10 Dietary Fiber and Coronary Heart Disease

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10.1 DIETARY FIBER DEFINITION AND CLASSIFICATION

Dietary fiber is generally described as plant material that is resistant to human digestive enzymes. Most of these plant materials fall into the category of non-starch polysaccharides, with the exception of plant lignins, which are actually polyphenolic in nature. Dietary fiber also may include resistant starches inherent in foods or created during processing of foods.

Several definitions of dietary fiber exist in the United States, based on analytical methods used to isolate and quantify fiber and physiological effects. The following are definitions proposed by the Panel on the Definition of Dietary Fiber, assembled by the Food and Nutrition Board, under the oversight of the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes1:

1 Dietary Fiber consists of non-digestible carbohydrates and lignin that are intrinsic and intact in plants, (2) Functional Fiber consists of isolated, non-digestible, and carbohydrates that have beneficial physiological effects in humans, and (3) Total Fiber is the sum of Dietary Fiber and Functional Fiber.

The Food and Drug Administration (FDA) defines dietary fiber as “non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants” or if not intact and intrinsic, must be “isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health.”2

The FDA has a definitive list of non-digestible carbohydrates that meet their dietary fiber definition (Table 10.1). These consist of non-digestible carbohydrates that can be declared as dietary fiber and also those that currently under consideration as dietary fiber.

The National Academy of Medicine (formerly the Institute of Medicine) recommended phasing out the terms soluble fiber and insoluble fiber, although food labels may still include soluble and insoluble fiber data.3 Soluble (water) fibers include pectin (pectic substances), gums, and mucilages, whereas the insoluble fibers include cellulose, hemicellulose, lignin, and modified cellulose.
The concept of soluble and insoluble fibers were introduced as an attempt to assign physiologic effects to chemical types of fiber; soluble fibers (from oat, barley, and psyllium) have health claims for their ability to lower blood lipid levels, while wheat bran and other more insoluble fibers are typically linked to laxation. Some of the better food sources of soluble fibers are fruit, legumes, oats, and some vegetables. Meanwhile, those foods noted to be richer sources of insoluble fibers include cereals, grains, legumes, and vegetables. A third category of fiber, resistant starches, are now an accepted member of the fiber family, and are found in foods such as oats, rice, and legumes. Some of these foods are also good sources of soluble and insoluble fibers. The term “resistant starch” was first used to describe the fraction of starch that resisted hydrolysis by α-amylase and pullulanase in vitro. Resistant starch (RS) is any starch not digested in the small intestine. RS is a broad and diverse range of materials and a number of different types exist, categorized as RS type 1–5. Food sources of RS include a variety of plant sources including oats, rice, grains, legumes, potatoes and potato starch, and green bananas.

### 10.1.1 Fiber Consumption and Recommendation

The amount of fiber present within the human diet can vary geographically. In more industrially developed countries, such as the United States, fiber consumption is relatively lower than in other societies as a direct result of Western dietary patterns. For example, the average intake of fiber in the United States is only about 12 to 15 g daily. Table 10.2 provides the percentage of the total weight of select foods that is attributable to fiber. This consumption falls well below current recommendations of the World Health Organization of 25 to 40 g of fiber daily. The American diet tends to derive less than one-half of its dietary carbohydrate intake from fruit, vegetables, and whole grains. In contrast, the people of some African societies are known to eat as much as 50 g of fiber daily.
Dietary reference intakes (DRIs) for total fiber by life stage group are shown in Table 10.3. The adequate intakes for total fiber are based on the intake level observed to protect against coronary heart disease based on epidemiologic, clinical, and mechanistic data.

### 10.1.2 Description of Common Dietary Fibers

Digestible polysaccharides in plant foods, such as starch, and to a much lesser degree glycogen in meats, have repeating monosaccharide units bonded by 1–4 linkages (Figure 10.1). These bonds are readily digested by amylase in both salivary and pancreatic secretions. Branch points in the starch and glycogen chains are joined through 1–6 linkages that are hydrolyzed by the enzyme 1–6 dextrinase (isomaltase) in pancreatic secretions. On the contrary, 1–4 linkages are formed by plants between monosaccharides in fibrous polysaccharides (Figure 10.1). Both salivary and pancreatic amylases are unable to hydrolyze 1–4 covalent bonds efficiently. This renders such polysaccharides resistant to human digestive action. However, bacteria inhabiting the large intestine can indeed metabolize some polysaccharide fiber and create short-chain fatty acids (acetic, propionic, and butyric acids) as metabolites. Table 10.4 summarizes the fermentation of common types of fiber. These short-chain fatty acids are now being recognized to have important roles in mediating diverse metabolic effects that impact inflammation, immune function, and gut health. A review of these effects is outside the scope of this chapter, but there are many excellent reviews on this topic available that have been published in the last few years.

