BRITISH
Nutrition
FOUNDATION

The evidence for the
cholesterol lowering effects of

Plant Stanol Esters

British Nutrition Foundation

Highlights

- Cholesterol and cardiovascular risk
- What are plant stanol esters?
- Studies investigating the cholesterol lowering effects of plant stanol esters
- Table of studies
- History of safe use
- Claims approved and recommendations made by regulatory and medical bodies around the world
- Conclusions
- References

Acknowledgement

The British Nutrition Foundation is a registered charity. It promotes the wellbeing of society through the impartial interpretation and effective dissemination of scientifically based knowledge and advice on the relationship between diet, physical activity and health.

The BNF wishes to thank McNeil Nutritionals Ltd. for financial support in the publication and dissemination of the finished report.

Cholesterol and cardiovascular risk

Cardiovascular disease (CVD), including stroke and coronary heart disease (CHD), is the leading cause of morbidity and mortality globally. An estimated 17.5 million people died from cardiovascular disease in 2005, representing 30% of all deaths worldwide. Of these deaths, 7.6 million were due to heart attacks and 5.7 million were due to stroke (WHO 2008). An elevated blood cholesterol concentration is one of the principal risk factors for CHD (see Frayn & Stanner 2005). Diet plays a key role in helping to lower blood cholesterol concentration (Buttriss 2005a; van Horn *et al*. 2008) and recently, particular attention has been paid to the role that plant stanol and sterol esters can have in lowering blood cholesterol concentrations.

What is cholesterol?

Cholesterol is a lipid which in small amounts is essential for many body processes. For example, it is a structural component of cell membranes and nerve sheaths. Cholesterol is also required for the synthesis of bile acids and steroid and adrenocortical hormones such as oestrogen and cortisol. Some of the body's supply of cholesterol is from dietary sources but diet usually makes only a minor contribution to the total cholesterol concentration in the blood. Animal-derived foods such as eggs, meat, shellfish, and organ meats such as liver, are the primary sources of dietary cholesterol. The remainder (typically the majority) has been synthesised 'endogenously', predominantly in the liver. Cholesterol synthesis is primarily driven by dietary saturated fatty acid intake (saturates). The major dietary sources of saturates are meat products, whole-milk products, and cereal products and fried foods made with fats rich in saturates (in particular butter, coconut oil and palm oil).

Cholesterol is carried around the body, in the blood, by specific transport proteins. These lipid-protein complexes, known as lipoproteins, can be classified based on their density. There are three main types of lipoproteins. Very low-density lipoproteins (VLDL) supply the body with energy from the triglyceride (derived from dietary fat) they carry, during the fasting state. Low-density lipoproteins (LDL) transport cholesterol to peripheral tissues. High levels of VLDL and LDL are associated with increased CHD risk. Finally, the function of high-density lipoproteins (HDL) is to transport cholesterol from peripheral tissues back to the liver for processing, e.g. excretion via the gall bladder as a constituent of bile. High levels of HDL reduces CHD risk.

Although there are a number of risk factors for CHD, high blood cholesterol concentration (especially high LDL cholesterol coupled with low HDL) is one of the primary modifiable risk factors. Mortality data indicates that 45% of people in Western Europe and 35% from Central and Eastern Europe who die from heart attacks have abnormal blood lipids, sometimes referred to as dyslipidaemia (BHF 2007). Among European men aged 15 or over, mean total cholesterol ranges between 4.5mmol/l and 6.2mmol/l. Among European women, the corresponding range is between 4.6mmol/l and 6.1mmol/l, compared to the target concentration of less than 5mmol/l (WHO 2006). Blood cholesterol concentration can be decreased by a combination of dietary change and increased physical activity.

Dietary Changes to Reduce Blood Cholesterol Concentration

- Reduce consumption of all types of fat, for example by selecting lean cuts of meat and lower fat dairy products, by reducing use of oil and full fat spreads (margarine, butter), by eating fewer fried foods, and by moderating consumption of high fat foods such as cakes, biscuits and savoury snacks.
- Opt for oils/spreads that are higher in monounsaturates and polyunsaturates and lower in saturates.
- Include oil-rich fish in the diet once per week. (Those with heart disease may benefit from higher intakes*.)
- Include more fruit and vegetables in the diet, aiming for at least 5 portions of a variety of fruits and vegetables each day.
- Use less salt at the table and in cooking, and look for lower salt alternatives of manufactured foods. Reduce intake to below 6g/day (less for children).
- Include more starchy fibre-rich foods in the diet, e.g. bread, potatoes, yams, rice, pasta and oats, so that at least 50% of energy intake comes from carbohydrate and increase consumption of wholegrain foods.
- Drink alcohol sensibly, i.e. no more than 2-3 units per day for women and no more than 3-4 units per day for men. Avoid binge drinking.

*The National Institute for Health and Clinical Excellence recommends that patients who have suffered a heart attack should consume two to four portions of oil-rich fish per week (NICE 2007).

What are plant stanol esters?

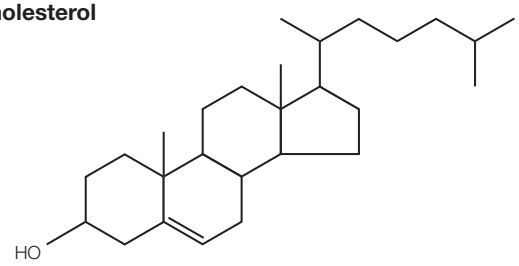
Although plants usually contain only small amounts of fat, seeds are relatively concentrated sources and provide essential fatty acids. One particular group of plant-derived lipids comprises plant stanols and sterols. Considerable interest in these has developed because of their possible beneficial effects, particularly with respect to CVD (see Wahle *et al*. 2001).

Sterols are essential components of cell membranes that play a key role in controlling membrane fluidity and permeability. Over 250 different sterols have been isolated from plants; the most abundant are sitosterol, campesterol and stigmasterol.

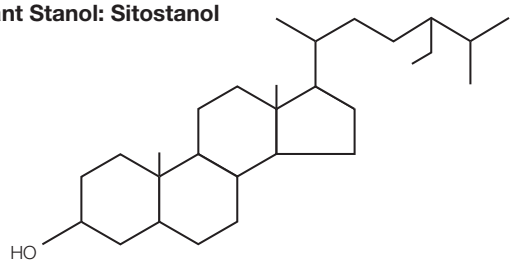
Stanols are saturated sterols (i.e. there are no double bonds in the structure). They are naturally occurring compounds that are found in very small amounts in plant products such as nuts, seeds and legumes. To improve their solubility, plant stanols are often combined with a fatty acid ester to produce plant stanol esters (see figure 1).

