Functional foods with added plant sterols for treatment of hypercholesterolaemia and prevention of ischaemic heart disease

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Background. A spread with added plant sterols, Pro-activ, is marketed in South Africa as an adjunct to low-fat diets for lowering of total and low-density lipoprotein (LDL) cholesterol concentrations and to decrease risk of ischaemic heart disease (IHD).

Objectives. The need for this functional food in South Africa, its efficacy, safety and target market, are evaluated in this review.

Results. The high, and probably increasing incidence of hypercholesterolaemia and cardiovascular disease in South Africa motivates the need for appropriate functional foods. There is convincing evidence in the literature that an average daily intake of about 2 g plant sterols in about 20 g of spread significantly lowers total and LDL cholesterol concentrations by approximately 10 - 15%, without influencing high-density lipoprotein (HDL) cholesterol and triglyceride concentrations. There is some concern about the effects on absorption of lipid-soluble vitamins and pro-vitamins, but safety tests lasting for up to 3 years found no serious adverse effects.

Conclusions. The target market for this spread should be non-pregnant, non-lactating adults with hypercholesterolaemia and/or increased risk of IHD. If it is considered for use in hypercholesterolaemic children, fat-soluble vitamin status should be monitored. It is recommended that post-marketing surveillance should be established to determine long-term effects and safety.

Functional foods are food products designed and developed to enhance or promote health or to contribute to reduction of a specific disease risk.[1] A new functional food, a spread or margarine with added plant sterols, Pro-activ (Unifoods (Pty) Ltd, Durban), was launched in South Africa during 2000. Plant sterols are known to inhibit absorption of both exogenous and endogenous cholesterol, reducing blood cholesterol concentrations. Levels of plant sterols normally present in the diet are insufficient to lower blood cholesterol concentrations, but added to a suitable food vehicle, desired levels may be obtained. The product was developed in The Netherlands, motivated by the high incidence of hypercholesterolaemia and consequent ischaemic heart disease (IHD). The manufacturer claims that an average daily intake of 20 g of the spread, providing approximately 2 g plant sterols, will lower total and low-density lipoprotein (LDL) cholesterol by about 10 - 15% and the relative risk of IHD by about 25% after 2 years.[2]

The objectives of this review are to evaluate the need for this and similar products in South Africa, based on the epidemiology of dyslipidaemia and IHD in this country; to evaluate the efficacy of the product based on results of clinical trials; to assess its safety based on its composition and safety tests; and to look at practical issues such as target groups, affordability and long-term surveillance needs.

Need for a cholesterol-lowering functional food in South Africa

Murray and Lopez[3] estimated that globally, in the year 2020, IHD will be the leading contributor to the burden of disease, moving from fifth place in 1990 to first place in 2020. Based on what is known about the epidemiological and health transition during development and industrialisation of populations, these authors estimate that annual deaths from cardiovascular disease will rise from 14 million in 1990 to 23 million in 2020, accounting for one-third of all deaths worldwide.

Bradshaw and co-workers[4] showed that in 1990 cerebrovascular events and IHD were the third and fifth leading causes of death in South Africa, accounting for 7% and 5% of total deaths in that year.

It is generally accepted that the increase in morbidity and mortality from chronic diseases in developing populations is,

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in addition to changes in population age structure, a result of changes in lifestyle during industrialisation and economic development, namely increased levels of smoking, sedentary occupations, adoption of high-fat, high-animal protein, low-fibre diets and increased exposure to stressful situations. All these factors are known to increase the risk of cardiovascular disease and specifically IHD because they lead to obesity, hypertension, diabetes mellitus and hyperlipidaemia, the major IHD risk factors.

