Phytosterols: natural compounds with established and emerging health benefits

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Abstract: *Phytosterols (plant sterols and stanols) are naturally occurring compounds which are found in all foods of plant origin. The term phytosterols refers to more than 200 different compounds. The most abundant ones in the human diet are sitosterol and campesterol. Their saturated counterparts, sitostanol and campestanol, are found in much lower amounts. Good food sources of phytosterols include vegetable oils, cereal grains, nuts, legumes, and fruits and vegetables. Phytosterols are structurally similar to cholesterol. Despite this structural similarity, they are not absorbed in significant quantities. Absorption is less than 2% for phytosterols, while it is 30-60% for cholesterol. Phytosterols are known to have various bioactive properties, which may have an impact on human health, and as such boosted interest in phytosterols in the past decade. The most important benefit is their blood cholesterol-lowering effect via partial inhibition of intestinal cholesterol absorption. The recommended daily intake of 2 g of phytosterols reduces cholesterol absorption by 30-40% and LDL-cholesterol by 10% on average. Other claimed benefits of phytosterols are possible anti-atherogenic effects as well as, particularly for beta-sitosterol, immune stimulating and anti-inflammatory activities. Furthermore, there is emerging evidence suggesting that particularly plant sterols may have beneficial effects against the development of different types of cancers, like colorectal, breast and prostate cancers. It is not clear whether mechanisms other than the established cholesterol-lowering action of phytosterols as such also contribute to these potential health benefits.*

Key words: *phytosterols, health benefits, cholesterol-lowering, LDL-cholesterol, atherosclerosis, immunity, inflammation, cancer, benign prostate hyperplasia*

Introduction

Phytosterols (plant sterols and stanols) are naturally occurring compounds that resemble cholesterol both in structure and biological function. They are structural components of the cell membrane, where they regulate membrane fluidity and permeability as well as membrane-associated metabolic processes. Phytosterols are products of the isoprenoid biosynthesis pathway and are, as cholesterol, synthesized from acetyl coenzyme-A via squalene. The synthesis of phytosterols involves more than 30 enzyme-catalysed reactions all taking place in plant cell membranes [1].

The term phytosterols refers to more than 200 different compounds which are found in various plants and marine sources [2]. They all have a steroid nucleus, a hydroxyl group at carbon 3 in the β-position and a double bond mostly located between the C-atoms five and six in the B-ring. Major differences are found in the alkyl side chain, which can vary by the absence or presence of a methyl or ethyl group on C24, saturation and position of a double bound and geometry of the substitution at C24. Plant stanols are the saturated forms of plant sterols, lacking the double bonds in the steroid nucleus and the alkyl side chain.

In this review, the term phytosterols refers to both plant sterols and their saturated counterparts, the plant stanols. The most biologically relevant phytosterols are sitosterol, campesterol, stigmasterol and brassicasterol. Sitostanol and campestanol, the major plant stanols, are 5,6-saturated analogues of sitosterol and campesterol *(figure 1)*.

The present review will focus on the established and emerging health benefits of phytosterols. Safety aspects have been previously reviewed [3, 4] and will not be addressed.

Occurrence and dietary intake of phytosterols

A comprehensive review of important food sources of phytosterols including aspects of ripening, post-harvest and processing changes in phytosterol contents has recently been published [5]. Appreciable amounts of phytosterols are found in the lipid-rich and fibre-rich fractions of all plant foods. In particular, vegetable oils and products made from oils like spreads and margarine are good sources of plant sterols [1]. Other foods which contribute to the daily intake of plant sterols are cereal grains, cereal-based products, nuts, legumes, vegetables and fruits [6, 7]. Plant stanols are also found in some foods, but at much lower concentrations. They are found in some cereals grains like rye, corn and wheat and in non-hydrogenated vegetable oils [1]. Plant stanols are also found in plant material from coniferous trees such as pine and spruce.

Dietary intake of plant sterols ranges from 150 to 400 mg/day with 65% of intake as β-sitosterol, 30% as campesterol and 5% as stigmasterol [8, 9]. The daily intake of plant stanols is in the magnitude of about 25 mg/day [10].