Cellulose is known to be the most abundant organic molecule on Earth. The molecular structure is similar to amylose in that it is made up of repeating units of the hexose glucose. However, again, the linkages will be 1–4 in nature. Cellulose is produced as a component of the plant cell wall by an enzyme complex called cellulose synthase. Once cellulose chains are formed, they quickly assemble with other cellulose molecules and form microfibrils that strengthen the cell wall. Cellulose, along
TABLE 10.3
Dietary Reference Intakes (DRI) for Total Fiber\(^a\) by Life Stage Group, Expressed as Adequate Intake\(^b\)

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Males (g/1000 kcal/d)</th>
<th>Females (g/1000 kcal/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year(^c)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>1–3 years</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>4–8 years</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>9–13 years</td>
<td>31</td>
<td>26</td>
</tr>
<tr>
<td>14–18 years</td>
<td>38</td>
<td>26</td>
</tr>
<tr>
<td>19–30 years</td>
<td>38</td>
<td>25</td>
</tr>
<tr>
<td>31–50 years</td>
<td>38</td>
<td>25</td>
</tr>
<tr>
<td>51–70 years</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>&gt;70 years</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>NA</td>
<td>28</td>
</tr>
<tr>
<td>Lactation</td>
<td>NA</td>
<td>29</td>
</tr>
</tbody>
</table>

Abbreviation: ND, not determined; NA, not applicable.

\(^a\) Total fiber is a combination of dietary fiber and functional fiber.

\(^b\) Adequate intake is provided when there is insufficient scientific evidence to calculate the Recommended Dietary Allowance.

\(^c\) There is no adequate intake for fiber for infants 0–12 months because there is not theoretical reason to establish one, as human milk is recognized as the optimal source of nourishment during this life stage.

FIGURE 10.1 (a) The \(\alpha\) 1–4 bond between glucose monomers of starch and glycogen and (b) the \(\beta\) 1–4 linkage between glucose units in cellulose.
with certain other fibers (hemicellulose and pectin) and proteins, is found within the matrix between the cell wall layers. This concept is somewhat similar to connective tissue matrix found within bone, tendons, and ligaments in humans. Hemicellulose is different from cellulose in that its monomers are heterogeneous. Hemicellulose will contain varied amounts of pentose and hexose covalently bound in a 1–4 linkage, as well as some branching side chains. Some of the more common and familiar monosaccharides in hemicelluloses are xylose, mannose, and galactose (Figure 10.2). Other monosaccharide subunits include arabinose and 4-O-methyl glucuronic acids.

Lignin stands alone as a fiber in that it is not a carbohydrate; yet it is considered an insoluble dietary fiber. Lignin is made up of aromatic polymers of chemicals from plant cell walls and provides plants with their “woody” characteristics. Lignin molecules are highly complex and variable polymers and are composed of three major aromatic alcohols: Coumaryl, coniferyl, and sinapyl. In plants, lignin provides structure and integrity, thus allowing the plant to maintain its form. A typical lignin monomer is presented in Figure 10.3.

The soluble fiber pectin, commonly found in the fleshy part of fruits such as apples and pears, is composed mostly of galactouronic acid that has been methylated. These units are also connected by 1–4 linkages in pectin. The degree of methylation increases during the ripening of fruit and allows for much of the gel-formation properties of soluble fibers. Gum and mucilage are also soluble fibers and are composed of hexose and pentose monomers. The physical structure and properties of these fibers are similar to pectin. Interestingly, gums are polysaccharides that are synthesized by plants at the site of trauma and appear to function in a manner similar to scar tissue in humans. Meanwhile, mucilage is produced by plant secretory cells to prevent excess loss of water through transpiration.

Resistant starch type 1 (RS1) are starches that are not accessible to amylase in its native form (e.g., whole grains) and can be made digestible through milling. RS type 2 (RS2) are starches that are accessible to α-amylase following gelatinization (e.g., raw potatoes). RS type 3 (RS3) are retrograded starches that are formed from cooking and cooling of starchy foods such as potatoes and rice. RS

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**TABLE 10.4**

<table>
<thead>
<tr>
<th>Types of Fiber</th>
<th>Characteristics</th>
<th>Food Sources</th>
<th>Degradation(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Soluble</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pectins</td>
<td>Rich in galacturonic acid, rhamnose, arabinose, galactose; characteristic of middle laminae and primary wall</td>
<td>Whole grains, legumes, cabbage, root vegetables, apples</td>
<td>+</td>
</tr>
<tr>
<td>Gums</td>
<td>Composed mostly of hexose and pentose monomers</td>
<td>Oatmeal, dried beans, other legumes</td>
<td>+++</td>
</tr>
<tr>
<td>Mucilages</td>
<td>Synthesized by plant cells and can contain glycoproteins</td>
<td>Food additives</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Insoluble</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td>Structural basis for cell wall; only monomer is glucose</td>
<td>Whole grains, bran, cabbage family, peas, beans, apples, root vegetables</td>
<td>+</td>
</tr>
<tr>
<td>Hemicellulose</td>
<td>Component of primary and secondary cell walls; different types vary in monomer content</td>
<td>Bran, cereals, whole grains</td>
<td>+</td>
</tr>
<tr>
<td>Lignin</td>
<td>Composed of aromatic alcohols; cements, other cell wall components</td>
<td>Vegetables, wheat</td>
<td>0</td>
</tr>
</tbody>
</table>


