



Benecol® Products
Effective
and **easy**
dietary solution
to lower
cholesterol



FOR HEALTHCARE PROFESSIONALS



Dear Reader,

Cardiovascular disease (CVD) is the major cause of premature death both in Europe and globally. Lowering of cholesterol is one of the most important means of decreasing the risk of developing cardiovascular disease.

Lifestyle changes, such as heart-healthy diet, are one of the cornerstones in the treatment of hypercholesterolemia. A heart-healthy diet is low in saturated fat and cholesterol but high in dietary fibre. Foods enriched with Plant stanol ester are recommended especially when cholesterol target levels are not achieved with ordinary dietary changes. Benecol® products may also be the first, motivating step towards healthier lifestyles.

The disease risk reduction claim awarded to Plant stanol ester was among the first disease risk reduction claims authorised by the European Commission in 2009:

“Plant stanol ester is proven to lower serum cholesterol. High cholesterol is a risk factor for coronary heart disease.”

This brochure provides basic information about Plant stanol ester, its cholesterol lowering effect and Benecol products for healthcare professionals. Benecol products are the first cholesterol lowering functional foods based on strong scientific evidence. These products are a result of a unique Finnish innovation and they entered the Finnish market already in 1995. At the moment, millions of people in over 30 countries use Benecol products to lower their cholesterol.

*European guidelines on cardiovascular disease prevention in clinical practice (2007)
WHO 2009
Finnish Diabetes Association: Nutrition recommendation for diabetes (2008)
Commission regulation (EC) No 983/2009, amended by (EU) No 376/2010*

Plant stanol ester effectively lowers cholesterol and reduces the estimated risk of cardiovascular disease

The efficacy of Plant stanol ester in cholesterol lowering has been proven in over 60 peer-reviewed clinical studies with the stringent scientific requirements.

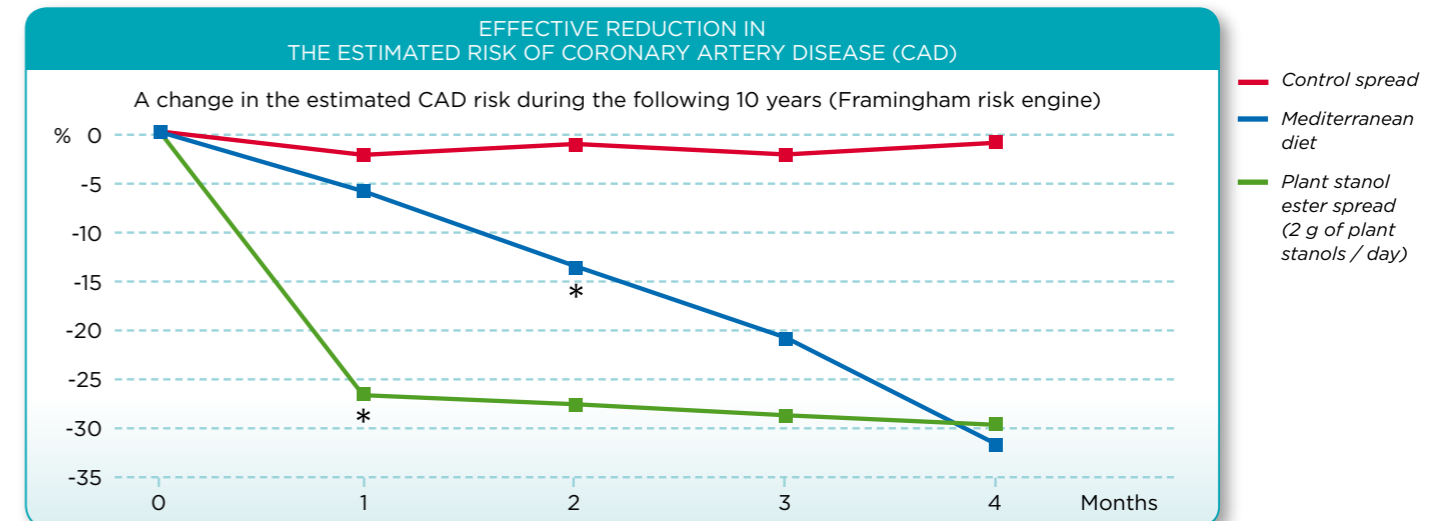
Studies show that the daily intake of 2 g plant stanols (as Plant stanol ester) reduces serum LDL cholesterol by 10-15 %.

Effective lowering of cholesterol predicts a significant reduction in the CVD risk: according to a recent study, the use of Benecol® products reduces the estimated CVD risk by 26-30 %, i.e. as much as by following a Mediterranean diet.*

“Framingham and PROCAM risk engines estimate the 10 year risk of getting coronary artery disease, whereas the Reynold risk engine estimates the 10 year risk of getting coronary artery disease or stroke. Athyros et al. has chosen to refer to these risk estimates collectively as CVD risks. This brochure follows the terminology used by Athyros et al.”

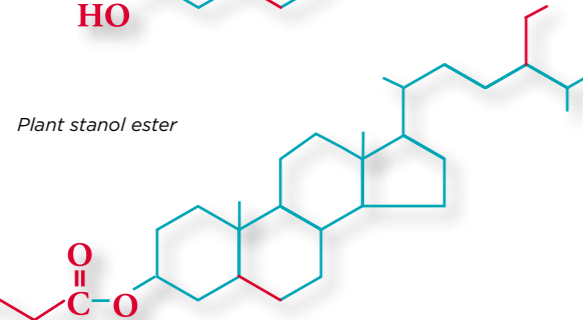
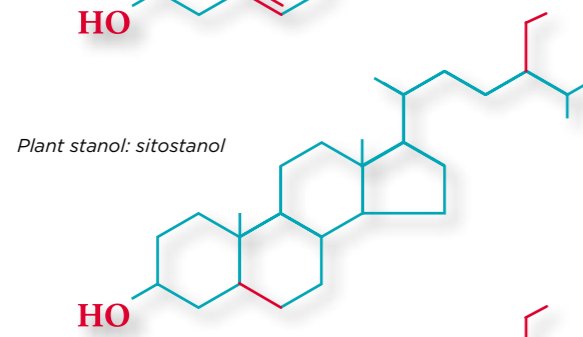
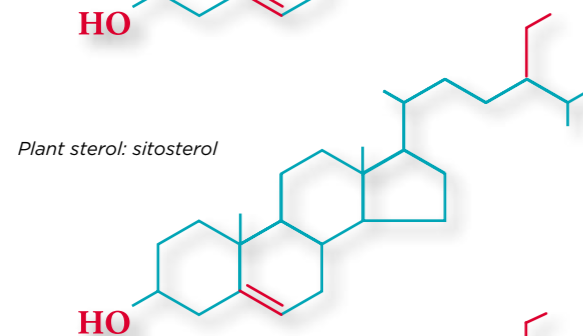
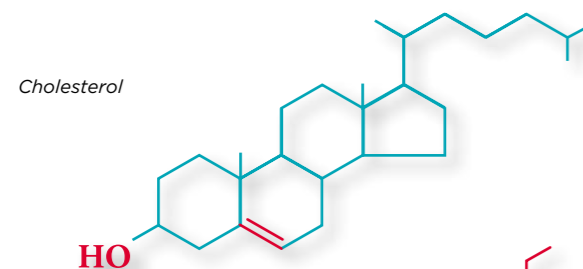
*Miettinen et al. 1995
Hallikainen et al. 2008
Athyros et al. 2011*

Figure 1.
Use of Plant stanol ester (2 g of plant stanols per day) reduced the estimated CAD risk equally but more rapidly than a Mediterranean diet (*p<0.01 compared with a control diet) (Athyros et al. 2011).



