

Plant stanols in Benecol® Buttery Spreads are proven to reduce cholesterol.

Defining Plant Stanol Esters

Plant sterols, plant stanols, and their esterified forms (**plant sterol ester/plant stanol ester**) are classified as **phytosterols**, which are naturally occurring components of plant cell membranes. Sterols/stanols are found in trace amounts in foods such as cereals and grains, vegetables, fruits and legumes. Because plant sterols/stanols hold a similar molecular structure to cholesterol, they compete for absorption in the intestine, and in turn lower blood cholesterol levels.^{1,2} As high blood cholesterol is a major contributor to Coronary Heart Disease (CHD), the Food & Drug Administration (FDA) recommends the use of plant stanols/sterols as a strategy to lower cholesterol, in turn reducing overall risk of CHD.³ Though both plant sterol ester and plant stanol ester are effective in lowering total and LDL cholesterol, **plant stanol ester** on average has been shown to cause a greater reduction in cholesterol compared to that of plant sterol ester.⁴

Plant sterols/stanols occur naturally in the Western diet however only provide an average of 0.6 grams daily, which is not enough to achieve the desired cholesterol-lowering effect. Summarizing evidence-based conclusions across 60+ clinical studies, the FDA recommends 2g per day of plant stanols to attain significant reduction in low-density lipoprotein (LDL) cholesterol and total cholesterol.³ **Benecol®** is the only buttery spread that contains plant stanol, providing the recommended 2g plant stanol ester in 4 tablespoons of spread.

¹ Ostlund RE Jr. Phytosterols and cholesterol metabolism. *Curr Opin Lipidol*. 2004;15 (1): 37-41.

² Katan, Martijn B. et al. Efficacy and Safety of Plant Stanols and Sterols in the Management of Blood Cholesterol Levels. *Mayo Clinic Proceedings*. 2003;78 (8): 965 – 978

³ Food Labeling; Health Claims: Phytosterols and Risk of Coronary Heart Disease. 75 Fed. Reg. 235 (December 8, 2010).

⁴ Musa-Veloso Kathy et al. A comparison of the LDL-cholesterol lowering efficacy of plant stanols and plant sterols over a continuous dose range: Results of a meta-analysis of randomized, placebo-controlled trials. *Prostaglandins, Leukotrienes and Essential Fatty Acids*. 2011; Volume 85(1): 9 – 28

Support from the Food & Drug Administration for Plant Stanol Use

The FDA assigns categories for food product claims, which include **Structure Function Claims, Nutrient Content Claims, and Health Claims that meet Significant Scientific Agreement (SSA)**. The SSA claim is by far the strongest of these three as it identifies a proven, significant health-related relationship between an ingredient and a documented health condition. In this instance, the FDA assigns the **Significant Scientific Agreement claim to the relationship between plant stanol/sterol esters and reduced risk of Coronary Heart Disease (CHD)**. The foundation of the Significant Scientific Agreement is a body of over 60+ clinical studies published in peer-reviewed scientific and medical journals, including the *American Journal of Clinical Nutrition*, the *American Journal of Cardiology* and *Atherosclerosis*.

While there are non-responders in any study, the overwhelming body of scientific evidence suggests that on average, for most people, there is a significant reduction in LDL and total cholesterol in response to consuming plant stanols.³

Across the clinical studies supporting the use of plant stanol/plant sterol in lowering cholesterol and risk of CHD, there has been proven efficacy with no known side effects in a variety of populations, including but not limited to:

- *Healthy women, men and children*
- *Subjects with normal, healthy cholesterol levels*
- *Subjects with moderate to high cholesterol levels*
- *People living with Type 1 and 2 Diabetes Mellitus*
- *Subjects with Metabolic Syndrome (collective occurrence of multiple diet-related diseases)*
- *Coronary Artery Disease (CAD) patients*
- *As a part of normal western diet*
- *As a part of strict cholesterol-lowering diet*
- *Paired with statin medication*
- *Globally diverse populations*

The text of the health claim authorized by the FDA with respect to plant stanols is as follows: “Foods containing at least 0.5g per serving of plant stanols eaten with meals or snacks for a daily total intake of 2g as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease.” One serving of Benecol® spread supplies 0.5g of plant stanols.