Figure 1: Chemical structures of cholesterol and plant stanols and sterols

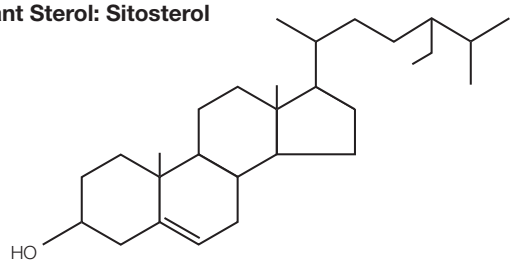
Cholesterol



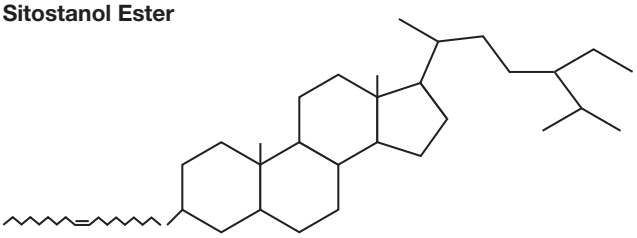
Plant Stanol: Sitostanol



Plant Sterol: Sitosterol

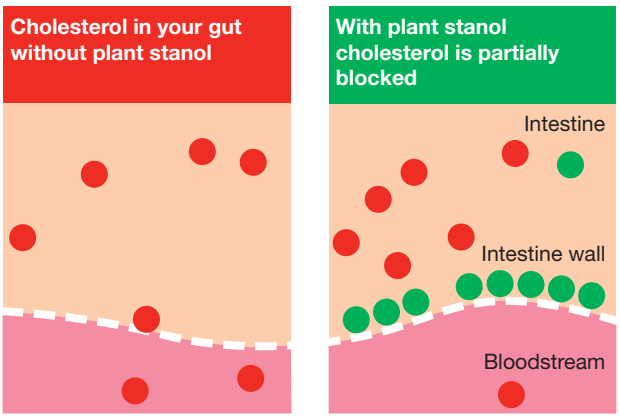


Sitostanol Ester



Both plant stanols and sterols have a structure very similar to that of cholesterol with only a few notable differences: they have a slightly different side chain configuration to cholesterol (Trautwein *et al*. 2003); and unlike cholesterol and plant sterols, plant stanols have a chemical structure that is completely saturated (Webb 2008). These structural differences affect absorption. Approximately 30-60% of total cholesterol is absorbed from the intestine into the blood, compared to only an estimated 0.15% of plant stanols and up to about 2% of plant sterols (Ostlund *et al*. 2002). Plant stanols and sterols are able to inhibit the absorption of both dietary cholesterol and the cholesterol incorporated into bile salts by the liver (Hallikainen *et al*. 2000). When plant stanol and sterol esters are present, absorption of cholesterol falls to approximately 20% (Plat 2001).

Figure 2: Mechanism of action of plant stanols



More cholesterol is absorbed so higher blood cholesterol levels

Less cholesterol is absorbed so lower blood cholesterol levels

Key: **Cholesterol** **Plant stanol**

What is the Mechanism of Action?

As stated earlier, plant stanols and sterols are poorly absorbed from the gut. They are also capable of significantly reducing the amount of cholesterol that is absorbed. This ultimately leads to lower blood total and LDL cholesterol concentrations. Prior to being absorbed, cholesterol is firstly incorporated into a mixed micelle (the transportation vehicle for cholesterol absorption) in the upper part of the small intestine. Research findings suggest that plant stanols and sterols compete with cholesterol for space in the micelle and that this results in much less of the cholesterol reaching the blood supply and it passes unabsorbed into the large bowel. Potential mechanisms have been described by Trautwein *et al*. (2003) (see figure 2).

Whilst the exact mechanism of action of these plant stanols and sterols is not fully understood, studies have shown that consuming approximately 2g of plant stanols or sterols each day results in a lowering of cholesterol concentrations in individuals with elevated cholesterol (Law 2000; Katan *et al*. 2003; Weingärtner *et al*. 2008). Furthermore, plant stanols and sterols lower total and LDL cholesterol without affecting HDL (Miettinen *et al*. 1995), and therefore are thought to have beneficial effects on reducing CHD risk. Because of their low concentrations in plant foods, it is not possible to acquire the amount of plant stanols or sterols needed to effectively lower cholesterol by consuming plant foods alone. Some manufacturers now add plant stanol or sterol esters to particular food products, such as some spreads, yogurts and yogurt drinks. When consumed regularly with meals, these products have the potential to significantly reduce both total and LDL cholesterol concentrations. When plant stanol or sterol esters are consumed, the active plant stanol and sterol component is released from the plant stanol or sterol ester molecule, allowing it to interfere with the absorption of cholesterol. The remaining fatty acid ester is absorbed like a normal fat.

Studies investigating the cholesterol-lowering effects of plant stanol esters

The cholesterol-lowering effects of plant sterol esters have recently been reviewed by Weingärtner *et al*. (2008); the body of evidence shows that regular consumption of 1 to 3 grams of plant sterols per day lowers LDL by 5-15%. Data from published human clinical trials studying the effects of plant stanol esters on LDL concentration in healthy adults with normal to moderately-elevated total cholesterol concentrations are summarised in Table 1. Studies investigating intakes of around 2-3g per day of plant stanols, provided as their esters, have demonstrated an average control-adjusted reduction in serum LDL concentration of 10% (see table 1). Findings from these studies indicate that the beneficial effect of plant stanols on LDL concentration is established within a few weeks, and remains stable over the duration of plant stanol ester consumption (Miettinen *et al*. 1995).

The effect of the frequency of intake

Data from clinical studies indicate that optimal LDL lowering is attained with a plant stanol intake of approximately 2g per day, and increasing the dose above this level does not further reduce serum LDL concentrations to a significant degree (Law 2000; Katan *et al*. 2003). The majority of studies on plant stanol consumption have assessed the effect of giving plant stanols on two or more occasions per day. However, Plat *et al*. (2000) showed that consuming 2.5g of plant stanols on a single occasion during the day for 4 weeks was just as effective in lowering serum LDL concentrations as when the dose was divided over 3 meals. The authors hypothesised that plant sterol or stanol esters may remain in the intestinal lumen or the cells of the intestinal wall for some time, allowing their impact to be prolonged.

The effect of the formulation

The form of the plant stanol (free or esterified) does not seem to be important in determining the ability of the dose to reduce plasma cholesterol concentrations; both the free and esterified forms are effective; manufacturers often combine the plant stanol with a fatty acid ester to improve solubility (Jones *et al*. 2000). The food matrix in which the plant stanols are eaten is also of little importance; the efficacy of plant stanol is preserved in both high and low fat matrices (Salo & Wester 2005; Miettinen *et al*. 1995). Spreads, low-fat dairy products, mayonnaise and pasta have all been shown to be effective carrier foods (table 1).