\(^a\) Denotes the degree of bacterial fermentation.
10.2 PHYSICAL AND PHYSIOLOGICAL PROPERTIES OF FIBER

The physiological attributes of fiber largely depend upon their physical characteristics, namely the molecular design and solubility. Although the physiological influences of dietary fibers were once thought to be limited to the intestinal lumen, which is anatomically exterior, newer evidence suggests that derivatives of intestinal fiber metabolism can influence more internal operations as well. The physical characteristics of dietary fiber can produce various gastrointestinal responses depending upon the segment of the digestive tract. Among these responses are gastric distention, influences upon the rate of gastric emptying, and enhancement of residue quantity (feces bulk) and moisture content. Furthermore, dietary fiber can influence fermentation by bacteria in the colon as well as the turnover of specific bacteria ecology. With regarding to bacterial enterotypes, Western diets

**FIGURE 10.2** Carbohydrate monomers common to polysaccharide fibers.

**FIGURE 10.3** A typical phenolic monomer of a lignin molecule.

Type 4 (RS4) are chemically modified starch (e.g., via conversion, substitution, and cross-linking). Finally, RS type 5 (RS5) describes amylase-lipid complexes that are formed during food processing.
Dietary Fiber and Coronary Heart Disease

characterized by higher meat consumption favor more Bacteriodes, whereas plant-based diets favor Prevotella. Such changes are evidence that the microbiome diversity is altered in response to dietary habits and fiber intake. A review of the impact of fiber upon microbiota is outside the scope of this chapter; however, the reader is referred to an excellent review by Makki et al. on this topic.

Different fiber molecules are subject to varying levels of bacterial degradation in the colon (Table 10.3). For instance, pectin, mucilages, and gums seem to be almost completely fermented. Meanwhile, cellulose and hemicellulose are only partly degraded and the non-carbohydrate nature of lignin allows it to go virtually unfermented. Similarly, some RSs escape colonic fermentation and are excreted in the feces. The degree of fermentation is dependent on the category and source of RS consumed. The physical structure of the plant itself may be associated with the degree of degradation of food fibers by intestinal bacteria. As an example, fibers derived from fruits and vegetables appear to be, in general, more fermentable than those from cereal grains. VFAs, namely acetic acid (2:0), propionic acid (3:0), and butyric acid (4:0), are among the products of bacterial fermentation. As mentioned above, these fatty acids can be oxidized for ATP production in mucosal cells of the colon wall. Furthermore, these fatty acids are fairly water soluble and can be absorbed into the portal circulation. Other products of bacterial fermentation of dietary fibers include hydrogen gas (H₂), carbon dioxide (CO₂), and methane (CH₄). These products may lead to occasional uncomfortable gas buildup in the colon that may occur with high fiber consumption. The presence of H₂ in the breath (hydrogen breath test) is often used clinically as an estimation of bacterial fermentation. Once produced, H₂ dissolves into the blood and circulates to the lungs.

Among some of their more interesting physical properties is the water-holding capacity or the hydration of fibers. The ability of the different fibers to associate with water molecules is largely attributable to the presence of sugar residues that have free polar groups (i.e., OH, COOH, SO, and C=O groups). These polar groups allow for the formation of hydrogen bonds with adjacent water molecules. It seems that pectic substances, mucilages, and hemicellulose have the greatest water-holding capacity. Cellulose and lignin also can hold water, but not to the extent of other fibers. However, as soluble fibers are generally more fermentable, the associated water is liberated and absorbed in the colon. Thus, it is the insoluble fibers that hold onto water throughout the total length of the intestinal tract and give the fecal mass greater water content.

In the small intestine, the hydration of fiber will allow for the formation of a gel matrix. Theoretically, the formation of a gel in the small intestine could increase viscosity of the food-derived contents and slow the rate of absorption of nutrients. It has been suggested this mechanism may slow down the rate of carbohydrate absorption and decrease the magnitude of the postprandial spike in blood glucose. This notion then may have application to individuals with diabetes mellitus, as discussed in this chapter.

10.3 RELATIONSHIP BETWEEN CHOLESTEROL LEVELS AND CORONARY HEART DISEASE

Coronary heart disease is estimated to cause 1 in 6 deaths in the United States, according to the American Heart Association’s 2017 Heart and Stroke update. In contrast to popular dogma among the lay public, heart disease is also the leading cause of death among women as well. Many risk factors can influence CHD, such as smoking, age, male sex, menopause, diabetes, serum cholesterol levels, and hypertension. Some of these risk factors are modifiable, such as smoking and serum cholesterol levels, and some are not, such as male sex or menopause. Among the most important risk factors that may be controlled are serum cholesterol levels. Many studies have established that high total cholesterol levels and low-density lipoprotein cholesterol levels are risk factors for CHD and mortality. The well-known Framingham Study was among the first to establish a statistical relationship between serum lipoproteins and CHD. Other important studies using very large cohorts from the Multiple Risk Factor Intervention Trial (MRFIT), and from various countries, have since strengthened the notion that serum cholesterol is a risk factor for CHD.
Elevated serum cholesterol levels can result from a variety of influences. Severely high serum cholesterol is usually due to familial hypercholesterolemia, a condition characterized by genetic defects in LDL receptor activity that result in accumulation of LDL cholesterol in the blood. Elevated serum cholesterol may also occur as a secondary effect of disorders such as diabetes or hypothyroidism, and in alcoholics. More commonly, cholesterol disorders are characterized by mild or moderate hypercholesterolemia and are generally dietary in origin, and recent evidence has shifted the dietary culprits away from simple intake of saturated fats and more toward eating patterns that include increased intake of processed carbohydrates and sugars, both of which are more common in a Western diet.

