Phytosterols and Health: Current Status and Future Perspectives

Dietary phytosterols (plant sterols and stanols) are known LDL-cholesterol lowering agents. Consequently, food products containing these plant compounds are widely used as a therapeutic dietary option to reduce plasma cholesterol and, potentially, cardiovascular risk. In this special issue, several manuscripts review the progress to date in research on the use of phytosterol fortified foods in clinical practice and the molecular mechanisms underlying the cholesterol-lowering effects of phytosterols as well as the recent findings that support the antitumorigenic and anti-inflammatory actions of phytosterols. This special issue also includes three manuscripts that review the recent findings on the therapeutic potential of phytosterols on multiple sclerosis and Alzheimer’s disease, the investigation and management of the inherited metabolic disorder sitosterolemia and the methodological aspects of phytosterol measurements in biologic samples, respectively.

Cofan et al. [1] update the consistent scientific evidence on the cholesterol-lowering efficacy and safety of functional foods supplemented with phytosterols. They conclude that two to three grams of phytosterol consumption, preferably with meals, is associated with a nine-to-twelve % of reduction in LDL-cholesterol in a wide range of clinical situations. This response is equivalent to that found with an upward titration x 2 of any statin dose. Furthermore, it has been reported that phytosterols reduce plasma triglycerides when they are high. The use of these plant compounds has been shown to be safe, with no drug–nutrient interactions. Therefore, although the long-term effects of dietary phytosterols on cardiovascular risk remain unknown, these compounds provide a clinical opportunity for the prevention of cardiovascular disease.

The cholesterol-lowering action of dietary phytosterols is thought to occur, at least in part, through competition with dietary and biliary cholesterol for intestinal absorption in mixed micelles. Cedó et al. [2] show that strong evidence indicates that dietary phytosterols may improve other atheroprotective pathways in the hepatocytes and enterocytes, such as a reduced liver VLDL production and an enhanced transintestinal cholesterol excretion. Furthermore, these plant compounds may alter the conversion of bile acids into secondary bile acids, thereby lowering the bile acid hydrophobic/hydrophilic ratio and reducing intestinal cholesterol absorption.

Beyond the phytosterol-mediated effects on LDL-cholesterol, the new findings reported by Vilahur et al. [3] support the anti-inflammatory effects of phytosterols on cell- and experimental animal-based approaches, mainly by reducing cytokine secretion and the expression of vascular adhesion molecules. However, human intervention studies have yield divergent results on C-reactive protein and inflammatory cytokine levels and, therefore, well-designed controlled human studies examining the effect of phytosterols on inflammatory-related markers are necessary.

Blanco et al. [4] also review and update the current knowledge on the molecular mechanisms involved in the anticancer action of phytosterols and their potential in cancer prevention or treatment. Experimental data provide evidence that phytosterols may modulate proliferation and apoptosis of tumor cells, but only a few human clinical studies have addressed this point. As discussed above, further studies are required to investigate the exact mechanisms of phytosterol action as well as to assess the long-term effects of these compounds on the prevention of tumor initiation, growth, and angiogenesis.

Recent evidence indicates that phytosterols may be transported to the brain and modulate its cholesterol metabolism and, thus, they could modulate neurological diseases such as multiple sclerosis and Alzheimer’s disease. Dierckx et al. [5] also discuss in a manuscript the new evidence that suggests a direct effect of phytosterols on neuroinflammation, neurodegeneration, and central nervous system repair independent of their role in modulating cholesterol metabolism.

On the other hand, some studies have raised the hypothesis that high levels of circulating plant sterols may be an atherogenic risk factor. Evidence in support of this hypothesis stems mainly from observations in sitosterolemic subjects who hyperabsorb phytosterols and may suffer premature atherosclerosis. Bastida et al. [6] review the main
clinical features of sitosterolemia related to cardiovascular disease and hematological abnormalities and report the relevance of the phytosterol assays and genetic testing in these pathological situations. More importantly, most of the physicians do not associate these hematological abnormalities with sitosterolemia and these patients may suffer long-term misdiagnosis of immune thrombocytopenia and be at high risk of not receiving the standard treatment with ezetimibe.

In this context, Gylling et al. [7] review the basic methods for the measurement of phytosterols in biologic samples. Since the main basic methods are well validated, the authors indicate that the challenge is to develop a practical and functioning standardization system between the sterol research laboratories.

In summary, beyond the established effects of dietary phytosterols on intestinal cholesterol absorption and LDL-cholesterol levels, it is also plausible that phytosterols may exert beneficial effects on inflammatory and oxidative stress markers and on tumorigenic processes, multiple sclerosis and Alzheimer’s disease (Fig. 1). However, phytosterols may be injurious at very high levels as occurred in sitosterolemic patients.

![Fig. (1). Dietary phytosterols reduce intestinal cholesterol absorption and LDL-cholesterol levels. Other biological actions, such as anti-inflammatory and antitumorigenic properties, have also been ascribed to these plant compounds. A number of studies have also indicated the potential of phytosterols to be used as a supplementary therapy for Multiple sclerosis and Alzheimer’s disease.](image)

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