

## Functional Foods and Dietary Management of LDL Cholesterol

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*This article reviews the safety, effectiveness, and proposed mechanisms of action of four functional foods with the most robust evidence of their effects in reducing low-density lipoprotein cholesterol (LDL-C). Dietetics professionals should consider prescribing functional foods as an adjunct to a heart-healthy diet for optimal dietary management of LDL-C and for improving cardiovascular disease (CVD) risk.*

### Support of Cholesterol-Lowering Functional Foods

Government and health organizations have shown support for cholesterol-lowering functional foods (FFs) as an adjunct to a heart-healthy diet for optimal dietary treatment and management of elevated LDL-C (the primary target of therapy for primary and secondary prevention of CVD events). The National Cholesterol Education Program Adult Treatment Panel III (ATP III) recommends therapeutic lifestyle changes (TLC) as *the first line of therapy* for hypercholesterolemia.<sup>1</sup> The TLC program advocates a combination of several FFs, such as viscous soluble fiber (VSF) and plant sterols/stanols (PS), to enhance the effectiveness of its prescribed diet. Maximal application of TLC therapy can result in estimated LDL-C reductions of 25% to 30%.<sup>2</sup> This substantial decrease obtained through lifestyle therapy is extremely valuable, considering that an approximate 1% reduction in LDL-C is associated with a 1% to 3% decrease in CVD risk.<sup>3</sup> Thus, FFs applied with a diet low in saturated fat and cholesterol have proven to be effective in maximizing LDL-C reduction in patients with hypercholesterolemia.

The American Heart Association also recommends FFs to enhance the effectiveness of its dietary guidelines.<sup>4</sup> The U.S. Food and Drug Administration (FDA) has issued health claims for several FFs (phytosterols, VSF, soy protein [SP], and tree nuts),<sup>5</sup> stating that each can reduce CVD risk when consumed as part of a diet low in saturated fat and cholesterol.

The four functional food categories with the greatest scientific support for their safety and efficacy in reducing LDL-C are plant sterols, viscous soluble fiber, soy protein, and tree nuts.

### Plant Sterols

The cholesterol-lowering effect of PS has been documented extensively in the literature since the 1950s.<sup>2</sup>

A meta-analysis of 41 clinical trials indicates that 2 g/day of sterols or stanols reduced LDL-C by 10%.<sup>6</sup> ATP III recommends a dietary intake of 2 g/day of PS as an adjunct to a diet low in saturated fat and cholesterol for better prevention of CVD.<sup>1</sup>

The exact mechanism responsible for the LDL-C reduction associated with PS consumption is not yet fully elucidated. PS exert their cholesterol-lowering effects through interference of dietary and biliary cholesterol uptake from the intestinal tract via micellar absorption. PS are structurally similar to cholesterol and compete for incorporation into the limited spaces in the mixed micelles in the intestinal lumen. Micellar competition results in decreased enterocyte cholesterol absorption and increased fecal excretion.<sup>6</sup> PS also increase gene expression of ATP-binding cassette (ABC) transporter genes, which direct the production of transport proteins that regulate cholesterol's efflux from the enterocytes back into the intestinal lumen.<sup>2,6</sup>

Some concern exists over the potential for reduced absorption of certain fat-soluble vitamins, most notably tocopherols and carotenoids. However, consumption of the recommended  $\geq 5$  daily servings of fruits and vegetables has been shown to offset this potential side effect.<sup>2</sup> PS are considered safe and effective and are listed on the FDA generally recognized as safe (GRAS) list.

### Viscous Soluble Fiber Foods

There are four major types of VSF: 1) -glucan (found in cereals, particularly oatmeal and barley); 2) psyllium (consumed in dietary supplement form); 3) gums (found in legumes); and 4) pectin (found in fruits such as apples and pears).<sup>7</sup> VSF consumption significantly lowers LDL-C (10%-15%) when added to a heart-healthy diet.<sup>8</sup> The TLC program suggests 5 g/day to 10 g/day VSF, with the goal of 10 g/day to 25g/day for maximum LDL-C lowering benefits. (The estimated average soluble fiber intake in the United States is 3-4 g/day.)<sup>9</sup> The FDA permits health claims on food products containing -glucan and psyllium (two of the four major categories of VSF).<sup>5</sup>

VSFs are polysaccharides that thicken and form a gel when mixed with fluids. There are several proposed mechanisms for the cholesterol-lowering effect associated with VSF consumption,<sup>7,8</sup> with the action purportedly occurring primarily in the gastrointestinal tract. The common underlying mechanism is the ability of VSFs to

increase elimination of bile acids. Interruption of enterohepatic circulation produces a deficit in bile acid return, stimulating hepatic conversion of cholesterol to new bile acids. This is evident by the increased activity of 7  $\alpha$ -hydroxylase. Ultimately, this cascade of events increases hepatic uptake of circulating LDL-C and a subsequent reduction in serum LDL-C level.<sup>7</sup>