Plant stanols in nutrition

Gylling et al. 1997
Piironen et al. 2000
Ostlund 2002
Katan et al. 2003



Plant stanols and sterols are cholesterol-like compounds, with only slight differences in their molecular structures. Major natural sources of plant stanols and sterols are cereals and vegetable oils. In a typical Western diet, the daily intake of plant stanols varies between 30 and 50 mg and that of plant sterols between 150 and 400 mg. Cholesterol intake generally ranges from some 300 to 500 mg per day.

Plant stanols and sterols have been shown to reduce the absorption of cholesterol from the digestive tract. This applies to both dietary and biliary cholesterol.

Intakes of plant stanols and sterols from an ordinary diet are not sufficient to effectively lower serum cholesterol, and this is why they are added to food. Plant stanols are added to Benecol® products as Plant stanol ester, in which fatty acids from a vegetable oil have been attached to the plant stanol. With the use of Plant stanol ester, both the good sensory property of Benecol products and their effective cholesterol lowering effect can be ensured.

Small structural differences have a considerable effect on the behaviour of different sterols in the body. Approximately 50 % of cholesterol is absorbed whereas plant sterols, and especially plant stanols, are much less absorbed. When the diet includes foods enriched with plant sterols or stanols, some 0.5-2 % of plant sterols and only 0.04-0.2 % of plant stanols are absorbed. Plant stanols reduce the absorption of both cholesterol and plant sterols. They leave the body rapidly and effectively.

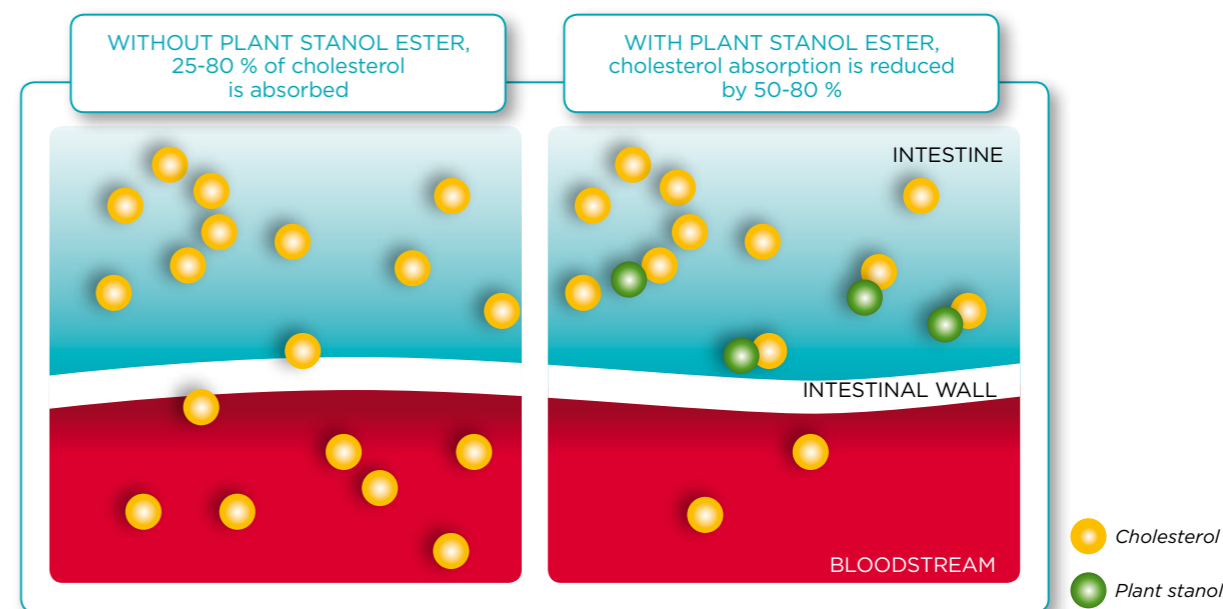
Mechanism of action of Plant stanol ester

Plant stanol ester is hydrolysed into plant stanols and fatty acids in the digestive tract where plant stanols block the absorption of cholesterol. Due to the structural similarity of plant stanols and cholesterol, plant stanols can replace cholesterol from so-called mixed micelles. A pre-requisite for cholesterol absorption is that it is solubilised into the lipid core of the mixed micelles. Additionally, plant stanols may activate certain transport proteins in the enterocytes. These transport proteins excrete cholesterol from an enterocyte back into the intestinal lumen and out of the body. Fatty acid part of Plant stanol ester is absorbed into the body

in the same way as other fatty acids in the food. Plant stanol ester reduces the absorption of both dietary and biliary cholesterol. When Benecol® products are included in the diet, cholesterol is excreted from the body by some 250 mg / day above the normal quantity.

Reduced cholesterol absorption results in significant reduction in serum total and LDL cholesterol concentrations. The use of Plant stanol ester does not cause any changes to the size distribution of the LDL lipoprotein particles.

Ilkeda et al. 1989
Miettinen and Kesäniemi 1989
Heinemann et al. 1991
Blomqvist et al. 1993
Gylling et al. 1997
Plat and Mensink 2002
Plat and Mensink 2009



Effective and easy dietary solution to lower cholesterol

According to research, two grams of plant stanols per day (as Plant stanol ester) is enough to produce a clinically relevant cholesterol lowering effect. For this reason sufficient amount of Benecol® product should be consumed daily.

In most studies, the daily dose of plant stanols has been consumed with two or more meals. However, the LDL cholesterol lowering is equally effective when the daily dose is taken as one serving as part of a meal.

Total and LDL cholesterol lowering effects have been shown

- in normal, healthy and hypercholesterolemic individuals
- in women, men and children of different ages
- in patients with coronary artery disease
- in patients with type 1 and 2 diabetes
- in patients with metabolic syndrome
- in patients with kidney transplantation
- as part of ordinary Western diets
- as part of a strict cholesterol lowering diet
- together with cholesterol lowering statin medication

In most studies HDL cholesterol and triglyceride levels have remained unchanged. However, recent evidence strongly indicates that a regular use of Plant stanol ester as part of the diet reduces elevated triglyceride levels.