10.3.1 Role of Fiber in Reducing Serum Cholesterol

Fiber has been implicated in reducing the risk for CHD. Many large epidemiological studies such as the Nurses’ Health Study and the Scottish Heart Health Study have demonstrated a reduced risk for CHD in both men and women who consume higher amounts of dietary fiber. The soluble fibers in particular are thought to exert a preventative role against heart disease, as they appear to have the ability to lower serum cholesterol levels. A recent meta-analysis examining soluble fiber sources from pectin, oat bran, guar gum, and psyllium reported a small but significant reduction in serum cholesterol levels. Many other studies have found that a high intake of soluble fiber results in decreased serum cholesterol levels. These studies generally report a decrease in total cholesterol and LDL cholesterol with no changes in high-density lipoprotein (HDL) or triglycerides. Indeed, it is now recognized that soluble fiber is a viable intervention to reduce serum cholesterol levels in clinically significant amounts, thereby reducing a known risk factor for CHD.

Oat bran in particular has received a great deal of attention over the years as a fiber source with an appreciable level of soluble fiber that has been shown to reduce plasma cholesterol levels under controlled conditions. Early studies examining the role of oats in reducing plasma cholesterol focused on supplementing oats without a great deal of dietary fat modification. In 1963, DeGroot and colleagues published a study that supplemented rolled oats in the form of bread to be consumed daily by 21 male volunteers between the age of 30 and 50. Over a 3-week period, an 11% reduction in serum cholesterol was observed. Another early study by Anderson et al. compared oat bran to fiber from beans in their ability to lower serum cholesterol. After consuming 17 g of soluble fiber per day for 3 weeks, a 19% decrease in total cholesterol and a 23% decrease in LDL cholesterol was observed.

A review of the literature demonstrates that oat bran has been repeatedly proved to play a role in reducing serum cholesterol levels and is generally recommended by the nutrition and medical community as an important part of the diet. A meta-analysis done by Ripsin and colleagues reviewed results from 10 trials and concluded that a significant amount of cholesterol reduction occurred when at least 3 g of soluble fiber from oat bran was consumed daily. Furthermore, the researchers observed that those subjects who had the most dramatic decrease in cholesterol levels were those who had the highest initial serum cholesterol concentrations. In spite of the wealth of data supporting the role of oat bran in decreasing serum cholesterol, one issue remains ambiguous for the typical American consumer, and that is the amount of oat bran needed to reduce serum cholesterol levels by clinically significant amounts. The lay public must realize that several servings of oat bran are required daily to reduce plasma cholesterol by an appreciable amount. Indeed, many of the studies that report significant decreases in serum cholesterol levels use very high intakes of soluble oat bran fiber. Most studies have used anywhere from 3.4 to 17 g of soluble fiber from oat bran to achieve total cholesterol and LDL-cholesterol reductions, with the most severe declines observed with the highest use of soluble fiber. A recent meta-analysis indicated that the amounts of oat bran used in well-controlled and powered studies to produce significant LDL reductions were equivalent to 45–90 g of oat cereal and 60–150 g of oatmeal. When one considers that the typical serving of instant oatmeal (0.5 cups) contains 1 to 2 g of soluble fiber, the reality of the magnitude of the dietary change involved becomes more apparent. In practice, it may be difficult for the average individual to
consume levels of soluble fiber equivalent to the highest amounts used in certain studies. However, with moderate dietary changes that focus on whole oats rather than processed versions, it is possible to consume enough oat bran to fall in the lower range of experimental amounts previously used, which would result in a statistically significant reduction in serum cholesterol.

The long-term interest in oat bran has led to the identification of beta-glucan as the active compound responsible for LDL reduction. In addition to oat bran, yeast has also been identified as a concentrated source of beta-glucan and has been investigated in a number of clinical studies. According to recent research, doses of 3–13 g/d produce reductions in total cholesterol of 8.15–15.13 mg/dL, and LDL reductions of 7.76–13.2 mg/dL. Commercial products based on beta-glucan are also available, and are marketed as additives to food or beverages. Once such product is known by the patented name Fibercel is composed of purified glucan derived from the yeast *Saccharomyces cerevisiae*, the species found in baker’s and brewer’s yeast. A serving of Fibercel contains 5 g of beta-glucan fiber, which is in the effective dose range reported to reduce plasma LDL.

