken down by the body's digestive enzymes. Dietary fiber can be grouped into two main categories, those that are soluble and those that are insoluble in water. The soluble fibers include pectins, gums, some hemicelluloses, and storage polysaccharides (starch and glycogen). The insoluble fibers include cellulose, most hemicelluloses, and lignins.

Cellulose is a major structural component of plant cell walls. Cellulose is a long, linear polymer of glucose (β-D-glucopyranose) units that are joined by β(1→4) glycosidic bonds (Figure 25-1a). Cellulose molecules have an

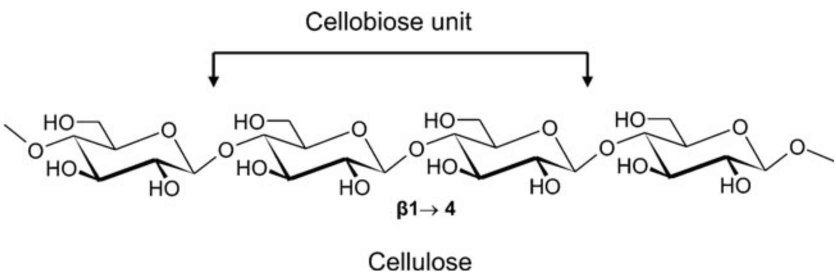


Figure 25-1a. The molecular structure of cellulose, indicating the repeating disaccharide unit, cellobiose.

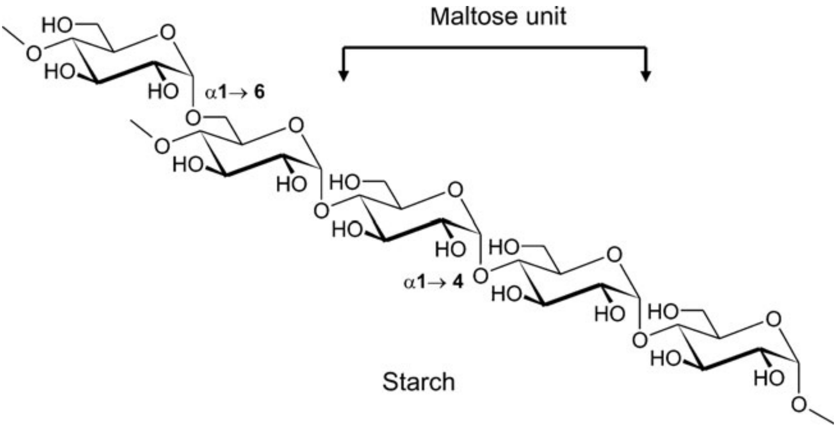


Figure 25-1b. The molecular structure of starch, indicating the repeating disaccharide unit, maltose, as well as the α-1,6-glycosidic bond present in the branch points of amylopectin.

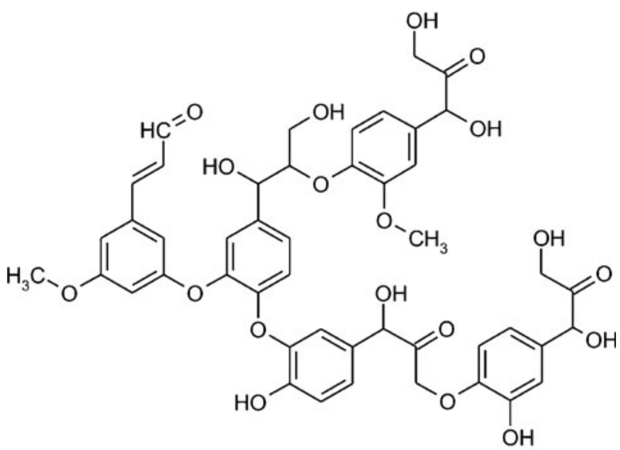
extended, rigid structure that is stabilized by interchain hydrogen bonds. Starch, the plant storage polysaccharide, which is also a polymer of glucose, differs in its structure in that the glucose monomer units are joined by α(1→4) glycosidic bonds (Figure 25-1b). Starch is composed of two types of polymers, amylose, which has a nonbranched helical structure, and amylopectin, which is branched with α(1→6) glycosidic bonds joining the branches to the main polymer chain. Although starch is easily digested by salivary and pancreatic amylase and the disaccharidases present on the brush border of intestinal mucosal cells, cellulose cannot be hydrolyzed. The β(1→4) glycosidic bonds of the cellulose chain cannot be cleaved by the amylases present in the digestive tract.

Hemicelluloses are also polysaccharides that are structural components of plant cell walls. However, unlike what their name implies, they are unrelated to cellulose. They are polymers that are made up of a variety of sugar monomers that include glucose, galactose, mannose, arabinose, and xylose, as well as acidic forms of these monosaccharides. Xylose is the monosaccharide that is most abundant. Hemicelluloses have a random, amorphous structure that is suitable for their location in the plant cell wall matrix. Depending on their molecular structure, hemicelluloses are partially digestible.

Lignins are formed by the irreversible dehydration of sugars that result in aromatic structures. The remaining alcohol or phenol OH groups can react with each other and with aldehyde and ketone groups to form polymers. An example of a lignin molecule in the early stage of condensation is shown in Figure 25-2. These polymers cannot be broken down by the digestive enzymes and, like cellulose and the indigestible portion of hemicelluloses, form the stool bulk.