Plat et al. 2000
Gylling and Miettinen 1994
Gylling et al. 1997
Andersson et al. 1999
Hallikainen and Uusitupa 1999
Blair et al. 2000
Hallikainen et al. 2000
Miettinen et al. 2000
Tammi et al. 2000
Vuorio et al. 2000
Mensink et al. 2002
Hallikainen et al. 2008
Naumann et al. 2008
Plat et al. 2009
Sutton et al. 2009
Theuwissen et al. 2009
Gylling et al. 2010
Mensink et al. 2010



2 grams per day with meals

EFFECTIVE IN DIFFERENT FOOD MATRICES (2 G PLANT STANOLS A DAY)

Product	Plant stanol g / day	LDL change (%)	Reference
Margarine	2	-13	Hallikainen et al. 2000
Low-fat spread	2	-14	Hallikainen and Uusitupa 1999
Yoghurt drink	2	-13*	Plat et al. 2009
Yoghurt	2	-10	Huyn et al. 2005
Pasta	2	-11	Salo and Wester 2005

* non-HDL cholesterol

Effective, fast and sustained cholesterol reduction

Miettinen et al. 1995
Hallikainen and Uusitupa 1999
Blair et al. 2000
Hallikainen et al. 2002
Mensink et al. 2002
Fransen et al. 2007
de Jong 2007
de Jong et al. 2008
Hallikainen et al. 2008

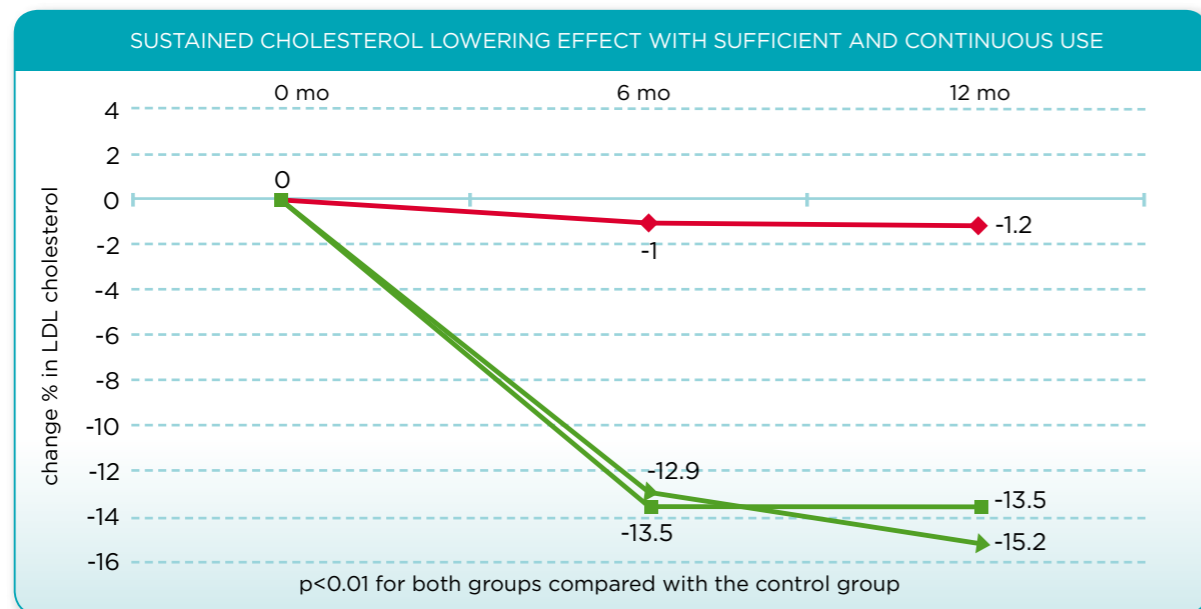
The effect of Plant stanol ester can be seen in the cholesterol levels already after two or three week's daily consumption. Most importantly, the effect is lasting when Plant stanol ester is consumed in sufficient amounts and continuously on a daily basis.

The sustained cholesterol lowering effect of Plant stanol ester has been shown in two long-term double-blind, placebo controlled clinical trials.

Durations of the intervention periods in the studies were 12 and 18 months. The sustained effect was also shown in a 5-year follow-up study, during which consumers used Benecol® products as part of their normal diet.

Studies show that the daily intake of 2 g plant stanols (as Plant stanol ester) reduces serum LDL cholesterol by 10-15 %.

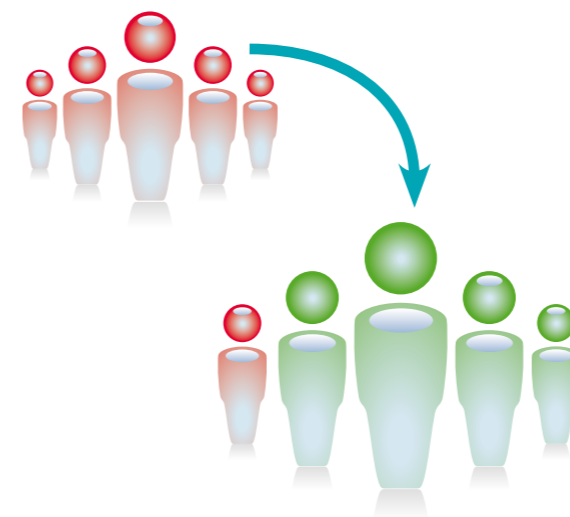
Figure 2.
LDL cholesterol lowering effect of Plant stanol ester is effective and sustained (adapted from Miettinen et al. 1995).



Four out of five hypercholesterolemic individuals achieved the cholesterol target level by using Benecol® products

When cholesterol levels are only mildly elevated, dietary changes are often sufficient. According to a recent research, 80 % of mildly hypercholesterolemic subjects achieved the total cholesterol target level (NCEP guideline: <math>< 200 \text{ mg/dl}</math>, <math>< 5.2 \text{ mmol/l}</math>) by including Plant stanol ester spread (2 g plant stanols / day) in their daily diet.

Athyros et al. 2011
NCEP Guideline: US National Cholesterol Education Program NCEP, 2002.



Plant stanol ester and enhanced efficacy

Naumann et al. 2008
Gylling et al. 2010
Mensink et al. 2010

Until recently it has generally been thought that increasing the intake of plant stanols or sterols to greater than 2 grams per day does not further enhance the cholesterol lowering effect. However, this assumption is not valid for Plant stanol ester. According to the most recent studies, the cholesterol lowering effect of plant stanols is further increased with daily doses higher than the current

recommendation: two studies showed that a daily intake of 9 g plant stanols lowered LDL cholesterol by over 17 % without any adverse effects. Currently there is no corresponding data available for plant sterols. Thus, the new research data showing a linear dose-response concerns only plant stanols and Benecol® products.

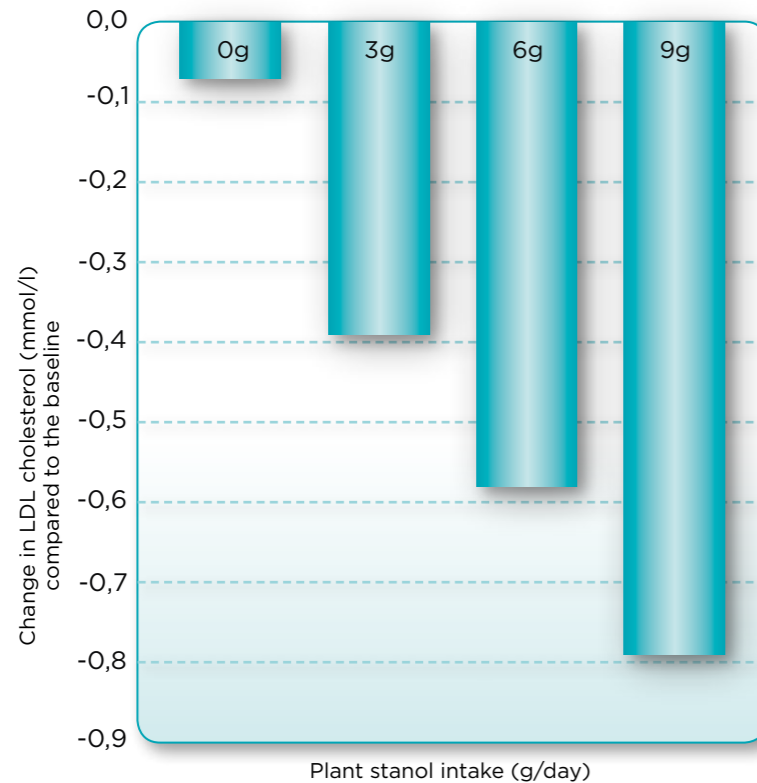


Figure 3.
LDL cholesterol lowering effect is enhanced with the increased daily intake of Plant stanol ester (Mensink et al. 2010).