In South Africa, the inter-ethnic difference in prevalence and incidence of IHD (high in the Indian and white populations, intermediate in the coloured population and low in black South Africans) is probably related to differences in patterns of dyslipidaemia.[5] However, several studies[6-8] have shown that hypercholesterolaemia, obesity, hypertension, tobacco smoking and diabetes mellitus are rapidly increasing in black South Africans and that the emergence of future IHD is already apparent.[9]

The same risk factors also predispose to stroke.[10] The highest documented stroke rates are in coloured and Asian communities (with age-standardised mortality rates of 125 - 175/100 000 per annum) and the lowest in the white community (70/100 000 per annum).[10] Unfortunately, few data are available for black South Africans but small studies suggest that the stroke rate may be as high as 300/100 000 per annum in this population.[10] In addition to lifestyle-related dyslipidaemias, major genetic disorders such as familial hypercholesterolaemia, which powerfully predispose to IHD, have been well described in many South African communities, including the black population.[9]

From the above it is evident that hypercholesterolaemia and its cardiovascular consequences are well documented, major public health problems in South Africa. Therefore, two working groups have recently published guidelines for the diagnosis, management and prevention of the common dyslipidaemias in South Africa[9,11] and another working group has documented a 'stroke therapy clinical guideline'.[10] In each of these guidelines, the prevention and treatment of hypercholesterolaemia is prominent. The two key elements in the management of hypercholesterolaemia (dyslipidaemia) are lifestyle modification and the use of appropriate lipid-modifying drugs in patients at high risk.[9] Lifestyle or behaviour modification includes cessation of tobacco use, a healthy prudent diet, regular aerobic exercise and weight loss where indicated.

Changes in behaviour are never easy. The low-fat, low-sodium, high-fibre and high-complex carbohydrate diet prescribed for the treatment of hypercholesterolaemia[11] is usually less attractive than the typical Western diet in which fat increases palatability. Consequently, worldwide compliance with this prudent diet has been disappointing.[12] Although there is no doubt that treatment of hypercholesterolaemia using the modern statins and/or fibrates reduces both total and cardiovascular morbidity and mortality, the introduction of these drugs for treatment of high-risk individuals should be approached with care, considering the expense, possible side-effects and the necessity for lifetime compliance.[9]

It seems, therefore, that based on *(i)* the high and increasing prevalence of hypercholesterolaemia, IHD and stroke; *(ii)* disappointing compliance with the prudent diet; and *(iii)* potential difficulties with drug treatment, there is a need for specific, palatable and affordable food products that can effectively and safely lower blood cholesterol levels, thereby reducing the risk of IHD and stroke. Such a food should not be seen as a single, magic bullet that will solve a particular health problem on its own, but rather as part of a healthy diet (and drug treatment where necessary), which will enable individuals to comply better with effective treatment and/or preventive measures.

Plant sterols and functional foods

In 1954 Best and co-workers[13] showed that plant sterols, also known as phytosterols, lower blood cholesterol levels. Sterols are essential components of cell membranes. Plant sterols are structurally related to cholesterol, the main animal-derived sterol, but differ in their side chain configuration. More than 40 plant sterols have been identified. The unsaturated sterols most frequently found in nature are β-sitosterol, campesterol and stigmasterol. The stanols are saturated sterols with no double bonds in the sterol ring. They are less abundant in nature but can be produced by hydrogenating sterols. Dietary intake of plant sterols varies from 200 - 300 mg/day in Northern European countries,[14] to 300 - 450 mg/day in Japan[15] depending on the amount of plant food in the diet. Esterification of plant sterols with fatty acids (e.g. from sunflower oil) increases their solubility in lipids and improves incorporation in the lipid phase of food vehicles. Suitable food vehicles will therefore be those with an oil or fat base such as spreads, salad dressings, cream cheese and yoghurt. These foods should be eaten in sufficient quantities in a prudent diet to provide between 1 g and 3 g plant sterols daily at levels that will not affect the acceptability and sensory characteristics of the product.

Efficacy of plant sterols in lowering blood cholesterol

The recent evidence that plant sterols in food vehicles effectively lower blood (serum or plasma) total and LDL cholesterol comes from approximately 20 clinical trials in humans, reviewed by Law[16] and Moghadasian and Frohlich.[17] Law[16] selected 14 randomised, double-blind trials, conducted between 1993 and 2000 which reported on the difference in serum cholesterol when using polyunsaturated spreads (margarines) (N = 9), mayonnaise (N = 3), olive oil (N = 1) or