Metabolism of phytosterols and their effects on cholesterol absorption

Despite the structural similarity between cholesterol and the major phytosterols, their absorption by mammalian intestine is low. Absorption rates are 0.5% for sitosterol, 1.9% for campesterol, 0.04% for sitostanol and 0.16% for campestanol, compared to a choles-

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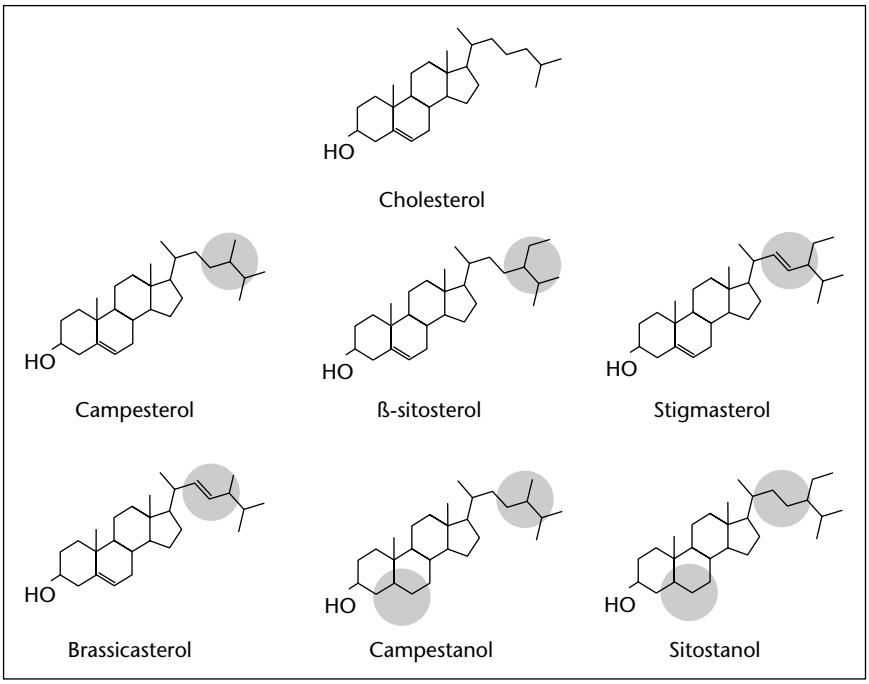

Figure 1. *Chemical structure of the most biologically relevant phytosterols.*

terol absorption rate of, on average, 56% [9, 11]. The low absorption of phytosterols as compared to cholesterol is explained by their rapid re-secretion from the intestinal cells back into the gut lumen via the ATP-binding cassette (ABC) transporters ABC G5 and ABC G8 [12].

Phytosterols are absorbed under the same conditions that exist for cholesterol. Like cholesterol, they are taken up in the so-called dietary mixed micelles, which typically contain mixtures of free cholesterol, mono- and di-glycerides, fatty acids, phoshoplipids and bile acids. Like esterified cholesterol, phytosterol esters ingested with the diet need to be hydrolysed by pancreatic cholesterol esterase.

Inhibition of intestinal cholesterol absorption is the mechanism of action responsible for the cholesterol-lowering effect of phytosterols. As a consequence, the faecal excretion of cholesterol and its intestinal breakdown products is increased. In several studies, the effect of dietary phytosterol intake on intestinal cholesterol absorption has been directly measured. Intakes of 0.7 to 9 g/day of phytosterols resulted in a reduction in cholesterol absorption in the range of 7-69% [13]. The recommended daily intake of 2 g of phytosterols reduces cholesterol absorption by 30-40%, leading to a 10% lowering of LDL-cholesterol [3, 13].

Although not all details are yet fully elucidated, several mechanisms are thought to contribute to the overall inhibition of intestinal cholesterol absorption by phytosterols [14]. The key mechanism of action is displacement of cholesterol from the micellar phase. As there is limited capacity in dietary mixed micelles to embody sterols, the competition between phytosterols and cholesterol reduces the cholesterol content of micelles and hence decreases its transport towards the intestinal brush border membrane [15]. Outside the micellar phase, cholesterol is no longer soluble and can form co-crystals with phytosterols and is then excreted together with the non-absorbed phytosterols.

