Plant Sterol
Scientific Review

This list includes publications of studies that investigated the cholesterol-lowering efficacy of plant sterols which were commissioned/initiated/sponsored by Unilever or for which the test products with added plant sterols were provided by Unilever. A description of each study with the main findings is provided. This list is organized chronologically. Studies are categorized based on the food format used: spreads/margarines, dairy products (milk, yoghurt and yoghurt drinks) and other food formats. A separate category is created for studies that used plant sterols as part of a dietary approach.

Efficacy of Flora ProActiv

SPREADS

Plant sterol-enriched margarines and reduction of plasma total- and LDL-cholesterol concentrations in normocholesterolaemic and mildly hypercholesterolaemic subjects.
Weststrate JA et al., Eur J Clin Nutr 1998; 52(5): 334-343.
In a randomized, double-blind, placebo-controlled study, 95 healthy normocholesterolaemic or mildly hypercholesterolaemic subjects consumed 30 g plant sterol-enriched spread daily (3.2 g plant sterols/day) as part of their normal diet over a 3.5 week period. Using regular Flora/Flora as a control spread, plasma total and LDL-cholesterol concentrations were reduced by 8% and 13% respectively without affecting HDL-cholesterol concentrations.

Spreads enriched with three different levels of vegetable oil sterols and the degree of cholesterol lowering in normo-cholesterolaemic and mildly hypercholesterolaemic subjects.
Hendriks HFJ et al., Eur J Clin Nutr 1999; 53(4): 319-327.
The dose response relationship between cholesterol-lowering and intake of plant sterols was investigated in this randomized double-blind placebo-controlled study of 100 subjects using three experimental spreads fortified with three different concentrations of plant sterols. The daily intake of plant sterols was 0.8 g, 1.6 g or 3.2 g taken in 25 g of spread over a period of 3.5 weeks. Compared to control (regular Flora), the average LDL-cholesterol reduction achieved as a result of enriching the spread with different plant sterols dosages was 6.7%, 8.5% and 9.9%, respectively, without seriously affecting lipid soluble (pro)vitamins. The three dosages of plant sterols significantly reduced LDL-cholesterol, whereas no significant differences were found between the three doses.

Modulation of plasma lipid levels and cholesterol kinetics by phytosterol versus phytostanol esters.
Jones PJ et al., J Lipid Res 2000; 41(5): 697-705.
In a randomized, crossover, double-blind study of 15 hypercholesterolaemic males using 1.8 g of plant sterols/stanols per day (23 g spread) as part of a healthy diet, effects on plasma cholesterol, cholesterol absorption and synthesis were determined. After 3 weeks of consuming the plant sterol-enriched spread, there was a significant 13% reduction in LDL-cholesterol and for plant stanols a 6% reduction in LDL-cholesterol. The plant sterol and stanol esters lowered circulating total- and LDL-cholesterol by suppression of cholesterol absorption (-36% for sterol spread and -26% for stanol spread) and enhanced cholesterol synthesis. Both spreads are efficacious in reducing circulating cholesterol concentrations in hypercholesterolemic subjects.

Safety and tolerability of esterified phytosterols administered in reduced-fat spread and salad dressing to healthy adult men and women.
Davidson, MH et al., J Am Coll Nutr 2001; 20(4): 307-319.
In a randomized, double-blind, placebo-controlled, parallel study, 84 free-living subjects consumed for 8 weeks reduced-fat spread (14 g/d) and salad dressing (46 g/d) providing either 0, 3, 6 or 9 g/d of plant sterols in their ester form. Total cholesterol non-significantly decreased by 3.9%, 0.9% and 4.6% and LDL-cholesterol by 3.7%, 1.5%, and 7.7%, compared with control in the 3, 6, and 9 g/d groups, respectively, with no significant differences between the 3 plant sterol groups. These effects were less pronounced than expected, but may have been related in part to the low baseline cholesterol concentrations of the participants in this study. HDL-cholesterol levels were not significantly increased by 4.8%, 3.3%, and 7.8% with the consumption of 3, 6 and 9 g/d plant sterols vs. control, respectively. As a result, doses of 3, 6 and 9 g/d plant sterols lowered the total cholesterol:HDL-cholesterol ratio by 8.3%, 5.4%, and 12.2% compared with control, and this effect reached statistical significance for the 9 g/d group. In addition with plasma lipid, blood concentrations of fat soluble vitamins, carotenoids and plant sterols were measured. All fat-soluble vitamins (retinol, 25-hydroxyvitamin D, alpha-tocopherol, gamma-tocopherol and phylloquinone) remained within normal reference ranges. Among the carotenoids, alpha- and trans-beta-carotene concentrations were reduced in the 9.0 g/d group vs. control, but all carotenoids remained within the normal range during the study. Significant increases in campesterol were observed in all groups consuming plant sterols vs. control, but beta-sitosterol concentrations were not significantly affected.

Lipid responses to plant sterol-enriched reduced fat spreads incorporated into a National Cholesterol Education Program Step I diet.
Maki KC et al., Am J Clin Nutr 2001; 74(1): 33-43.
This study was designed as a randomized, double-blind, placebo-controlled, parallel-group study of 5 weeks including 224 subjects with an initial LDL-cholesterol level between 3.4 and 5.2 mmol/L. Subjects followed a low-fat Step I diet from the National Cholesterol Education Programme (NCEP). The groups received 14g of reduced-fat spread either enriched with a low dose of plant sterol esters (1.1 g plant sterols/day) or a higher dose (2.2 g plant sterols/day), or the control spread. Subjects in the low- and high-sterol groups who consumed ≥80% of the scheduled servings had total cholesterol reductions of 5.2% and 6.6%, and LDL-cholesterol reductions of 7.6% and 8.1% respectively. This study showed that a reduced-fat spread containing plant sterol esters incorporated into a low-fat NCEP diet is a beneficial adjunct in the dietary management of hypercholesterolemia.

Randomized controlled trial of use by hypercholesterolaemic patients of a vegetable oil sterol-enriched fat spread.
Neil HAW et al., Atherosclerosis 2001; 156(2): 329-337.
A randomized, double-blind, placebo-controlled, crossover trial over two 8-week periods was undertaken in 58 subjects with hypercholesterolemia. The intake of spread was 25 g/day (2.5 g plant sterols/day). Significant LDL-cholesterol reduction from plant sterol-enriched spread was 14% at 4 weeks and 10% at 8 weeks compared to control. No difference in the response was observed between hypercholesterolaemic patients prescribed statins and those not taking lipid-lowering drug therapy. This study concludes that plant sterols may be a useful additive therapy in the treatment of hypercholesterolaemic patients.

Plant sterol-enriched margarine lowers plasma LDL-cholesterol in hyperlipidemic subjects with low cholesterol intake: effect of fibrate treatment.
Nigon F et al., Clin Chem Lab Med 2001; 39(7): 634-40.
This study was designed as a randomized, double-blind placebo-controlled 2-period crossover trial with 53 hypercholesterolemic patients with or without fibrate treatment. The aim of the study was to test the cholesterol-lowering effect of a plant sterol-enriched spread in hypercholesterolemic subjects and to test the combined effect with cholesterol-lowering drugs (fibrates). Plasma total and LDL-cholesterol concentrations were significantly reduced by 6.4% and 8.8% respectively, for plant sterol-enriched spread (intake 1.6 g /day) compared to control margarine. When subjects were divided in two subgroups according to fibrate treatment, plant sterol supplementation decreased plasma total and LDL-cholesterol by 8.5% and 11.1% respectively in the subgroup treated with fibrates. In the subgroup who did not receive fibrates, the total and LDL-cholesterol was reduced by 5.5% and 7.7% respectively. This study shows that plant sterol ester-enriched spread is a useful adjunctive therapy for hypercholesterolemic patients on fibrate treatment.

Effect of plant sterol-enriched margarine on plasma lipids and sterols in subjects heterozygous for phytosterolaemia.
Stalenhoef AFH et al., J Intern Med 2001; 249(2): 163-166.
In a 4-week study, 2 subjects with heterozygous sitosterolemia received a diet that included 40g plant sterol-enriched spread (3 g plant sterols/day). Total plasma cholesterol levels were decreased by 11 and 12% respectively, mainly due to a decrease in LDL-cholesterol. Plasma concentrations of plant sterols remained at similar levels as found in normal subjects.

Plant sterol-esters in a low fat spread are efficacious in lowering blood cholesterol levels in normal cholesteroelmic subjects.
Tijburg LBM et al., FASEB J 2001; published abstract only.
The cholesterol-lowering efficacy of plant sterol-esters in a low-fat spread format has not been reported earlier. Subjects were divided in a control group (n=15) and in a group (n=47) receiving 20 g/d of a low-fat spread with added plant sterols (1.6 g/d) for three weeks. Plant sterol intake significantly reduced serum total- and LDL-cholesterol by 5.8% and 10%, respectively. These results are similar as reported for full-fat spreads. HDL-cholesterol and triglycerides were not affected.

Plant sterol ester-enriched spread lowers plasma total and LDL cholesterol in children with familial hypercholesterolemia.
Amundsen AL et al., Am J Clin Nutr 2002; 76(2): 338-344.
In a randomized, double-blind, controlled crossover study lasting for two 8-week periods, 38 children aged 7-12 years with familial hypercholesterolemia consumed 18.2 g plant sterol-enriched spread daily (1.5 g plant sterols/day), achieving an average LDL-cholesterol reduction of 10.2% compared to control. In this important study, it was shown that children with familial hypercholesterolemia already following a cholesterol-lowering diet can achieve an additional reduction in LDL-cholesterol of about 10% without any adverse effects from a daily intake of ~1.5 g plant sterols as plant sterol-enriched spread. This effect persisted in an open-label 6-month follow-up period in free living conditions simulating normal behaviour (see Amundsen et al., 2004).