butter (N = 1) with and without added plant sterols. Of these, 6 were cross-over trials and 8 were parallel group trials. In total, 473 subjects took a sterol-enriched product and 423 a product without sterols. The mean ages of the participants varied from 33 to 58 years, and the duration of the trials ranged from 1.4 to 52 weeks. The average daily intake of added plant sterols was between 0.8 g and 4.0 g. The mean placebo (control)-adjusted reduction in serum LDL cholesterol varied from 0.20 (95% confidence interval (CI): 0.10 - 0.31) to 0.64 (CI: 0.06 - 1.22) mmol/l. The trial with the smallest LDL cholesterol reduction of 0.20 (CI: 0.10 - 0.31) mmol/l, was that of Hendriks *et al*.[18] in which 80 subjects with a mean age of 37 years consumed 1.6 g plant sterols daily in margarine for 3.5 weeks in a cross-over design. The largest reduction was reported by Jones and co-workers[19] in a parallel trial with 16 experimental and 16 control subjects with a mean age of 50 years. The experimental subjects consumed 1.9 g plant sterols daily in margarine for 4 weeks and showed a reduction of 0.64 (CI: 0.06 - 1.22) mmol/l in LDL cholesterol when compared with the control group which consumed margarine without added plant sterols. Law's[16] review pointed out that the LDL cholesterol reductions in these 14 studies were greater in older subjects, and that there is a dose-response effect continuous up to a dose of about 2 g per day. This amount of plant sterols added to an average daily portion of margarine reduced LDL cholesterol by an average of 0.54 mmol/l in subjects aged 50 - 59 years, 0.43 mmol/l in those aged 40 - 49 years and 0.33 mmol/l in those aged 30 - 39 years. No effects on high-density lipoprotein (HDL) cholesterol or triglyceride levels were observed.

Moghadasian and Frohlich[17] reviewed 16 human studies published in 1999 and earlier, with a total of 590 subjects. They found that on average, plant sterol therapy resulted in a 10% reduction in total cholesterol and a 13% reduction in LDL cholesterol concentrations. The three trials in Law's review,[16] which compared the efficacy of sterols with that of stanols, indicated that the stanols may be slightly better. However, the results were inconclusive. Since publication of these reviews a number of other human studies[20-22] have confirmed the total cholesterol and LDL cholesterol reductions. One of these studies[21] also compared the effect of unsaturated plant sterol esters with that of saturated plant stanol esters. This cross-over clinical trial involving 15 hypercholesterolaemic patients showed that compared with an 'unfortified' margarine, consuming a margarine with added sterol esters (1.84 g/day) for 21 days lowered plasma total cholesterol by 13.4% (significantly: $P < 0.05$). The observed 10.2% reduction with an equal dose of the stanol esters was not significant. Cholesterol absorption was reduced significantly by both sterol and stanol esters (36.2% and 25.9% respectively). Cholesterol biosynthesis was reciprocally increased by 53.3% and 37.8% compared with 'unfortified' margarine indicating the compensatory adjustments when cholesterol is not absorbed. Cholesterol turnover was not influenced by the diet.

It has also been shown[23] that plant sterols have an additional, clinically significant cholesterol-lowering effect when taken as part of a low-fat diet. In this parallel, double-blind trial, 55 hypercholesterolaemic subjects randomly assigned to three groups after 4 weeks on a high-fat baseline diet, consumed a low-fat diet with and without added wood stanol or vegetable oil stanol-fortified margarines for 8 weeks. The daily mean stanol intakes were 2.31 g and 2.16 g respectively. Compared with the low-fat diet, the significant reductions in LDL cholesterol of the groups consuming the two fortified margarines were 13.7% and 8.6% greater.

However, some studies[24-26] have shown no or only small non-significant effects of phytosterols. The most recent example is the study by Denke[26] in which a daily dose of 3 g sitostanol suspended in safflower oil, taken in 12 gelatin capsules by 33 mildly hypercholesterolaemic men on a cholesterol-restricted diet, had no effect on any of the serum lipids. This author speculated that the lack of effect could be related to the type of patients (mildly polygenic hypercholesterolaemic), their low-cholesterol diet (< 200 mg/day) or the sitostanol preparation taken as gelatin capsules. If the stanol does not mix sufficiently with the intestinal contents, significant inhibition of intestinal cholesterol absorption would not be possible.