Stimulation of bile flow prompted by food intake is a crucial step for the formation of dietary mixed micelles. This plays an important role in the overall mechanism of action and consequently for the optimal cholesterol-lowering efficacy of phytosterols when consumed with various background diets and in the form of different enriched food formats. For instance, ingestion of a (fatty) meal stimulates bile flow, resulting in a release of (endogenous) cholesterol into the gut lumen, which increases the likelihood for phytosterols to compete with cholesterol for micellisation.

There is also emerging evidence that phytosterols interfere with transporter-mediated processes of cholesterol uptake [16]. Recent insights into the role of so-called influx and efflux sterol transporters in the gut, like the Niemann-Pick C1 Like 1 (NPC1L1) protein and the ABC transporters ABCG5 and ABCG8 have shown that phytosterols and cholesterol share the same transport processes [17]. *Figure 2* summarises the various putative mechanisms by which phytosterols lower cholesterol absorption.

As phytosterols interfere with intestinal cholesterol absorption, and fat-soluble vitamins and carotenoids share the same absorption pathway as cholesterol, a potential concern relates to the effects of phytosterols on fat-soluble vitamin and carotenoid absorption. Several studies have shown that intakes of phytosterol-enriched foods does not affect plasma concentrations of retinol, vitamin D and K, but significantly lower plasma concentrations of carotenoids and vitamin E [3, 13]. As carotenoids and vitamin E are transported by lipoproteins, usually their concentrations are standardised for plasma lipid concentrations. After such lipid standardisation, plasma concentrations of tocopherols remain normally unaltered, while the concentrations of alpha- and beta-carotene and lycopene are up to 20% lower with phytosterol intake. Carotenoid con-

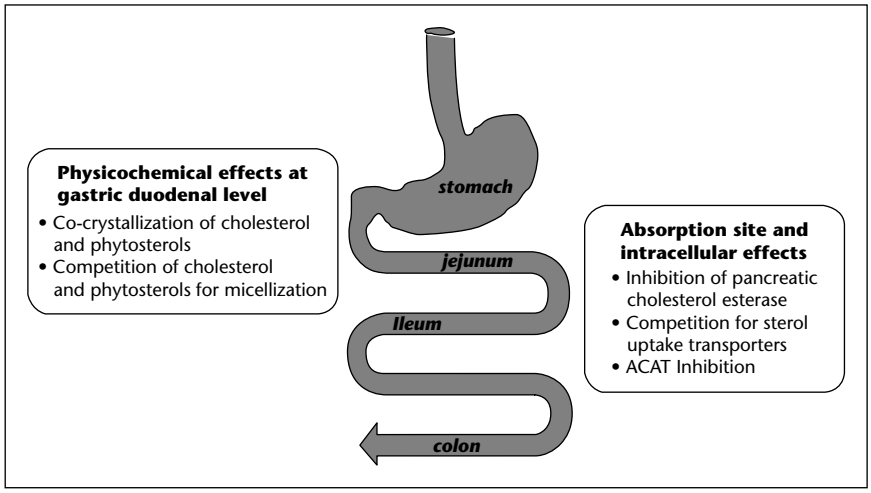

Figure 2. *Potential sites of action and mechanisms by which phytosterols may lower cholesterol absorption. Adapted from Trautwein et al. [14].*

centrations remain, however, still within the normal inter-individual range and typical seasonal variations. Moreover, the phytosterol-induced decrease in plasma carotenoid concentrations can be counterbalanced by consuming more fruits and vegetables [3].

Health benefits of phytosterols

Beneficial effects of phytosterols related to cholesterol metabolism and atherosclerosis risk next to other metabolic processes in the human body have been reviewed recently [18, 19].