The soluble fibers such as pectin and true plant gums are mucilaginous and are digestible. Pectins are predominantly polygalacturonic acids with varying amounts of other hexose or pentose residues. True plant gums are complex polysaccharides composed of primarily arabinose, fucose, galactose, mannose, rhamnose, and xylose. The gums are soluble in water and are digestible by the enzymes in the intestinal tract. Both pectins and gums are mucilaginous; they absorb water to form viscous gels in the stomach that decrease the rate of gastric emptying.

Although cellulose and hemicellulose are insoluble, they absorb water to swell and increase the stool bulk. This results in larger, softer stools. It has been shown that diets plentiful in insoluble fiber also increase the transit time of food in the digestive tract and decrease intracolonic pressure. Lignins, in addition to increasing stool bulk, also bind organic molecules such as cholesterol and many potential carcinogens. The mucilaginous nature of the soluble fibers, pectins, and gums tends to decrease the rate at which carbohydrates are digested and absorbed, thus decreasing both the rise in blood glucose levels and the ensuing increase in insulin concentration.



Lignin

Figure 25-2. A lignin molecule in an early stage of condensation. The aromatic rings are a result of irreversible dehydration of sugar residues.

COMPREHENSION QUESTIONS

[25.1] A patient with type I diabetes mellitus has fasting and postprandial blood glucose levels that are frequently above the normal range despite good compliance with his insulin therapy. He was referred to a dietician that specialized in diabetic patients. The patient was recommended to incorporate foods high in dietary fiber. Which of the following dietary fibers would be most helpful in maintaining a normal blood glucose level?

A. Cellulose
B. Hemicellulose
C. Lignins
D. Pectins

[25.2] Some individuals complain of flatulence following a meal plentiful in beans, peas, soybeans, or other leguminous plants. All legumes contain the oligosaccharides raffinose and stachyose that contain glycosidic linkages that are poorly hydrolyzed by intestinal enzymes but are good sources of energy for intestinal bacteria that convert these sugars to H_2. Which of the following glycosidic bonds are contained in raffinose and stachyose and are not hydrolyzed by our intestinal enzymes but can be by intestinal flora?

A. Galactose ($\alpha1\rightarrow6$) glucose
B. Galactose ($\beta1\rightarrow4$) glucose
C. Glucose ($\beta1\rightarrow2$) fructose
D. Glucose ($\alpha1\rightarrow4$) glucose
E. Glucose ($\beta1\rightarrow4$) glucose

[25.3] Cellulose is the most abundant polysaccharide and is an important structural component of cell walls. Strict vegetarians consume a large amount of cellulose, but it is not a source of energy because it is indigestible by the human intestinal tract. Cellulose is indigestible because it contains which of the following glycosidic bonds?

A. Galactose ($\beta1\rightarrow4$) glucose
B. Galactose ($\beta1\rightarrow6$) galactose
C. Glucose ($\alpha1\rightarrow4$) glucose
D. Glucose ($\beta1\rightarrow2$) fructose
E. Glucose ($\beta1\rightarrow4$) glucose

Answers

[25.1] **D.** Pectins and gums are soluble dietary fibers that absorb water and form mucilaginous gels. In doing so, they delay gastric emptying and decrease the rate at which monosaccharides such as glucose and fructose and disaccharides are absorbed by the intestinal tract. By decreasing the rate of sugar absorption, postprandial spikes in blood glucose concentration are avoided.

[25.2] **A.** Raffinose and stachyose are sucrose molecules that have one and two galactose residues in an $\alpha 1 \rightarrow 6$ glycosidic linkage. These bonds are not hydrolyzed by intestinal enzymes, but can be broken down by intestinal bacteria to produce CO_2 and H_2. Although they contain the glucose ($\beta 1 \rightarrow 2$) fructose link, sucrase can hydrolyze that bond. The galactose ($\beta 1 \rightarrow 4$) glucose, glucose ($\alpha 1 \rightarrow 4$) glucose, and glucose ($\beta 1 \rightarrow 4$) glucose linkages are not found in these oligosaccharides.

[25.3] **E.** Cellulose is a polymer of glucose in β1,4 glycosidic linkages. This bond is not hydrolyzed by intestinal enzymes or the flora of the human intestine. It makes up the bulk of the stool.

BIOCHEMISTRY PEARLS

❖ Dietary fiber comprises those components that are not digestible, which can be grouped into two main categories, those that are soluble and those that are insoluble in water.

❖ The soluble fibers include pectins, gums, some hemicelluloses, and storage polysaccharides (starch and glycogen). The insoluble fibers include cellulose, most hemicelluloses, and lignins.

❖ Cellulose is a long, linear polymer of glucose (β-D-glucopyranose) units that are joined by **$\beta(1 \rightarrow 4)$ glycosidic bonds, which cannot be broken by human enzymes.**

❖ Starch, the plant storage polysaccharide, which is also a polymer of glucose, differs in its structure in that the glucose monomer units are joined by $\alpha(1 \rightarrow 4)$ glycosidic bonds.

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