The Role of Phytosterols in Cholesterol Management

Approximately 1 in 3 adults 20 years and older has elevated low-density lipoprotein cholesterol (LDL-C), and two-thirds of this population has an LDL-C that is uncontrolled, putting them at an increased risk for heart disease. A core recommendation in the most recent National Cholesterol Education Program (NCEP) guidelines is centered on therapeutic lifestyle changes (TLCs) to reduce LDL-C to less than 100 mg/dL for all individuals, including weight control, increased physical activity, reductions in saturated fats and cholesterol, and therapeutic dietary (TLC diet) options (eg, plant stanols/sterols, fiber) to help individuals achieve their LDL-C goals. The NCEP recommends a daily intake of 2000 mg of plant stanols/sterols as part of a treatment plan to enhance LDL-C lowering. According to the FDA, products containing at least 400 mg per serving of plant sterols and stanols, eaten twice a day with meals for a daily intake of at least 800 mg as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.

The Influence of Phytosterols on Serum Cholesterol

Phytosterols, also referred to as stanols or sterols, are plant-derived substances that are structurally similar and functionally analogous to cholesterol in humans. When ingested, phytosterols displace cholesterol on binding sites within the digestive tract, inhibiting intestinal cholesterol absorption and increasing biliary excretion. This results in a reduction of circulating LDL-C and other apolipoprotein B–containing lipoprotein particles in the bloodstream. Based on a typical Western diet, many people consume as little as 200 mg of phytosterols daily through food intake. The most common sources include unrefined vegetable oils, nuts, fruit, and whole grains. Vegetable oils (eg, corn oil, olive oil) contain the most concentrated amount of phytosterols (Table). Others sources of phytosterols include fortified foods, which most commonly include margarines. Consuming sufficient amounts of phytosterol through fortified or unfortified foods to meet the NCEP recommendation (2000 mg daily) may be challenging for patients, especially for those on calorie-restricted diets. One option that may offer more convenience as well as a reduced caloric burden is the use of phytosterol dietary supplements.

CholestOff® as Part of a Treatment Plan

Available phytosterol-only CholestOff formulations include the original formulation (2 tablets contain a total of 900 mg of free-form sterols/stanols) and CholestOff Plus (2 softgel capsules contain a total of 900 mg of sterols/stanols in an esterified form). Available over the counter, CholestOff provides 1800 mg of sterols/stanols when taken twice daily with meals.

Use of CholestOff as part of an NCEP-recommended diet was shown to significantly reduce LDL-C, non-high-density lipoprotein cholesterol (non-HDL-C), and total cholesterol (TC) in randomized, double-blind, placebo-controlled crossover studies among patients with hypercholesterolemia. The studies were similar in design. After a 5-week run-in period during which participants received placebo and were instructed to follow the TLC diet, patients who had baseline LDL-C between 130 mg/dL and 220 mg/dL were randomized to treatment with CholestOff or placebo for 6 weeks, then crossed over to the opposite groups for 6 additional weeks of treatment. Use of lipid-altering treatments was prohibited for at least 4 weeks prior to study entry. Patients were asked to take the supplement with meals, twice daily, at consistent times. In addition, patients were counseled to follow the TLC diet and to maintain usual physical activity throughout the study. Fasting blood samples were collected at baseline and at the end of weeks 5, 6, 11, and 12.

One of these studies evaluated esterified plant sterol/stanol use in 28 patients with hypercholesterolemia. Patients were randomly assigned to receive CholestOff Plus (esterified sterols/stanols 2.9 g/day, equivalent to nonesterified plant sterols/stanols 1800 mg/day) or placebo. As shown in the Figure, treatment with CholestOff was associated with improvements in LDL-C, non-HDL-C, TC, and triglycerides (TG). The percentage change between groups was 9.2% for LDL-C (baseline, 153.6 mg/dL; P < .001), 9.0% for non-HDL-C (baseline, 178.6 mg/dL; P < .001), 7.4% for TC (baseline, 222.5 mg/dL; P < .001), and 9.1% for TG (baseline, 124.6 mg/dL; P = .042). Adverse events were reported by 6 subjects in the treatment phase and 4

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<thead>
<tr>
<th>TABLE: QUANTITY OF PHYTOSTEROLS FOUND NATURALLY IN FOODS</th>
<th>(mg)</th>
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<tbody>
<tr>
<td>Corn oil, 1 tablespoon</td>
<td>134</td>
</tr>
<tr>
<td>Olive oil, 1 tablespoon</td>
<td>24</td>
</tr>
<tr>
<td>Corn, 1 ear</td>
<td>63</td>
</tr>
<tr>
<td>Apple, 1 whole</td>
<td>22</td>
</tr>
<tr>
<td>Tomato, 1 whole</td>
<td>9</td>
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subjects in the placebo phase. These events included fatigue, gingivitis, headache, hypertension, infection, and insomnia during the sterol/stanol treatment period, and myalgia, rhinitis, salivary duct obstruction, and upper respiratory infection while taking placebo. None of these events were serious, and all were considered to be unrelated to treatment with CholestOff.  

A separate crossover study evaluated the use of nonesterified sterols/stanols (CholestOff Original) in 32 adults with hypercholesterolemia. Patients were randomized to treatment with nonesterified sterol/stanols 900 mg twice daily or placebo for 6 weeks before crossing over to the opposite group for 6 additional weeks of treatment. Between-group differences in response were 4.9% for LDL-C (baseline, 155.5 mg/dL; \( P = .002 \)), 3.6% for non-HDL (baseline, 182.1 mg/dL; \( P = .008 \)), and 2.8% for TC (baseline, 227.4 mg/dL; \( P = .024 \)). Eight adverse events were reported during the treatment phase; 7 were reported during the placebo phase. The most common adverse events were related to respiratory issues, such as rhinitis and sinusitis, and none of the events were serious. With the exception of 1 case of increased appetite, the adverse events were considered to be unrelated to study treatment.  

**Role of the Pharmacist**

Use of a dietary supplement such as CholestOff, along with a heart-healthy diet, is a practical part of a treatment regimen for patients with elevated LDL-C. Given the low amount of phytosterols found in most foods, CholestOff can help patients meet the level recommended by the NCEP by offering 1800 mg of plant sterol/stanol daily. Pharmacists should stress dietary changes as part of overall cholesterol management, and should review treatment expectations with patients, including average cholesterol reductions. Advise patients to take CholestOff with meals.  

Although phytosterols have been studied in conjunction with cholesterol-lowering medications, patients should be advised to notify their health care provider if they are taking CholestOff. Pharmacists can also help to educate patients by recommending that they check the directions of use on the nutrition or supplement facts panel and aim toward 2000 mg of phytosterols daily. Patients with an allergy to pine trees (or any other product ingredients) should not take CholestOff. In addition, CholestOff should not be used in pregnant or lactating women, or in children.  

**References**