Apolipoprotein E polymorphism and serum lipid response to plant sterols in humans.
Geelen A et al., Eur J Clin Invest 2002; 32(10): 738-742.
This randomized, crossover, placebo-controlled study investigated whether the cholesterol-lowering effect of plant sterols could differ between subjects with different apoE phenotypes. Eighty-eight subjects with different apoE phenotypes (E3/4, n=31, or E4/4, n=57) consumed for 3 weeks a plant sterol-enriched margarine providing 3.2 g/d plant sterols or a control margarine. The subjects consumed the test margarines as part of their usual diet, which was low in cholesterol. The responses of total and LDL-cholesterol was not significantly affected by the apoE polymorphism. LDL-cholesterol was lowered by 12.2% in the E3/4 subjects and 9.8% in the E4/E4 subjects. This study showed that the cholesterol-lowering efficacy of plant sterols is not affected by the apoE polymorphism in healthy subjects who consume a low-cholesterol diet.

Food phytosterol ester efficiency on the plasma lipid reduction in moderate hypercholesterolemic subjects.
Lottenberg AM et al., Arq Bras Cardiol 2002; 79(2): 139-142. (Journal in Portuguese)
The relation between the cholesterol-lowering effect of plant sterol esters and different apoE polymorphisms was investigated. In a double-blind crossover study, 60 moderately hypercholesterolemic subjects received 20 g/day of a plant sterol-enriched spread (containing 1.68 g plant sterols/day) and a control spread for 4 weeks. Total cholesterol and LDL-cholesterol concentrations levels were significantly reduced by 10% and 12%, respectively, when compared to baseline, and by 6% and 8% in comparison with the control treatment. HDL-cholesterol and triglyceride levels were not modified by the active treatment. No significant difference in cholesterol-lowering ability was found between apoE3/3 and apoE4/3. Thus, it can be concluded that plant sterols lower blood cholesterol levels regardless of the apoE polymorphism.

Effects of phytosterol ester-enriched margarine on plasma lipoproteins in mild to moderate hypercholesterolemia are related to basal cholesterol and fat intake.
Mussner MJ et al., Metabolism 2002; 51(2): 189-194.
In this randomized, double-blind, placebo-controlled, crossover study, the effect of a 20g/day phytosterol ester-enriched spread (1.82 g plant sterols/day) on plasma lipoproteins was investigated in 63 healthy subjects after 3 weeks of intervention. Plant sterol ester-enriched spread significantly reduced total cholesterol by 3.4% and LDL-cholesterol by 5.4% compared with control. The findings of this study suggest that through lowering total and LDL-cholesterol the daily consumption of a plant sterol ester-enriched margarine may lower the risk of atherosclerosis in subjects with mild to moderate hypercholesterolemia.

An increase in dietary carotenoids when consuming plant sterols or stanols is effective in maintaining plasma carotenoid levels.
Noakes M et al., Am J Clin Nutr 2002; 75(1): 79-86.
This double-blind, randomized crossover trial with 46 hypercholesterolemic subjects compared the efficacy of 25g of spread enriched with plant sterols esters and plant stanol esters on plasma and carotenoid concentrations. Subjects were advised to eat at least 5 servings of fruit and vegetables daily, with at least one of the servings as carotenoid-rich carrots, sweet potato, pumpkin, tomato, apricots, spinach or broccoli. The plant sterol ester enriched spread (2.3 g sterols/day) significantly lowered LDL-cholesterol by 7.7% compared to control. The plant stanol enriched spread (2.5 g stanols/day) significantly lowered LDL-cholesterol by 9.5% compared to the control spread. There was no difference in cholesterol-lowering between the spreads and no difference in plasma carotenoids compared with baseline. The advice to increase of fruit and vegetable intake was effective in maintaining plasma carotenoid levels within baseline values while lowering LDL-cholesterol concentrations.

A spread enriched with plant sterol-esters lowers blood cholesterol and lipoproteins without affecting vitamins A and E in normal and hypercholesterolemic Japanese men and women.
Ntanios FY et al., J Nutr 2002; 132(12): 3650-3655.
The efficacy of a plant sterol-ester enriched spread (15 g/day containing 1.8 g of plant sterols) in lowering blood cholesterol was examined in 53 Japanese volunteers consuming a traditional Japanese (low-fat) diet. Plasma total and LDL-cholesterol concentrations were significantly decreased by 5.8 and 9.1%, respectively, when subjects consumed the plant sterol-enriched spread compared to the control spread. This study showed that patients already on a low-fat diet can reduce their LDL-cholesterol further by introducing a plant sterol-enriched spread into their traditional Japanese diet.

Additive effect of plant sterol-ester margarine and cerivastatin in lowering low-density lipoprotein cholesterol in primary hypercholesterolemia.
Simons LA et al., Am J Cardiol 2002; 90(7): 737-740.
In this multi-centre, randomized double blind study, the additive or interactive effect of plant sterol ester-enriched margarine (25 g containing 2 g plant sterols/day) in combination with a statin drug on LDL-cholesterol reduction was investigated in 152 primary hypercholesterolemic subjects. Cerivastatin (vs. placebo) significantly reduced LDL-cholesterol by 32% and sterol ester-enriched margarine (vs. regular margarine) by 8%. The effect of sterol ester-enriched margarine and cerivastatin together on LDL-cholesterol reduction was additive (39%); there was no significant interactive effect. The addition of a sterol ester-enriched margarine to statin therapy offers LDL-cholesterol reduction equivalent to doubling the dose of statin.

Effects of a plant sterol-enriched spread on serum lipids and lipoproteins in mildly hypercholesterolaemic subjects.
Temme EHM et al., Acta Cardiol 2002; 57(2): 111-115.
In this randomized double-blind placebo-controlled crossover study, the effects of plant sterol-enriched spreads (25 g containing 2 g plant sterols/day) on concentrations of serum lipids, lipoproteins and apolipoproteins were determined in 42 Belgian subjects. Serum total and LDL-cholesterol concentrations significantly reduced by 7% and 10%, respectively, with the plant sterol-enriched spread compared to the control spread. These findings indicate that a daily intake of 25 g low-fat spread containing 2 g plant sterol per day is effective in lowering blood total and LDL-cholesterol.

Plant sterol-enriched spread enhances the cholesterol-lowering potential of a fat-reduced diet.
Cleghorn CL et al., Eur J Clin Nutr 2003; 57(1): 170-176.
In this randomized double-blind crossover study, the effect of replacing butter with plant sterol-enriched spread on plasma cholesterol concentrations was investigated in subjects on a diet containing 30% of energy as fat. After 3 weeks on butter, fifty free-living men and women consumed 25 g of polyunsaturated spread with or without 2 g of plant sterols daily during 4 week periods. Replacing butter with a plant sterol-enriched spread significantly reduced plasma total cholesterol by 8.9% and LDL-cholesterol by 12.3% which is more than the effect achieved with polyunsaturated spread without plant sterols. Thus, in people with moderately raised plasma cholesterol concentrations consuming reduced-fat diets, the reduction in plasma total and LDL-cholesterol concentrations achieved by replacing butter with a polyunsaturated spread is enhanced by the addition of plant sterols.

Plant sterols lower LDL-cholesterol without improving endothelial function in prepubertal children with familial hypercholesterolaemia.
Jongh de S et al., J Inh Metab Dis 2003; 26: 343-351.
In a double-blind crossover trial, the effect of plant sterol-enriched spread on plasma cholesterol and vascular function was evaluated in 41 pre-pubertal children with familial hypercholesterolemia. During 4-week periods, children consumed 15 g of plant sterol-enriched spread (2.3 g plant sterols/day) and a placebo spread. Total cholesterol concentrations significantly decreased by 11% and LDL-cholesterol concentrations by 14% as compared to placebo spread. The present study shows a clear reduction of LDL-cholesterol by plant sterol-enriched spread in children with familial hypercholesterolemia. However, short-term plant sterol treatment did not improve the endothelial function in these children.

Safety of long-term consumption of plant sterol esters-enriched spread.
Hendriks HFJ et al., Eur J of Clin Nutr 2003; 57(5): 681-692.
The efficacy and safety of long-term consumption of spreads containing plant sterol esters were evaluated in a randomized double-blind placebo controlled parallel trial. One hundred and eighty-five healthy volunteers consumed daily 20 g spread enriched with 1.6 g plant sterols as fatty acid esters or a control spread for 1 year. Consumption of the plant sterol-enriched spread consistently lowered total and LDL-cholesterol during the 1 year period on average by 4 and 6%, respectively. This study concludes that the consumption of plant sterol-enriched spread is safe to use over a long period of time and an effective way to consistently lower blood cholesterol concentrations.

Impact of margarine enriched with plant sterols on blood lipids, platelet function, and fibrinogen level in young men.
Kozlowska-Wojciechowska M et al., Metabolism 2003; 52(11): 1373-1378.
In this randomized, parallel trial, the effects of a polyunsaturated fatty acid (PUFA)-rich margarine and a plant sterol-enriched margarine were evaluated in 42 men who had consumed butter during a 2-wk stabilisation period. After the stabilisation period, the subjects were allocated to one of the 2 groups consuming 30 g/d of a PUFA-rich margarine or 30 g/d margarine providing 2.6 g plant sterols. The fatty acid composition of the PUFA-rich and plant sterol-enriched margarines were different, and therefore the PUFA margarine could not be considered as a control for the plant sterol margarine. The effects of each of the margarines were evaluated by comparing the lipid concentrations at the end of the intervention vs. the baseline lipid levels following consumption of butter. Compared with baseline, the PUFA margarine resulted in 6% reduction in LDL-cholesterol, whilst the plant sterol-enriched margarine resulted in a significant 11% decrease. In addition, the plant sterol-enriched margarine prolonged the adhesion and aggregation time of blood platelets after collagen-epinephrine activation, suggesting that plant sterols could have anti-platelet activity which would contribute to reducing the risk of circulatory diseases.