Plasma cholesterol-lowering

The early findings

The most important physiological effect of phytosterols relates to their cholesterol-lowering action. The cholesterol-lowering properties of plant sterols were observed in humans in the early 1950s [20]. Due to the crystalline nature and poor solubility of the pure phytosterol preparations, high doses of up to 50 g/day were required to achieve a significant cholesterol-lowering effect [21]. A major breakthrough occurred when it was shown in the 1980s that the esterification of phytosterols with fatty acids from vegetable oils could ease their incorporation into a variety of food products.

Cholesterol-lowering efficacy of phytosterol esters

A vast number of human studies have shown that phytosterol esters, when incorporated into various food products, significantly lower total and LDL-cholesterol. A recent meta-analysis of 41 clinical trials with fat-based foods like spreads, margarine, mayonnaise or salad dressings enriched with phytosterol esters has shown a non-linear dose-response relationship between the daily dose of phytosterols consumed and cholesterol-lowering efficacy [3]. On average, 2 g/day phytosterols (the equivalent dose expressed as free sterols based on 3.3 g/day phytosterol esters) lowered LDL-cholesterol concentrations by about 10% [3]. The effect appeared to taper off at intakes of about 2 g/day or more, with little additional benefit at intakes higher than 2.5 g/day *(Figure 3)*. Phytosterol esters incorporated in low-fat food matrices such as milk, yoghurt and once-a-day yoghurt/yoghurt drinks have also been shown to significantly lower LDL-cholesterol, with effects ranging from – 5 to – 16% for doses of 1.6 to 3.0 g/day [22-25].

Cholesterol-lowering efficacy of free phytosterols

In recent years, considerable effort has been spent to formulate free phytosterols into both liquid and solid food formats. Different formulations of free phytosterols (phospholipid – lecithin – micelles, micro-crystallised, finely dispersed, or dissolved and then re-crystallised in oil) have been tested in recent human trials. Except for one study which did not show a significant effect of low-fat and non-fat dairy beverages [26], free phytosterols provided in multiple daily doses of fat-free or low-fat beverages such as orange juice and milk have been shown to lower LDL-cholesterol [27, 28] to an extent similar to that reported for plant sterol esters in fat-based food formats [3]. Phytosterols incorporated in their free form in fat-based food matrices (margarine, butter) [29, 30] and other fat-rich foods (tortilla chips, chocolate, cold cuts and sausages) [31-33] were also shown to be efficacious in lowering LDL-cholesterol. Overall, properly formulated free phytosterols may be as effective as plant sterol and stanol esters in lowering blood cholesterol. However, further studies with a direct head-to head comparison of free vs. esterified phytosterols would be useful to fully clarify this aspect.

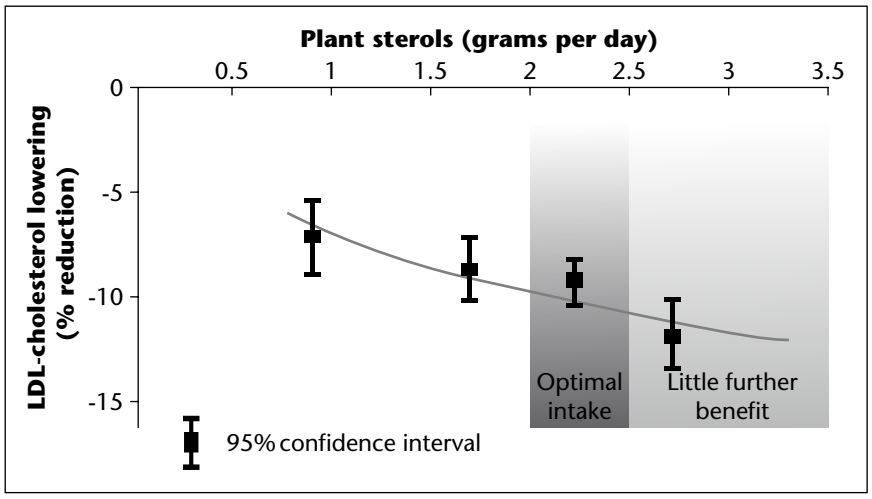

Figure 3. *The dose-response relationship between phytosterol intake and LDL-cholesterol lowering effect. Based on Katan et al. [3].*