The effect of plant stanol esters in combination with a low fat, cholesterol-reducing diet

A good diet is one of the best ways to help prevent ill health. Dietary changes such as reducing saturated fatty acid intake and consuming more wholegrain foods can be effective in reducing cholesterol concentrations (Buttriss 2005b; van Horn *et al*. 2008), but the cholesterol lowering effects of plant stanol esters are independent of background diet (Hallikainen & Uusitupa 1999).

Studies have shown that consuming plant stanol esters in addition to a low-fat cholesterol-reducing diet leads to an even greater effect on LDL than consuming a low-fat cholesterol-reducing diet alone (Andersson *et al*. 1999; Hallikainen *et al*. 2000). For example, a study in a Finnish population demonstrated that the addition of 2.3g plant stanols to a low fat diet [less than 30% total fat, less than 10% saturated fat and less than 300mg cholesterol per day] brought about a 23% reduction in plasma LDL concentration, of which 10% was attributed to the diet and 13% to the plant stanols (Hallikainen & Uusitupa 1999).

The effect of plant stanol esters in combination with cholesterol lowering drugs

Statins are a class of drug that helps to protect healthy, but high risk, people from heart disease and prevent repeated problems in people who've already had a heart attack, a stroke or peripheral artery disease (BHF 2008). They act by reducing the amount of cholesterol produced in the body.

As with a healthy diet, consuming plant stanol esters in addition to statins has a greater effect on lowering cholesterol than with statins alone. One study demonstrating this effect is that by Blair *et al*. (2000). In this study, 176 patients, all of whom were taking statins, consumed either 3 servings per day of plant stanol ester spread (providing them with 5.1g per day of plant stanol ester, equivalent to 3g of plant stanols) or a control spread. The combination of the plant stanol ester enriched spread with the statins resulted in a 10% greater reduction in cholesterol concentrations than the effect seen with the control spread. A similar effect has also been found in a smaller group of participants with a history of myocardial infarction and people with diabetes (Gylling *et al*. 1997; Gylling & Miettinen 1996). Consuming plant stanol esters in combination with statins appears to be a more effective method of reducing cholesterol than simply doubling the statin dose, which usually only results in an additional reduction in LDL cholesterol concentrations of approximately 6% (Bradford *et al*. 1991).

Future research

Plant stanol esters have been shown to reduce cholesterol concentrations but there is currently no direct evidence that consumption of plant stanol esters actually reduces CVD events (*i.e.* heart disease and stroke) at an intake of 2g per day. The UK's National Institute for Health and Clinical Excellence (NICE) has called for trials to test both the efficacy and effectiveness of plant stanols and sterols in people who are at high risk of a first CVD event. Such trials should test the efficacy of advising people who are at high risk of experiencing a first CVD event to include food items containing plant stanols or sterols in a low-fat diet. NICE advises that the trial, which should follow a randomised placebo-controlled design, should last for at least 2 years and should consider appropriate outcomes (NICE 2008).

Table 1: Summary of studies investigating the cholesterol-lowering effects of plant stanols