From the above it seems reasonable to conclude that there is convincing evidence from randomised, cross-over or parallel clinical trials that phytosterols, when added to a functional food such as a spread or salad dressing, effectively lower total and LDL cholesterol in adult men and women. These effects are not dependent on baseline cholesterol levels or background diet. It also seems that phytosterols do not lower HDL cholesterol concentrations, nor do they affect triglyceride levels. The reasons why a few studies could not show cholesterol-lowering properties may be related to the form of intake, but more research is needed for clarity.

Other effects and safety issues

The main mechanism thought to be responsible for the total and LDL cholesterol-lowering effects of functional foods with added phytosterols, is the inhibition of exogenous (dietary) and endogenous (biliary) cholesterol absorption in the small intestine.[16,17,21] The serum cholesterol-lowering effect may also have other associated beneficial, anti-atherogenic effects.[17] But theoretically, the inhibitory effect on intestinal cholesterol and related lipid absorption (such as fat-soluble vitamins and pro-vitamins), possible effects on cellular cholesterol and steroid hormone metabolism and function, possible absorption of phytosterols, and possible influences of increased phytosterol concentrations in the large gut (where they are excreted) may lead to potential toxic or harmful side-effects. A daily portion of the available functional foods with added phytosterols provides approximately 10 times more phytosterols than normally present in the diet. Therefore, the question whether

cholesterol reduction may be hazardous in certain circumstances should also be addressed.

Because of these possible detrimental effects, the safety of functional foods with added phytosterols has been extensively evaluated in a number of clinical trials in humans and rats. Eleven of the more recent trials[20,22,27-35] are summarised in Table I. The results of these trials indicate that the small amounts of phytosterols absorbed are excreted through the bile and eventually both absorbed and unabsorbed fractions through the faeces, without affecting large gut microflora, short-chain fatty acid production or formation of secondary sterol metabolites. The adrenal glands, ovaries and intestinal epithelium showed the highest levels of phytosterols in rats after ingestion of a mixture of labelled sterols. However, no study could find any evidence that sterol hormone functions or reproductive characteristics are influenced in the doses tested, which were generally substantially higher in the animal models than in humans.

There is concern about the reduction in absorption of lipid-soluble vitamins and pro-vitamins by phytosterols. No effects on absorption of vitamins D and K have been observed. The reductions in vitamin E, α- and β-carotenes are generally non-significant when standardised for plasma lipids, but the significant reduction of serum lycopene may be a problem. Vitamin E as well as α- and β-carotenes and lycopene are antioxidants, and may be protective against diet-related chronic diseases.[36] Law[16] advises that eating more fruit and vegetables, a major recommendation in many dietary guidelines, would counter this decrease in absorption of lipid-soluble antioxidants. The fortification of functional foods with some of these antioxidants could be another possible solution to the problem.

The question whether blood cholesterol concentrations can be reduced to undesirable low levels, needs attention. Ratnayake and co-workers[37] used the haemorrhagic stroke-prone spontaneously hypertensive rat model (SHRSP rats) to test the hypothesis that the high concentration of phytosterols in canola oil compared with soybean oil are responsible for the shortened lifespan of these rats when fed diets rich in canola oil. Their results showed that the addition of phytosterols to the rat diet was associated with a lower red blood cell membrane deformability index (more rigid membranes), which correlated with the shorter survival times and cholesterol concentration. It is possible that the deficiency of membrane cholesterol and/or replacement of cholesterol by phytosterols are responsible for this effect. However, in a follow-up study[38] the same group of researchers found that this response was probably unique to the SHRSP rats, since normal healthy laboratory animals (Wistar rats and gerbils) showed no alterations in red blood cell deformability, platelet number or other haematological variables on diets supplemented with phytosterols. No similar data from human studies could be found, but Law and co-workers[39] assessed the possible hazards of reducing serum cholesterol in a systematic review of data from 10 cohort studies, 2 international trials and 28 randomised trials. They found that the only cause of death attributable to low serum cholesterol concentration was haemorrhagic stroke. The excess risk was associated with concentrations below 5 mmol/l (relative risk 1.9, 95% CI: 1.4 - 2.5), affecting about 6% of people in the Western world. The authors concluded that the benefit of low serum cholesterol and consequent low IHD risk, will outweigh the increased risk for haemorrhagic stroke. However, the above emphasise the importance of targeting functional foods with powerful cholesterol-lowering properties to appropriate consumers with high serum cholesterol concentrations and increased risk of IHD.