Recent studies using glucomannan (also known as Konjac-mannan) fiber have also yielded very promising results by reducing risk factors for CHD. Subjects supplemented with a daily average of 23 g of glucomannan in the form of biscuits experienced a lower total:HDL cholesterol ratio and LDL cholesterol, lower systolic blood pressure, and improved glycemic control. These results were significantly better than those achieved with an identical diet using wheat bran instead of glucomannan diet, thereby demonstrating the effectiveness of the soluble fiber in influencing not only cholesterol, but other CHD risk factors as well. A more recent meta-analysis indicated that supplementation with 1.2–15.1 g/day of glucomannan can reduce LDL cholesterol by an average of 16 mg/dL. Glucomannan fiber itself is well known for having among the highest viscosity of all the soluble fiber types. The use of glucomannan fiber may also lead one to speculate that highly soluble fibers, such as glucomannan, may be more effective at reducing cholesterol levels than other soluble fibers. It must be borne in mind, however, that the use of glucomannan entails supplementation in existing foods, such as breads or biscuits, rather than eating an actual product such as oatmeal cereal. This may have practical relevance since it is far simpler for the typical consumer to buy instant cereal and eat it daily for breakfast than to buy glucomannan fiber and supplement it in baked goods on a daily basis.

Other types of soluble fibers have been extensively studied for their ability to lower serum cholesterol amounts. Psyllium has received attention over the years as a soluble fiber that can reduce cholesterol levels. Psyllium is a plant whose stalks contain tiny seeds, also called psyllium, covered by husks, which is the source of the fiber. There is a great deal of soluble fiber in psyllium; in fact, 71% of the weight of psyllium is derived from soluble fiber. In contrast, only 5% of oat bran by weight is made of soluble fiber; in other words, the soluble fiber in 1 tablespoon of psyllium is equal to 14 tablespoons of oat bran. The active fraction of psyllium seed husks that is thought to be responsible for the cholesterol-lowering effects is a highly branched arabinoxylan that is composed of a xylose backbone with arabinose and xylose containing side chains. Interestingly, arabinoxylan from psyllium is not fermented by colonic bacteria, apparently due to an as yet to be identified structural feature of the molecule.

A number of animal studies have demonstrated that rats fed controlled diets supplemented with psyllium fiber experience a significant decrease in serum cholesterol levels. A study done by Anderson et al. even found reductions of up to 32% in cholesterol levels in rats fed 6% dietary psyllium. Many studies in humans have also found psyllium to be an effective agent. Supplementation of 10.2 g of psyllium per day for 8 weeks in men consuming a 40% fat diet has resulted in a 14.8% reduction in total cholesterol and 20.2% reduction in LDL cholesterol. Another study using higher amounts of dietary psyllium (15 g/day) observed a change of LDL cholesterol from 184 to 169 mg/dL. Another study has demonstrated that men with type 2 diabetes supplemented with 10.2 g of psyllium daily for 8 weeks also experienced an 8.9% drop in total cholesterol and a 13% decline in LDL cholesterol. This group of men with type 2 diabetes displayed an improvement in glycemic control as well. Improvements in insulin sensitivity and glucose tolerance have also
been reported in both animal studies and human trials examining subjects with metabolic syndrome supplemented with psyllium. A large meta-analysis that examined 12 published and unpublished studies has concluded that consumption of dietary psyllium is linked with reductions in serum total and LDL cholesterol. Even though psyllium has not achieved as much attention in the popular press compared with oat bran, there is evidence that it may actually be more effective as a dietary agent to lower cholesterol levels. Anderson et al. compared 10 different dietary fiber types in the rat model and found psyllium to be the most effective at lowering serum cholesterol levels. A study in humans using psyllium and oat bran demonstrated an equivalent reduction in total and LDL cholesterol when psyllium was used in one-half the amount of oat bran. These studies could lead one to conclude that psyllium fiber may actually be more effective at reducing cholesterol levels and therefore could be consumed in lesser amounts to achieve desirable results. In fact, FDA-approved labels have been present on psyllium-supplemented cereals since 1998 that state regular consumption of psyllium as part of a low-fat diet can reduce cholesterol levels.

Several clinical trials have investigated the associations between RS and blood cholesterol. A meta-analysis conducted in 2018 showed that RS supplementation has an effect on lowering total cholesterol (mean difference, −7.33 mg/dL [95% confidence interval −12.15 to −2.52 mg/dL], 19 studies) and LDL-cholesterol (mean difference: −3.40 mg/dL [95% confidence interval, −6.74 to −0.07 mg/dL], 16 studies). Compared to control, RS intake did not affect HDL cholesterol (weighted difference, −0.98 mg/dL; 95% confidence interval, −2.44 to 0.49 mg/dL, 17 studies) or triglyceride (weighted difference: −7.50 mg/dL [95% confidence interval, −16.93 to 1.92 mg/dL]). Eighteen of the 20 trials included in this meta-analysis tested RS2 (high amylase RS in 12 studies and foods rich in RS in 6 studies), while the remaining two tested RS3 from corn. A subgroup analysis on just RS3 did not reveal changes in total cholesterol, LDL-cholesterol, HDL-cholesterol, or triglycerides. Additionally, further analysis suggest that a longer time (>4 weeks) of RS supplementation can generate more obvious effects on TC and LDL-C levels, and higher dose (>20 g/d) of RS also had a lowering effect on TG level. One study on wheat-based RS4 demonstrated reductions in total cholesterol, LDL-cholesterol, and HDL-cholesterol following consumption of a blend of 70% wheat flour/30% wheat-based RS4 for 26 weeks.

