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Review

Phytosterols and cardiovascular health

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A B S T R A C T

Phytosterols are typical constituents of plants' cell walls. When ingested with plant foods, they reduce cholesterol absorption from the gut, due to their structural similarity with cholesterol. In the last decades, purified plant sterols or stanols have been added to various foods items to obtain functional foods with remarkable hypocholesterolemic activity. A daily intake of plant sterols or stanols of 1.6–2 g/day, incorporated in these foods, is able to reduce cholesterol absorption from the gut by about 30%, and plasma LDL cholesterol levels by 8–10%. Since the action of plant sterols or stanols on plasma LDL cholesterol is additive to that of statins, the former can be used to increase the latter's hypocholesterolemic action in patients needing a marked reduction in plasma LDL cholesterol levels. Phytosterols, up to 3 g/day, are safe and effective cholesterol-lowering agents.

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1. Introduction

Non-pharmacological control of plasma lipid profile is being actively explored with the use of a variety of agents/nutrients/nutraceuticals/functional foods [1–3]. Among such agents, phytosterols are being widely employed and are part of several food items and supplements.

The hypocholesterolemic effects of phytosterols (plant sterols and stanols, PS) have been known since about 1950, when a fall of about 27% was observed in the plasma cholesterol levels of 26 healthy subjects supplemented with 5–10 g/day of PS, for 2 weeks. Subsequent studies demonstrated that high doses of PS (over 10 g/day), taken for 3–5 weeks, were able to decrease blood cholesterol levels, on average, up to 20% [4].

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The doses of PS recommended to reduce blood cholesterol, consequently, ranged between 9 and 30 g/day up to the late '70s. The first PS preparations were quite heterogeneous in terms of both composition and source, but they all appeared to be effective and safe. Their pharmacological application was limited, at those times, to severe hypercholesterolemias, mainly due to the elevated cost of high-purity compounds.

Calculations of the large amounts of PS in the ancestral diet stimulated research on their role in human health, notably with the aim to correct the low intake of these compounds in modern diets. Hence, PS shifted from being natural food components to being formulated into medications and supplements or incorporated in conventional foods. Firstly, they were incorporated into lipid-based products, mostly margarines. Subsequently, the progress of food technologies has allowed to improve their solubility and incorporation in different food products such as fruit juice, ice cream, oven baked products, etc. [5].

2. Biochemistry

Like cholesterol, to which they are related both structurally and biosynthetically, PS belong to the family of triterpenes, with a tetracyclic ring and a side chain linked to carbon 17. They can be classified into sterols and stanols, according to the presence or absence of a double bond at the Δ5 position. PS exist in free or esterified forms: free sterols form part of the cellular wall, where they play important structural functions, whereas sterol esters represent storage products within the cell [6] (Fig. 1).

More than 250 different PS molecules have been identified to date; β-sitosterol is the most abundant among them. The only structural difference between sitosterol and cholesterol consists of an additional ethyl group present at position C-24 in sitosterol, which is probably responsible for its poor absorption. Other plant sterols such as campesterol, stigmasterol, and dihydrobrassicasterol are present in vegetal foods at much lower concentrations; the saturated derivatives campestanol and sitostanol are found in almost negligible amounts in plants [7]. In turn, the most common dietary PS are sitosterol, campesterol, and stigmasterol, that contribute to about 98% of the total dietary intake.