In conclusion, the safety evaluation studies,[20,22,27-35] some of which tested phytosterol doses up to 3 g/day for periods up to 3 years, provided no evidence of any toxic effects. The only concerns seem to be about the possible inhibition of absorption of some dietary vitamins and pro-vitamins and of increasing risk of haemorrhagic stroke in individuals with low serum cholesterol. Both these concerns can be addressed by including more fruit and vegetables in the diet and by targeting the phytosterol-rich functional food at individuals with increased serum cholesterol. Law[16] mentioned that phytosterol margarines have been sold for 3 years in Finland without evidence of hazard. However, there may be some individuals with a genetic defect resulting in abnormally high absorption of phytosterols. These individuals will develop sitosterolaemia, hypercholesterolaemia and Achilles tendon xanthomas. Unfortunately, the genetic defect is not well described and it is not known if individuals heterozygous for this condition would absorb higher amounts of phytosterols. The Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association advises that homozygous individuals with tendon xanthomas should be counselled against the use of products fortified with phytosterols.[40]

Practical issues

The nutritional information[41,42] and price per 100 g of some South African margarines and butter are compared with those of the functional food spread with added phytosterols (Pro-activ) in Table II. Pro-active and the 'extra light' margarine, products aimed at lowering blood cholesterol concentration and approved as part of the Heart Foundation eating plan, have a much higher moisture and therefore lower fat and energy content than 'harder' margarines and butter. Their ratios of polyunsaturated fatty acids (PUFAs) are also much higher and their trans fatty acid content is very low or nil. All these properties are known to decrease serum cholesterol levels.[11] With the added plant sterols at a level of 8 g per 100 g in Pro-activ, its reported efficacy in lowering circulating total

Table I. Summary of studies evaluating safety of margarines with added plant sterols

Characteristics evaluated	Study design and methods	Results	Reference
Oestrogenic activity/potential	Binding of plant sterol to oestrogen receptor, sterol effects on transcriptional activation of oestrogen-responsive genes, and effects on oestrogen-responsive tissues; a mixture of β-sitosterol, campesterol and stigma sterol tested in *in vitro* and *in vivo* assays	No evidence of any oestrogenic activity found; no binding to oestrogen receptor, no transcriptional activity and no uterotrophic effects demonstrated	Baker *et al.*[27]
Toxicity in rats: food and water consumption, body weights, organ weights, histology of various tissues	Wistar rats were fed diets containing 0.16, 1.6, 3.2 and 8.1% plant sterols for 90 days – equivalent to a dose of 6.6 g/kg body weight phytosterol esters or 4.1 g/kg/day phytosterol	No treatment-related changes of toxicological significance were found	Hepburn *et al.*[28]
Two-generation reproduction performance in male and female Wistar rats	Effects of plant sterols at levels of 0, 1.6, 3.2 and 8.1% (w/w) measured in a wide range of reproductive and developmental parameters over two successive generations of Wistar rats	No effects observed on pup mortality, precoital time, mating index, fertility index, female fecundity index, gestation index, etc., and pup development. Also no effects on sexual maturation parameters. Concluded that a daily oral dose of up to 1.54 - 5.62 g phytosterol/kg body weight was the no observed-effect level	Waalkens-Berendsen *et al.*[29]
Faecal bile acid and neutral steroid concentrations of healthy normolipidaemic volunteers	Comparative study with two randomised parallel groups after run-in period consuming 40 g margarine with and without added phytosterols for 21 days (males) and 28 days (females). Background diets standardised. Faecal neutral steroids, bile acids and sterol metabolites measured	Significant increases in neutral faecal steroids observed as expected in phytosterol consumers. No increased formation of bile acids or sterol metabolites observed	Weststrate *et al.*[30]
Faecal short chain fatty acids (SCFA) bacterial enzyme activities, microflora counts, female sex hormones, serum cholesterol levels	A randomised, placebo-controlled, two-period, parallel dosed study in healthy men and women, consuming 40 g margarine for 21 and 28 days with and without added plant sterols: a test and control group	The test group showed significant reductions in total and LDL serum cholesterol, faecal lactic acid and serum progesterone. No other significant treatment effects. Although both groups showed significant changes compared with baseline, none was considered to be of biological importance	Ayesh *et al.*[31]
The fate of phytosterols (in rats)	Oral dose of ^{14}C-labelled cholesterol, β-sitosterol, β-sitostanol or ^{3}H-labelled β-sitostanol, campesterol, campestanol or stigmasterol dissolved in sunflower seed oil. Urine and faecal samples collected; tissue and carcass remains examined	Overall absorption of phytosterols low. Eliminated via faeces. Absorption slightly greater in females. Adrenal glands, ovaries and intestinal epithelium showed highest levels and longest retention of radioactivity	Sanders *et al.*[32]
Cholesterol and phytosterol metabolism in colectomised patients: serum, biliary and faecal sterols	Eleven colectomised patients consumed margarine with added stanol (stanol intake was 2 g/day) for 7 - 18 days	Inhibition of cholesterol absorption and lowering of serum cholesterol occurred within 1 day of stanol consumption; composition of major bile lipids was unchanged; gallstone formation unlikely. The small amounts of plant sterols detected in serum, excreted through bile	Miettinen *et al.*[22]