Significantly better maximal efficacy with Benecol® products

Recent published studies show that Plant stanol ester reduces serum LDL cholesterol dose dependently over a broad range of daily intakes of plant stanols. Thus, the earlier assumptions that no further serum LDL cholesterol is obtainable with higher than currently recommended daily intakes of plant stanols and that Plant stanol ester and plant sterol ester show equal cholesterol lowering efficacy appear to be wrong.

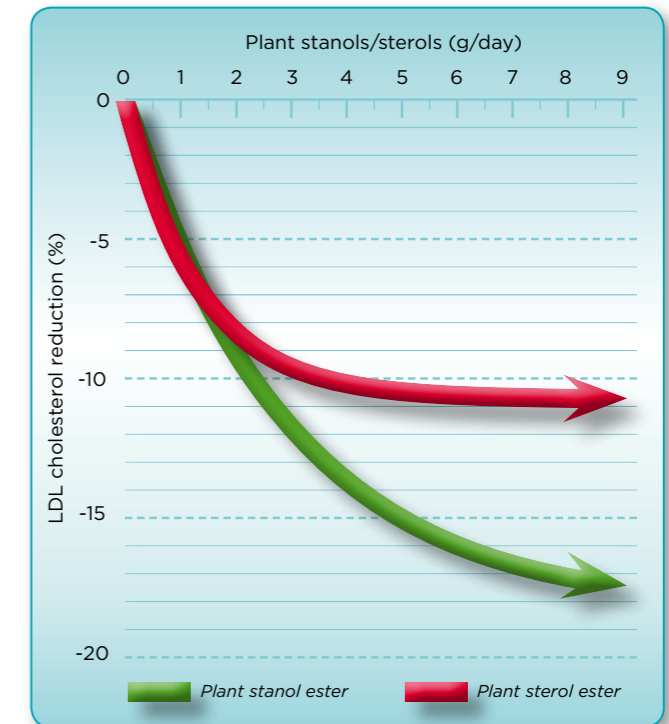
The aim of the meta-analysis of Musa-Veloso et al. 2011a and 2011b was to determine if plant stanols and plant sterols differ with respect to their LDL cholesterol lowering efficacy across a continuous dose range. It was shown that the maximal LDL cholesterol lowering efficacy of Plant stanol ester is significantly better than that of plant sterol ester (-18.3 % vs -10.7 %). Plant stanol ester in Benecol® products reduces LDL cholesterol dose-dependently. The same effect was not recorded for plant sterols.

The relationship between reduction in LDL cholesterol and a reduced risk of coronary heart disease is near to linear. For every 1 % reduction in LDL cholesterol concentration, there is a corresponding 1-2 % decrease in the risk of CHD.

Daily consumption of Plant stanol ester containing Benecol products will help your patients to reach their cholesterol targets.

Mensink et al. 2010
Musa-Veloso et al. 2011a
Musa-Veloso et al. 2011b
Grundy et al. 2004
Robinson et al. 2005
LaRosa 2007
Clark 1986

Figure 4.
The estimated relative LDL cholesterol lowering efficacy of Plant stanol ester and plant sterol ester. Results from a meta-analysis based on end of treatment data for weighted strata. (Musa-Veloso et al. 2011b)



Plant stanol ester, an effective dietary way to lower cholesterol

Modified from Model of steps in TLC, JAMA 2001; 285:No. 19
Musa Veloso et al 2011

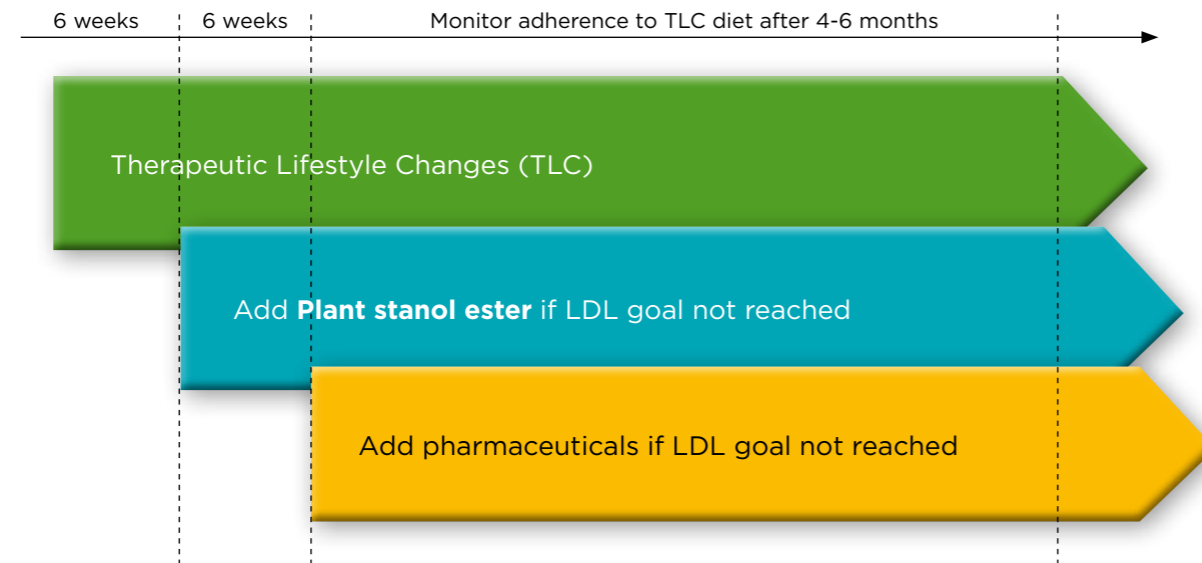
In the National Cholesterol Education Program (NCEP) a Therapeutic Lifestyle Changes (TLC) approach to reduce CHD is recommended. It includes following steps:

Visit 1: To initiate TLC, intakes of saturated fats and cholesterol are reduced first to lower LDL cholesterol. Also physical activity is encouraged.

Visit 2: After 6 weeks, the LDL response is determined; if the LDL cholesterol goal has not been achieved, other therapeutic options for LDL lowering such as plant stanols and viscous fiber can be added.

Visit 3: After maximum reduction of LDL cholesterol with dietary therapy, emphasis shifts to management of the metabolic syndrome and associated lipid risk factors.

It is important to note that healthy nutrition and physical activity always should be part of the actions when aiming to reduce CHD.