Impact of frequency of intake and intake occasion on the cholesterol-lowering efficacy of phytosterol-enriched foods

From a practical point of view, an important aspect to consider is the extent to which the frequency of intake (*i.e.* once daily or in divided doses throughout the day) affects the cholesterol-lowering efficacy of phytosterol-enriched foods. A study specifically designed to address this question did not show a significant difference in the effects of a phytosterol-enriched spread consumed once a day with lunch or three times a day with breakfast, lunch and dinner [34]. Other food formats enriched with phytosterols and consumed once-a-day (yoghurt drink, ground meat) were also shown to significantly lower LDL-cholesterol [25, 35]. One factor that may affect the cholesterol-lowering efficacy of phytosterols-enriched foods is their intake occasion. Indeed, consumption of a once-a-day yoghurt drink with lunch was shown to lower LDL-cholesterol concentrations more markedly than consumption on an empty stomach, 30 minutes before breakfast [25]. It may be hypothesized that the stimulation of bile release consequent to the presence of food in the upper part of the gut facilitates the action of phytosterols by stimulating the formation of mixed micelles which are crucial to the process of cholesterol absorption. Moreover, bile contains significant amounts of cholesterol which are less effectively reabsorbed in the presence of phytosterols and are therefore excreted in faeces.

Combination of phytosterols with other cholesterol-lowering approaches

The LDL-cholesterol lowering effect of phytosterol-enriched foods appears to be additive to that of some other dietary approaches to lower plasma cholesterol. The impact of phytosterols on LDL-cholesterol was evaluated as part of a "heart-healthy" diet (*e.g.* low or moderate intakes of total and saturated fat) in various clinical trials. When compared with the baseline, usual diet, the healthy diet-phytosterol combination led to decreases in LDL-cholesterol of up to 24% for doses of phytosterols ranging from 1.5 to 2.3 g/day [3, 36]. The LDL-cholesterol lowering effect attributed to the healthy diet in these studies was about 10% [3, 36], suggesting an additive effect of phytosterols with the healthy diet.

A more effective way to optimise dietary-induced cholesterol lowering is to combine phytosterols with other ingredients and func-

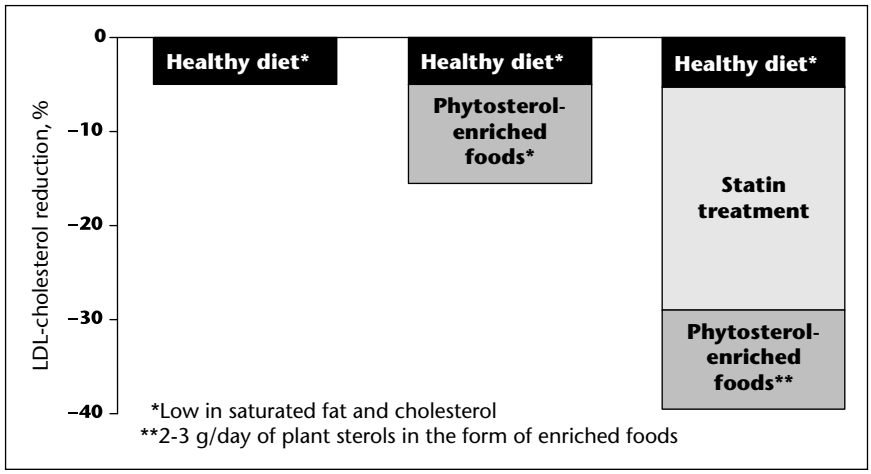

Figure 4. *The cholesterol-lowering effect of phytosterols is additive to that of a healthy diet and lipid-lowering medications such as statins. Based on: Katan et al. [3] and Edwards and Moore [44].*

tional foods that have different cholesterol-lowering mechanisms. A good example of such a combination is the "Portfolio diet" which includes viscous dietary fibers such as psyllium or beta-glucan from oats, soy protein, almonds and phytosterols. This diet was shown to lower LDL-cholesterol in hypercholesterolemic individuals by around 30% within one month [37]. On a longer term (one year), the LDL-cholesterol lowering obtained in free-living individuals was about 13% on average, but reductions in LDL-cholesterol of more than 20% were achieved in more than 30% of the fully compliant participants [38]. These results confirmed the contribution of phytosterols to the beneficial effect of the "Portfolio diet" on the long term. Phytosterol ester intake had indeed been shown to consistently lower total and LDL-cholesterrol in long-term efficacy studies lasting up to one year [39, 40].