	Author, (year)	Study type	Country of research	No. of subjects included in analyses	Study population	Baseline LDL concentration (mmol/L)		Intervention			Intervention group		Control group		Overall change in LDL concentration[1] (mmol/L)	Overall % reduction in LDL concentration[2]
						Intervention group	Contol group	Test product	How much plant stanol (g per day)?	Length of time diet followed for (weeks)	Final LDL concentration (mmol/L)	Change from baseline (mmol/L)	Final LDL concentration (mmol/L)	Change from baseline (mmol/L)		
1	Alhasson *et al*. (2006)	RDB PC II	US	26	Healthy sedentary middle-aged men and postmenopausal women with TC < 6.2mmol/L	3.31±0.18	2.92±0.26	Spread	3.0	4	2.87 ± 0.18	–0.44	3.13±0.23	+0.21	–0.65	19.6%
2	Andersson *et al*. (1999)	RDB PC II	Sweden	40	TC > 5mmol/L, < 8.5mmol/L	4.68±0.78	5.07±0.91	Low-fat spread + lipid-lowering diet	1.9	8	3.80 ± 0.53	–0.88	4.48±0.83	-0.59	–0.29	6.2%
3	Hallikainen & Uusitupa (1999)	RDB PC II	Finland	35	Hypercholesterolaemic adults with TC 5.4–7.5mmol/L	4.54±0.72	4.27±0.59	Low-fat spread	2.3 (WSE)	8	3.48±0.77	–1.06	3.82±0.56	-0.45	–0.61	13.4%
				37		4.25±0.85	4.27±0.59	Low-fat spread	2.1 (PSE)	8	3.45±0.76	–0.80	3.82±0.56	-0.45	–0.35	8.2%
4	Hallikainen *et al*. (2006)	RDB PC XO	Finland	76	Hypercholesterolaemic adult men and women with baseline TC < 8mmol/L	3.31±0.16	4.41±0.13	Spread	1.92	10	3.09±0.15	–0.22	3.50±0.15	+0.09	–0.31	9.4%
5	Homma *et al*. (2003)	RDB PC II	Japan	69	Healthy adult Japanese men and women with baseline TC 5.4–7.2mmol/L	3.96±0.49	4.06±0.59	Spread	2.0	4	3.58	–0.38	4.02	–0.04	–0.34	8.6%
				71		3.96±0.44	4.06±0.59		3.0		3.66	–0.30	4.02	–0.04	–0.26	6.6%
6	Hyun *et al*. (2005)	RDB PC II	Korea	51	Korean young male and female adults with normocholesterolaemia and mild hypercholesterolaemia (Baseline TC 4.5–6.5mmol/L)	3.08±0.12	2.98±0.09	Low-fat yogurt	2.0	4	2.78±0.12	–0.30	2.93±0.09	–0.05	–0.25	8.1%
7	Jauhiainen *et al*. (2006)	RDB PC II	Finland	67	Mildly hypercholeterolaemic adult men and women (Baseline TC 5.0–6.5mmol/L)	3.58±0.09	3.60±0.10	Low-fat cheese	2.0	5	3.10±0.10	–0.48	3.48±0.10	–0.12	–0.36	10.1%
8	Jones *et al*. (2000)	RDB PC XO	Canada	15	Hyperlipidemic adult males (Baseline TC 6.0–10.0mmol/L)	4.35±0.23	4.46±0.25	Spread	1.8	3	3.95±0.19	–0.40	4.22±0.18	–0.24	–0.16	3.7%
9	Lagström *et al*. (2006)	RDB PC II	Finland	42	Adult subjects with normo- to mild hypercholesterolaemia (Baseline TC 4.5–7mmol/L)	3.4±0.5	3.6±0.8	Capsules taken with food	2.0	3	3.1±0.5	–0.30	3.5±0.8	–0.10	–0.20	5.9%
10	Miettinen & Vanhanen (1994)	RDB PC II	Finland	15	Hypercholesterolaemic adults with TC > 6.0mmol/L	3.39±0.25	4.34±0.25	Mayonnaise	0.83	9	4.42	–0.20	3.19	+0.08	–0.28	8.3%
11	Miettinen *et al*. (1995)	RDB PC II	Finland	153	Adult men and women with baseline TC ≥ 5.6mmol/L	4.14±0.10	4.12±0.10	Spread	2.6	52	3.47±0.08	–0.67	4.07±0.10	-0.05	–0.62	15.0%
12	Niinikoski *et al*. (1997)	RDB PC II	Finland	24	Normocholesterolaemic adult subjects	3.8±1.1	3.9±1.1	Spread	2.2	5	3.0±1.1	–0.80	3.6±1.0	–0.30	–0.50	13.1%
13	Noakes *et al*. (2005)	RDB PC XO	Australia	40	Modestly hypercholesterolaemic adults with baseline TC 5–7.5mmol/L	4.48±0.75		Low-fat yogurt	1.7	3	4.22±0.76	–0.26	4.45±0.74	–0.03	–0.23	5.1%
14	Plat & Mensink (2000)	RDB PC II	The Netherlands	78	Non-hypercholesterolaemic adult men and women with TC < 6.5mmol/L	2.94±0.74	2.96±0.73	Spread & shortening	3.8 (PSE)	8	2.51±0.66	–0.43	2.90±0.73	–0.06	–0.37	12.6%
				76		2.94±0.90	2.96±0.73		4.0 (WSE)	8	2.54±0.72	–0.41	2.90±0.73	–0.06	–0.35	11.9%
15	Vanhanen *et al*. (1993)	RDB PC II	Finland	67	Modestly hypercholesterolaemic adults with baseline TC > 6.0mmol/L	3.71±0.11		Mayonnaise	3.4	6	3.34±0.14	–0.37	3.67	–0.04	–0.33	8.9%
16	Vanhanen *et al*. (1994)	RDB PC II	Finland	15	Mildly hypercholesterolaemic adults with baseline TC > 6.0mmol/L	3.39±0.25	4.34±0.25	Mayonnaise	0.8	9	3.19	–0.20	4.42	+0.08	–0.28	8.3%
						3.39±0.25	4.34±0.25	Mayonnaise	2.0	6	3.00	–0.39	4.49	+0.15	–0.54	15.9%
17	Woodgate *et al*. (2006)	RDB PC II	Canada	30	Mild to modestly hypercholesterolaemic adults with baseline TC > 5.0mmol/L	5.35±1.0	5.21±0.7	Soft gels	1.6	4	4.86±1.0	–0.49	5.11±0.6	–0.10	–0.39	7.3%
															Overall change in LDL concentration[3] (mmol/L)	
18	Cater *et al*. (2005)	RDB PC XO	US	8	Adult men and women with baseline LDL ≥ 3.4mmol/L	DNI	DNI	Spread	2.0	6	3.67 ± 0.65	DNI	4.19±0.52	DNI	–0.52	12.4%
						DNI	DNI		3.0	6	3.65 ± 0.52	DNI		DNI	–0.54	12.9%
						DNI	DNI		4.0	6	3.62 ± 0.36	DNI		DNI	–0.57	13.6%
		RDB PC XO	US	13	Postmenopausal women with moderately elevated LDL (> 3.9mmol/L).	DNI	DNI	Spread	3.0	6	3.65 ± 0.39	DNI	4.19±0.65	DNI	–0.54	12.9%
19	Gylling & Miettinen (1999)	RDB PC XO	Finland	23	Postmenopausal women with elevated TC (5.5–8.0mmol/L).	DNI	DNI	Butter	2.4	5	3.70±0.16	DNI	4.15±0.18	DNI	–0.45	10.8%
20	Hallikainen *et al*. (2000)	RDB PC XO	Finland	34	Free-living adult men and women with baseline TC 4.8–7.0 mmol/L	DNI	DNI	Spread	1.9	4	3.65±0.69	DNI	4.19±0.61	DNI	–0.54	12.9%
21	Mensink *et al*. (2002)	RDB PC II	The Netherlands	60	Non-hypercholesterolaemic adults with TC < 6.5mmol/L	2.92±0.87*	2.86±0.87	Low-fat yogurt	2.98	4	2.68±0.74	–0.34	2.92±0.87	+0.06	–0.40	13.7%
22	Nguyen *et al*. (1999)	RDB PC II	US	159	Adult men and women with baseline TC 5.2–7.3mmol/L	DNI	DNI	Spread	3.0	8	DNI	DNI	DNI	DNI	DNI	11.7%
				157		DNI	DNI		3.0	8	DNI	DNI	DNI	DNI	DNI	5.2%
				162		DNI	DNI		2.0	8	DNI	DNI	DNI	DNI	DNI	6.7%
23	Plat *et al*. (2000)	RDB PC XO	The Netherlands	39	Adult subjects with normocholesterolaemia and mild hypercholesterolaemia with TC < 6.5mmol/L	DNI	DNI	Spread & shortening	2.5 (1X a day)	4	2.74±0.81	DNI	3.04±0.86	DNI	–0.29	9.5%
				39					2.5 (3X a day)	4	2.73±0.87	DNI		DNI	–0.31	10.2%
24	Salo & Wester (2005)	RDB PC II	Germany	39	Adult subjects with normocholesterolaemia and mild hypercholesterolaemia with TC 4.5–7mmol/L	DNI	DNI	Yogurt drink	2.0	6	DNI	DNI	DNI	DNI	DNI	12.6%
25	Salo & Wester (2005)	RDB PC II	Finland	37	Adult subjects with normocholesterolaemia and mild hypercholesterolaemia with TC 4.5–7mmol/L	DNI	DNI	Pasta	2.0	2	DNI	DNI	DNI	DNI	DNI	10.9%
26	Salo & Wester (2005)	RDB PC II	Finland	60	Adult subjects with normocholesterolaemia and mild hypercholesterolaemia with TC 4.5–7mmol/L	DNI	DNI	Meat-based low-fat prepared meal	2.0	2	DNI	DNI	DNI	DNI	DNI	10.1%
27	Seppo *et al*. (2007)	RDB PC II	Finland	202	Adults with mild or moderate hypercholesterolaemia (TC 5.0–6.5mmol/L)	3.4±0.1	3.5±0.1	Yogurt	2.0	5	DNI	DNI	DNI	DNI	DNI	2.9%
								Yogurt drink			DNI	DNI	DNI	DNI	DNI	3.2%
								Yogurt drink			DNI	DNI	DNI	DNI	DNI	11.8%
								Milk			DNI	DNI	DNI	DNI	DNI	6.2%
28	Theuwissen & Mensink (2007)	RDB PC XO	The Netherlands	40	Healthy adult men & women with slightly elevated TC (TC 5.0–8.0mmol/L)	DNI	DNI	Muesli	1.5	4	3.89 ± 0.90	DNI	4.09 ± 0.91	DNI	–0.18	4.4%
29	Weststrate & Mejer (1998)	Incomplete Latin Square	The Netherlands	95	Normocholesterolaemic and mildly hypercholesterolaemic adults with TC < 8.0mmol/L	DNI	DNI	Spread	2.7	3.5	2.96	DNI	3.36	DNI	–0.40	11.9%
															Average	**9.8%**
															Min	**2.9%**
															Max	**19.6%**