Response of obligate heterozygotes for phytosterolemia to a low-fat diet and to a plant sterol ester dietary challenge.
Kwiterovich PO et al., J Lipid Res 2003; 44(6): 1143-1155.
The response of obligate heterozygotes for phytosterolemia to a low-fat (Step I) diet and to a plant sterol ester-enriched spread was investigated in 12 subjects who underwent two single-blind protocols of different durations. In the first protocol, a 4-week run-in period (step I diet with placebo spread) preceded 6 weeks on a Step I diet and plant sterol-enriched spread consumption, which was followed by 4 weeks of a Step I diet with placebo spread consumption. Protocol II was similar, except that treatment phases were 12 weeks long. In both protocols, 28 g/d of spread was consumed, providing 2.2 g plant sterols/d. When comparing the plant sterol phase and the placebo phase, decreases in LDL-cholesterol concentrations of 9% and 14% were observed in protocol I and II, respectively. Plasma plant sterol (campesterol and sitosterol) concentrations increased with consumption of the plant sterol spread, but returned to baseline levels during the placebo spread wash-out at the end of the study. Although the plant sterol and placebo spread phases were not randomized, this study provides an indication that phytosterolemic heterozygous individuals have a response to plant sterol consumption similar to that of normal subjects.

A phytosterol-enriched spread improves the lipid profile of subjects with Type 2 diabetes mellitus. A randomized controlled trial under free-living conditions.
Lee YM et al., Eur J Nutr 2003; 42(2): 111-117.
In this randomized, placebo-controlled, double-blind trial, the effect of a phytosterol-enriched spread in 85 subjects with Type 2 diabetes mellitus on serum lipids was investigated. The participants consumed 20 g of spread with or without 1.6 g plant sterol esters daily for 12 weeks. Total cholesterol concentrations and LDL-cholesterol concentrations were significantly reduced by 5.2% and 6.8% respectively compared to baseline after 4 weeks. After 8 and 12 weeks, the reductions became smaller, but there was still a significant difference between the control and plant sterol groups. This clinical study showed that plant sterol-enriched spread is effective in lowering total and LDL-cholesterol in subjects with Type 2 diabetes. Although the effect is modest, it may contribute to decreasing the elevated risk of cardiovascular disease in Type 2 diabetes.

The human cholesteryl ester transfer protein I405V polymorphism is associated with plasma cholesterol concentration and its reduction by dietary phytosterol esters.
Lottenberg AM et al., J Nutr 2003; 133(6): 1800-1805.
The aim of the study was to investigate the effect of plant sterol ester consumption on blood lipids, cholesteryl ester transfer protein (CETP) concentration and lecithin-cholesterol acyltransferase (LCAT) activity and their relationships with I405V CETP, Taq1B CETP and apoE polymorphisms. In a double-blind crossover study, 60 moderately hypercholesterolemic subjects received 20 g/day of a plant sterol-enriched spread (containing 1.68 g plant sterols/day) and a control spread for 4 weeks. Total cholesterol and LDL-cholesterol concentrations levels were significantly reduced by 10% and 12%, respectively, when compared to baseline, and by 6% and 8% in comparison with the control treatment. This pattern of response of plasma lipids was related to the I405V CETP polymorphism. The reductions in total cholesterol for the II, IV and VV phenotypes were 7.2%, 4.2% and not significant, respectively, whereas a significant reduction in LDL-cholesterol occurred only for the II phenotype (9.5%). These data suggest that CETP polymorphisms can modulate the effect of plant sterols on plasma cholesterol concentrations.

Long-term compliance and changes in plasma lipids, plant sterols and carotenoids in children and parents with FH consuming plant sterol ester-enriched spread.
Amundsen AL et al., Eur J Clin Nutr 2004; 58(12): 1612-20.
In a 26-week open-label follow-up of children with familial hypercholesterolemia (who had previously been studied in a controlled crossover study design, AbumWeis et al, 2002), compliance and changes in plasma lipids were studied in 37 children and 20 of their parents. Subjects were recommended to eat 20g/day of plant sterol ester-enriched spread (1.8 g plant sterols/day) as part of their lipid lowering diet. Nineteen of the parents, but no children, used statins. The mean intake of plant sterol-enriched spread was 13.7 and 16.5 g/day in the children and parents respectively, corresponding to 1.2 g and 1.5 g/day of plant sterols. Plasma total cholesterol was significantly decreased by 9.1% in both children and parents. The corresponding decreases in LDL-cholesterol were 11.4% and 11.0% respectively. In this study, sustained cholesterol-lowering efficacy and long-term compliance to plant sterol ester enriched spread intake was demonstrated in a free-living, less controlled setting.

Increased intake of fruit and vegetables and a low-fat diet, with and without low-fat plant sterol-enriched spread consumption: effects on plasma lipoprotein and carotenoid metabolism.
Colgan HA et al., J Hum Nutr Diet 2004; 17(6): 561-569.
This randomized, crossover double blind study determined the effect of specific dietary advice to increase daily fruit and vegetable intake on plasma carotenoid concentrations while following a low-fat National Cholesterol Education Programme (NCEP) Step 1 diet including plant sterol ester enriched spread intake. Forty-eight hypercholesterolemic men consumed 21 g/day of a low-fat plant sterol ester-enriched spread (1.3 g plant sterols/day) or placebo for 3 weeks. Plasma total and LDL-cholesterol were significantly reduced by 4.6% and 7.1%, respectively. Plant sterol ester consumption was associated with significantly lowered plasma beta-carotene concentrations, but this change was not significant after lipid standardisation. Hence, dietary advice to increase fruit and vegetable consumption was effective in preventing a reduction in plasma carotenoid concentrations previously associated with plant sterol ester consumption. In addition, plant sterol ester-enriched low-fat spread consumed as part of a low-fat NCEP Step 1 diet is effective in reducing total and LDL-cholesterol.

Effect of phytosterol ester-enriched margarine and diet compared to diet on plasma lipids in hypercholesterolemic subjects.
Vogt A et al., Atherosclerosis J 2004; published abstract only.
This randomized, double-blind, placebo-controlled study investigated the cholesterol-lowering effect of plant sterols on top of a low-fat (Step I) diet. Sixty-five hypercholesterolemic subjects consumed plant sterol-enriched spread in addition to a heart healthy diet or only the diet. Changes in the lipoprotein profile were measured. Total- and LDL-cholesterol were significantly reduced by 8.5% and 13.7% in the plant sterol group. No changes were observed in the diet group.

Inhibition of cholesterol absorption by the combination of dietary plant sterols and ezetimibe: effects on plasma lipid levels.
Jakulj L et al., J Lipid Res 2005; 46: 2692-2698.
In this study, the combination of the cholesterol absorption inhibitor ezetimibe (Ezetrol®) and plant sterols was tested in mildly hypercholesterolemic adult subjects with baseline LDL-cholesterol concentrations between 3.5 and 5.0 mmol/L. Forty volunteers were randomly divided into four groups: ezetimibe alone, ezetimibe plus plant sterols, plant sterols alone, or placebo. The study was a double-blind, placebo-controlled crossover study for the plant sterol treatment with an open-label ezetimibe treatment. After a 2- or 6-week run-in, depending on the pre-use of plant sterols, volunteers received four weeks of treatment and afterwards crossed over to the next study treatment. The amount of plant sterols was 2 g/day provided as 25 grams of spread, while the ezetimibe dose was 10 mg/day. Compared to the placebo, ezetimibe, plant sterols and the combination reduced plasma LDL-cholesterol by 22%, 5% and 25%, respectively. There was no significant effect on HDL-cholesterol or triglycerides. Plasma sitosterol and campesterol concentrations increased with plant sterols while, with ezetimibe, plasma plant sterol concentrations were lower than the placebo treatment. With the combination of ezetimibe plus plant sterols, plasma sitosterol and campesterol concentrations were higher compared to ezetimibe alone, but lower compared to placebo. In conclusion, in this study the combination of plant sterols plus ezetimibe did not show an additional cholesterol-lowering benefit as compared to ezetimibe treatment alone. Based on these findings, it is uncertain whether subjects will benefit from consuming plant sterol-enriched foods together with taking ezetimibe.

Isocaloric substitution of plant sterol-enriched fat spread for carbohydrate-rich foods in a low-fat fibre-rich diet decreases plasma low-density lipoprotein cholesterol and increases high-density lipoprotein concentrations.
Skeaff CM et al., Nutr Metab Cardiovasc Disease 2005; 15(5): 337-344.
This randomized crossover study compared the effect of replacing a plant sterol-enriched spread with carbohydrate-rich foods relative to a diet high in saturated fat. Twenty-nine subjects completed the three 4-week interventions where all foods were provided. The three diets were a typical New Zealand diet (high in total and saturated fat), a cholesterol-lowering diet including plant sterol-enriched spread (2 g plant sterols/day) and the same cholesterol-lowering diet enriched with carbohydrates instead of the plant sterol-enriched spread. LDL-cholesterol concentrations decreased by 20% on the plant sterol diet which was significantly greater than the 12% decrease on the carbohydrate diet. The study concluded that including a plant sterol-enriched spread in a cholesterol-lowering diet produces a more favourable plasma lipid profile than the same diet made lower in total and saturated fat by replacing the spread with carbohydrate rich foods.

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.
AbuMweis SS et al., J Nutr 2006; 136(4): 1012-1016.
Most plant sterols available on the market are esterified to vegetable oil fatty acids. A new approach consists in esterifying plant sterols to fatty acids from other sources, such as fish oil fatty acids, which are known to have their own beneficial effects on plasma triglyceride concentrations and cardiac mortality. This study tested the lipid-lowering effects of fish oil fatty acid esters of plant sterols in 30 overweight, hypercholesterolemic subjects. The study had a randomized, crossover, placebo-controlled single-blind design, with 5 different treatments: (I) control, (II) free plant sterols, (III) plant sterols esterified to sunflower oil fatty acids, (IV) plant sterols esterified to fish oil fatty acids, and (V) free plant sterols in combination with fish oil fatty acids. All treatments were incorporated into margarine and consumed under supervision for 4 weeks, at breakfast. Washout periods of 2 to 4 weeks separated each treatment phase. Surprisingly, none of the plant sterol treatments had a statistically significant effect on plasma total, LDL-cholesterol and triglyceride concentrations. However, the dose of plant sterols in each of the four plant sterol treatment phases was based on body weight, resulting in a wide range of doses, from 1.0 to 1.8g/d, which may have caused a large variability in the cholesterol-lowering efficacy of the plant sterol treatments.