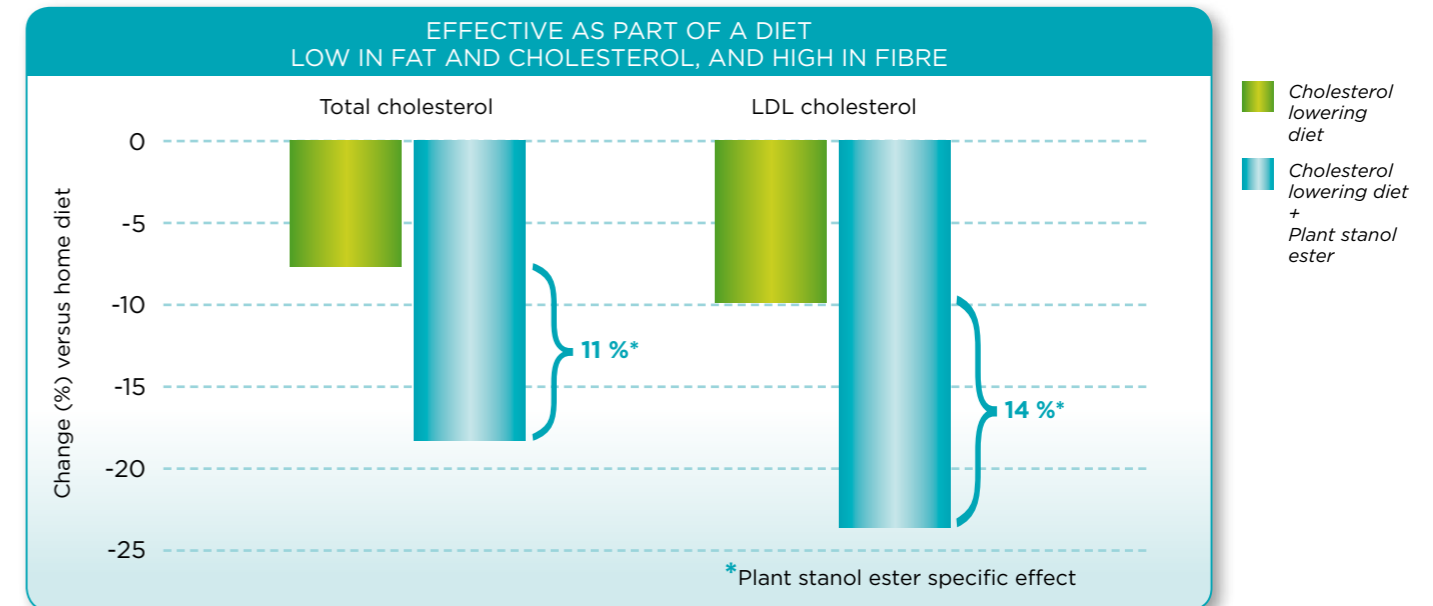
Effective in all diets

Plant stanol ester is effective when used as part of different kind of diets; it works with both “typical Western” diets and recommended diets. Therefore, Benecol products can be the first solution to a cholesterol lowering diet or an effective addition to an already healthy diet.



Miettinen et al. 1995
Andersson et al. 1999
Hallikainen and Uusitupa 1999
Athyros et al. 2011

Figure 5. Plant stanol ester further reduced serum total and LDL cholesterol when it was incorporated into a strict cholesterol-lowering diet (Hallikainen and Uusitupa 1999).



Complementing the effect of statin medication

Blair et al. 2000
 Castro Cabezas et al. 2006
 de Jong et al. 2008
 Plat et al. 2009

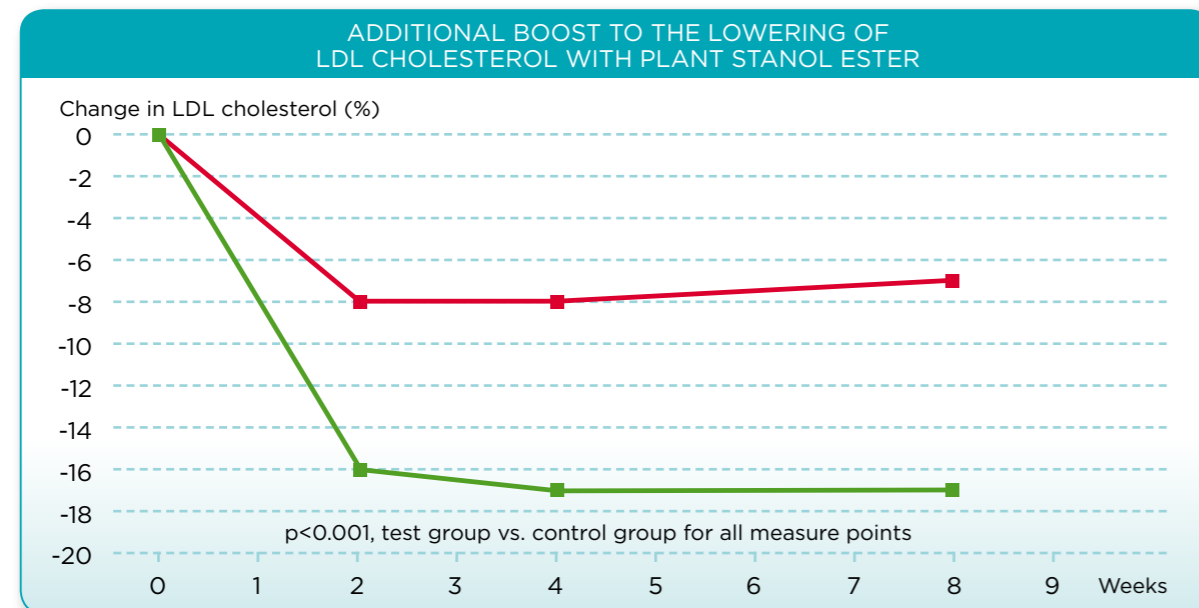
According to the international guidelines, diet and other lifestyle changes are always the basis of therapy for dyslipidemia. In some cases, however, cholesterol lowering medication is required. Statins are the most widely used cholesterol lowering medications.

Statins inhibit the synthesis of cholesterol in the liver while Plant stanol ester blocks the absorption of cholesterol from the digestive tract. Because of

the different mechanisms of action, the cholesterol lowering effects of statins and Plant stanol ester are additive. Adding Plant stanol ester to the diet of subjects already on statin medication further reduces serum LDL cholesterol by up to 10-12 %.

By adding Benecol® products to their diets statin users can further decrease their cholesterol levels and may avoid an increase in the statin dose.

Figure 6. Incorporating a margarine-type spread enriched with Plant stanol ester into the diet of statin users further reduced LDL cholesterol by 17 % and compared with the control spread by 10 % (Blair et al. 2000).