Phytosterol-enriched foods may also be a useful adjunct to specific lipid-lowering medications. Additional cholesterol-lowering benefits have been observed with statins [41] and fibrates [42]. In one large multi-centre clinical trial, statins alone, a phytosterol-enriched spread alone, and the statin-phytosterol combination lowered LDL-cholesterol by 32%, 8% and 39%, respectively, showing that the effects of phytosterols and statins are additive [41]. Phytosterols and ezetimibe, however, were not shown to have additive effects [43], possibly due to the fact that both ezetimibe and phytosterols lower cholesterol absorption, and that a "ceiling" effect may be achieved in lowering cholesterol absorption. *Figure 4* shows the cholesterol-lowering effects that can be expected by combining phytosterol-enriched foods with a healthy diet and statins [3, 44].

Anti-atherogenic effects of phytosterols

So far, no long-term studies on the effect of phytosterols on atherosclerosis and thus CHD risk reduction in humans are available. However, animal studies have convincingly shown beneficial, anti-atherogenic effects.

Over 30 studies have investigated the effect of phytosterols on experimental atherosclerosis models in different animals, such as chicken, rabbits, hamsters and more recently knockout mouse models [4]. These studies have shown clear protective effects, such as a reduction in arterial lipid accumulation and a reduction in the development of atherosclerosis, *e.g.* lesser plaque development or reduced lesion size, an inhibition of lesion formation and progression and even regression of existing lesions resulting from the cholesterol-lowering action of phytosterols [45-50]. The key findings related to the evidence from these animal studies are summarised in *table 1*.

In the more recent studies, different types of genetically modified, so-called knockout mice were studied. In ABC G5/G8 and LDL-receptor double knockout mice fed for 7 months a Western diet, the size of the atherosclerotic lesions was similar to that observed in control mice, despite greatly elevated plasma phytosterol concentrations (> 20-fold higher than control mice) [51]. In LDL receptor-deficient mice fed for 35 weeks an atherogenic diet with phytosterols alone or in combination with atorvastatin, less aortic lesion development was observed compared to mice fed the atherogenic diet without phytosterols, despite the 4 to 11-fold increase in plasma sitosterol and campesterol concentrations resulting from phytosterol intake [52]. Moreover, consumption of phytosterols alone for an additional period of 12 weeks resulted in lesion regression [52]. These findings suggest that elevated plasma sitosterol and campesterol concentrations caused by feeding dietary phytosterols alone or in combination with a statin have no atherogenic effects.

Table 1. *Anti-atherosclerotic effects of dietary phytosterols in various animal models.*

Animal studies	Dose (% weight of diet)	Sterols or stanols	Source	Effects on atherosclerosis development[a]
Hamsters				
Nanios *et al.*, 2003 [49]	0.24-2.84%	Pure sterols	Vegetable oil	Reduced lesion formation
Mice				
Moghadasian *et al.*, 1997 [45]	2%	Mainly sterols	Tall oil	Reduced lesion formation
Moghadasian *et al.*, 1999 [47]	2%	Mainly sterols	Tall oil	Reduced lesion formation
Moghadasian *et al.*, 1999 [48]	2%	Mainly sterols	Tall oil	Reduced lesion size
Volge *et al.*, 2001 [50]	1%	Mainly sterols	Vegetable oil vs Wood	Reduced extent and severity of lesions
Plat *et al.*, 2001 [52]	1-2%	Both sterols and Stanols	Tall oil	Inhibited lesion formation & progression regression of existing lesions
Rabbits[b]	0.2-3%	Sterols/ stanols	Not well describeb	Reduced development of lesions
Chicken[b]	1-5%	Sterols/ stanols	Not well describeb	Reduced lesion formation

[a] With respect to control group (where applicable).
[b] As summarised by Pollak and Kritchevsky [53].