Fish-oil esters of plant sterols improve the lipid profile of dyslipidemic subjects more than do fish-oil or sunflower oil esters of plant sterols.
Demonty I et al., Am J Clin Nutr 2006; 84(6): 1534-1542.
Plant sterols have been previously shown to lower blood total- and LDL-cholesterol concentrations, and fish oil fatty acids have been shown to lower triglyceride concentrations. The present study investigated the effects on blood lipids of a combination treatment consisting in plant sterols esterified to fish-oil fatty acids (FO-PS). Twenty-one hypercholesterolemic persons were fed an olive oil (OO)-based diet and consumed 4 different treatment oils during 4 successive periods in a semi-randomized order: OO, fish oil, FO-PS and sunflower oil esters of plant sterols (SU-PS). The plant sterol oils provided ~1.7 g/d of free plant sterols. Triglyceride concentrations were significantly lower after fish oil and FO-PS supplementation compared to OO and SU-PS. Both FO-PS and SU-PS supplementation resulted in a significant decrease in LDL-cholesterol compared to OO, as well as a significantly lower ratio of total to HDL-cholesterol and lower apoB concentrations compared to OO and fish oil. Furthermore, the ratio of apoB to apoA was significantly lower after SU-PS supplementation compared to OO and fish oil. HDL-cholesterol was not affected by both plant sterol oils; however, HDL2 and the ratio of HDL2 to HDL3 were significantly higher after FO-PS supplementation compared to OO, fish oil and SU-PS. These results show that both the traditional vegetable oil esters of plant sterols and the novel fish oil esters of plant sterols included in an olive-oil based diet improve the plasma lipid and apolipoprotein profile in comparison with fish oil or the control diet alone. Due to the beneficial effects of FO-PS on the HDL sub fractions, the authors concluded that FO-PS supplementation may reduce cardiovascular disease risk more than does fish oil or SU-PS supplementation. However, cardiovascular disease risk was not directly investigated in this study (only markers of cardiovascular disease risk were measured), and this hypothesis would need to be verified.

Olive oil containing olive oil fatty acid esters of plant sterols and dietary diacylglycerol reduces low-density lipoprotein cholesterol and decreases the tendency for peroxidation in hypercholesterolaemic subjects.
Chan YM et al., Br J Nutr 2007; 98(3): 563-570.
This study aimed at evaluating the effect of novel esters of plant sterols (olive-oil fatty acid esters of plant sterols) on blood lipid profile and lipid peroxidation. The study was realized in the context of a healthy, Mediterranean-like diet, with 70% of the fat being provided by olive oil. Twenty-one subjects consumed in a random way 3 consecutive treatment oils (olive oil as the control oil, plant sterols (1.7 g/d) esterified to sunflower oil (PS-SO) and plant sterols (1.7 g/d) esterified to olive oil (PS-OO)) for 4 weeks each, separated by 4-week washout periods. The PS-SO and the PS-OO treatments resulted in significant reductions in LDL-cholesterol (-6.3% and -9.1%, respectively) and in non-significant reductions in total cholesterol (-4.9% and -6.9%, respectively) compared with the control olive oil. There were no differences across diets in lipoprotein (a) and lipid peroxidation levels. These data suggest that olive oil esters of plant sterols may be as effective as the traditional sunflower oil esters in lowering LDL-cholesterol. However, the evidence for beneficial effects of the novel olive oil esters of plant sterols on other cardiovascular disease risk markers was less convincing.

Spreads fortified with a brassicasterol-rich phytosterol mixture from rapeseed oil lower total and LDL-cholesterol concentrations in mildly hypercholesterolemic subjects.
Demonty et al., FASEB J 2007; published abstract only.
This double-blind, placebo-controlled, parallel study with a 2-week run-in and a 3-week intervention period aimed to investigate the effect on cholesterol and plasma fat-soluble vitamins of a brassicasterol-rich plant sterol mixture from rapeseed oil. A total of 53 mildly hypercholesterolemic subjects completed the study. Subjects consumed either a control spread or a low-fat spread enriched with 2.1 g rapeseed plant sterols in their ester form. Serum total and LDL-cholesterol were significantly reduced by 7% and 12%, respectively, vs. control. No significant effect was observed on HDL-cholesterol, triglycerides, and cholesterol-adjusted retinol, α-tocopherol and carotenoid concentrations, except for α-carotene which was significantly lower (-19%) vs. control. Plasma concentrations of plant sterols were modestly increased in the plant sterol group, but returned to baseline values after a 4-week washout. Brassicasterol-rich PS mixtures from rapeseed oil have cholesterol lowering properties similar to those reported previously with plant sterols from other sources.

Similar serum plant sterol responses of human subjects homozygous for a mutation causing sitosterolemia and controls to diets enriched in plant sterols or stanols.
Kratz M et al., Eur J Clin Nutr 2007; 61(7): 896-905.
This randomized, double-blind crossover study including seven heterozygous relatives of sitosterolemic patients and 10 controls was performed to investigate the serum phytosterol responses to phytosterol or -stanol-enriched spread (2 g/d). After 6 weeks of intervention, serum plant sterol concentrations increased by more than 20% with plant sterol intake vs. control, with no significant difference between heterozygotes and controls. Serum plant sterol concentrations were decreased after intake of plant stanols, similarly for heterozygotes and controls, whereas serum plant stanol concentrations increased. Total cholesterol was significantly reduced after the plant stanol intake, but not after the plant sterol intake. LDL-cholesterol only tended to be lower, particularly after plant stanol intake.

The effect of a combination of plant sterol-enriched foods in mildly hypercholesterolemic subjects.
Madsen MB et al., Clin Nutr 2007; 26(6): 792-798.
The objective of the study was to evaluate the impact on coronary heart disease risk of a combination of two different plant sterol-enriched foods (spread and milk) as part of a low-fat diet. Fifty moderately hypercholesterolemic, otherwise healthy, men and women were recruited to participate in the study. The study was a randomized, double-blind, placebo-controlled, crossover trial consisting of two 4-week intervention phases, with no wash-out between phases. During both the placebo and the plant sterol phases, participants followed the NCEP Step I diet. A 4-week run-in period preceded the intervention. The treatments consisted in two 10 g portions of low-fat spread and one 250 mL serving of low-fat milk, to be consumed in three different occasions each day, with main meals. The plant sterol-enriched products provided a daily dose of 2.3 g plant sterols. Serum total cholesterol, LDL-cholesterol, apoB and apoB:apoA-I ratio decreased significantly by 5.5%, 7.7%, 4.6% and 3.4%, respectively, after consumption of plant sterol-enriched products compared to placebo. There was no significant difference in HDL-cholesterol and triglycerides between the intervention and the placebo phases. Neither apo A-I, Lp(a) nor hsCRP were affected by plant sterol consumption. The present data support the additional role that plant sterols may play in reducing cardiovascular disease risk as part of a low-fat diet, and show that low-fat, plant sterol-enriched food formats such as milk can be combined with fat-based food formats to efficiently lower elevated LDL-cholesterol concentrations.

Dose-response effects of different plant sterol sources in fat spreads on serum lipids and C-reactive protein and on the kinetic behavior of serum plant sterols.
Clifton PM et al., Eur J Clin Nutr 2008; 62(8): 968-977.
This study tested the cholesterol-lowering effect of two doses of plant sterols (1.6 g/d and 3.0 g/d) from different sources incorporated in a low-fat spread. The different plant sterol sources were soybean oil sterols, tall oil sterols and a mix of tall oil and rapeseed oil sterols. The study had a placebo-controlled parallel design and the 151 subjects either received placebo spread for 6 weeks or a spread enriched with 1.6 g/d plant sterols for 3 weeks followed by 3.0 g/d plant sterols for another 3 weeks. LDL-cholesterol was lowered significantly by 7-11% with the intake of 1.6 g/d plant sterols. Increasing the dose to 3.0 g/d modestly lowered LDL-cholesterol further to 10-15%. There was no difference in the cholesterol-lowering effect between the tested plant sterol sources differing in their plant sterol composition. Interestingly, fasting triglyceride concentrations were significantly lower in subjects receiving the tall oil/rapeseed oil sterol mix while triglycerides were not statistically different with intake of the other plant sterol sources. There is no clear explanation for this effect. Next to plasma lipids, serum plant sterol concentrations were also measured after the intake of 1.6 g/d and 3.0 g/d plant sterols as well as 6 weeks after discontinuation of plant sterol intake. With the increasing intakes of plant sterols from different sources, serum sitosterol and campesterol concentrations increased in a distinctive extent depending on the plant sterol source. After plant sterol withdrawal, serum plant sterol levels decreased rapidly by 50% within 2 weeks.

Effects of long-term plant sterol or stanol ester consumption on lipid and lipoprotein metabolism in subjects on statin treatment.
Jong de A et al., Br J Nutr 2008; 100(5): 937-941.
The study was a double-blind, randomized, parallel 3-arm intervention study with a 5-week run-in period with control spread followed by an 85-week intervention period with either control, plant sterol-enriched or plant stanol-enriched spreads. Spread intake was 30 g/day delivering 2.5 g/day of plant sterols or stanols. Fifty-four patients on stable statin treatment (32 men, 22 women) completed the study. After the run-in period, 17 subjects continued with the control spread, 18 consumed the plant sterol- and 19 the plant stanol-enriched spread. Only data of 47 subjects were suitable for analysis. Halfway the study, at 45 weeks, LDL-cholesterol was significantly lowered by 11.6% in the plant sterol group and by 8.7% in the plant stanol group compared to the control group. At the end of the study, after 85 weeks, LDL-cholesterol was decreased by 8.7% in the plant sterol group and by 13.1% in the plant stanol group compared to the control group. No changes were found in HDL-cholesterol and triglyceride concentrations between the 3 groups. No effects were found on plasma concentrations of bile acid synthesis markers, which were measured to see whether differences in these markers could explain a possible difference in efficacy between plant sterols and -stanols. As expected, plasma plant sterol concentrations (expressed as sitosterol or campesterol to cholesterol ratios) increased with plant sterol intake, and plasma sitostanol and campestanol concentrations were significantly increased with plant stanol intake. However, no differences were noted between 45 and 85 weeks of intervention demonstrating no further increase in plasma plant sterol concentrations with continuous intake. In conclusion, as stated by the authors this long-term study demonstrated that both plant sterol- and stanol-ester enriched spreads are equally effective in lowering LDL-cholesterol over a period of 85 weeks in statin users.