Table I. (continued)

Characteristics evaluated	Study design and methods	Results	Reference
Serum carotenoid levels in 60 hypercholesterolaemic patients selected of which 55 completed the study	Randomised, parallel, double-blind study with 4 weeks run-in period and 8 weeks experimental: 3 groups daily consuming wood stanol ester (2.31 g) vegetable oil stanol ester (2.16 g) and control margarine. Serum α-, and β-carotene and lycopene measured	In stanol ester groups, α-carotene did not change, β-carotene significantly lower, but ratio of carotenoids to total cholesterol did not change. No change in serum lycopene	Hallikainen *et al*.[33]
Effects on lipid-soluble (pro) vitamins	Randomised, double-blind placebo-controlled study using 5 spreads and 4 periods. Plant sterol ingestions were 0.83, 1.61 and 3.24 g/day; *N* = 100 subjects	Significant decreases in total and LDL cholesterol with sterol ingestion. No effect on vitamins K_1, D, lycopene and E, but decreases in α- and β- carotene	Hendriks *et al*.[34]
Body weight, weight gain of rats; reproduction performance and variety of reproductive parameters; malformations	A mixture of vegetable oil-derived stanol fatty acid esters in female Wistar rats fed at levels of 0, 1.75, 4.38 and 8.76% from day 0 to 21 of gestation	No effects in low-dose group but decrease in weight of high-dose group. No effects on reproductive variables and malformation or development	Slesinski *et al*.[35]
Effects of soyabean and sheanut oil sterols on plasma lipids plus α- and β-carotene, lycopene	76 healthy adult subjects with mean age of 44 (SD 11) years and total cholesterol below 8 mmol/l ingested 0.8 g plant sterols daily in a double-blind cross-over study, comparing effects of sterols from soyabean and sheanut oils, added to margarines	Soyabean oil steroids, but not sheanut oil steroids significantly lowered total and LDL cholesterol (3.8 and 6%). No effects on HDL cholesterol. Plasma lipid standardised α- and β-carotenes not significantly influenced, but lycopene levels (also standardised) showed a 9.5% significant reduction	Sierksma *et al*.[20]

w/w = weight of solute in weight of solvent; LDL = low-density lipoprotein; SD = standard deviation.

and LDL cholesterol is not surprising. The major sterols in the product are campesterol (10 - 40%), stigmasterol (6 - 30%) and β-sitosterol (30 - 65%).

The South African dietary guidelines for the treatment of dyslipidaemia[11] do not include a specific recommendation regarding this functional food, probably because the guidelines were published before the launch of the product. However, it seems reasonable to recommend that in the prescribed low-saturated, low trans-fat diet, with or without prescribed drug treatment, at least 20 g of this margarine should be included in the daily diet. This amount will provide only 270 kJ and 7 g total fat and will cost R1.40 per day. Compared with other spreads it is expensive, but compared with hypolipidaemic drugs it is extremely cost-effective. The relatively high cost of the product is because 2 500 parts of raw material are needed to extract one part of sterol.

Because of the cost, and also because of its high water content, this spread should not be used for baking or frying of foods (preparation methods which should be limited in a cholesterol-lowering diet). The addition of phytosterols to spreads does not change the taste, consistency or acceptability of the spread, which ensures that compliance should not be a problem. It can be expected that such a small change in diet, replacing an existing spread with the phytosterol-fortified spread, would result in better compliance than dramatic dietary interventions.