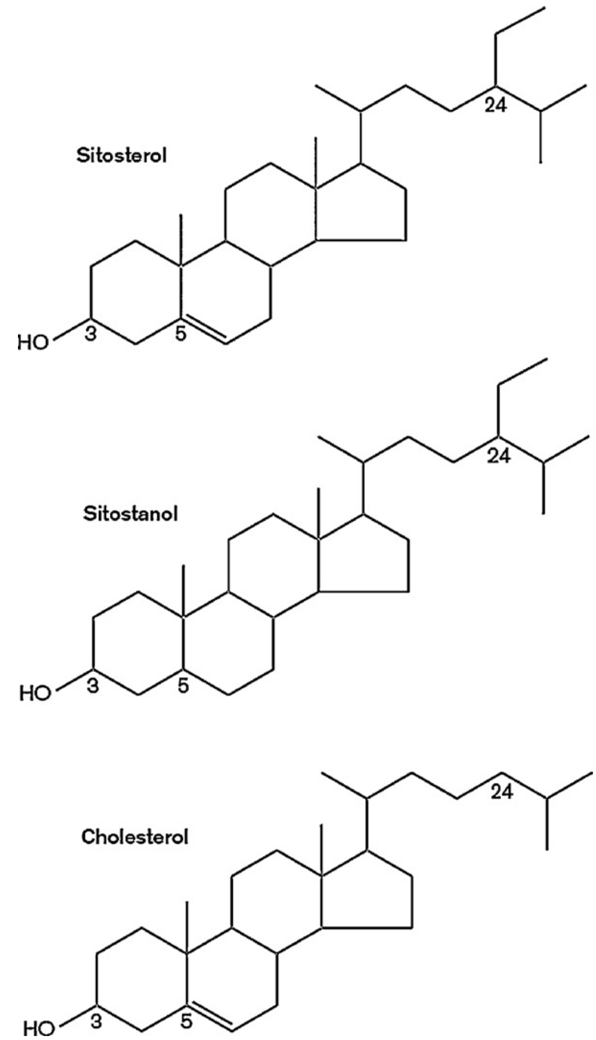

Fig. 1. Structures of sitosterol and sitostanol.

3. Dietary sources and intake

The main PS sources are vegetable oils, nuts, grains, and grain-derived products; also sprouts, cabbages, cauliflowers, green and black olives contain plant sterols and stanols (Table 1). Among non-vegetable foods, egg yolks, mammalian liver and crustaceans represent important sources of PS in Western diets. In walnuts, PS represent 0.1–0.2% of the total lipid fraction; about 87% of the total PS is represented by sitosterol. Macadamia nuts contain about 1.3 mg of PS per gram of lipids [8].

The major sources of plant sterols used for incorporation into commercial products are tall oil – which contains up to 80% β-sitosterol – and the by-products of soybean oil production. Both sterols and stanols are frequently used in esterified forms, as fatty acid esters: this increases their solubility and allows their incorporation into lipid-based foods [7].

Due to large differences in the consumption of plant foods throughout the world, the dietary intake of PS ranges from 167 mg/day in Britain (mainly from vegetable oils) to 375 mg/day in Japan [9]. However, it varies greatly also within Western population groups, being markedly higher (+50%) in vegetarians. In the large sample of the EPIC study (European Prospective Investigation into Cancer), performed on 22,256 subjects, PS intake ranged from 463 mg/day (highest quintile) to 178 mg/day (lowest quintile) [10,11]. The dietary intake of plant stanols is much lower, about 50 mg/day [10].

As PS cannot be endogenously synthesized by humans, their circulating levels are only dependent upon diet and absorption efficiency. Miettinen and coworkers [12] found a positive correlation between the circulating concentration of campesterol and sitosterol and the amount of dietary PS ingested, as well as the polyunsaturated/saturated fatty acid ratio of dietary fat and the linoleic acid contents of plasma and dietary lipids. Depending on the type and amount of plant foods consumed, PS consumption, and therefore PS blood levels, may vary greatly within and between populations.

Results from intervention studies suggest that higher PS intake in the form of supplements increases circulating levels of PS, while plant stanol supplementation decreases them [9].

Inter-individual variability affects phytosterols' absorption: it is known that the absorption route of PS is similar to that of cholesterol, whose efficiency is affected by ApoE polymorphisms. Therefore different ApoE phenotypes may modify plasma concentrations of PS, even if data from studies in different populations are inconsistent and not as yet conclusive. However, it is likely that the ApoE phenotype plays a role in explaining why variations in PS concentrations exist within and across different population groups [13].