Key: RDB PCII – Randomised double blind placebo controlled parallel design
RDB PC XO – Randomised double blind placebo controlled cross over study
PSE = Plant Stanol Ester
WSE = Wood Stanol Ester
TC = Total Cholesterol
DNI = Data not included in paper
*As reported

Studies 1-17: Overall change and overall % reduction calculated by [1] and [2]
Studies 18-29: Overall change and overall % reduction calculated using [3]

[1] Overall change = Change in the Intervention group – change in the Control group
[2] Overall % reduction = ((Change in the Intervention group – change in the Control group) divided by baseline LDL concentration of Intervention group) x 100
[3] Difference between final LDL concentration of Intervention group and final LDL concentration of Control group

History of safe use

Foods with added plant stanol esters were launched in the UK and Ireland in 1999, following a successful launch in Finland in 1995. A range of dairy products containing plant stanol esters are now on the market, including yogurts, yogurt drinks, spreads and cream cheese style spreads. Millions of Europeans are regular consumers. The body of available evidence demonstrates that the cholesterol lowering effects are most beneficial at an intake of at least 2g per day, eaten with a meal (Law 2000).

Foods with added plant stanol esters have been approved for use by many regulatory agencies, including the Scientific Committee on Foods of the European Union (EC 2000) and the US Food and Drug Administration (FDA 2000). Evidence of the safety and efficacy of plant stanol esters has come from extensive animal and human research.

Initial concerns about the safety of plant stanol and sterol esters centred on their possible interference with the absorption of nutrients (particularly fat soluble vitamins) and therapeutic drugs, as well as the possible effects of unabsorbed cholesterol and plant stanols and sterols and their metabolites in the large intestine.

It has been suggested that the absorption of other substances, including fat-soluble vitamins, might be reduced by plant stanol and sterol esters (Plat & Mensink 2005). However, studies have found the absorption of the fat-soluble vitamins A, D and K to be largely unaffected by plant stanol ester intake (Katan *et al*. 2003). Some studies have shown a slight reduction in plasma levels of beta-carotene, although levels always remained within normal limits (Katan *et al*. 2003). Indeed, the slight deficit in beta-carotene can easily be compensated by the regular consumption of fruit and vegetables, important components of a heart-healthy diet (Noakes *et al*. 2002).

Information about the effect of plant stanol esters on the absorption of therapeutic drugs is limited. However, one eight-week study of 318 hypercholesterolaemic subjects reported no adverse effects on the absorption of therapeutic drugs when plant stanol esters were consumed (Nguyen *et al*. 1999).

As plant stanol esters inhibit the absorption of cholesterol, they consequently result in an increased faecal excretion of cholesterol and its metabolites. These substances therefore enter the large intestine in larger quantities than would normally occur in the absence of foods with added plant stanol and sterol esters. Although many studies have been conducted investigating gut health and potential cancer risk (for example Drasar & Hill 1972; Awad & Fink 2000), at present there are no convincing data to suggest that plant stanol esters have any effect on colon cancer risk (Katan *et al*. 2003).

The evidence published to date on the safety of plant stanol esters demonstrates that an intake of 2g per day effectively lowers LDL concentration, produces no adverse effects, and poses no health risks. However, intakes above 3g per day are not recommended, as higher levels have little additional effect on LDL levels (Katan *et al*. 2003).

The safety of foods containing plant stanol esters is continually being monitored to ensure their safety. For example, a prospective longitudinal study in Finland is currently investigating long-term health effects of consumption of stanol spreads (Attolainen *et al*. 2001).

Claims approved and recommendations made by regulatory and medical bodies around the world

Products enriched with plant stanol esters sometimes carry claims about the health promoting effects associated with the ingredients they contain. A number of regulatory and medical bodies around the world have issued position statements, recommendations or regulatory frameworks, to ensure that any claims made are underpinned with robust scientific evidence, in order to protect consumers. By following these recommendations and by adopting labelling rules that regulate the information about the health benefits of foods and their nutritional value, it is hoped that consumers will be able to make informed and meaningful choices.

All foods sold in Europe with added plant stanols or sterols must include the statement: *'foods with added plant stanol/sterol esters may not be nutritionally appropriate for pregnant and breast feeding women, and children under 5 years. If you take cholesterol lowering medication seek you doctor's advice. Eat no more than 3g of plant stanol per day. Eating more does not provide additional cholesterol lowering benefit'*. This is to ensure that consumers are provided with information to help them to set the potential health benefits of the product in context, as well as advice on how to incorporate such products into a healthy, balanced diet.

Claims approved by national bodies

The Table below sets out the detail of claims that have been approved for use in the USA, Netherlands, Japan and Sweden. As evident from the detail of the claims, the regulatory bodies have made sure that any beneficial health effects of the product are matched with clear conditions of use, including recommended amounts (see table 2).

A new European Commission (EC) regulation on nutrition and health claims (1924/2006/EC) came into force in July 2007. The regulation provides a legal framework for nutrition and health claims that applies across the European Union (EU). In due course a list of approved claims will be published that can be used on foods, provided the product in question contains enough of the nutrient to have a health benefit and its nutrient profile is deemed healthy enough to support a claim.

Health claims, which refer to a health benefit from a food or food constituent, are divided into two types. One category comprises claims that refer specifically to reduction of disease risk or to children's health. The other category excludes these types of claims and instead comprises health claims that are supported by generally accepted scientific evidence and concern the function of the food or its components (e.g. in relation to growth, development, function or behaviour). It is not yet certain into which category claims relating to the cholesterol lowering potential of plant stanol esters will fall, but it is thought likely that they will be considered to be disease risk reduction claims. Manufacturers wishing to make such a claim will need to submit a detailed dossier describing the scientific evidence for the claim to the EC. For more information see Aisbitt 2007.

Recommendations regarding plant stanol esters

Due to the potential of foods with added plant stanol esters to have a beneficial effect on blood cholesterol concentrations, a number of medical authorities have described their value in the treatment and management of elevated cholesterol. Table 3 outlines recommendations from around the world.