### 10.3.2 Mechanisms for Lowering of Serum Cholesterol by Fiber

There are several possible mechanisms in which soluble fiber is thought to reduce serum cholesterol levels; many are related to the ability of soluble fibers to form viscous gels in the intestinal tract. Among these potential mechanisms are reduced cholesterol absorption in the presence of soluble fiber, increased excretion of bile acids, an alteration of bile acid type present in the gut, and possible influences of short-chain fatty acid production by intestinal flora upon cholesterol synthesis.

It has been proposed that soluble fiber reduces plasma cholesterol through its ability to bind bile acids in the gastrointestinal tract. As soluble fibers bind bile acids in the intestinal tract, micelle formation is altered and reabsorption of bile acids is subsequently impaired, resulting in the excretion of the fiber–bile complex through the feces. There are two classes of bile acids, primary and secondary. Primary bile acids (cholic and chenodeoxycholic acid) are those synthesized directly from the liver, whereas secondary bile acids (deoxycholic and lithocholic acid) are produced after modification of primary bile acids by bacterial action in the colon. It has been demonstrated that consumption of oat bran increases the loss of bile acids by twofold and specifically increases the loss of deoxycholic acid (secondary bile acid) by 240% in human subjects. It was also concluded that the pool of bile acids was not decreased, even though bile acid excretion is increased. Another human study done with soluble fiber from psyllium found increased bile acid turnover of both primary bile acids as well. These studies point to the fact that bile excretion is increased when high amounts of soluble fiber are eaten. Usually bile is reabsorbed in the large intestine and reused in emulsification of fats; however, since a constant pool is required, the excreted bile must be replaced to keep bile levels adequate for digestive
Dietary Fiber and Coronary Heart Disease needs. Theoretically, this would indicate that bile acid synthesis would be increased under these conditions and, indeed, an increase in bile acid synthesis has also been observed in individuals consuming high amounts of soluble fiber. Specifically, the synthesis of deoxycholic acid has been found to increase with consumption of a high-fiber diet. This may have further beneficial effects, as deoxycholic acid has been shown to decrease absorption of dietary cholesterol. Replacement of bile can be achieved two ways: (1) more hepatic cholesterol can be dedicated for bile synthesis instead of being exported in the circulation as very low-density lipoprotein, and (2) increased hepatic cholesterol demand will upregulate synthesis and activity of LDL receptors, allowing for greater amounts of VLDL remnants and LDL to be removed from circulation. The overall effect of these alterations is a reduction in LDL and total cholesterol levels. With regard to the first point, data from animal studies demonstrate an increased rate of cholesterol synthesis in the livers of psyllium-fed hamsters. Specifically, the enzymatic activity of HMG CoA reductase, the rate-limiting enzyme for hepatic cholesterol synthesis, is observed to be increased three- to fourfold in hamsters fed soluble fiber. This effect is thought to be transcriptionally mediated, as mRNA levels have been found to be similarly increased in the same model. Alterations of LDL receptor activity are also possible under the influence of psyllium fiber; however, this has been found to occur in experimental animals fed high-fat and high-cholesterol diets. Usually consumption of a high-fat diet tends to depress LDL receptor activity, but hamsters fed high-fat and high-cholesterol diets in conjunction with high dietary soluble fiber demonstrate a restoration of LDL receptor expression to normal levels. Examination of the effects of oat bran consumption reveals a divergence in the mechanism of action between soluble fiber from oats vs. that of psyllium. Both have the ability to bind to bile acids and facilitate their excretion; however, they differ in their secondary influence on hepatic cholesterol synthesis. As mentioned above, psyllium fiber fed to animals has been found to increase hepatic cholesterol synthesis. Paradoxically, soluble fiber from oat bran has been found to depress hepatic cholesterol synthesis. Bacterial fermentation of soluble fiber from oats results in the production of short-chain fatty acids, specifically propionate, that are absorbed in the colon and travel to the liver via the portal vein. Data from in vitro studies demonstrate an inhibition of hepatic cholesterol and fatty acid synthesis under the influence of propionate. The apparent paradox of psyllium fiber increasing cholesterol synthesis and oat fiber decreasing cholesterol synthesis may be explained by the fact that psyllium is very poorly fermented by bacteria in the colon; hence, little propionate is produced to decrease hepatic cholesterol synthesis.