Basal plasma concentrations of plant sterols can predict LDL-C response to sitosterol in patients with familial hypercholesterolemia.
Fuentes F et al., Eur J Clin Nutr 2008; 60: 495-501.
In 30 familial hypercholesteromic subjects, the effect of plant sterol intake on blood lipids, endothelial function and LDL particle size was investigated. This study was designed as a randomized, crossover, controlled-feeding trial with 4 periods/diets (each lasting 4 weeks): low cholesterol (150 mg/d) + low sitosterol (<0.5 g/d) diet, low cholesterol + high sitosterol (2.5 g/d) diet, high cholesterol (280-300 mg/d) + low sitosterol diet, and high cholesterol + high sitosterol diet. Plant sterols were provided in a spread format. After intervention, no diet effect was found on LDL-cholesterol. However, when comparing the high cholesterol + low sitosterol diet with the high cholesterol + high sitosterol diet, LDL-cholesterol was significantly reduced by 7.7%. In fact, reductions in LDL-cholesterol were largest in the subjects in the upper and intermediate tertiles of basal plasma sitosterol concentrations compared to the subjects in the lower tertile. No effects on endothelial function were found. LDL particle size appeared to be larger and less dense after the 2 plant sterol-enriched dietary periods.

Effect of plant sterols in combination with other cholesterol-lowering foods.
Jenkins DJ et al., Metabolism 2008; 57(1): 130-139.
The contribution of plant sterols to the overall cholesterol-lowering effect of the portfolio diet (high in soy protein, viscous fibers, almonds and plant sterols) was studied in subjects consuming that diet for one year under free living conditions. After eliminating plant sterols (consumed as enriched spread) from the portfolio diet, LDL-cholesterol increased; when the plant sterol-enriched spread was again introduced into the diet, LDL-cholesterol decreased. In the 18 subjects of whom a complete data set was available, LDL-cholesterol reductions were 16.7±3.1% ($P<0.001$) before and 10.3±2.6% ($P<0.001$) after plant sterol elimination, resulting in a 6.4±1.3% ($P<0.001$) difference attributable to plant sterols. This demonstrates that plant sterols are a major contributor to the cholesterol-lowering benefit of the portfolio diet.

Plant sterol consumption frequency affects plasma lipid levels and cholesterol kinetics in humans.
AbuMweis SS et al., Eur J Clin Nutr 2009; 63(6): 747-755.
In this study, the effect of frequency of plant sterol intake on lowering LDL-cholesterol and on cholesterol absorption was investigated. The study compared the effects of 1.8 g/d plant sterols (in the form of a spread) given once in the morning and given 3 times throughout the day with breakfast, lunch and dinner. The study design was a placebo-controlled, 3-phase crossover, diet-controlled, supervised trial. Each treatment phase lasted 6 days. Compared to the control spread, plasma LDL-cholesterol concentrations were 6% lower after consuming plant sterols 3-times per day, while they were not significantly different from control when plant sterols were consumed once-a-day with breakfast. Interestingly, cholesterol absorption efficiency decreased comparably by 36% and 39% after the trice-a-day and the once-a-day plant sterol intake compared to control, respectively, despite the fact that no significant lowering in LDL-cholesterol was seen with the single daily intake. In conclusion, the present data suggest that the frequency of intake may affect the cholesterol-lowering efficacy of plant sterols.

Phytosterol intake and dietary fat reduction are independent and additive in their ability to reduce plasma LDL cholesterol.
Chen SC et al., Lipids; 2009; 44(3): 273-281.
In this randomized controlled crossover trial, the effects of 3.3 g/d plant sterols, a low-fat Step 1 type of diet and their combination on blood lipids/lipoproteins and carotenoids were investigated in mildly hypercholesterolemic men and postmenopausal women. The subjects consumed an American diet with plant sterols, a Step 1 diet with plant sterols (combination), a Step 1 diet without plant sterols and an American diet without plant sterols (control) for 23 days each. The Step 1 diet significantly lowered total, HDL-, LDL-cholesterol, ApoA1 and ApoB by 4.3, 5.3, 4.5, 2.8 and 2.5%, independent of plant sterol intake. Plant sterol intake significantly lowered total and LDL-cholesterol and ApoB by 9.0, 12.4 and 6.1%, independent of type of diet, without affecting HDL-cholesterol and ApoA1. No interaction of plant sterol intake and diet was found, demonstrating that the effects of plant sterols and diet on plasma lipoprotein cholesterol concentrations are additive.

Baseline plasma plant sterol concentrations do not predict changes in serum lipids, C-reactive protein (CRP) and plasma plant sterols following intake of a plant sterol-enriched food.
Houweling AH et al., Eur J Clin Nutr 2009; 63(4): 543-551.
This study aimed to examine whether baseline plasma plant sterol concentrations are related to subsequent changes in serum lipids, plasma plant sterol concentrations and C-reactive protein (CRP) concentrations following the intake of 2 g/d of plant sterols (as esters) in the form of an enriched spread. Hypercholesterolemic but otherwise healthy men (n=82) were selected based on having low (LPS) vs. high (HPS) basal plasma plant sterol concentrations. The randomized, diet-controlled study consisted of two 4-week intervention periods separated by a 4-week washout. At baseline, men with HPS had higher mean serum total, LDL- and HDL-cholesterol concentrations while men with LPS had a higher BMI. After plant sterol intake, absolute sitosterol plus campesterol plasma concentrations were increased both in men with HPS and LPS but percent changes were not different between groups. Baseline plant sterol concentrations did not correlate with absolute and percent changes in campesterol and sitosterol following plant sterol intake. Total and LDL-cholesterol was lowered significantly by 6.3% and 7.8%, respectively, after plant sterol intake when data from all men were analyzed together. Changes in lipid parameters were not statistically different between men with HPS and LPS basal concentrations. Thus, baseline plant sterols were not predictive of changes in LDL-cholesterol following plant sterol intake. No effects on CRP were seen subsequent to plant sterol intervention. In conclusion, this study demonstrated that baseline plasma plant sterol concentrations are not associated with changes in cholesterol or plant sterol concentrations following plant sterol intake.

Effects of margarines and butter consumption on lipid profiles, inflammation markers and lipid transfer to HDL particles in free-living subjects with the metabolic syndrome.
Gagliardi AC et al., Eur J Clin Nutr 2010; 64(10): 1141-1149.
In this parallel study, 75 metabolic syndrome patients were randomized into 1 of the following intervention groups: butter (15 g/d), no-trans-fat margarine (36 g/d) or plant sterol margarine (30 g/d with 2.4 g/d plant sterols), for 35 days. Out of 75 subjects, only 53 subjects completed the protocol; drop-out rate was high mainly due to problems with consuming the required amount of spread per day. The findings show that, in free-living subjects with the metabolic syndrome, consumption of plant sterol and no-trans-fat margarines within recommended amounts reduce Apo-B levels and the ability of HDL to accept lipids, respectively. Possibly due to the limited number of subjects that completed the protocol, there was not enough power to show statistically significant changes in total and LDL-cholesterol after consumption of the plant sterol margarine vs. the other margarines.

Consumption of a plant sterol-based spread derived from rice bran oil is effective at reducing plasma lipid levels in mildly hypercholesterolaemic individuals.
Eady S et al., Br J Nutr 2011; 105(12): 1808-1818.
This publication describes the results of two crossover studies with mildly hypercholesterolemic patients. Study 1 (n=40) aimed at investigating the effect of rice brain oil spread (RBOS), plant sterol-enriched spread (1.6 g/d of plant sterols) and standard spread (control) on cholesterol levels. Study 2 (n=40) was designed to investigate whether the cholesterol-lowering benefit of RBOS could be enhanced by including a supplementary serving of rice bran oil (RBO). In study 1, after 3x4 weeks of intervention, total and LDL-cholesterol levels were reduced by 2.2 and 3.5%, respectively, after RBOS treatment compared to control, whereas significant reductions of 4.1 and 5.6%, respectively, were observed after plant sterol treatment, with no effects on HDL-cholesterol and triglycerides. In study 2 (also 3x4 weeks), no enhanced lipid-lowering effects of the addition of RBO to RBOS were shown.

A spread containing bioactive milk peptides Ile-Pro-Pro and Val-Pro-Pro, and plant sterols has antihypertensive and cholesterol-lowering effects.
Turpeinen AM et al., Food Funct 2012; 3(6): 621-627.
In a randomized, placebo-controlled double-blind study, the effect of bioactive milk peptides (Ile-Pro-Pro and Val-Pro-Pro) and plant sterols on cholesterol concentrations and blood pressure was investigated. One hundred subjects consumed for a period of 10 weeks either 20 g/d of placebo spread or 20 g/d of a spread containing 4.2 mg IPP and VPP and 2 g plant sterols. LDL-cholesterol and total cholesterol were significantly reduced compared to placebo (by ~9 and ~7%, respectively). Also home systolic blood pressure was significantly reduced compared to placebo; however, office blood pressure and ambulatory blood pressure measurements did not reveal significant reductions in blood pressure. The findings of this study suggest that functional foods with both milk peptides and plant sterols may address two major risk factors at the same time. However, more research especially into the blood pressure lowering effects of this combination is warranted.