■ **-glucan.** Oatmeal and barley are rich sources of the VSF -glucan, which has been shown to significantly lower LDL-C. The cholesterol-lowering effect of consuming oats in particular is well-documented. In 1997, following an extensive literature review, the FDA approved the oat health claim for prevention of CVD. Andon and Anderson recently reaffirmed the FDA's conclusion that consumption of oats and oat-based products significantly reduces blood cholesterol concentrations.<sup>3</sup> Human clinical trials also have demonstrated that using barley as the food source of -glucan is equally effective in lowering LDL-C.<sup>8</sup> The FDA health claim for soluble fiber specifies a serving size of at least 3 g/day of -glucan soluble fiber from whole oats or barley, or a combination of whole oats and barley as part of a diet low in saturated fat and cholesterol, to potentially reduce heart disease risk.<sup>5</sup>

■ **Psyllium.** Psyllium is a gelatinous substance derived from the *Plantago ovata* plant. The husk of the psyllium seed is a rich source of the VSF *psyllium hydrophilic mucilloid*.<sup>7</sup> Psyllium has an excellent safety record and has attained FDA GRAS status as a food substance. It is one of the most effective LDL-C-lowering VSFs, with the fewest adverse effects.<sup>10</sup> A meta-analysis of 8 clinical studies on the hypocholesterolemic effect of psyllium adjunctive to a low-fat diet showed that 10.2 g/day psyllium (~7 g VSF) was well-tolerated and resulted in a 7% mean reduction in LDL-C.<sup>11</sup> The FDA health claim for foods containing soluble fiber from psyllium seed husk was based on a large body of research using this quantity of psyllium; hence, the health claim specifies 7 g/day or more of VSF from psyllium seed husk.

### Soy Protein

The cholesterol-lowering effects of SP have been documented for some time now, with a 1995 meta-analysis of 38 studies concluding that ingestion of 47 g/day of SP reduces LDL-C by an average of 12.9%.<sup>12</sup> However, a recent AHA meta-analysis<sup>13</sup> revealed a much more modest reduction in LDL-C (~3%). The cholesterol-reduction mechanism may be related to one or both of the major groups of bioactive components in soy: SP and soy isoflavones (SI). With regard to SP, the  $\alpha'$  subunit of the 7S fraction of a major soy storage protein, beta-conglycinin, is postulated to upregulate hepatic LDL receptors.<sup>14</sup> Regarding SI, a meta-analysis of 11 clinical trials showed that consumption of SP with a higher content of isoflavones decreased LDL-C significantly more compared

with the same SP amount low in isoflavones.<sup>15</sup> Hence, ingesting 102 mg/day SI (the amount in 2 glasses of soymilk) reduced LDL-C by 3.8%, independent of the amount of SP consumed. Note that the mild LDL-C reduction observed with frequent SP consumption also may be the result of simply displacing some cholesterol-raising animal fats in the diet with SP.

The FDA health claim for SP specifies that 25 g/day as part of a diet low in saturated fat and cholesterol to potentially reduce the risk of heart disease.<sup>5</sup>

### Tree Nuts

Pooled analyses of clinical human nutrition studies show that adding a variety of tree nuts to a healthy diet reduces LDL-C by 3% to 19% compared with either a low-fat or Western diet.<sup>16</sup> Although the exact mechanism of action for reducing LDL-C is not fully established, it has been proposed that it relates primarily to the favorable fatty acid profile of nuts (most are low in saturated fat, some are high in monounsaturated fatty acids, and others contain a considerable amount of omega-3 and omega-6 polyunsaturated fatty acids). Moreover, nuts contain a substantial amount of dietary fiber in addition to numerous bioactive components (antioxidants, vitamins, minerals, PS, and polyphenols) that would favorably affect the lipid profile.<sup>16</sup>

The FDA has granted a qualified health claim for most tree nuts and peanuts, specifying a serving size of 1.5 oz/day as part of a diet low in saturated fat and cholesterol to potentially reduce heart disease risk.<sup>5</sup>

### Dietary Combination Therapy

To achieve maximum reduction of LDL-C by dietary means, a multicomponent diet is the best strategy and is comparable to low-dose statin therapy in the potential magnitude of LDL reduction that can be achieved. Daily consumption of a combination of functional ingredients rather than a single FF has been shown to be more effective in lowering LDL-C. For example, research on the effects of combining psyllium with PS revealed a significant 10% reduction in LDL-C,<sup>17</sup> whereas each individual food had previously been shown to contribute only a 4% to 7% reduction in LDL-C. Thus, the investigators propose that an additive effect in LDL-C reduction occurs when FFs are combined.

■ **Functional foods in a dietary "portfolio."** Jenkins et al introduced this novel dietary strategy for reducing LDL-C.<sup>18</sup> Termed the "portfolio diet," a collection of FFs (almonds: 23 g/1,000 kcals; soy protein: 22.5 g/1,000 kcals; VSF: 10 g/1,000 kcals; and PS: 1 g/1,000 kcals), all consumed with a diet low in saturated fat and cholesterol, showed dramatic LDL-C reductions comparable to that achieved with first-generation statin medication. Thus, a combination of FFs and a heart-healthy diet may provide an effective therapeutic alternative to drug therapy for some patients.