In the final analysis, it seems that oat bran may be able to reduce cholesterol levels in a two-part fashion: increasing bile loss and decreasing endogenous hepatic cholesterol synthesis, thus resulting in a shift of serum cholesterol for bile synthesis. Psyllium may reduce serum cholesterol levels through only one relevant mechanism, the loss of bile acids. Furthermore, in spite of the increase in HMG CoA reductase activity and cholesterol synthesis under the influence of psyllium, hepatic cholesterol content continues to be markedly reduced in animals fed a high-psyllium diet. Therefore, it seems that this upregulation is barely enough to meet the demands of bile acid synthesis, and obviously not enough to contribute significantly to VLDL exportation and hence LDL cholesterol levels. As one can conclude after careful consideration of the cited studies in this section, even though the net effect of soluble fiber consumption is well established, the specific biochemical events that occur in cholesterol metabolism are still incompletely understood and require more thorough testing.

10.3.3 Other Relevant Considerations for Fiber and Coronary Heart Disease Risk

Fiber has also been implicated in reducing risk for CHD through mechanisms other than plasma cholesterol modification. One such example is through modification of blood clotting ability. An enhanced clotting ability coupled with atherosclerosis increases the risk of developing an occlusion in the coronary arteries and subsequent myocardial infarction. The ability of the blood to clot
is dependent upon fibrinogen levels and quality of the resulting fibrin network. Pectin has been found to influence the concentration and quality of fibrin networks in the blood and reduce the tensile strength of these networks. Pectin supplements have been shown to decrease the strength and quality of fibrin networks; these types of networks are thought to be less atherogenic than fibrin networks under normal conditions and thus may represent another vehicle for reducing risk for CHD.40,41

It has been demonstrated that individuals consuming 18.5 g or more of dietary fiber had a 42% risk for elevated plasma C-reactive protein compared to those consuming 8.5 g or less. Similar findings were reported after analysis of survey data from the National Health and Nutrition Examination data as well. Using this data, a 41% lower risk of elevated C-reactive protein was found in individuals consuming high-fiber diets, after adjusting for smoking, BMI, physical activity, total energy, and fat intake.36 Finally, a meta-analysis also reported that six out of seven clinical trials examined reported significant reductions in plasma C-reactive protein resulting from high-fiber dietary interventions.42 Given the role of C-reactive protein as a plasma marker of inflammation, and as a marker of atherosclerosis, it is noteworthy that dietary fiber may act in ways beyond its cholesterol lowering ability.

Since the 1980s, it has been proposed that LDL particle size could play an important role in increasing risk for coronary heart disease. However, the most recent reviews that have examined all the evidence to date state that LDL particle size has not been independently associated with CHD risk.43 Therefore, clinical practice does not yet include LDL particle size as a risk factor that should be screened. Nonetheless, the impact of dietary fiber on LDL particle size has been studied, and there are reports that indicate fiber and food sources of fiber can increase, decrease, or not affect LDL particle size. For example, soluble fiber has been shown to significantly reduce the levels of small dense LDL particles. In a study that gave 14 g fiber per day from oat cereal to overweight middle aged men, overall LDL levels were reduced by 5%, but more importantly, levels of small LDL particles were reduced by 17%.44 In contrast, a dietary portfolio containing fiber, nuts, phytosterols, and vegetable protein did not demonstrate a greater reduction in small LDL particles compared to overall LDL levels.45 Finally, a recent study that added almonds (a source of dietary fiber) to an existing statin regimen found that LDL particle size actually increased.46 Given the limited number of studies published thus far, more research is needed to define the role of fiber effects on small LDL particle content, and whether any changes in particle size are clinically relevant to disease risk.

Whole grains have also been shown to be protective against CHD, as demonstrated by an inverse relationship between whole grain consumption CHD.47–49 However, it still remains unclear whether this association is due to the fiber content of whole grains or other components of whole grains such as phytochemicals, antioxidants, folate, vitamin B6, monounsaturated fatty acids, or n-3 polyunsaturated fatty acids that may act to reduce CHD risk. In spite of a certain degree of confusion regarding the individual contribution of whole grain–derived fiber in reducing CHD risk, the overall beneficial effect of whole grains in general should not be overlooked.

10.3.4 Fiber as Adjunct Therapy to Statin Medication

Current medical practice is to use statin drugs to reduce elevated plasma cholesterol levels. There are many types of statin drugs used today, but they all share the common feature of inhibiting the hepatic enzyme HMG CoA reductase. Since dietary fiber is thought to reduce cholesterol levels through other mechanisms in addition to HMG CoA inhibition, it has been proposed that combining fiber therapy with medication may be an effective approach to reduce cholesterol. A recent study examined the precise role of dietary fiber as adjunct therapy to statin medication and found that hypercholesterolemic patients taking 10 g of psyllium per day along with a 10 mg dose of simvastatin had the same degree of cholesterol reduction as those taking 20 mg of simvastatin alone.43 Other
studies have reported that fiber (carboxymethyl cellulose) in combination with statin drugs can further lower LDL. However, guar gum supplementation combined with lovastatin increased the rate of endogenous cholesterol production, while overall LDL levels remained unchanged. Finally, pectin and oat bran consumption combined with lovastatin actually increased LDL compared to just lovastatin alone. These data demonstrate that dietary fiber may have differential effects based on the type of fiber consumed and the type of statin taken. Therefore, it may be prudent to be cautious with fiber supplementation, beyond what is present in a normal healthy diet. Furthermore, given the ambiguity on how various types of statins respond to adjunct fiber supplementation therapy, it is also recommended for individuals to check cholesterol levels after a period of fiber supplementation to verify that cholesterol levels are improving.