Table 2: Claims approved by national bodies

National Body	Food	Claim
US Food and Drug Administration (FDA) September 2000 and February 2003	Diets that include plant stanol esters	Foods containing at least 1.7g per serving of plant stanol esters, eaten twice a day with meals for a total daily intake of at least 3.4g, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. A serving of [product name] supplies [x] grams of plant stanol esters. In 2003, FDA stated it will leverage its enforcement discretion on products that contain 0.8g of plant stanols/plant sterols.
Netherlands Nutrition Centre May 2001	Spread or yogurt drink	Two to three servings of [product name] daily lower serum total and low-density lipoprotein cholesterol concentrations and may consequently reduce the risk of coronary heart disease.
Ministry of Health, Labor and Welfare, Japan February 2002	Spread	This product contains plant stanol ester which restrains the body of absorption of blood cholesterol and lowers blood cholesterol level, especially LDL cholesterol (bad cholesterol). We recommend the product for people who tend toward a high level of cholesterol.
Swedish Nutrition Foundation December 2006	Spread or yogurt drink	[Product name] effectively reduces blood cholesterol. [Product name] has a sustained blood cholesterol lowering effect. [Product name] effectively reduces blood cholesterol.

Table 3: Recommendations regarding plant stanol esters

Medical Body	Recommendation
National Cholesterol Education Programme Adult Treatment Panel III, USA	In the third report on the detection, evaluation and treatment of high blood cholesterol, published in 2002, the authors include a statement on plant stanol esters. They recommend that plant stanol esters are a therapeutic option to enhance serum cholesterol lowering; daily intakes of 2-3g of plant sterols or stanols will reduce serum LDL cholesterol by 6-15% (NCEP 2002).
Joint European Societies	The third Joint Task Force Report of European and other societies on cardiovascular disease prevention provides general recommendations regarding fat in the diet. In the case of dyslipidemia specifically, the importance of lowering serum LDL cholesterol by dietary means is stressed and the fact that plant sterols can help to achieve this is mentioned (De Backer *et al*. 2003).
Joint British Societies	The Task Force reports that consumption of 2g plant sterols or stanols per day by individuals with established cardiovascular disease would be expected to lower serum LDL cholesterol by approximately 0.5mmol/L and reduce the risk of cardiovascular disease by 25% over a 2 year period (Wood *et al*. 2005).
American Heart Association	The American Heart Association recommends that all patients with coronary or other forms of atherosclerotic vascular disease should add 2g daily of plant stanols or sterols to a low saturated fat, low cholesterol diet, to lower LDL cholesterol further (Lichtenstein *et al*. 2006).
World Health Organization	The World Health Organization recognises the cholesterol lowering ability of plant sterol and stanol esters and indicates that there is the probability that plant sterol and stanol esters may lower the risk of cardiovascular disease, in its report on diet, nutrition and the prevention of chronic diseases (WHO/FAO 2003).
International Atherosclerosis Society	After reviewing numerous recent studies, a report published by the International Atherosclerosis Society indicates that plant sterols and stanols lower cholesterol concentrations beyond what can be achieved by reducing dietary saturated fatty acids and cholesterol alone (IAS 2003).
Finnish Internal Medicine Society	The treatment guidelines of the Finnish Internal Medicine Society state that if regular dietary treatment is not enough to lower cholesterol in patients with dyslipidemia, products containing plant sterol or plant stanol esters can be added (FIMS 1996).
Australian Heart Foundation	In their recent position statement, the Australian Heart Foundation recommends that adult Australians with high absolute risk of CVD would benefit from the cholesterol-lowering effects of consuming plant sterol and stanol esters naturally occurring in plant foods and food products enriched with plant sterol and stanol esters (2-3g of plant stanols or sterols per day) (AHF 2007).

Conclusions

Foods and drinks with added plant stanol or sterol esters reduce blood cholesterol and are a promising addition to interventions aimed at lowering heart disease risk. Maximum effects are observed at intakes of approximately 2-3g per day. The reduction in LDL cholesterol concentration ranges between 6-15%. Therefore, individuals wishing to reduce their blood cholesterol level may benefit from inclusion of foods with added plant stanol esters (e.g. spreads, mini drinks and yogurts) in a healthy, varied and balanced diet.

References

Aisbitt B (2007) Nutrition and Health Claims: the facts on your food. EuroFIR Synthesis Report No. 5. EuroFIR/British Nutrition Foundation: London, UK.

AHF (Australian Heart Foundation) (2007) Position statement on phytosterol/stanol enriched foods. Available at: http://www.heartfoundation.org.au/document/NHF/HF_Phytosterols_Stanols_CVD_PositionSt_2007_Aug_FINAL.pdf (accessed June 2008).

Alhassan S, Reese KA, Mahurin J *et al*. (2006) Blood Lipid response to plant stanol ester supplementation and aerobic exercise training. *Metabolism Clinical and Experimental*. **55**: 541-549.

Andersson A, Karlstrom B, Mohsen R *et al*. (1999) Cholesterol-lowering effects of a stanol ester-containing low-fat margarine used in conjunction with a strict lipid-lowering diet. *European Heart Journal Supplements*. **1**: S80-S90.

Attolainen M, Luoto R, Uutela A *et al*. (2001) Characteristics of users of and nonusers of plant stanol ester margarine in Finland: an approach to study functional foods. *Journal of the American Dietetic Association*. **101**(11): 1365-8.

Awad AB and Fink CS (2000) Phytosterols as anticancer dietary components: evidence and mechanisms of action. *Journal of Nutrition*. **130**: 2127-2130.

Blair SN, Capuzzi DM, Gottlieb SO *et al*. (2000) Incremental reduction of serum total cholesterol and low-density lipoprotein cholesterol with the addition of plant stanol ester-containing spread to statin therapy. *American Journal of Cardiology*. **86**: 46-52.

Bradford RH, Shear CL, Chremos AN *et al*. (1991) Expanded Clinical Evaluation of Lovastatin (EXCEL) Study results. I. Efficacy in modifying plasma lipoproteins and adverse event profile in 8245 patients with moderate hypercholesterolemia. *Archives of Internal Medicine*. **151**(1): 43-49.

BHF (British Heart Foundation) (2007) Coronary Heart Disease Statistics. Available at: http://www.ws3.heartstats.web.baigent.net/uploads/documents%5C48160_text_05_06_07.pdf (accessed 09/06/08).

BHF (British Heart Foundation) (2008) All about statins. Available at: http://www.bhf.org.uk/living_with_heart_conditions/treatment/medicines_for_the_heart/statins.aspx (accessed 09/06/08).