In vitro studies utilizing vascular smooth muscle cells (VSMC) isolated from rats have shown that phytosterols stimulated prostacyclin release from VSMC, suggesting that natural phytosterols may prevent VSMC hyperproliferation, which could play a beneficial role against atherosclerosis development [54]. Another in-vitro study with macrophages found a reduced release of prostaglandins, possibly offering protection from atheroma development via affecting platelet aggregation or vasodilatation of blood vessels [55].

Human studies have not demonstrated yet clear possible benefits of phytosterols on other risk factors related to the development of atherosclerosis besides the substantial reduction of total and LDL-cholesterol. For instance, coagulation and fibrinolytic parameters as well as endothelial markers like vascular cell adhesion molecule 1 (VCAM) and intercellular adhesion molecule 1 (ICAM) were not significantly affected after plant sterol or stanol intake for up to 16 weeks [56, 57]. In studies with children with familiar hypercholesterolemia, short-term phytosterol intake did not improve endothelial dysfunction as measured by flow-mediated dilation (FMD) despite the clear reduction in LDL-cholesterol [58]. Besides LDL-cholesterol lowering, decreased levels of oxidized-LDL were observed with the intake of phytosterols for 4 weeks, suggesting a protection against LDL-oxidation [59]. Whether phytosterols indeed have distinct antioxidant properties and whether these have any relevance to human health awaits further investigation. Therefore, it is still uncertain whether other possible effects next to LDL-cholesterol lowering contribute to the anti-atherosclerotic properties of phytosterols.

Anti-inflammatory effects and effects on the immune system

Some evidence suggests that phytosterols, particularly beta-sitosterol, may have anti-inflammatory activity. In vitro studies showed an inhibition of secretion of inflammatory markers such as interleukin-6 (IL-6) or tumor necrosis factor alpha (TNF-α) by monocytes [60]. In ovalbumin-induced asthmatic mice, lung inflammation related to leukocytosis and eosinophil infiltration was reduced by intraperitoneal injection of beta-sitosterol [61]. Oral consumption or topic application of a single dose of a phytosterol mixture containing mainly beta-sitosterol was also shown to decrease or even inhibit oedema in murine models of inflammation [62]. However, results from other studies in animal models do not support a role for beta-sitosterol in preventing or reducing inflammation [63, 64]. In humans, data on the effects of consumption of phytosterol-enriched foods on inflammatory markers are scarce and conflicting. One trial showed a significant reduction in plasma C-reactive protein (CRP) concentrations following consumption, for 8 weeks, of 2 g/day phytosterols incorporated in a reduced-calorie orange juice [27]. However, in a longer term study, 16-wk consumption of 2.5 g/day phytosterols did not affect soluble adhesion molecules, CRP and monocyte chemotactic protein-1 concentrations [57]. These latter results suggest that at doses consumed for cholesterol-lowering, phytosterols may not exert noticeable effects on inflammation in human subjects. Nevertheless, further investigations would be useful to address this question in a more comprehensive manner.

To gain insight into the modulatory effects of phytosterols on the immune system, Bouic *et al.* undertook a series of in vitro, animal and humans studies, and published reviews on this topic [60, 65]. Beneficial effects of doses of beta-sitosterol as low as 60 mg/day in combination with negligible amounts (less than 1 mg/day) of sterolins (beta-sitosterol glucosides), were reported to improve the immune function in subjects affected by various pathologic processes such as pulmonary tuberculosis, HIV, stress-induced immune suppression, allergic reactions and rheumatoid arthritis [60, 65]. The mechanisms by which beta-sitosterol and beta-sitosterol glucosides would improve the immune response include increases in the proliferative response of blood lymphocytes and in the lytic/cytotoxic activity of natural killer cells, a modulation of the T-helper 1/T-helper 2 (Th1/Th2) balance [60, 65], as well as effects on macrophage function [66]. A recent study in a mouse model of acute, aseptic inflammation has given further support for a role of dietary phytosterols (a mixture containing 41% beta-sitosterol) in increasing the Th1/Th2 ratio [64]. However, considering that the phytosterol dose used in human studies (60 mg/day) [60, 65] is low compared with the dose used in the animal trial (2% of diet weight) [64], and that the normal dietary intake of phytosterols by humans is around 150-400 mg/day, it seems doubtful whether such low additional intakes of phytosterols could result in distinct effects on the immune function in human subjects. Further studies with doses of phytosterols used for cholesterol-lowering (2.0-2.5 g/day) would be useful to evaluate the effects of phytosterols on immune function in humans.