Low doses of eicosapentaenoic acid and docosahexaenoic acid from fish oil dose-dependently decrease serum triglyceride concentrations in the presence of plant sterols in hypercholesterolemic men and women.
Ras RT et al., J Nutr 2014; 144(10): 1564-1570.
This large (n=332), randomized, placebo-controlled parallel study aimed to investigate the dose-response relationship between various low doses of eicosapentaenoic acid and docosahexaenoic acid (0.9, 1.3 and 1.8 g/d) from fish oil and triglyceride concentrations, when incorporated in a plant sterol-enriched spread (dose of plant sterols: 2.5 g/d). In addition, effects on LDL-cholesterol were investigated. After 4 weeks of intervention, triglyceride concentrations were reduced in a dose-dependent manner. The triglyceride-lowering effects ranged from -9.3% to -16.2% compared to the placebo group. LDL-cholesterol was reduced by on average 11.5-14.7% in the various plant sterol groups compared to the placebo group. Combining both plant sterols and fish oil thus lowers two blood lipid risk factors simultaneously.

The effect of a low-fat spread with added plant sterols on vascular function markers: results of the Investigating Vascular Function Effects of Plant Sterols (INVEST) study.
Ras RT et al., Am J Clin Nutr 2015; 101(4): 733-741.
This study was a double-blind, randomized, placebo-controlled, 3-month, parallel-group study with the primary aim to investigate the effect of a low-fat spread with added plant sterols on endothelial function as measured by flow-mediated dilation (FMD). The study was conducted in 240 healthy male and post-menopausal female subjects with moderately elevated blood cholesterol who were not yet on lipid-lowering medication. Subjects consumed a low-fat spread enriched with 3 g/d plant sterols or spread without plant sterols. Regular intake of a low-fat spread with added plant sterols neither improved nor worsened FMD. Other markers of vascular function (arterial stiffness and blood pressure) were not significantly changed. Plant sterols intake led to a significant reduction in total- and LDL-cholesterol concentrations although smaller than anticipated. Plasma plant sterol concentrations were significantly increased upon plant sterol intake within the expected range. Explorative correlation analysis revealed that increases in plasma plant sterols were not related to changes in FMD while a larger reduction in LDL-cholesterol was modestly correlated with an increase in FMD.

The effect of plant sterols and different low doses of omega-3 fatty acids from fish oil on lipoprotein subclasses.
Jacobs DM et al., Mol Nutr Food Res 2015; doi: 10.1002/mnfr.201500152.
This study investigated the effect of a low-fat spread with plant sterols and fish oil fatty acids on lipoprotein subclasses. Triglycerides and cholesterol were determined in 13 serum lipoprotein subclasses in 282 hypercholesterolemic subjects consuming a placebo spread, a plant sterol-enriched spread (2.5 g/d) or the plant sterol-enriched spread with addition of fish fatty acids (0.9, 1.3 or 1.8 g/d). The plant sterol intervention lowered cholesterol in total LDL and total VLDL and in almost all LDL and VLDL particles. No changes in triglycerides in any of the lipoprotein subclasses were observed with plant sterols. The combinations with various doses of fish fatty acids dose-dependently reduced cholesterol and triglycerides in the larger VLDL particles. In LDL particles, cholesterol was not further changed, whereas triglycerides were slightly reduced. In the larger HDL particles, triglycerides and cholesterol were increased whereas they decreased in the smaller HDL particles. These changes in the lipoprotein subclasses point toward a lipoprotein profile that is beneficial for coronary heart disease risk.

DAIRY FOOD FORMATS (MILK, YOGHURT, YOGHURT DRINK)

Plant sterol ester-enriched milk and yoghurt effectively reduce serum cholesterol in modestly hypercholesterolemic subjects.
Noakes M et al., Eur J Nutr 2005; 44(4): 214-222.
Two studies were carried out to assess the cholesterol-lowering effect of a plant sterol ester enriched low-fat milk, a plant sterol ester enriched low-fat yoghurt and a plant stanol ester enriched low-fat yoghurt in modestly hypercholesterolemic subjects. In both studies, background diet was habitual dietary intake (30% energy). The first study (n=39) was a single-blind, placebo controlled, crossover trial with 3 week interventions. The interventions were 300ml/day of placebo or plant sterol (2 g/day) enriched low-fat milk, and 25g/day of placebo or plant sterol (2 g/day) enriched spread. Total cholesterol and LDL-cholesterol were lowered significantly by the plant sterol-enriched low-fat milk (5.5% and 7.9% respectively) compared to placebo group. The plant sterol-enriched spread lowered total cholesterol and LDL-cholesterol by 8.0% and 10.1% respectively, which was not significantly different from the effect of plant sterol-enriched low-fat milk. There was no effect on HDL-cholesterol or triglycerides during the intervention. The second study (n=40) was a randomized, placebo controlled, double-blind, crossover trial with 3 week interventions. Subjects consumed 300g/day of placebo low-fat yoghurt, low-fat yoghurt enriched with plant sterols (1.8g/day) and low-fat yoghurt enriched with plant stanols (1.7g/day). Total cholesterol and LDL-cholesterol were significantly reduced by the plant sterol ester enriched yoghurt (4.4% and 6.1%, respectively) and the plant stanol enriched yoghurt (3.5% and 5.2%, respectively) compared to placebo group. There was no effect on HDL-cholesterol or triglycerides. The authors conclude that plant sterol esters when provided in low-fat milk and yoghurt are effective in lowering total and LDL-cholesterol.

Intake occasion affects the serum cholesterol lowering of a plant sterol-enriched single-dose yoghurt drink in mildly hypercholesterolemic subjects.
Doornbos A et al., Eur J Clin Nutr 2006; 60(3): 325-333.
In a double-blind, randomized placebo-controlled parallel design study, the effect of intake occasion on the cholesterol-lowering efficacy of a plant sterol-enriched single-dose yoghurt drink was investigated. One hundred and eighty-four moderately hypercholesterolemic subjects completed one of five 4-week treatments. The treatments differed in product fat level and in intake occasion (yoghurt drink consumed with a lunch meal or on an empty stomach). LDL-cholesterol concentrations significantly decreased by 9.4% when the single-dose drink was taken with a meal independent of its fat content as compared to placebo treatment. When consumed without a meal, LDL-cholesterol was also significantly decreased by 6% as compared to placebo; however the effect was significantly smaller as compared to intake with a meal. This study concludes that consumption with a meal is important for optimal cholesterol-lowering of a plant sterol-enriched yoghurt drink.

Independent and interactive effects of plant sterols and fish oil n-3 long-chain polyunsaturated fatty acids on the plasma lipid profile of mildly hyperlipidaemic Indian adults.
Khandelwal S et al., Br J Nutr 2009; 102(5): 722-732.
The study aimed at investigating the independent and interactive effects of a yoghurt drink enriched with 2 g plant sterols (in their ester form) and fish oil capsules providing 2 g/d long chain omega-3 fatty acids. The subjects (200 at the start of the study) were divided in 4 groups receiving either a control drink or a plant sterol-enriched yoghurt drink in combination with either control capsules or fish oil capsules. The plant sterol-enriched yoghurt drink lowered LDL-cholesterol by 5% and plasma triglycerides by 15%. Fish oil lowered plasma triglycerides by 15% but did not affect plasma cholesterol concentrations. The combination of plant sterols and fish oil lowered plasma LDL-cholesterol by about 5% and triglycerides by 15%. Thus, there was no interaction between plant sterols and fish oil on plasma LDL-cholesterol concentrations, suggesting that a synergy between plant sterols and fish oil omega-3s in modulating LDL-cholesterol appears unlikely. The pronounced triglyceride-lowering effect of plant sterols observed in the present study (similar to that seen for fish oil, a well-known triglyceride-lowering ingredient) warrants further investigation.

Evaluation of cardiovascular risk and oxidative stress parameters in hypercholesterolemic subjects on a standard healthy diet including low-fat milk enriched with plant sterols.
Bañuls C et al., J Nutr Biochem 2010; 21(9): 881-886.
The effects of a healthy diet including plant sterol-enriched low-fat milk on cardiovascular risk and oxidative stress parameters were investigated in 40 hypercholesterolemic subjects. During 3 months, subjects consumed a healthy diet after which they were randomized to consume 500 mL of milk with or without added plant sterols (2 g/d) while continuing the consumption of a healthy diet, also for 3 months. The healthy diet itself significantly reduced total and LDL-cholesterol levels (-4.0% and -4.7% vs. baseline, respectively). The addition of plant sterols in a milk format further reduced total and LDL-cholesterol (-6.4% and -9.9% vs. baseline, respectively). Despite a decrease in cryptoxanthin with plant sterol supplementation, anti-oxidative defences were not impaired and oxidative stress was not enhanced.

Effects of phytosterol ester-enriched low-fat milk on serum lipoprotein profile in mildly hypercholsterolaemic patients are not related to dietary cholesterol or saturated fat intake.

Hernández-Mijares A et al., Br J Nutr 2010; 104(7): 1018-1025.

The aim of this study was to evaluate whether the efficacy of plant sterols is impacted by the type of diet consumed. The study was organised as a 3-month randomized, parallel trial with 3 arms. Eighty-four hypercholesterolemic subjects consumed a healthy diet, a healthy diet + plant sterols (2 g/d in a milk format) or a free diet (higher in saturated fatty acids and cholesterol compared to the healthy diet) + plant sterols, after a 3-month run-in period with a healthy diet (adaptation period). After intervention, the healthy diet + plant sterols and the free diet + plant sterols reduced total cholesterol (-6.7% and -5.5%, resp.) and LDL-cholesterol (-9.6% and -7.0%. resp.) to a similar extent, whereas no cholesterol changes were seen in the healthy diet group. Non-HDL-cholesterol, apoB-100 and the ratio apoB-100/apoA-I were also reduced in both plant sterol intervention groups. Following the healthy diet, B-carotene was increased, whereas it was not changed after the healthy diet + plant sterol treatment, and reduced after the free diet + plant sterol treatment. Thus, the type of background diet does not impact the efficacy of plant sterols; a healthy diet may however counterbalance the negative effects of plant sterols on carotenoid levels.