Buttriss J (2005a) *Diet and cardiovascular disease: where are we now?* In: Cardiovascular disease: diet, nutrition and emerging risk factors. The report of the British Nutrition Foundation Task Force (Stanner S ed.). Blackwell Publishing. Oxford. Pp 196-233.

Buttriss J (2005b) *A Public Health Approach to Cardiovascular Disease Risk Reduction* In: Cardiovascular disease: diet, nutrition and emerging risk factors. The report of the British Nutrition Foundation Task Force (Stanner S ed.). Blackwell Publishing. Oxford. Pp 234-265.

Cater NB, Garcia-Garcia AB, Vega GL *et al*. (2005) Responsiveness of plasma lipids and lipoproteins to plant stanol esters. *The American Journal of Cardiology*. **96**(1A): 23D-28D.

De Backer G, Ambrosioni E, Borch-Johnsen K *et al*. (2003) European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *European Heart Journal*. **24**: 1601-10.

Drasar BS and Hill MH (1972) Intestinal bacteria and cancer. *American Journal of Clinical Nutrition*. **25**: 1399-1404.

EC (European Commission) (2000) Opinion of the Scientific Committee on Food on a request for the safety assessment of the use of phytosterol esters in yellow fat spreads. Available at: http://ec.europa.eu/food/fs/sc/scf/out56_en.pdf (accessed June 2008).

FDA (Food and Drug Administration) (2000) FDA Authorizes New Coronary Heart Disease Health Claim for Plant Sterol and Plant Stanol Esters. Available at: http://www.fda.gov/bbs/topics/answers/ans01033.html (accessed June 2008).

FDA (Food and Drug Administration) (2003) FDA letter regarding enforcement discretion with respect to expanded use of an interim health claim rule about plant sterol/stanol esters and reduced risk of coronary heart disease. Available at: http://www.cfsan.fda.gov/~dms/ds-ltr30.html (accessed June 2008).

Frayn K & Stanner S (2005) *The Aetiology and Epidemiology of Cardiovascular Disease*. In: Cardiovascular disease: diet, nutrition and emerging risk factors. The report of the British Nutrition Foundation Task Force (Stanner S ed.). Blackwell Publishing. Oxford. Pp 10-13.

FIMS (Finnish Internal Medicine Society) (1996) Suomen Yhdistys, Suomen Seura, Suomen Verenpaineyhdistys, Kunnallislääkärit-yhdistys, Suomen Yhdistys, Suomen Sydäntautiliitto: Prevention of coronary heart disease in clinical practice [in Finnish]. *Suom Lääkäril* **51**: 783-802.

Gylling H and Miettinen TA (1999) Cholesterol reduction by different plant stanol mixtures and with variable fat intake. *Metabolism*. **48**(5): 575-580.

Gylling H, Radhakrishnan R and Miettinen TA (1997) Reduction of Serum Cholesterol in Postmenopausal Women with Previous Myocardial Infarction and Cholesterol Malabsorption Induced by Dietary Sitostanol Ester Margarine. *Circulation*. **96**: 4226-4231.

Gylling H and Miettinen T (1996) Effects of inhibiting cholesterol absorption and synthesis on cholesterol and lipoprotein metabolism in hypercholesterolemic non-insulin-dependent diabetic men. *Journal of Lipid Research*. **37**: 1776-85.

Hallikainen M and Uusitupa M (1999) Effects of 2 low-fat stanol-ester containing margarines on serum cholesterol concentrations as part of a low-fat diet in hypercholesterolaemic subjects. *American Journal of Clinical Nutrition*. **69**: 403-410.

Hallikainen M, Sarkkinen E, Gylling H *et al*. (2000) Comparison of the effects of plant sterol ester and plant stanol ester-enriched margarines in lowering serum cholesterol concentrations in hypercholesterolaemic subjects on a low-fat diet. *European Journal of Clinical Nutrition*. **54**: 715-725.

Hallikainen M, Lyyra-Laitinen T, Laitinen T *et al*. (2006) Endothelial function in hypercholesterolemic subjects : Effects of plant stanol and sterol esters. *Atherosclerosis*. **188**: 425-432.

Homma Y, Ikeda I, Ishikawa T *et al*. (2003) Decrease in plasma low-density lipoprotein cholesterol, apolipoprotein B, cholesterol ester transfer protein, and oxidized low-density lipoprotein by plant stanol ester-containing spread: a randomized, placebo controlled trial. *Nutrition*. **19**: 369-374.

Hyun YJ, Kim OY, Kang JB *et al*. (2005) Plant stanol esters in low-fat yoghurt reduces total and low-density lipoprotein cholesterol and low-density lipoprotein oxidation in normocholesterolemic and mildy hypercholesterolemic subjects. *Nutrition Research*. **25**: 743-753.

IAS (International Atherosclerosis Society) (2003) Harmonized clinical guidelines on the prevention of atherosclerotic vascular disease. Hamburg, Germany: International Atherosclerosis Society. pp. 1–28.

Jauhiainen T, Salo P, Niittynen L *et al*. (2006) Effects of low-fat hard cheese enriched with plant stanol esters on serum lipids and apolipoprotein B in mildly hypercholesterolaemic subjects. *European Journal of Clinical Nutrition*. **60**: 1253-1257.

Jones PJ, Raeini-Sarjaz M, Ntanios FY *et al*. (2000) Modulation of plasma lipid levels and cholesterol kinetics by phytosterol versus phytostanol esters. *Journal of Lipid Research*. **41**: 697-705.

Katan MB, Grundy SM, Jones P *et al*. (2003) Efficacy and Safety of Plant Stanols and Sterols in the Management of Blood Cholesterol Levels. *Mayo Clinical Proceedings*. **78**: 965-978.

Lagstrom H, Helenius H and Salo P (2006) Serum cholesterol-lowering efficacy of stanol ester incorporated in gelatine capsules. *Scandinavian Journal of Food and Nutrition*. **50**(3): 124-30.

Law MR (2000) Plant sterol and stanol margarines and health. *British Medical Journal*. **320**: 861-864.

Lichtenstein AH, Appel LJ, Brands M *et al*. (2006) Summary of American Heart Association Diet and Lifestyle Recommendations revision 2006. *Arteriosclerosis, Thrombosis and Vascular Biology*. **26**: 2186-91.

Maki KC, Davidson MH, Umporowicz DM *et al*. (2001) Lipid responses to plant-sterol-enriched reduced-fat spreads incorporated into a National Cholesterol Education Program Step I Diet. *American Journal of Clinical Nutrition*. **74**: 33-43.

Mensink RP, Ebbing S, Lindhout M *et al*. (2002) Effects of plant stanol esters supplied in low-fat yoghurt on serum lipids and lipoproteins, non-cholesterol sterols and fat soluble antioxidant concentrations. *Atherosclerosis*. **160**: 205-213.