It is important to emphasise that phytosterol-enriched spreads should not replace cholesterol-lowering drugs such as the statins where prescribed. The LDL cholesterol-lowering properties of the statins are superior, but taken together, the effects of the two are additive.[16]

Discussion and conclusion

There is sufficient and convincing evidence that spreads with added phytosterols effectively lower total and LDL cholesterol without adverse effects on HDL cholesterol. The ease and expected high compliance when using these spreads could play and extremely important role in the prevention of IHD. Law and co-workers[43] analysed 10 prospective, 3 international and 28 randomised control studies to assess by how much and how quickly a reduction in serum cholesterol concentration will

Table II. Comparison of nutritional information* and price† of some South African spreads

Nutrients per 100 g	Pro-activ	Flora tub margarine (extra light)	Rama tub margarine	Rama block/brick margarine	Butter
Energy (kJ)	1 351	1 354	2 995	2 995	3 040
Protein (g)	0.1			0.33	0.5
Carbohydrate (g)					
Total fat	35.0	35.0	80	80	81.8
Saturated fat (g)	8.0	9.0		18.92	47.77
Cholesterol (mg)					21.9
Trans fatty acids (g)	0.5	0.0	1.0	23.81	5.26
Unsaturated fat (g)					
MUFA (g)	9.0	8.0		42.0	20.56
PUFA (g)	17.5	18.0		17.34	1.61
Plant sterols (g)	8				
Sodium (g)	0.35		0.805	0.802	0.826
Vitamin A (mg RE)		691	691	691	753 (salted or unsalted)
Vitamin D (mg)		6	6	6	0.76
Vitamin E (mg TU)	66		5	5	1.58
Fibre	0.3				0.0
Moisture (%)		59		15.2	15.7
Price per 100 g	6.796	1.898	1.598	1.098	2.978

* Margarines (spreads) as given in the table, and butter according to South African Food Composition Tables.[41,42]
† Calculated for 100 g in rands; bought in 500 g or 250 g packs (Pro-activ) at Pick & Pay in December 2000 in Potchefstroom.
RE = retinol equivalents; TU = tocopherol units.

lower IHD risk. Their results from the prospective studies which included about 500 000 men and 18 000 IHD events, showed that a long-term reduction of 0.6 mmol/l (10%) in serum cholesterol concentration, will lower relative risk of IHD by 50% at age 40. At 50 years of age the reduction is 40%, 30% at 60 years and 20% at age 70 and older. The randomised trials, based on data from 45 000 men and 4 000 IHD events, showed that the full benefit of the reduction in relative risk is achieved by 5 years. The data for women were limited but indicated a similar effect.

Based on what is known about the safety of the product, the recommended target market should include adult, non-pregnant and non-lactating individuals with raised blood cholesterol concentrations and/or increased risk of IHD. This is in agreement with a statement for health care professionals from the American Heart Association (AHA).[40] The AHA also advises that the product can be used for secondary prevention after an atherosclerotic event, and that if it is considered for use in hypercholesterolaemic children, lipid-soluble vitamin status should be monitored. Before really long-term safety studies have been completed, routine ingestion by the general population to lower IHD risk is not advised.

At present the high price of the spread will probably dictate the target market – affluent people who are aware of their blood cholesterol level and IHD risk. But the future scenario in South Africa may change. As more people become urbanised and prosperous the known social drift phenomenon[44] may result in lower risk in the high socio-economic groups and higher risk in the lower socio-economic groups. Hopefully at that stage this functional food will be more affordable to those who need it most.

Although the safety of these products with added plant sterols has been evaluated extensively, no data on long-term safety are available. The situation is similar to that experienced with the introduction of polyunsaturated fatty acid (PUFA) diets. In contrast to Mediterranean people who consumed high mono-unsaturated fatty acid diets for generations, no populations following high PUFA diets for similar periods were available to assess long-term effects of PUFAs. Therefore, it is necessary to establish a post-marketing surveillance system or safety net[45] to monitor long-term effects of this functional food.

