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### **Phytosterols in Human Nutrition**

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#### **ABSTRACT**

Phytosterols are cholesterol-like molecules found in all plant foods, with the highest concentrations occurring in vegetable oils. They are absorbed only in trace amounts but inhibit the absorption of intestinal cholesterol including recirculating endogenous biliary cholesterol, a key step in cholesterol elimination. Natural dietary intake varies from about 167-437 mg/day. Attempts to measure biological effects in feeding studies have been impeded by limited solubility in both water and fat. Esterification of phytosterols with long-chain fatty acids increases fat solubility by 10-fold and allows delivery of several grams daily in fatty foods such as margarine. A dose of 2 g/day as the ester reduces low density lipoprotein cholesterol by 10%, and little difference is observed between Delta(5)-sterols and 5alpha-reduced sterols (stanols). Phytosterols can also be dispersed in water after emulsification with lecithin and reduce cholesterol absorption when added to nonfat foods. In contrast to these supplementation studies, much less is known about the effect of low phytosterol levels in the natural diet. However, reduction of cholesterol absorption can be measured at a dose of only 150 mg during otherwise sterol-free test meals, suggesting that natural food phytosterols may be clinically important. Current literature suggests that phytosterols are safe when added to the diet, and measured absorption and plasma levels are very small. Increasing the aggregate amount of phytosterols consumed in a variety of foods may be an important way of reducing population cholesterol levels and preventing coronary heart disease.

**KEY WORDS:** Sterols, cholesterol, Esterification, coronary Heart disease

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## **INTRODUCTION**

Phytosterols are compounds found in plants that resemble cholesterol. The National Institutes of Health report that there are over 200 different phytosterols, and the highest concentrations of phytosterols are found naturally in vegetable oils, beans and nuts.<sup>1</sup> Their benefits are so recognized that foods are being fortified with phytosterols. At the supermarket, you may see orange juice or margarine advertising phytosterol contents. After reviewing the health benefits, you may want to add phytosterol-rich foods to your diet.<sup>1,2</sup>

## **BENEFITS OF PHYTOSTEROLS**

### ***Cholesterol-Lowering Benefits***

The most well-known, and scientifically proven, benefit of phytosterols is their ability to help lower cholesterol. A phytosterol is a plant compound that is similar to cholesterol. A study in the 2002 issue of Annual Review of Nutrition explains that phytosterols actually compete for absorption with cholesterol in the digestive tract.<sup>3</sup> While they prevent the absorption of regular dietary cholesterol, they themselves are not easily absorbed, which leads to a total lower cholesterol level. The cholesterol-lowering benefit does not end with a good number on your blood work report. Having lower cholesterol leads to other benefits, such as a reduced risk for heart disease, stroke and heart attacks.<sup>3,4</sup>

### ***Cancer Protection Benefits***

Phytosterols have also been found to help protect against the development of cancer. The July 2009 issue of the European Journal of Clinical Nutrition offers encouraging news in the fight against cancer. Researchers at the University of Manitoba in Canada report that there is evidence that phytosterols help prevent ovarian, breast, stomach and lung cancer.<sup>5</sup> Phytosterols do this by preventing the production of cancer cells, stopping the growth and spread of cells that are already in existence and actually encouraging the death of cancer cells. Their high anti-oxidant levels are believed to be one way phytosterols help fight cancer. An anti-oxidant is a compound that fights free radical damage, which is negative effects on the body produced by cells that are unhealthy.<sup>6</sup>

### ***Breast Cancer***

Phytosterols were shown to be protective against breast cancer in a study. Two of the most common dietary phytosterols, beta-sitosterol and campesterol, were tested on advanced breast cancer cells, in a study by A.B. Awad, published in the 2003 "Journal of Nutritional Biochemistry." The cells that were exposed to

beta-sitosterol exhibited a 70 percent reduction in cell growth, while campesterol-treated breast cancer cells had a 6 percent decline in cell growth.<sup>6,7</sup>