Miettinen TA and Vanhanen H (1994) Dietary sitostanol related to absorption, synthesis and serum level of cholesterol in different apolipoprotein E phenotypes. *Atherosclerosis*. **105**: 217-226.

Miettinen TA, Puska P, Gylling H *et al*. (1995) Reduction of serum cholesterol with sitostanol-ester margarine in a mildly hypercholesterolemic population. *New England Journal of Medicine*. **333**:1308-12.

NCEP (National Cholesterol Education Programme) (2002) Detection, evaluation and treatment of high blood cholesterol in adults (adult treatment panel III). Available at: http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3full.pdf (accessed June 2008).

NICE (National Institute for Health and Clinical Excellence) (2007) MI: Secondary prevention: Secondary prevention in primary and secondary care for patients following a myocardial infarction. Available at: www.nice.org.uk (accessed June 08).

NICE (National Institute for Health and Clinical Excellence) (2008) National Institute of Health and Clinical Excellence clinical guideline 67 Lipid modification: Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease.

Nguyen TT, Dale LC, von Bergmann K *et al*. (1999) Cholesterol-Lowering Effect of Stanol Ester in a US Population of Mildly Hypercholesterolemic Men and Women: A Randomized Controlled Trial. *Mayo Clinic Proceedings*. **74**: 1198-1206.

Niinikoski H, Viikari J and Palmu T (1997) Cholesterol-lowering effect and sensory properties of sitostanol ester margarine in normocholesterolemic adults. *Scandinavian Journal of Nutrition*. **41**: 9-12

Noakes M, Clifton PM, Doornbos AME *et al*. (2005) Plant sterol ester-enriched milk and yoghurt effectively reduce serum cholesterol in modestly hypercholesterolemic subjects. *European Journal of Nutrition*. **44**: 214-222.

Noakes M, Clifton P, Ntanios F *et al*. (2002) An increase in dietary carotenoids when consuming plant sterols or stanols is effective in maintaining plasma carotenoid concentrations. *American Journal of Clinical Nutrition*. **75**: 79-86.

Ostlund RE, McGill JB, Zeng CM *et al*. (2002) Gastrointestinal absorption and plasma kinetics of soy Δ^5-phytosterols and phytostanols in humans. *American Journal of Physiology – Endocrinology and Metabolism*. **282**: E911-E916.

Plat J and Mensink RP (2000) Vegetable oil based versus wood based stanol ester mixtures: effects on serum lipids and hemostatic factors in non-hypercholesterolemic subjects. *Atherosclerosis*. **148**: 101-112.

Plat J, van Onselen E, van Heugten M *et al*. (2000) Effects on serum lipids, lipoproteins and fat soluble antioxidant concentrations of consumption frequency of margarines and shortenings enriched with plant stanols esters. *European Journal of Clinical Nutrition*. **54**: 671-677.

Plat J (2001) Plant Stanol Esters: *Effects on cardiovascular risk markers and cholesterol metabolism*. PhD Thesis. University of Maastrict, The Netherlands.

Plat J and Mensink RP (2005) Plant Stanol and Sterol Esters in the Control of Blood Cholesterol Levels: Mechanism and Safety Aspects. *American Journal of Cardiology*. **96**(1, S1): 15-22.

Salo P and Wester I (2005) Low-fat formulations of plant stanols and sterols. *The American Journal of Cardiology*. **96**(1A): 51D – 54D.

Seppo L, Jauhiainen T, Nevala R *et al*. (2007) Plant stanol esters in low-fat milk products lower serum total and LDL cholesterol. *European Journal of Nutrition*. **46**: 111-117.

Theuwissen E and Mensink RP (2007) Simultaneous intake of ß-glucan and plant stanol esters affects lipid metabolism in slightly hypercholesterolemic subjects. *The Journal of Nutrition*. **137**: 583-588.

Trautwein EA, Duchateau GS, Lin Y *et al*. (2003) Proposed mechanisms of cholesterol-lowering action of plant sterols. *European Journal of Lipid Science and Technology*. **105** (3-4): 171-85.

Turnbull D, Frankos VH, Leeman WR *et al*. (1999) Short-term tests of estrogenic potential of plant stanols and stanol esters. *Regulatory Toxicology and Pharmacology*. **29**(2): 211-215.

Vanhanen HT, Blomqvist S, Ehnholm C *et al*. (1993) Serum cholesterol, cholesterol precursors, and plant sterols in hypercholesterolemic subjects with different apoE phenotypes during dietary sitostanol ester treatment. *Journal of Lipid Research*. **34**: 1535-1544.

Vanhanen HT, Kajander J, Lehtovirta H *et al*. (1994) Serum levels, absorption efficiency, faecal elimination and synthesis of cholesterol during increasing doses of dietary sitostanol esters in hypercholesterolaemic subjects. *Clincial Science*. **87**: 61-67.

van Horn L, McCoin M, Kris-Etherton PM *et al*. (2008) The evidence for dietary prevention and treatment of cardiovascular disease. *Journal of the American Dietetic Association*. **108**(2): 287-331.

Wahle KWJ, Heys SD, Majumder B *et al*. (2001) Conjugated linoleic acids modulate apoptotic and anti-signal mechanisms in breast and prostate cells. 1st International Conference on CLA, Aleslund, Norway.

Webb GP (2008) Nutrition, a health promotion approach. Third Edition. Hodder Arnold, London, pp 525-527.

Weingärtner O, Böhm M and Laufs U (2008) Plant sterols as dietary supplements for the prevention of cardiovascular diseases. *Deutsche medizinische Wochenschrift*. **133**(22): 1201-4.

Weststrate JA and Meijer GW (1998) Plant sterol-enriched margarines and reduction of plasma total- and LDL-cholesterol concentrations in normocholesterolaemic and mildly hypercholesterolaemic subjects. *European Journal of Clinical Nutrition*. **52**: 334-343.

Wood D, Wray R, Poulter N *et al*. (2005) JBS 2: Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice. *Heart*. **91** (supp 5): 1-52.

Woodgate D, Chan CHM and Conquer JA (2006) Cholesterol-lowering ability of phytostanol softgel supplement in adults with mild to moderate hypercholesterolemia. *Lipids*. **41**(2): 127-132.

WHO/FAO (World Health Organization/Food and Agriculture Organisation) (2003) *Global Report on Diet, Nutrition and Prevention of Chronic Diseases*. Technical Report 916. Geneva:WHO

WHO (World Health Organization) (2006) WHO global infobase online. Available at: http://www.who.int/ncd_surveillance/infobase/web/InfoBasePolicyMaker/CountryProfiles/QCStart.aspx (accessed June 2008).

WHO (World Health Organization) (2008) Cardiovascular diseases. Available at: http://www.who.int/topics/cardiovascular_diseases/en/ (accessed June 2008).