10.4 HEALTH CLAIMS ASSOCIATED WITH FIBER AND CORONARY HEART DISEASE

The U.S. Food and Drug Administration allows food manufacturers to use certain health claims related to the link between dietary fiber and a reduced risk of heart disease. For example, upon review of the research literature, the FDA recognizes the relationship between fruit, vegetables, and grain products that contain fiber, particularly soluble fiber, and a reduced risk of CHD. Foods that apply for related health claims would include fruit, vegetables, and whole-grain breads and cereals. To qualify, foods must meet criteria for low saturated fat, low fat, and low cholesterol. The foods must contain, without fortification, at least 0.6 g of soluble fiber per reference amount, and the soluble fiber content must be listed on the label. The health claim must use the terms fiber, dietary fiber, some types of dietary fiber, some dietary fibers, or some fibers and coronary heart disease or heart disease in discussing the nutrient–disease link. The term soluble fiber may be added. A sample health claim may read:

Diets low in saturated fat and cholesterol and rich in fruits, vegetables, and grain products that contain some types of dietary fiber, particularly soluble fiber, may reduce the risk of heart disease, a disease associated with many factors.

More specific to soluble fiber, the FDA has to date reviewed and authorized three sources of soluble fiber (oat, barley, and psyllium) to be eligible for use of a health claim with regard to a reduction in the risk of CHD (Table 10.5). In doing so, the FDA acknowledges that in conjunction with a low-saturated-fat and low-cholesterol diet, certain soluble fiber foods may favorably influence total cholesterol and LDL levels and thus lower the risk of heart disease. Foods and supplements meeting this criteria may contain oat bran, whole oat flour, oatrim, whole grain barley, dry milled barley, barley betafiber, and psyllium seed husk. Again, in order for a food manufacturer to use such a health claim on a food label, the food must meet criteria for low saturated fat, low cholesterol, and low fat. The food must provide oat- and/or barley-based eligible ingredients in at least 0.75 g of soluble fiber per serving. Foods that contain psyllium seed husk must contain at least 1.7 g of soluble fiber per serving. In addition, a claim must indicate the daily dietary intake of the soluble fiber source necessary to reduce the risk of heart disease. Also, the claim must indicate the contribution that one serving of the product will make toward that intake level. Further still, the soluble fiber content must be stated in the nutrition label. In the health claim, the food manufacturer must state “soluble fiber” qualified by the name of the eligible source of soluble fiber and “heart disease” or “coronary heart disease” in describing the nutrient–disease association. A sample claim may read as follows:

Diets low in saturated fat and cholesterol that include 3 grams or more of beta-glucan soluble fiber from either oats or barley may reduce the risk of heart disease. One serving of dried oats provides 2 grams of this soluble fiber.
TABLE 10.5

Eligible Soluble Fiber Sources for the Health Claim on the Relationship between Soluble Fiber and Risk of Coronary Heart Disease

<table>
<thead>
<tr>
<th>Food Ingredient</th>
<th>Ingredient Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oat bran</td>
<td>Oat bran fraction is not more than 50% of the original starting material and provides at least 5.5% (dwb) β-glucan soluble fiber and a total dietary fiber content of 16% (dwb), and such that at least one-third of the total dietary fiber is soluble fiber</td>
</tr>
<tr>
<td>Rolled oat</td>
<td>Provides at least 4% (dwb) of β-glucan soluble fiber and a total dietary fiber content of at least 10%</td>
</tr>
<tr>
<td>Whole oat flour</td>
<td>Provides at least 4% (dwb) of β-glucan soluble fiber and a total dietary fiber content of at least 10% (dwb)</td>
</tr>
<tr>
<td>Oatrim</td>
<td>Has β-glucan soluble fiber content up to 10% (dwb) and not less than that of the starting material (dwb)</td>
</tr>
<tr>
<td>Whole grain barley</td>
<td>Has β-glucan soluble fiber content of at least 4% (dwb) and a total dietary fiber content of at least 10% (dwb)</td>
</tr>
<tr>
<td>Dry milled barley</td>
<td>Contain at least 4% (dwb) of β-glucan soluble fiber and at least 8% (dwb) of total dietary fiber, except barley bran and sieved barley meal, for which the minimum β-glucan soluble fiber content is 5.5% (dwb) and minimum total dietary fiber content is 15% (dwb)</td>
</tr>
<tr>
<td>Barley beta fiber</td>
<td>Has β-glucan soluble fiber content of at least 70% on a dry weight basis</td>
</tr>
<tr>
<td>Psyllium husk/psyllium seed husk</td>
<td>Has a purity of no less than 95%, such that it contains 3% or less protein, 4.5% or less of light extraneous matter, and 0.5% or less of heavy extraneous matter, but in no case may the combined extraneous matter exceed 4.9%</td>
</tr>
</tbody>
</table>

Abbreviation: dwb, dry weight basis.

REFERENCES