### ***Skin Protection Benefits***

A lesser known benefit of phytosterols involves skin care. One of the contributing factors in the aging of the skin is the breakdown and loss of collagen (the main component in connective skin tissue) and sun exposure is a major contributor to the problem. As the body ages, it is not able to produce collagen as it once did. The National Institutes of Health reports on a study out of Germany in which various topical preparations were tested on skin for 10 days.<sup>8</sup> The topical treatment that showed anti-aging benefits to the skin was the one that contained phytosterols and other natural fats. It is reported that phytosterols not only stopped the slow-down of collagen production that can be caused by the sun, it actually encouraged new collagen production.<sup>3,9</sup>

### ***Changing the Immune System***

Plant phytosterols play a role in how the immune system functions. Although they were chemically identified in 1922, their role in health has been grossly underestimated. In a review article published in November 2001 in "Current Opinion in Clinical Nutrition and Metabolic Care", author PJ Bouic notes that it was only in the previous 10 years that scientists were able to prove the direct activity that phytosterols have on lymphocytic activity, especially in the mechanism against cancer cells.<sup>10,11</sup> Phytosterols have also been used as supportive therapy in chronic conditions in which an inflammatory response plays a large role including cardiovascular conditions and cancer. Additionally, the Linus Pauling Institute reports that women diagnosed with breast or endometrial cancer had lower dietary phytosterol intakes than women who did not have cancer.<sup>6</sup>

## **FOOD SOURCES OF PHYTOSTEROLS**

Phytosterols are sterols occurring naturally in plants. They are similar to cholesterol in structure, but consumption of phytosterols has cardioprotective effect by lowering blood cholesterol levels. This is achieved through an inhibition of cholesterol absorption from the intestines. Due to this property, phytosterols are sometimes added to some premium brands of margarines, butters and spreads, and marketed as cholesterol-lowering foods.<sup>12</sup>

## ***Nuts***

Nuts contain high levels of phytosterols, especially almonds, walnuts, pistachios and macadamias. Sabate and Wien from the Loma Linda University, California, reviewed the scientific literature and concluded that there was strong evidence that nut consumption was associated with a decreased risk in coronary heart disease.<sup>12</sup> According to the authors, there is an 8.3 percent reduction in risk for every weekly serving of nuts. This is achieved through a lowering of total and low-density lipoprotein, or bad, cholesterol and an optimization of the LDL:HDL cholesterol ratio. Apart from phytosterols, other heart-protective nutrients found in nuts include fiber, alpha-tocopherol, folic acid, magnesium and copper.<sup>12, 13</sup>

## ***Flaxseed Oil***

Flaxseed oil is also a good source of phytosterols. This oil is also prized for its content of omega-3 fatty acids, which are associated with several health benefits. According to K. Prasad from the University of Saskatchewan, Canada, flaxseed oil protects against heart disease through a reduction in total cholesterol and LDL cholesterol and elevation of high-density lipoprotein, or good, cholesterol. Prasad reports that flaxseed oil reduces blood pressure and decreases the risk of stroke.<sup>14,15</sup> According to researchers from the Memorial Sloan-Kettering Cancer Center, New York, flaxseed oil consumption can also have significant anti-inflammatory effects in gout and lupus.<sup>9</sup>

## ***Broccoli***

Broccoli is a good source of phytosterols, fiber, antioxidants, vitamins K, C and A, and the minerals manganese, potassium, phosphorus, magnesium and iron. H.J. Cho and colleagues from Hallym University, Korea, also report that broccoli contains anti-cancer nutrients, such as diindolylmethane, indole-3-carbinole and glucoraphanin. Diindolylmethane also has antibacterial and antiviral properties while indole-3-carbinole aids DNA repair.<sup>10, 14</sup>

## ***Avocados***

Avocados are potent cholesterol-lowering fruits and this is believed to be achieved through three nutrients: the phytosterol beta-sitosterol, fiber and monounsaturated fat. In a study carried out by L.R. Ledesma and colleagues from the La Raza Medical Centre, Mexico, adults eating avocado every day demonstrated a decrease in total cholesterol after seven days. According to the same authors, patients with mild hypercholesterolemia put on an avocado-enriched diet exhibited not just a decrease in total cholesterol but also a reduction in triglycerides and an increase in HDL cholesterol.<sup>14, 16</sup>