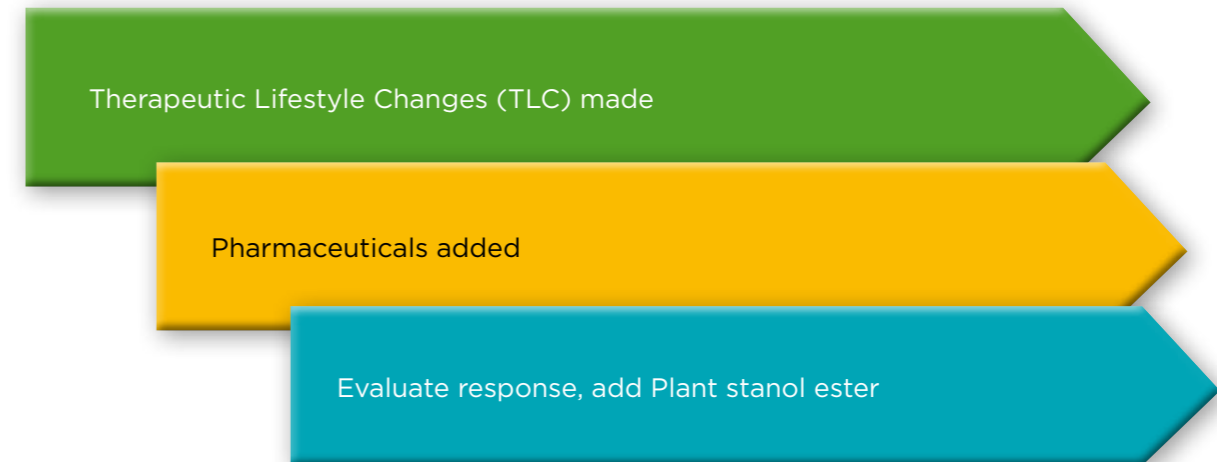
Combining statin treatment with Plant stanol ester gives additive cholesterol reduction

For patients already on statins, adding Plant stanol ester provides additional $\geq 10\%$ effect in LDL reduction.

The additive cholesterol lowering effect of Plant stanol ester has been shown to persist also in long-term in patients on stable statin treatment.

A greater reduction of cholesterol lowering can be achieved by combining Plant stanol ester with statin treatment than by doubling the dose of statin. Generally the doubling of statin dose produces 6 % additional cholesterol lowering.

Blair et al. 2000
 De Jong et al. 2008
 Dujovne. 1997
 Bradford et al. 1991
 Jacobson 1997

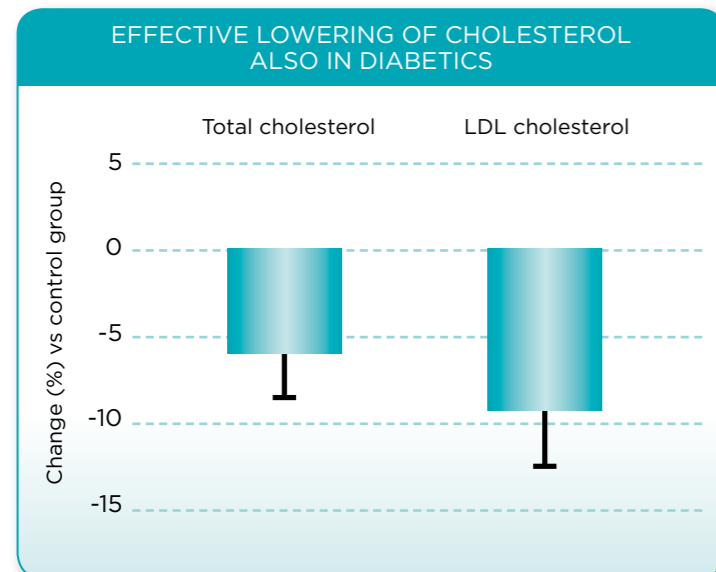


Diabetes

Especially type 2 diabetes is increasing rapidly worldwide as population age and unhealthy lifestyles are adopted. Diabetics have a multiple risk of developing CVD compared with healthy individuals. This is why it is very important to treat their risk factors as effectively as possible. Plant stanol ester effectively reduces serum cholesterol also in type 1 and type 2 diabetics. Plant stanol ester has been recognized in the guidelines of the American Diabetes Association & American College of Cardiology Foundation.

Gylling and Miettinen 1994
 Gylling and Miettinen 1995
 Gylling and Miettinen 1996
 de Jong 2007
 Hallikainen et al. 2008
 Guidelines of the American Diabetes Association & American College of Cardiology Foundation (2008)

Figure 7. Plant stanol ester effectively reduced serum total and LDL cholesterol in men with type 2 diabetes ($p < 0.05$) (Gylling and Miettinen 1994).

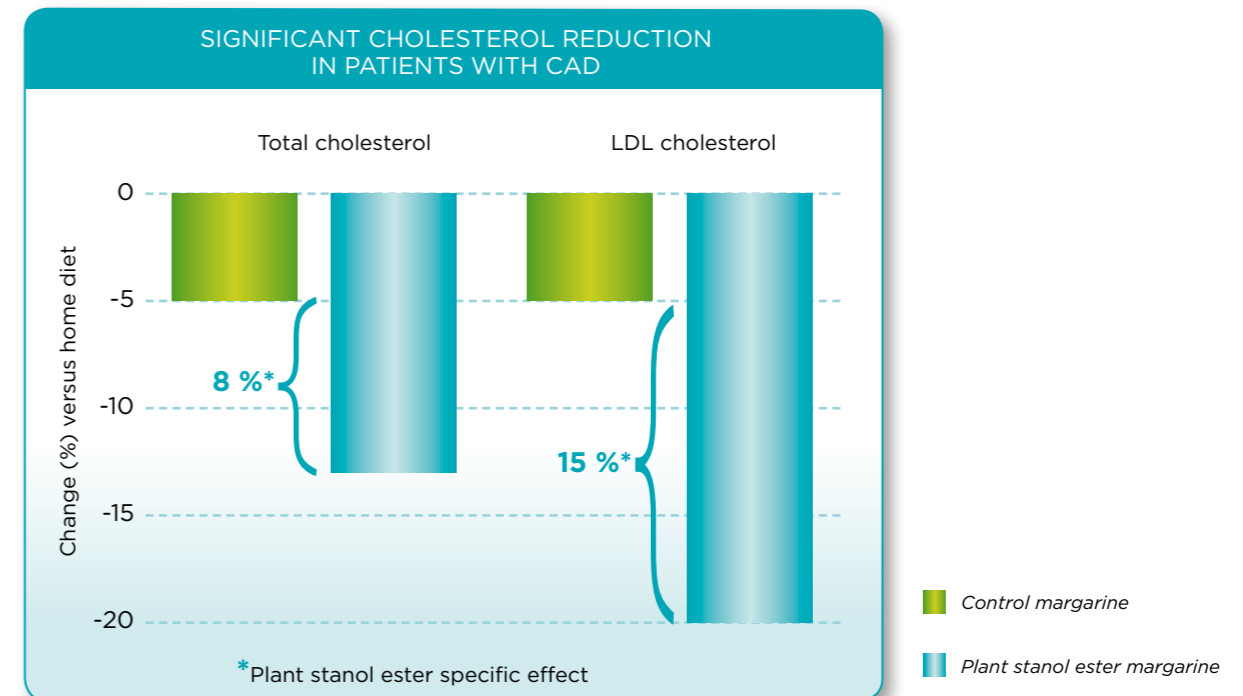


Patients with coronary artery disease

It is important to reduce all modifiable risk factors and to prevent the recurrence of a cardiac event especially in patients with existing cardiovascular disease. Plant stanol ester is an effective means of lowering serum total and LDL cholesterol also in these individuals.