In addition to the FDA support, the following recognized health-related organizations recommend consumption of plant stanols/sterols as a cholesterol-lowering strategy and overall method of reducing risk of CHD:

- *International Atherosclerosis Society, 2013*
- *American Diabetes Association, 2013*
- *European Atherosclerosis Society, 2013*
- *European Society of Cardiology, 2012*
- *National Heart, Lung, and Blood Institute & National Institutes of Health & American Academy of Pediatrics, 2011*
- *European Society of Cardiology & European Atherosclerosis Society, 2011*
- *The Australian Heart Foundation, 2009*
- *American Academy of Pediatrics, 2008*
- *American Diabetes Association & American College of Cardiology, 2008*
- *American Heart Association & American College of Cardiology, 2006*
- *Joint British Societies, 2005*
- *International Atherosclerosis Society, 2005*
- *Joint WHO/FAO Expert Consultation, 2003*
- *International Lipid Information Bureau, 2003*
- *National Cholesterol Education Program & National Institute of Health, 2002*

For reference, below is a subset of the clinical studies identified by the FDA as contributing to the **SSA** claim by demonstrating the link between consumption of plant stanols/sterols and the reduced risk of CHD:

1. National Heart, Lung, and Blood Institute, National Institutes of Health. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Pressure in Adults (Adult Treatment Panel III) Executive Summary. National Institutes of Health, Bethesda, MD, 2001. Available at <http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf>.
2. Clifton, P.M., M. Noakes, D. Sullivan, N. Erichsen, D. Ross, G. Annison, C.M. Fassoulakis, and P. Nestel. "Cholesterol-Lowering Effects of Plant Sterol Esters Differ in Milk, Yoghurt, Bread, and Cereal." *European Journal of Clinical Nutrition*, 58(3):503-509, 2004.
3. Jones, P.J., F.Y. Ntanios, M. Raeini-Sarjaz, and C.A. Vanstone. "Cholesterol-Lowering Efficacy of a Sitostanol-Containing Phytosterol Mixture With a Prudent Diet in Hyperlipidemic Men." *American Journal of Clinical Nutrition*, 69(6):1144-1150, 1999.
4. Vanstone, C.A., M. Raeini-Sarjaz, W.E. Parsons, and P.J.H. Jones. "Unesterified Plant Sterols and Stanols Lower LDL-Cholesterol Concentrations Equivalently in Hypercholesterolemic Persons." *American Journal of Clinical Nutrition*, 76:1272-1278, 2002.
5. Christiansen, L.I., P.L. Lähteenmäki, M.R. Mannelin, T.E. Seppänen-Laakso, R.V.K. Hiltunen, and J.K. Yliruusi. "Cholesterol-Lowering Effect of Spreads Enriched With Microcrystalline Plant Sterols in Hypercholesterolemic Subjects." *European Journal of Nutrition*, 40(2):66-73, 2001.
6. Tikkanen, M.J., P. Höglström, J. Tuomilehto, S. Keinänen-Kiukaanniemi, J. Sundvall, and H. Karppanen. "Effect of a Diet Based on Low-Fat Foods Enriched With Nonesterified