## ***Grains***

Wheat germ has one of the highest concentrations of phytosterols, containing 197 mg in a ½ cup serving, according to the Linus Pauling Institute. However, recent research has found that wheat germ is not a significant source of phytosterols for most people because they don't eat it often enough, according to a study published in the "Journal of Agricultural and Food Chemistry" in November 2005. Wheat bran is also a good option with 58 mg of phytosterols in a ½ cup serving and two slices of rye bread will give you 33 mg of phytosterols.<sup>17</sup>

## ***Enriched Foods***

Enriched margarines are among the richest sources of phytosterols available and can contain up to 1650 mg in a 1-tbsp. serving. Other phytosterol-rich options include enriched mayonnaise, yogurt, milk, cheese, chocolate, orange juice, vegetable oils, salad dressings, snack bars and soy milk. The amount of phytosterols in such products varies from brand to brand, so read the nutrition labels carefully to find out how much you're getting.<sup>12,13</sup>

## ***Phytosterol Additives and Supplements***

Phytosterols are very soluble in fatty substances. As a result, several products are available at most food stores that have added phytosterols, including some cheeses, margarines, salad dressings, yogurt and even snack bars. Phytosterol supplements are also available at health food stores, usually containing beta-sitosterol at concentrations of 60-130 mg per capsule. Foods with added phytosterols and phytosterol supplements are generally considered safe, although daily intake should not exceed 3 g per day, according to the Linus Pauling Institute. Consult your doctor to determine if consuming these phytosterol-fortified foods or supplements is advisable for you.<sup>18</sup>

## ***Doses***

According to the Linus Pauling Institute, our early human ancestors probably ate around 1,000 mg of plant sterols per day. Nowadays, people in western countries eat between 150 and 450 mg per day. If you are at risk for high cholesterol and heart disease, your doctor may tell you to use between 800 mg to 6 g of phytosterols daily, according to the University of Maryland Medical Center. While it is possible to achieve these doses through food sources, your doctor may recommend that you take a specific phytosterol supplement or use phytosterol-enriched foods like certain margarines and salad dressings.<sup>16, 18</sup>

## ***Recommendations***

Talk to your doctor to learn more about your risk for heart disease. If you have high cholesterol or other risk factors for heart disease, ask your doctor if you may benefit from using phytosterol-containing foods or supplements.<sup>19</sup> Phytosterols are typically very safe and free of side effects but can be dangerous to people with specific genetic conditions such as sitosterolemia. Pregnant mothers and people using certain prescription medications may also want to avoid plant sterols.<sup>16</sup>

## **WHAT ARE THE SIDE EFFECTS OF PHYTOSTEROL?**

Plants such as cabbage and corn contain cholesterol-like molecules called phytosterols. A typical U.S. diet delivers 200 to 300 mg/day. Phytosterols added to foods in amounts of 1000 to 3000 mg/day partially block cholesterol absorption. As a result, blood levels of low density lipoprotein cholesterol are reduced on average by 10 to 15 percent.<sup>20</sup> The Food and Drug Administration recognizes this proven benefit by allowing a health claim on product labels. While FDA approval implies that the products are safe, there are mild side effects and also a very rare serious side effects.

### ***Extreme Phytosterolemia***

According to Dr. Martin Katan's efficacy and safety review in the August 2003 "Mayo Clinic Proceedings," consumption of phytosterols in effective doses results in measurable increases in phytosterolemia, or blood phytosterol levels.<sup>21</sup> Extreme phytosterolemia is the result of a very rare genetic condition in which patients are unable to eliminate phytosterols from blood. These patients develop premature heart disease. Experts in this field wonder if for people without the genetic defect, the modest blood increase seen from consuming phytosterols results in modestly increased risk of heart disease, albeit masked by the larger reduced risk from lowering blood cholesterol. A review by Drs. Miettinen and Gylling in the January 2009 issue of *Current Atherosclerosis Reports* concluded that phytosterolemia is also increased by statin drugs. People taking a statin drug should talk to their doctor before adding a phytosterol-containing functional food to their daily regimen.<sup>22</sup>