Gylling et al. 1997
 Gylling et al. 2006

Figure 8. Margarine containing Plant stanol ester effectively reduced serum total and LDL cholesterol in CAD patients ($p < 0.05$ or lower) (Gylling et al 1997).



Familial hypercholesterolemia (FH)

The efficacy and safety of consuming products enriched with Plant stanol ester has been shown with both adults and children with FH. In a study with patients suffering from heterozygous FH, spread containing Plant stanol ester lowered serum LDL cholesterol by 11 % and in combination with statin medication by 20 %. According to a recent meta-analysis, Plant stanol ester may offer an effective adjunct to the cholesterol lowering treatment of FH patients.



Healthy Children

Atherosclerosis may start to develop early in life so it is important to follow a heart-healthy diet early in childhood. An ordinary healthy diet is sufficient for most children and Plant stanol ester is not generally recommended for healthy children younger than five years.

Safety

More than 60 published clinical studies, extensive safety studies, assessments conducted by food authorities, and the long experience of Benecol® products on the market have shown that the consumption of Plant stanol ester is safe, well-tolerated and without adverse effects.

Plant stanols are practically not absorbed, and are effectively excreted from the body. Levels of plant stanols in the blood remain very low even after continuous long-term use of Benecol products, and also when the daily intake of plant stanol exceeds the currently recommended 2 grams per day (up to 9 g per day).

Use of Plant stanol ester does not change serum concentrations of vitamins A, D, E and K. Serum concentration of β -carotene may be reduced, but it still remains within the reference values. It is also possible to prevent the reduction of β -carotene concentration by eating vegetables, berries and fruit according to nutrition guidelines.

Miettinen et al. 2000
Noakes et al. 2002
de Jong 2007
Mensink et al. 2010
Gylling et al. 2010



Recommended by international and national expert bodies

According to international guidelines, dietary intervention is the cornerstone of therapy for dyslipidemia. The diet also plays an important role when cholesterol medication has already been initiated since the diet has other beneficial effects beyond its effects on lipid concentrations.

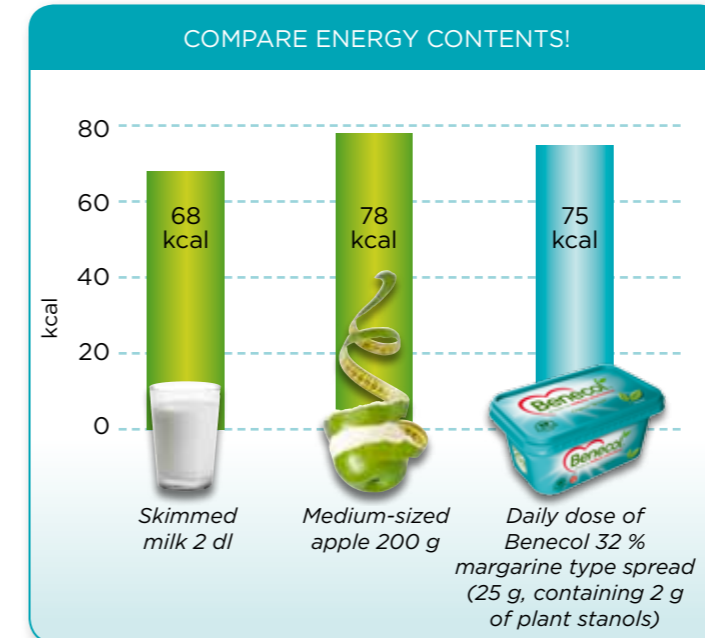
Several international and national organisations recommend the consumption of foods containing Plant stanol ester as part of cholesterol lowering diet. Examples of these are:

- *US National Cholesterol Education Program NCEP (2002)*
- *European Union Scientific Committee on Foods (2002)*
- *International Atherosclerosis Society (2003)*
- *International Lipid Information Bureau (2003)*
- *WHO/FAO (2003)*
- *American Heart Association & American College of Cardiology (2006)*
- *Fourth joint task force of European and Other Societies on Cardiovascular Disease (2007)*
- *American Diabetes Association (2008)*
- *American Heart Association & American College of Cardiology Foundation (2008)*
- *American Academy of Pediatrics (2008)*
- *Finnish Diabetes Association: Nutrition recommendation for diabetes*
- *Dyslipidemias: Current Care Guideline, Finland (2009)*
- *Australian Heart Foundation (2009)*
- *The Finnish National Nutrition Council: Guidelines for nutrition care (2010)*



Summary

- Plant stanol ester, the cholesterol lowering ingredient in Benecol® products, reduces serum LDL cholesterol by 10-15 %.
- Until now a daily intake of 2 g plant stanols has been considered sufficient. The most recent research results indicate that lowering of cholesterol is further enhanced by using higher daily intakes, up to 9 g per day.
- Use of Benecol products is recommended as part of meals and a healthy diet.
- The cholesterol lowering effect is lasting when sufficient amounts of Benecol products are consumed on a daily basis.
- Plant stanol ester is an effective, easy and safe dietary solution to lower cholesterol.
- Several international guidelines recommend the use of foods enriched with Plant stanol ester as part of dietary therapy of elevated cholesterol.
- Benecol products taste good and they fit extremely well into a heart-healthy diet.



Literature

American Academy of Pediatrics. *Pediatrics* 2008; 122: 198-208.

American Diabetes Association & American College of Cardiology Foundation. *J Am Coll Cardiol* 2008; 51: 1512-24.

American Diabetes Association. *Diabetes Care* 2008 31: S61-S78.

American Heart Association / American College of Cardiology. *Circulation* 2006; 113: 2363-72.

Andersson A, Karlström B, Mohsen R, Vessby B. *Eur Heart J Suppl* 1999; 1: S80-S90.

Athyros VG, Kakafika AI, Papageorgiou AA, Tziomalos K, Peletidou A, Vosikis C, Karagiannis A, Mikhailidis DP. *Nutr Metab Cardiovasc Dis* 2011; 21(3): 213-221.

Blair SN, Capuzzi DM, Gottlieb SO, Nguyen T, Morgan JM, Cater NB. *Am J Cardiol* 2000; 86: 46-52.

Blomqvist SM, Jauhiainen M, van Tol A, Hyvönen M, Torstila I, Vanhanen HT, Miettinen TA, Ehnholm C. *Nutr Metab Cardiovasc Dis* 1993; 3: 158-164.

Bradford RH, et al. *Arch Intern Med* 1991; 151:43- 49.

Castro Cabezas M, de Vries JH, van Oostrom AJ, lestra J, van Staveren WA. *J Am Diet Assoc* 2006; 106: 1564-1569.

Clark. *J. Natl. Med. Assoc.* 78 (1986) 743-751.

Dujovne CA. New lipid lowering drugs and new effects of old drugs. *Curr Opin Lipidol* 1997;8:362-368.

Dyslipidaemias: Current care guidelines, Finland (2009).

European guidelines on cardiovascular disease prevention in clinical practice, *Atherosclerosis* 194 (2007).

European Union Scientific Committee on Foods 2002. General view of the Scientific Committee on Food on the long-term effects of the intake of elevated levels of phytosterols from multiple dietary sources, with particular attention to the effects on β -carotene. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: *JAMA.* 2001; 285 (19):2486-2497.