Serum lipid responses to phytosterol-enriched milk in a moderate hypercholesterolemic population is not affected by apolipoprotein E polymorphism or diameter of low-density lipoprotein particles.

Bañuls C et al., Eur J Clin Nutr 2011; 65(2): 255-261.

This study aimed at investigating the influence of plant sterol-enriched milk on lipid profile and on LDL particle size according to apoE genotype as part of a healthy diet in moderately hypercholesterolemic patients. ApoE is an apolipoprotein which plays an essential role in the metabolism of cholesterol and triglycerides. Some researchers suggest that the apoE4 phenotype may result in larger LDL-cholesterol-lowering efficacy after plant sterol intervention. After a 3-month run-in period on a healthy diet, subjects (n=75) were randomly assigned to consume 2 g/d plant sterols in a low-fat milk or a placebo milk as part of the healthy diet during another 3 months. Subjects that consumed the plant sterol-enriched milk exhibited a significant reduction in total (5.1%), LDL- (8.1%), and non-HDL-cholesterol (7.4%) and apoB-100/apoA-1 ratio (7.7%) compared to baseline, whereas no blood lipid changes were found in the placebo group. The effect of plant sterols on lipid profile was independent of apoE phenotype (at least with the power available). In none of the groups, effects on HDL-cholesterol, triglycerides or LDL particle size were found.

Low intestinal cholesterol absorption is associated with a reduced efficacy of phytosterol esters as hypolipemic agents in patients with metabolic syndrome.

Hernández-Mijares A et al., Clin Nutr 2011; 30(5): 604-609.

This study aimed at investigating whether the addition of low-fat milk enriched with plant sterols improves cardiovascular risk factors in metabolic syndrome patients (n=24) and moderately hypercholesterolemic controls (n=24). After a 3-month run-in period on a healthy diet (NCEP-ATP III), participants were randomized to continue with the healthy diet or to combine the healthy diet with 500 mL low-fat milk which was enriched with plant sterols (2 g/d). At baseline, metabolic syndrome patients had larger waist circumference, elevated diastolic blood pressure, triglycerides and glucose, and smaller size of LDL particles and lower total and LDL-cholesterol levels, compared to the controls. Surprisingly, in metabolic syndrome patients, enrichment of a healthy diet with plant sterols did not induce any improvement in lipoprotein profile, whereas, in the control subjects, total and LDL-cholesterol concentrations were reduced, as well as concentrations of non-HDL-cholesterol, apoB and the apoB/apoA ratio. The authors suggest that this finding is the result of a reduced intestinal cholesterol absorption seen in metabolic syndrome patients which is likely to interfere with plant sterol mechanism of action. Indeed, baseline LDL-cholesterol concentrations between metabolic syndrome patients and controls were highly imbalanced (lower in patients).

Effects of plant sterol esters in skimmed milk and vegetable-fat-enriched milk on serum lipids and non-cholesterol sterols in hypercholesterolaemic subjects: a randomised, placebo-controlled, crossover study.

Casas-Agustench P et al., Br J Nutr 2012 107(12): 1766-1775.

In this randomized, placebo-controlled, crossover study, 43 hypercholesterolemic subjects consumed each of the following treatments during 4 weeks: placebo skimmed milk (SM), plant sterol-enriched SM or plant sterol-enriched SM with vegetable fat. The effects on serum lipids and non-cholesterol sterols were investigated. The daily dose of milk was 2 times 250 mL whereas the daily dose of plant sterols was 2 g. Compared to control, LDL-cholesterol was reduced by 8.0% and 7.4% in the plant sterol-enriched SM and in the one that was also enriched with vegetable oil. Furthermore, the LDL-cholesterol response to plant sterols seemed enhanced in subjects with low cholesterol synthesis and high cholesterol absorption at baseline.

Phytosterols supplementation decreases plasma small and dense LDL levels in metabolic syndrome patients on a westernized type diet.

Sialvera TE et al., Nutr Metab Cardiovasc Dis 2012; 22(10): 843-848.

In metabolic syndrome patients, the effect of plant sterol-enriched yoghurt-drinks on risk factors for coronary artery disease was investigated. In a 2-month randomized, single-blind, placebo-controlled, parallel-design study, 108 patients consumed either 2 plant sterol-enriched yoghurt-drinks (4 g/d of plant sterols) or placebo drinks whilst continuing their usual Westernized diets. Compared to placebo, plant sterol supplementation lowered total cholesterol by 15.9%, LDL-cholesterol by 20.3% and triglycerides by 19.1%. Also significant decreases in small dense LDL and in apoB levels were found. Usually, studies which are designed to show an LDL-cholesterol-lowering effect of plant sterols are not sufficiently powered to show a triglyceride-lowering effect (as the variation in triglycerides is large). The current study however does support a potential, relatively large triglyceride-lowering effect of plant sterols in metabolic syndrome subjects.

Impact of omega-2 fatty acids and/or plant sterol supplementation on non-HDL cholesterol levels of dyslipidemic Indian adults.
Khandelwal S et al., J Func Foods 2013; 5: 36-43.
In a 2x2 factorial, double-blind, placebo-controlled study, the independent and combined effects of plant sterols and fish oil omega-3 fatty acids on non-HDL-cholesterol were evaluated. Effects on LDL-cholesterol, HDL-cholesterol and triglycerides were reported earlier in the paper by Khandelwal et al. in 2009. Two hundred mildly hypercholesterolemic subjects consumed placebo, omega-3 fatty acids from fish oil (2 g/d in capsules), plant sterols (2 g/d in a yoghurt drink) or the combination for 4 weeks. Plant sterols significantly lowered non-HDL-cholesterol by 7.9%, whereas omega-3 did not significantly impact non-HDL-cholesterol (+3.8%). The combination resulted in a non-significant reduction in non-HDL-cholesterol of 3.9%. No significant interaction between plant sterols and omega-3 was observed. Despite this slight counteractive effect of omega-3 on the non-HDL-cholesterol lowering effect of plant sterols, the combination may still contribute to reducing coronary artery disease risk due to their previously reported triglyceride- and LDL-cholesterol lowering benefit.

OTHER FOOD FORMATS

Plant sterol esters lower plasma lipids and most carotenoids in mildly hypercholesterolemic adults.
Judd JT et al., Lipids 2002; 37(1): 33-42.
The cholesterol-lowering efficacy of plant sterol-enriched salad dressings with different fat contents was evaluated in this randomized controlled trial in which 53 subjects were allocated to one of two treatment arms receiving a dressing containing either 4 g or 8 g fat/serving. Within each arm, there was a randomized crossover between the control and the plant sterol-enriched dressing. The plant sterol-enriched salad dressings provided 2.2 g/d plant sterols in their ester form. The subjects consumed the control and the plant sterol dressings for 3 wks as part of a typical American diet providing 32% of energy from fat. The fat content of the salad dressings did not have an impact on cholesterol-lowering efficacy. On average, the plant sterol-enriched salad dressings lowered LDL-cholesterol by 7.9% compared with the control dressings. A decrease in triglycerides (7.3%) was also observed, with no effect on HDL-cholesterol concentrations. Plasma carotenoids were lowered by plant sterol consumption, but remained within the normal ranges.

Plant sterol-enriched milk tea decreases blood cholesterol concentrations in Chinese adults: a randomized controlled trial.
Li NY et al., Br J Nutr 2007; 98(5): 978-983.
This study investigated the effects of a new plant sterol-enriched format (milk tea) in the Chinese population. The study was a double-blind, randomized controlled trial including participants aged 18 to 65 years old who had a usual diet containing a significant amount of fat as part of the main meals and/or had a history of hypercholesterolemia. After a 10-20 days run-in period, 309 mildly hypercholesterolemic subjects were randomly allocated to one of the following dietary treatments: 1) a placebo milk tea, 2) a milk tea providing 1.5 g plant sterols per day or 3) a milk tea providing 2.3 g plant sterols per day. The milk tea was consumed with the two fattiest meals of the day with half the assigned daily dose taken on each occasion. The plant sterol-enriched milk tea had a significant effect on plasma total cholesterol concentrations (-3.8% and -4.4% for the 1.5 and 2.3 g/d doses, respectively) compared with the placebo. Reductions in LDL-cholesterol were -2.5% and -3.4% for 1.5 and 2.3 g/d, respectively, but the effect was not statistically significant with the lower dose. These effects were less than expected for such doses of plant sterols. Possible explanations for the lower efficacy observed in this study include, according to the authors, the food format and characteristics of the Chinese population studied.

PLANT STEROLS AS PART OF A DIETARY APPROACH

A dietary portfolio approach to cholesterol reduction: combined effects of plant sterols, vegetable proteins, and viscous fibers in hypercholesterolemia.
Jenkins DJ et al., Metabolism 2002; 51(12): 1596-1604.
In this study, the combined effect of plant sterols, soy proteins, viscous fibers and almonds on blood lipids was tested in 13 hyperlipidemic subjects who were already consuming a low-saturated fat, low-cholesterol diet before starting the study. The intake of spread was 24 g/day containing approximately 2 g plant sterols/day. After 4 weeks, the portfolio diet reduced LDL-cholesterol by 29% and the ratio of LDL-cholesterol to HDL-cholesterol by 26.5%. Near maximal effects were seen by week 2. This study shows that acceptable diets of foods from food retailers containing a combination of recognised cholesterol-lowering dietary components may be as effective as the starting dose of older first-line drugs in managing hypercholesterolemia.