Anticancer activity of phytosterols and beneficial effects on prostatic hyperplasia

The effects of plant sterols as anticancer compounds have been recently reviewed by Bradford and Awad [66]. Evidence for a protective role of especially plant sterols against various types of cancer in humans comes from epidemiological, case-control studies. In these studies, the consumption of total phytosterols was related, after controlling for major confounding factors, to a lower incidence of breast, lung, and stomach cancer [66]. Dietary intake of beta-sitosterol and stigmasterol was associated to lower risks of esophagus [67] and ovarian [68] cancer, respectively. On the other hand, a recent prospective cohort study failed to demonstrate a relationship between phytosterol intake and the risk of colon and rectal cancers [10]. Although the number of controlled studies is limited and the existence of a statistical relationship between phytosterol intake and a lower incidence of some cancers does not indicate a causal link, overall, the epidemiologic evidence suggests that phytosterols may exert a protective effect against certain types of cancer.

Additional evidence for the potential anticancer properties of phytosterols is provided by studies in animal models and in vitro experiments. Various studies in rats or mice administered carcinogenic stimuli, or injected or implanted with cancer cells showed that consumption of beta-sitosterol or a phytosterol mixture reduced the incidence of tumors, slowed down cell proliferation and/or lowered the number of metastases of colon, breast or prostate cancers [66]. Various mechanisms have been proposed to explain the potential anticancer properties of phytosterols: inhibition of cell cycle progression, promotion of cellular apoptosis possibly via activation of the sphingomyelin cycle and increased generation of ceramide, down-regulation of cholesterol synthesis, inhibition of cell invasion, migration and adhesion, as well as stimulation of the immune function [66, 69]. A possible estrogenic activity of phytosterols could also be involved, but reports are inconsistent [66] and this mechanism of action seems less likely.

Clinical evidence is lacking for a role of phytosterols in the management of cancers. However, supplementation with phytosterols appears to be useful in the treatment of benign prostatic hyperplasia (BPH). Symptomatic BPH is a common medical condition in older men. A meta-analysis of four randomised, placebo-controlled, double blind trials showed that oral consumption of small doses (60-130 mg/day) of beta-sitosterol for 4 to 26 weeks improved the clinical symptoms of BPH (flow rate and residual urinary volume) without reducing the prostate size [70]. A subsequent study showed that the beneficial effects of 60 mg/day beta-sitosterol were maintained over a period of 18 months [71]. This efficacy in improving the symptomatology of BPH is remarkable as such low doses of beta-sitosterol are small compared with the normal dietary intake of phytosterols

estimated at 150-400 mg/day. The mechanisms responsible for the putative beneficial effects of phytosterols on BPH remain unclear but may be related to an altered testosterone metabolism [72]. Moreover, data on long-term safety and ability to prevent complications related to BHP are lacking.

Conclusion

Phytosterols are naturally occurring compounds found in plants that include sitosterol and campesterol, and their saturated counterparts sitostanol and campestanol. Phytosterols have been used for the last half-century because of their cholesterol-lowering properties. They have been shown in a vast number of human studies to be safe and effective in lowering plasma total and LDL-cholesterol concentrations. The underlying mechanisms of the cholesterol-lowering action of phytosterols relate to the inhibition of intestinal cholesterol absorption. In addition to their well-established cholesterol-lowering effect, other potential health benefits of phytosterols have been described. However, evidence for such promising effects, *e.g.* antioxidant and anti-inflammatory actions, as well as benefits on the immune system and anticancer properties are still at a rudimentary stage and more research is clearly needed to draw firm conclusions.

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