## ■ Functional foods in combination with statin medication.

Additional research reveals that combining FFs with low-dose statin therapy can achieve a reduction in LDL-C comparable to that achieved with higher dosages of statins taken alone.<sup>19</sup> Psyllium supplements (18 g Metamucil® (5.1 g VSF) 3 times/day with meals) in combination with 10 mg simvastatin over 8 weeks reduced LDL-C to the same degree as 20 mg simvastatin. Simons demonstrated that combining a statin with PS produces a purely additive effect on LDL-C reduction equivalent to doubling the statin dosage.<sup>20</sup> Hence, FFs exert additive effects in combination with statin therapy and can be a safe and effective strategy for magnifying medicinal LDL-C reduction. Furthermore, adjunctive FFs can help patients achieve their LDL-C goals using lower dosages of statins, thereby decreasing the potential risk of pharmacotherapy adverse effects.

## Conclusion and Practical Applications

The preponderance of scientific evidence to date strongly supports the substantial potential of incorporating an array of FFs into the daily diet as an inexpensive, safe, and effective means to augment the cholesterol-lowering effect of standard dietary treatment to prevent CVD. Combining FFs either alone or as an adjunct to statin pharmacotherapy exerts an additive effect, magnifying the total LDL-C reduction—clearly a beneficial outcome for CVD risk management. Dietetics professionals should consider recommending a range of FFs in combination and as an adjunct to a heart-healthy diet to enhance the effectiveness of standard dietary management of hypercholesterolemia.

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# Functional Foods: Helping You Lower Your Cholesterol

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Association

## Key cholesterol-lowering functional foods

High cholesterol is a leading risk factor for heart disease. Keeping your cholesterol in check can help prevent heart disease.

A healthy diet is the first step toward prevention, and adding a few cholesterol-lowering “functional foods” to a heart-healthy diet can help keep your cholesterol where it needs to be.

Functional foods are foods or dietary components that may provide a health benefit beyond basic nutrition. Key cholesterol-lowering functional foods include:

■ **Plant sterols and stanols.** Plant sterols or “phytosterols,” found in plant foods, are sold as supplements or as an ingredient in various foods such as margarine, orange juice, and yogurt (look for “plant sterols and stanols” or “phytosterols” in the ingredient list). Up to 2 grams daily, preferably divided over 3 meals, is recommended to lower cholesterol.

■ **Viscous soluble fiber.** Like a sponge, this special fiber soaks up water and cholesterol in the intestine and is then excreted. Consuming at least 5 to 10 grams daily is recommended. Two types of this fiber are available as functional foods:

-**glucan soluble fiber:** aim for 3 grams daily from either whole oats or barley.

**psyllium seed husk:** build up to 10.2 grams of psyllium husk (about 7 grams of fiber). Psyllium generally is consumed through a dietary supplement (about 2 tablespoons of psyllium powder).

■ **Soy protein.** Soy beans are a highly nutritious vegetable source of plant protein, filled with fiber, vitamins, minerals, and essential omega-3 fat. Unlike animal sources of protein, soybeans have no cholesterol and very little cholesterol-raising saturated fat. Consume 25 grams daily for heart health.

■ **Tree nuts and peanuts.** Nuts are packed with nutrients: fiber, vitamins, minerals, protein, and the “good” type of polyunsaturated fat. How much is enough to keep your cholesterol in check? Aim for 1½ ounces daily (about 1 large handful).

## Tips for including these functional foods into your day

### ***Start at breakfast:***

Eat a bowl of whole grain oatmeal (-**glucan soluble fiber**) made with 1 cup of light soy milk (**soy protein**); drink a glass of orange juice with added **phytosterols**.

### ***Have a heart-healthy handful if you're on-the-go:***

Carry a packet of dry-roasted, unsalted **almonds** for a portable snack.

### ***Try a veggie burger instead of a regular burger for lunch:***

A soy-based veggie burger provides **soy protein** (about 10 grams)—and by eating plant protein rather than animal protein you'll reduce your intake of cholesterol-raising saturated fat and cholesterol.

### ***Enjoy a bowl of barley soup at dinner:***

Barley is another good source of -**glucan soluble fiber**. Try this delicious heart-healthy whole grain in soups, salads, or as a side dish.

### ***Add a sweet treat for dessert:***

Try psyllium-containing wafers with a cup of tea for a cholesterol-lowering sweet treat.

## **Take it slow**

Incorporating functional foods into a daily heart-healthy diet is an inexpensive, safe, and effective way to optimize your lifestyle management of heart disease risk. However, many of these foods are high in fiber and sometimes result in unpleasant gastrointestinal side effects if too much is taken, too soon. Therefore, start slowly and gradually increase your intake. If you're taking prescription medications or have a chronic medical condition, be sure to ask your physician about potential drug-nutrient interactions.