- Plant Sterols and Mineral Nutrients on Serum Cholesterol.”*American Journal of Cardiology*, 88(10):1157-1162, 2001.
7. Miettinen, T.A. and H.T. Vanhanen. “Dietary Sitostanol Related Absorption, Synthesis and Serum Level of Cholesterol in Different Apolipoprotein E Phenotypes.”*Atherosclerosis*, 105:217-226, 1994.
 8. deGraaf, J., P.R.W. deSavage Nolting, M. vanDam, E.M. Belsey, J.J.P. Kastelein, P.H. Pritchard, and A.T.H. Stalenhoef. “Consumption of Tall Oil-Derived Phytosterols in a Chocolate Matrix Significantly Decreases Plasma Total and Low-Density Lipoprotein-Cholesterol Levels.”*British Journal of Nutrition*, 88(5):479-488, 2002.
 9. Nestel, P., M. Cehun, S. Pomeroy, M. Abby, G. Weldon. “Cholesterol-Lowering Effects of Plant Sterol Esters and Non-Esterified Stanols in Margarine, Butter and Low-Fat Foods.”*European Journal of Clinical Nutrition*, 55(12):1084-1090, 2001.
 10. Korpela, R., J. Tuomilehto, P. Högström, L. Seppo, V. Piironen, P. Salo-Väänänen, J. Toivo, *et al.* “Safety Aspects and Cholesterol-lowering Efficacy of Low Fat Dairy Products Containing Plant Sterols.”*European Journal of Clinical Nutrition*, 60:633-642, 2006.
 11. AbuMweis, S.S., C.A. Vanstone, N. Ebine, A. Kassis, L.M. Ausman, P.J.H. Jones, and A.H. Lichtenstein. “Intake of a Single Morning Dose of Standard and Novel Plant Sterol Preparations for 4 Weeks Does Not Dramatically Affect Plasma Lipid Concentrations in Humans.”*Journal of Nutrition*, 136:1012-1016, 2006.
 12. Jones, P.J., M. Raeini-Sarjaz, F.Y. Ntanos, C.A. Vanstone, J.Y. Feng, and W.E. Parsons. “Modulation of Plasma Lipid Levels and Cholesterol Kinetics by Phytosterol Versus Phytostanol Esters.”*Journal of Lipid Research*, 41:697-705, 2000.
 13. Noakes, M., P. Clifton, F. Ntanos, W. Shrapnel, I. Record, and J. McInerney. “An Increase in Dietary Carotenoids When Consuming Plant Sterols or Stanols is Effective in Maintaining Plasma Carotenoid Concentrations.”*American Journal of Clinical Nutrition*, 75(1):79-86, 2002.
 14. Doornbos, A.M.E., E.M. Meynen, G.S.M.J.E. Duchateau, H.C.M. van der Knaap, and E.A Trautwein. “Intake Occasion Affects the Serum Cholesterol Lowering of a Plant Sterol-Enriched Single-Dose Yoghurt Drink in Mildly Hypercholesterolaemic Subjects.”*European Journal of Clinical Nutrition*, 60:325-333, 2006.
 15. Vanhanen, H.T. and T.A. Miettinen. “Effects of Unsaturated and Saturated Dietary Plant Sterols on Their Serum Contents.”*Clinica Chimica Acta; International Journal of Clinical Chemistry*, 205:97-107, 1992.
 16. Law, M. “Plant Sterol and Stanol Margarines and Health.”*British Medical Journal*, 320:861-864, 2000.
 17. Ostlund, R.E. “Phytosterols in Human Nutrition.”*Annual Review of Nutrition*, 22:533-549, 2002.
 18. Katan, M.B., S.M. Grundy, P. Jones, M. Law, T. Miettinen, and R. Paoletti. “Efficacy and Safety of Plant Stanols and Sterols in the Management of Blood Cholesterol Levels.”*Mayo Clinic Proceedings*, 78:965-978, 2003.
 19. Plat, J., E.N.M. van Onselen, M.M.A. van Heugten, and R.P. Mensink. “Effects on Serum Lipids, Lipoproteins and Fat Soluble Antioxidant Concentrations of Consumption Frequency of Margarines and Shortenings Enriched With Plant Stanol Esters.”*European Journal of Clinical Nutrition*, 54(9):671-677, 2000.
 20. Matvienko, O.A., D.S. Lewis, M. Swanson, B. Arndt, D.L. Rainwater, J. Stewart, *et al.* “A Single Daily Dose of Soybean Phytosterols in Ground Beef Decreases Serum Total Cholesterol and LDL Cholesterol in Young, Mildly Hypercholesterolemic Men.”*American Journal of Clinical Nutrition*, 76(1):57-64, 2002.