### ***Interference with Fat-Soluble Vitamins***

According to a Linus Pauling Institute review on phytosterol safety, blood vitamin A was not affected by consumption of therapeutic amounts of phytosterols, vitamin D was either not affected or modestly lowered, vitamin K was decreased by 14 percent based on evidence from one study, and vitamin E was consistently lowered.<sup>16,18</sup>

### ***Interference with Carotenoids***

According to the same Linus Pauling Institute review, blood levels of carotenoids such as beta-carotene and lycopene are reduced by 10 to 20 percent when people use phytosterols to lower blood cholesterol. Benefits of carotenoids and lycopene are not proven, but both are thought to reduce the risk of some types of cancer.<sup>18</sup>

### **ALLERGIES TO PHYTOSTEROLS**

As with any medication, you are at risk of experiencing an allergic reaction while using phytosterols. An allergic reaction may not occur during the first or second dose, but symptoms may appear in sequent doses. If you experience any adverse reactions while taking phytosterols, call your doctor immediately. A severe allergic reaction to phytosterols is uncommon, but could lead to death if not treated promptly.<sup>8,9</sup>

### ***Allergic Reaction***

An allergic reaction to medication typically develops signs after the first few doses. The introduction of a new substance to the body can cause the immune system to mistake the substance as harmful. If it does, the immune system will begin to develop antibodies against that substance. Once ingested, the immune system unleashes an attack against the phytosterols and causes a chemical chain reaction throughout the body, causing common allergy symptoms, according to the American Academy of Allergy, Asthma and Immunology.<sup>8,9,22</sup>

### ***Effects***

The main chemical released in the body that causes an allergic reaction is histamine. Histamine is a hormone that helps to ward off infection and disease, but when produced in high rates, it causes inflammation and swelling in soft tissue. Increased histamine levels leads to common allergy symptoms, such as digestive difficulties, skin rashes, rhinitis and asthma, according to Medline Plus.<sup>23</sup>

### ***Symptoms***

You may experience diarrhea, vomiting, stomach cramping and nausea after taking phytosterols. Skin rashes may appear within a few minutes in the form of eczema, hives or general skin inflammation and irritation. Nasal congestion, sneezing, a runny nose, eye irritation and a tickle in the throat are rhinitis

symptoms. Asthma can develop, causing shortness of breath, wheezing, chest tightness and wheezing, according to Medline Plus.<sup>8,9,23,24</sup>

### **Testing**

If you experience an allergic reaction to phytosterols, your doctor may recommend allergy testing to determine the severity of the reaction and the cause. Allergy tests are performed by an allergist, using blood tests and skin prick tests. The doctor will expose your body to a small amount of the drug and observe how your body responds to the medication. Your doctor may recommend a different drug to lower your cholesterol or diet modification.<sup>25,8,9</sup>

### **CONCLUSION**

Phytosterols are a family of compounds similar to cholesterol which have been shown to lower cholesterol levels when supplemented in the diet. A daily dose of 2–3 g of phytosterols has been shown to reduce LDL-cholesterol levels by 5–15%. Phytosterol supplementation can be undertaken using phytosterol enriched functional foods or nutraceutical preparations. The type of phytosterol supplemented, such as plant sterol or saturated plant stanol appear to be equally effective in lowering cholesterol levels.<sup>26</sup> Phytosterols, whether in esterified or free form have both been shown to lower cholesterol levels, with esterified phytosterol formulations having a greater number of clinical trials demonstrating efficacy.<sup>27</sup> The functional food or nutraceutical matrix which is used to deliver supplemental phytosterols can significantly affect cholesterol lowering efficacy. Effective cholesterol lowering by phytosterols depends on delivery of phytosterols to the intestine in a form which can compete with cholesterol for absorption.<sup>27, 28</sup> New phytosterol functional food and nutraceuticals products should always be tested to demonstrate adequate delivery of phytosterol dose and effective total and LDL-cholesterol lowering. Phytosterol products which do not effectively lower cholesterol will negatively impact the perception and use of phytosterols, and must not be allowed on the marketplace.<sup>13, 26, 29</sup>

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