At present all available evidence indicates that proven benefits far outweigh possible hazards. The food or nutrient function claim on the South African product is that it contains plant sterols which actually lower cholesterol and that it is approved as part of the Heart Foundation eating plan. With long-term surveillance and more research, a future health claim

that it reduces risk of IHD and other cardiovascular diseases seems promising.

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CONTINUING PROFESSIONAL DEVELOPMENT ACTIVITY FOR DIETITIANS

SAJCN CPD activity No 20 – July 2003

You can obtain 3 CPD points for reading the article: **"Functional foods with added plant sterols for treatment of Hypercholesterolaemia and prevention of Ischaemic Heart Disease"** and answering the accompanying questions. This article has been accredited for CPD points for dietitians. (Ref number: 03/3/080/12)

1. Check your name and HPCSA number.
2. Read the article and answer all the questions.
3. Indicate your answers to the questions by coloring the appropriate block(s) in the cut-out section at the end of this questionnaire.
4. You will earn 3 CPD points if you answer more than 75% of the questions correctly. If you score between 60-75% 2 points will be allocated.
5. A score of less than 60% will not earn you any CPD points.
6. Make a photocopy for your own records in case your form is lost in the mail.
7. Send the cut-out answer form **by mail,** NOT BY FAX to: SASPEN Secretariat, SAJCN CPD activity **No 20**, c/o Department of Human Nutrition, PO Box 19063, Tygerberg, 7505 to ***reach the office not later than 15 October 2003***. Answer sheets received after this date will not be processed.

PLEASE ANSWER ALL THE QUESTIONS

(There is only ONE correct answer per question.)

1. Functional foods are designed and developed to promote health and/or to reduce disease risk.
   [a] true
   [b] false
2. Functional foods can be seen as "magic bullets" that are able to reduce specific risk factors for disease.
   [a] true
   [b] false
3. Stanols are saturated plant sterols that can be produced by hydrogenating sterols.
   [a] true
   [b] false
4. Existing evidence shows that plant sterols significantly lower total and LDL-cholesterol levels, without affecting HDL-cholesterol or triglycerides.
   [a] true
   [b] false
5. Plant sterols are a normal dietary constituent.
   [a] true
   [b] false
6. In hypercholesterolaemic patients who already follow low-fat diets, additional intake of plant sterols has no effect on serum cholesterol levels.
   [a] true
   [b] false
7. Plant sterols effectively lower serum cholesterol levels because they inhibit absorption of both exogenous and endogenous cholesterol in the small gut.
   [a] true
   [b] false
8. Because of their mechanism of action, plant sterols have no effect on the absorption of any dietary constituent other than cholesterol.
   [a] true
   [b] false
9. Individuals with a genetic defect resulting in increased absorption of plant sterols may develop sitosterolaemia and should be advised not to use products fortified with plant sterols.
   [a] true
   [b] false
10. The safety evaluation of margarines with added plant sterols indicated that hypercholesterolaemic children may use it under certain circumstances.
    [a] true
    [b] false
11. Margarines with added plant sterols are so safe and effective that routine ingestion by the general population is advised.
    [a] true
    [b] false
12. Pregnant and lactating women, even when they are hypercholesterolaemic, are advised not to consume products fortified with plant sterols.
    [a] true
    [b] false

✂ Cut along the dotted lines and send to: SASPEN Secretariat, SAJCN CPD activity **No 20**, c/o Department of Human Nutrition, PO Box 19063, Tygerberg, 7505 to **reach the office not later than 15 October 2003**

HPCSA number: DT |__|__|__|__|__|__|__|

Surname as registered with HPCSA: _____ Initials: _____

Postal address: _____

_____ Code: _____

Full member of ADSA: |__| yes |__| no If yes, which branch do you belong to? _____

Full member of SASPEN: |__| yes |__| no Full member of NSSA: |__| yes |__| no

"Functional foods with added plant sterols for treatment of Hypercholesterolaemia and prevention of Ischaemic Heart Disease"
Vorster HH, Raal FJ, Ubbink JB, Marais AD, Rajput MC, Ntanios FY
Please color the appropriate block(s) for each question
(e.g. if the answer to question 1 is a: 1) a ■ b)

1) a b	2) a b	3) a b	4) a b
5) a b	6) a b	7) a b	8) a b
9) a b	10) a b	11) a b	12) a b