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Review

Plant sterols in food: No consensus in guidelines



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ABSTRACT

Plant sterols are supplemented in foods to reduce cardiovascular risk. Randomized controlled trials show 2 g of plant sterols a day reduce serum cholesterol by about 10%. This reduction in serum cholesterol levels is achieved at the expense of increased serum plant sterol levels. Findings in patients with phytosterolemia, in experimental studies and in clinical trials have lead to speculations that plant sterols might be atherogenic. In view of emerging safety issues the role of plant sterols in cardiovascular prevention has become controversial. This review reflects the ongoing controversial scientific debate and points out recent developments in guidelines of national and international societies.

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1. Introduction

High cholesterol levels are a known risk factor for cardiovascular diseases [1]. Only recently a consensus panel of the *European Atherosclerosis Society (EAS)* published a position paper on the impact of plant sterols and stanols on cholesterol homeostasis and cardiovascular risk [2]. The *EAS Consensus Panel* concludes that based on the LDL-C lowering effects and due to “absence of adverse signals” functional foods with plant sterols may be considered in patients with high cholesterol levels at intermediate and low global cardiovascular risk who do not qualify for pharmacotherapy. Moreover, plant sterols may be considered as adjunct to pharmacotherapy in high and very high risk patients who do not reach LDL-C targets and in adults and children above 6 years with familial hypercholesterolemia.

2. Discussion

The conclusions of the *EAS Consensus Panel* come as a surprise since highly esteemed international societies such as the *American Heart Association* which had previously recommended the use of phytosterols as a food additive [1] do not explicitly advise this option in newer recommendations [3]. In addition, the German Drug Commission and the updated guidelines from the *National Institute of Health and Clinical Excellence (NICE)* in the United Kingdom advise against the general recommendation that plant sterols should be taken as a dietary supplement [4,5]. Health Canada the federal department responsible for helping Canadians maintain and improve their health went as far as rising significant safety issues not to allow functional foods enriched with plant sterols to be sold in Canada, shortly after market release in the year 2000 [6]. Moreover, the new joint guidelines for the management of hypercholesterolemia of the *European Society of Cardiology* and the *European Atherosclerosis Society (ESC/EAS)*—even though clearly acknowledging the LDL-lowering capability of phytosterols—come to the

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conclusion that long term studies would be needed to guarantee the safety of foods enriched with plant sterols [7]. Finally, the newly revised guidelines for cholesterol management of the *American College of Cardiology* and the *American Heart Association* clearly state that there are no atherosclerotic vascular disease outcome studies identified for plant sterols and clearly step back from a general recommendation [8].

The background for the currently controversial scientific debate are the phytosterols themselves [9]. In clinical trials, phytosterols can indeed produce a reduction in LDL cholesterol levels [10]. However, new studies show that this effect is not always reproduced with certainty and that phytosterol supplementation in some individuals can also lead to a paradoxical increase in cholesterol levels [11]. Moreover, the effectiveness of a reduction in cholesterol depends not only on the quantity of the phytosterols taken, but also on genetic differences in sterol metabolism [12]. Patients with ApoE4 homozygosity show a clearer reduction in cholesterol levels under phytosterol supplementation [13]. For this genotype in particular, the reduction in cholesterol is, however, associated with an extremely elevated phytosterol serum elevation. The significance of elevated serum phytosterols is unclear and highly controversial [14–16].

The discovery of phytosterolemia, a rare inherited disorder, has raised curiosity as to whether phytosterols could be a possible risk factor for cardiovascular disease [17,18]. Elevated phytosterol concentrations, xanthomas and the premature onset of atherosclerosis are the significant findings in patients with homozygous phytosterolemia. Specific gene mutations are the cause, resulting in the increased consumption and reduced excretion of phytosterols [19,20]. The fact that patients with this disease experience the aggressive progression of atherosclerosis despite normal cholesterol levels, would suggest that phytosterols themselves may have a potentially atherogenic capability. More recent results of experimental studies and data from individual epidemiological and clinical studies support this hypothesis [21–27].

On the contrary, other studies could not detect a relationship between plant sterol serum concentrations and an increased cardiovascular risk and some studies even indicated an association with a lower cardiovascular risk [28–30]. Of note, a great shortcoming is that the measurement of plant sterols, in contrast to cholesterol, in different laboratories around the world is not standardized. This makes the comparison of results from various laboratories with each other difficult and necessitates a harmonization of sterol measurements [31]. This has stirred up a great controversy in the scientific community with pro and contra discussions at international meetings, in the end being completely inconclusive in regard to a scientific consensus [32,33].

Against a backdrop of increasing evidence that phytosterols could be harmful as a food supplement, back in 2008, the *German Federal Institute for Risk Assessment* called for these products to be recommended with restriction to individuals with elevated cholesterol levels only [34]. In December, 2011, after additional results from clinical and experimental studies were published [22–27] the *German Federal Institute for Risk Assessment* called for the general scrutiny of the use of phytosterols as a food additive at the European level and for a reassessment by the *European Food and Safety Authority (EFSA)* [35].

Due to the more relaxed approval and control conditions, investigation into the interactions of individual food additives, whether with each other or with drugs, has been mainly unsatisfactory. This is important especially for consumption by elderly and infirm patients, by children and by individuals who are chronically ill due to liver or kidney disease, high risk patients and patients taking a number of different drugs.

Positive lifestyle changes by incorporating physical activity and increasing the consumption of fresh fruits, vegetables and fish,

bring health benefits, a fact only recently demonstrated by the PREDIMED Study of the Mediterranean Diet [36]. Clear evidence for the efficacy of dietary supplements in the prevention of cardiovascular diseases is as yet unavailable and individual studies show that they may even be harmful [37,38]. For drugs, such questions must be clarified prior to authorization for market circulation and it is only when the benefit outweighs the risk that a drug will actually be released onto the market. According to the much slackened food legislation, which also governs dietary supplements and functional foods, however, there is no provision for this type of investigation into product safety. In individual cases, supplements might do more harm than good. Different interpretations of the currently available scientific data resulting in contradictory guideline recommendations will not be of help for medical practice. As long as results of trials testing relevant clinical endpoints for phytosterols are pending the general recommendation of these products will continue to be a matter of controversial debate and will become a more and more challenging scientific issue.

Conflicts of interests

None.

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