The effect of combining plant sterols, soy protein, viscous fibers, and almonds in treating hypercholesterolemia.
Jenkins DJ et al., Metabolism 2003; 52(11): 1478-83.
This study aimed to assess the contribution of reduced saturated fat and dietary cholesterol to the effect on plasma lipid concentrations seen with the portfolio diet. Twenty-five hyperlipidemic subjects consumed either a portfolio diet (n=13) which is very low in saturated fat and high in plant sterols (1.2 g/1000 kcal), soy protein, viscous fibers, and almonds, or a low-saturated fat diet (n=12). LDL-cholesterol was significantly reduced by 12% on the low-fat diet and by 35% on the portfolio diet. The reduction in LDL-cholesterol was significantly larger with the portfolio diet than with the control diet. Combining a number of foods and food components in a single dietary portfolio may lower LDL-cholesterol similarly to treatment with first-generation statins and can thus increase the potential effectiveness of dietary therapy.

Effects of a dietary portfolio of cholesterol-lowering foods vs. lovastatin on serum lipids and C-reactive protein.
Jenkins DJ et al., JAMA 2003; 290(4): 502-510.
In this 4-week randomized controlled trial, 46 hyperlipidemic adults were assigned to 1 of 3 interventions: a very low-saturated fat diet (control), the same diet plus lovastatin, or a diet high in plant sterols, soy protein, viscous fibers, and almonds (dietary portfolio). LDL-cholesterol concentrations were reduced by 8.0% in the control group, by 30.9% in the statin group and by 28.6% in the dietary portfolio group. This data confirms that use of diets low in saturated fat together with plant sterols and viscous fibers, soy protein and nuts can greatly enhance the cholesterol-lowering effect of dietary intake.

Combined effects of a dietary portfolio of plant sterols, vegetable protein, viscous fibre and almonds on LDL particle size.
Lamarche B et al., Br J Nutr 2004; 92(4): 657-663.
The changes in LDL particle size in response to a diet very low in saturated fat and incorporating simultaneously viscous fibres (9 g/4.2 MJ), soybean protein (23 g/4.2 MJ), plant sterols (1 g/4.2 MJ) and almonds (15 g/4.2 MJ) were evaluated in hyperlipidemic subjects. The treatment phase was 4 weeks long, with blood draws taken at baseline, 2 and 4 weeks. The diet resulted in a mean (average of data from weeks 2 and 4) decrease in LDL-cholesterol concentrations of 30% compared with baseline, which was attributed to concurrent reductions in cholesterol content of large, medium and small LDL particles. These data showed that the portfolio diet including plant sterols is effective in lowering serum concentrations of all LDL fractions including small dense LDL which are known for their atherogenic effect.

Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants.
Jenkins DJ et al., Am J Clin Nutr 2005; 81(2): 380-387.
In a randomized crossover design, this study compared the cholesterol-lowering effect of a dietary portfolio with that of a statin. Thirty-four hyperlipidemic subjects completed three 1-month treatments in random order as outpatients: a very low saturated fat diet, the same diet plus 20mg lovastatin (statin diet) and a diet high in plant sterols (1.0 g/1000 kcal, delivered in a spread), soy-protein foods, almonds and viscous fibres. LDL-cholesterol concentrations were significantly reduced by 8.5%, 33.3%, and 29.6% after 4 weeks on the control, statin, and portfolio diets, respectively. The statin and portfolio diets did not differ in their ability to reduce LDL-cholesterol below the 3.4 mmol/L primary prevention cut-off. This study concludes that dietary combinations may not differ in potency from first-generation statins in achieving lipid goals for primary prevention.

Effects of a diet high in plant sterols, vegetable proteins, and viscous fibers (dietary portfolio) on circulating sterol levels and red cell fragility in hypercholesterolemic subjects.
Jones PJ et al., Lipids 2005; 40(2): 169-174.
This (uncontrolled) study investigated the effect of a dietary portfolio (a diet high in plant sterols (1 g/1000 kcal), soy protein (23 g/1000 kcal), viscous fiber (9 g/1000 kcal), and almonds (14 g/1000 kcal)) on serum sterols and red cell fragility in 13 hypercholesterolemic subjects. Subjects followed a 4-week run-in diet, then the portfolio diet for 4 weeks followed by a run-out period of 4 weeks. After the portfolio diet intervention, serum campesterol and sitosterol concentrations were raised by on average 50% and 27%, respectively. The portfolio diet did however not alter red cell fragility. Jenkins et al. 2002 earlier reported the lipid results of this study.

Assessment of the longer-term effects of a dietary portfolio of cholesterol-lowering foods in hypercholesterolemia.
Jenkins DJ et al., Am J Clin Nutr 2006; 83(3): 582-591.
The authors reported new data on the cholesterol-lowering efficacy of the portfolio diet in free-living conditions. The subjects were prescribed diets high in plant sterols (1.0 g/1000 kcal), soy protein (22.5 g/1000 kcal), viscous fiber (10 g/1000 kcal), and almonds (23 g/1000 kcal). The portfolio diet consistently lowered LDL-cholesterol by 14% and 13% at 12 and 48 weeks, respectively. In 32% of the subjects, who were the most compliant to the diet, LDL-cholesterol was lowered by more than 20%. These data indicated that compliance may be a key factor in achieving large cholesterol reductions with the portfolio diet. They also showed that the hypocholesterolemic effect of plant sterols may be additive to that of other cholesterol-lowering ingredients such as soy protein, viscous fibers and almonds.

Comparison of a dietary portfolio diet of cholesterol-lowering foods and a statin on LDL particle size phenotype in hypercholesterolaemic participants.
Gigleux I et al., Br J Nutr 2007; 98(6): 1229-1236.
The primary objective of this study was to investigate the impact of a dietary portfolio of cholesterol-lowering foods and a statin on LDL size electrophoretic characteristics. Thirty-four hyperlipidemic subjects consumed in a random order each of the three experimental treatments: a control diet low in saturated fat (NCEP Step II diet), the same diet with 20 mg lovastatin and a dietary portfolio diet high in plant sterols, soya proteins, soluble fibres and almonds. Each treatment phase was 1-month long. The portfolio and the statin treatments both significantly reduced LDL-cholesterol levels by about 21% and 25%, respectively, compared to the control diet. These reductions in LDL-cholesterol could be attributed to reductions in the concentration of cholesterol within the subclass of smallest LDL (portfolio -0.69 mmol/L and statin -0.99 mmol/L). These data suggest that the portfolio diet, similarly to the statin treatment, may provide additional benefits on cardiovascular health compared to the NCEP Step II low-fat diet.

Effect on hematologic risk factors for coronary heart disease of a cholesterol reducing diet.
Jenkins DJ et al., Eur J Clin Nutr 2007; 61(4): 483-492.
This study investigated the effect of a 1-year intake of a cholesterol-lowering diet on hematological indices. A growing body of evidence suggests that these indices may be considered risk factors for coronary heart disease. The diet consisted of a combination of plant sterols, soy proteins, soluble fibers and almonds, also known as the portfolio diet. Out of the 66 subjects who started the 1-year intervention, 55 subjects completed the study. The diet intervention significantly reduced hemoglobin, hematocrit, red cell number and neutrophils whereas it significantly increased platelet volume. Although the observed effect sizes of the hematological indices were modest, they indicate additional improvements in non-lipid risk factors and therefore may contribute to reduced coronary heart disease risk.

Long-term effects of a plant-based dietary portfolio of cholesterol-lowering foods on blood pressure.
Jenkins DJ et al., Eur J Clin Nutr 2008; 62(6): 781-788.
In this study, the effect of the portfolio diet (a combination of plant-based cholesterol-lowering foods, including almonds, soy proteins, viscous fibers and plant sterols) on blood pressure was investigated. The portfolio diet was consumed for 1 year by 66 subjects (no control group). Measurements related to blood pressure, body weight and nutrient intake were done monthly and then every 2 months throughout the study. Fifty subjects completed the study. Body weight was reduced significantly (0.7 ± 0.3 kg). Furthermore, both systolic and diastolic blood pressure were reduced significantly (-4.2 ± 1.3 mmHg and -2.3 ± 0.7 mmHg, respectively). The weight change was significantly related to diastolic blood pressure reduction. Furthermore, only the compliance with almond intake was significantly related to the blood pressure reduction. Although plant sterols are important cholesterol-lowering components of the portfolio diet, these data suggest that they may not play a role in the blood pressure lowering effect of the portfolio diet.

Effect of a dietary portfolio of cholesterol-lowering foods given at 2 levels of intensity of dietary advice on serum lipids in hyperlipidemia: a randomized controlled trial.
Jenkins DJ et al., JAMA 2011; 306(8): 831-839.
The effect on cholesterol of different intensities of counselling for the use of a dietary portfolio of cholesterol-lowering foods was investigated in 351 hyperlipidemic subjects. In a randomized controlled trial, subjects received advice to follow a control diet or a dietary portfolio at two levels of intensity (2 or 7 counselling visits) for a 6-months intervention period. After intervention, LDL-cholesterol was reduced by -13.8% in the intensive dietary portfolio group and by -13.1% in the routine dietary portfolio group. In the control group, LDL-cholesterol was reduced by 3%. Regardless of the intensity of counselling, a dietary portfolio is beneficial to lower cholesterol concentrations in real world conditions.

Consumption of a dietary portfolio of cholesterol lowering foods improves blood lipids without affecting concentrations of fat soluble compounds.
Ramprasath VR et al., Nutr J 2014; 13(1): 101.
Because plant sterols affect cholesterol metabolism by inhibition of intestinal cholesterol absorption, it is possible that the absorption of other fat-soluble compounds, such as vitamins, is also compromised by the intake of plant sterols. In the current study, the effect of two levels of intensity of a portfolio diet (i.e. plant sterols, soy proteins, soluble fibers and almonds) on fat-soluble vitamin status in hypercholesterolemic subjects. The effects on blood lipids within this study were earlier reported by Jenkins et al., 2011. After 6 months of intervention, no changes in plasma concentrations of α and γ tocopherol, lutein, lycopene and retinol were observed after various intensities of counselling for a portfolio diet. Only β-carotene was significantly decreased after intensive and routine portfolio diet counselling vs. control diet, but this reduction was not significant anymore after adjustment for the reduction in cholesterol.