Fourth joint task force of European and Other Societies on Cardiovascular Disease. *European Journal of Cardiovascular Prevention & Rehabilitation* 2007; 14 (suppl 2):S1-S113.

Fransen HP, de Jong N, Wolfs M, Verhagen H, Verschuren WM, Lütjohann D, von Bergmann K, Plat J, Mensink RP. *J Nutr* 2007; 137: 1301-1306.

Grundy et al. *Circulation* 110 (2004) 227-239.

Gylling H, Hallikainen M, Nissinen MJ, Miettinen TA. *Clinical Nutrition* 2010; 29: 112-118.

Gylling H, Miettinen T. *Diabetologia.* 1994; 37: 773-80.

Gylling H, Miettinen TA. *Atherosclerosis* 1995; 117: 305-308.

Gylling H, Miettinen TA. *J Lipid Res* 1996; 37: 1776-1785.

Gylling H, Radhakrishnan R, Miettinen TA. *Circulation* 1997; 96: 4226-4231.

Gylling H, Rajaratnam RA, Vartiainen E, Puska P, Miettinen TA. *Menopause* 2006; 13: 286-293.

Gylling H, Siimes M, Miettinen TA. *J Lipid Res* 1995; 36: 1807-1812.

Hallikainen M, Lyyra-Laitinen T, Laitinen T, Moilanen L, Miettinen TA, Gylling H. *Atherosclerosis* 2008; 199: 432-439.

Hallikainen MA, Sarkkinen ES, Gylling H, Erkkilä AT, Uusitupa MI. *Eur J Clin Nutr* 2000; 54: 715-725.

Hallikainen MA, Sarkkinen E, Wester I, Uusitupa M. *BMC Cardiovascular Disorders* 2002; 2: 14.

Hallikainen MA, Uusitupa MI. *Am J Clin Nutr* 1999; 69: 403-410.

Heinemann T, Kullak-Ublick GA, Pietruck B, von Bergmann K. *Eur J Clin Pharmacol* 1991; 40 Suppl 1: S59-S63.

Hyun JY, Oh YK, Joo BK, Lee JH, Jang Y, Liponkoski L, Salo P. *Nutrition Research* 2005; 25: 743-753.

Ikeda I, Tanabe Y, Sugano M. *J Nutr Sci Vitaminol* 1989; 35: 361-369.

International Atherosclerosis Society 2003. *Harmonized Guidelines on Prevention of Atherosclerotic Cardiovascular Diseases.*

International Lipid Information Bureau 2003. *Gotto AM et al. Dyslipidemia and Coronary Heart Disease, 3. edition.*

Jacobson TA. *Curr Opin Lipidol* 1997;8:369 -374.

Jakulj L, Vissers MN, Rodenburg J, Wiegman A, Trip MD, Kastelein JJ. *J Pediatr* 2006; 148: 495-500.

Commission regulation (EC) No 983/2009, amended by (EU) No 376/2010.

de Jong A. *Doctoral Dissertation, Maastricht University* 2007.

de Jong A, Plat J, Bast A, Godschalk RW, Basu S, Mensink RP. *Eur J Clin Nutr* 2008; 62: 263-273.

de Jong A, Plat J, Lütjohann D, Mensink RP. *Br J Nutr* 2008;100:937-41.

Katan MB, Grundy SM, Jones P ym. *Mayo Clinic Proc* 2003; 78: 965-978.

Ketomäki A, Gylling H, Miettinen TA. *Clin Chim Acta* 2005; 353: 75-86.

LaRosa. *Am. J. Cardiol.* 100 (2007) 240-242.

Mensink RP, Ebbing S, Lindhout M, Plat J, van Heugten MMA. *Atherosclerosis* 2002; 160: 205-213.

Mensink RP, de Jong A, Lütjohann D, Haenen GRMM, Plat J. *Am J Clin Nutr* 2010; 92: 24-33.

Miettinen TA, Kesäniemi YA. *Am J Clin Nutr* 1989; 49: 629-635.

Miettinen TA, Puska P, Gylling H, Vanhanen H, Vartiainen T. *N Engl J Med* 1995; 333: 1308-1312.

Miettinen TA, Vuoristo M, Nissinen M, Järvinen HJ, Gylling H. *Am J Clin Nutr* 2000; 71: 1095-1102.

Musa Veloso et al, *PLEFA, 2011a, 2011b.*

Moruisi KG, Oosthuizen W, Opperman AM. *J Am Coll Nutr* 2006; 25: 41-48.

Naumann E, Plat J, Kester AD, Mensink RP. *J Am Coll Nutr* 2008; 27: 117-26.

Noakes M, Clifton P, Ntanos F, Shrapnel W, Record I, McInerney J. *Am J Clin Nutr* 2002; 75: 79-86.

Ostlund RE Jr. *Annu Rev Nutr* 2002; 22: 533-549.

Piironen V, Toivo J, Lampi A-M. *J Food Compos Anal* 2000; 13: 619-624.

Plat J, Brufau G, Dallinga-Thie GM, Dasselaar M, Mensink RP. *J Nutr* 2009; 139: 1143-1149.

Plat J, van Onselen ENM, van Heugten MMA, Mensink RP. *Eur J Clin Nutr* 2000; 54: 671-667.

Plat J, Mensink RP. *FASEB J* 2002; 16: 1248-1253.

Plat J, Mensink RP. *Lipids* 2009; 44(12): 1149-1153.

Robinson et al. *J. Am. Coll. Cardiol.* 46 (2005) 1855- 1862.

Salo P, Wester P. *Am J Cardiol* 2005; 96: 51-54.

Sutton D, Davey T, Venkatraman G, Hart K. *J Ren Care* 2009; 35: 42-47.

Tammi A, Rönnemaa R, Gylling H, Rask-Nissilä L, Viikari J, Tuominen J, Pulkki K, Simell O. *J Pediatr* 2000; 136: 503-510.

Theuwissen E, Plat J, van der Kallen CJ, van Greevenbroek MM, Mensink RP. *Lipids* 2009; 44(12): 1131-1140.

US National Cholesterol Education Program NCEP. *NIH Publication No. 02-5215. September 2002, updated 2004.*

Vuorio AF, Gylling H, Turtola H, Kontula K, Ketonen P, Miettinen TA. *Arterioscler Thromb Vasc Biol* 2000; 20: 500-506.

WHO/FAO Expert Consultation. *WHO Technical Report Series* 2003, No.797 - TRS 797.

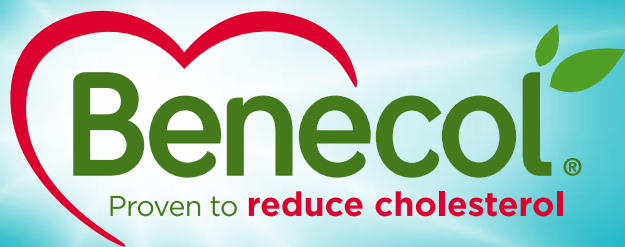
WHO: *Fact sheet of cardiovascular diseases* (2009).

Williams CL, Bollella MC, Strobino BA, Boccia L, Campanaro L. *J Am Coll Nutr* 1999; A sufficient amount of plant stanol (2 g) is obtained by a daily use of one of the following.

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