

Editorial

Plant Sterols, Health Claims and Strategies to Reduce Cardiovascular Disease Risk

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In this issue of the journal, Williams and colleagues report the results of their study of nineteen two- to five-year old healthy children who received three grams of stanol in a margarine or five grams of wheat fiber in breakfast cereal for one month periods in a randomized crossover design [1]. Stanol margarine reduced total cholesterol by 12.4% and LDL cholesterol by 15.5%, while wheat bran resulted in a non-significant 4% reduction in serum cholesterol. Reductions in LDL cholesterol of this order of magnitude are not unexpected in children at this dose of stanol.

Plant Sterols and Stanols

The ability of plant sterols to lower serum cholesterol has been recognized for almost half a century [2]. Early studies have focussed on β -sitosterol rather than other plant sterols such as campesterol and stigmasterol, which are also present in plant foods [3,4]. Early studies used very large amounts, 10 to 15 g/d, of unesterified sitosterol with reductions in serum cholesterol of 10% to 20% [2,5–9]. These sitosterol dosages were well tolerated and provided effective treatment for periods of up to five years or more [9,10]. It then became apparent that 3 g/d gave reductions in cholesterol that were not improved on by raising the intake in excess of 9 g/d [8]. Finally, interest switched from sterols to stanols, which are found in much smaller quantities in plant foods, since these were suggested to be more effective in cholesterol lowering. Thus an early study by Becker *et al.* in children with familial hypercholesterolemia [11], showed that 6 g/d sitosterol lowered LDL-C by 20% while 1.5 g/d sitostanol lowered LDL-C by 33% [11]. Emphasis has stayed with stanols. In a recent study, sitostanol interesterified with margarine at a dose of 1.9 to 2.6 g/d lowered plasma cholesterol by 10.2% over one year in 102 mildly hypercholesterolemic patients [12]. However, most recently the advantage of stanols over sterols has been blurred with the demonstration of similar LDL cholesterol reduction using esterified soybean oil sterols as was seen the esterified stanols derived from hydrogenation of pine wood pulp sitosterol [41].

Plant sterols resemble cholesterol, but have ethyl or methyl groups or unsaturation in the side chain. They are considered to lower serum cholesterol by inhibiting cholesterol absorption, being very poorly absorbed themselves. Stanols are the products of 5 α -saturation of the sterols. This can be achieved commercially.

Plant sterols have proved safe and effective and do not appear to cause significant malabsorption of nutrients including fat soluble vitamins. In the rare recessively transmitted familial hyperphytosterolemia, absorption of both cholesterol and plant sterols is high [13] and premature arteriosclerosis is common [14–19]. However, the major sterol accumulating in atheroma is cholesterol. It has also been reported that increased sterol absorption is associated with increased cholesterol absorption, even in subjects without familial hyperphytosterolemia, and that this tracks in families with premature CHD [13].

The Lipid Lowering Portfolio

However, the thrust of this study was not to explore detailed mechanism of action of plant sterols in children, but to find a safe, effective and acceptable dietary means of lowering serum cholesterol in children who in adulthood may suffer premature cardiovascular disease. Reference was also made to dietary fiber, soy protein and garlic [20,21]. Plant sterols added to margarines, viscous fibers in various foods, naturally occurring in oats and barley, and soy proteins in dairy and meat replacements, may all make a significant contribution to reducing LDL-C and hence CHD risk. Individually, taken in modest amounts, their effects may not be large [22]. However, their cumulative action is likely to be very worthwhile if each contributes 5% to 10% to serum LDL cholesterol reduction (Table 1). Indeed, if these effects are additive, then combined with the reductions in dietary saturated fat and cholesterol advocated in NCEP Step 1 [23] and, even more importantly, NCEP Step 2 diets [23], the total LDL reduction may be equivalent to or better than that from the routine dose of a

Table 1. Portfolio of Dietary Factors for Cholesterol Reduction

Diet Component	Dietary Change	Approximate LDL Reduction
Saturated Fat*	<7% of calories	10%
Dietary Cholesterol	<200 mg/d	5%
Body Weight	lose 10 lb (5 kg)	5%
Plant Sterols**	1–3 g/d	5%
Viscous Fiber	5–10 g/d	5%
Soy Protein	25 g/d	5%
Total	Full Portfolio†	35%

* Reduce trans fatty acids as close to zero as possible.

** Depending on the sterol and stanol.

† Assuming the effects are additive.

Adapted from Jenkins DJ, *et al.*, 1998[42].

statin, the current first line drugs of choice in the treatment of hypercholesterolemia (Table 1).

Functional Foods: A Role for Health Claims

A number of the most promising functional foods or food components, i.e., foods with a physiological function in lowering serum cholesterol, already have or are being considered for health claim status by the United States Food and Drug Administration (FDA) [24–26], the claim being cardiovascular disease risk reduction. At present, plant sterols are not on the FDA list. It is possibly for this reason that Williams and colleagues have gone to considerable lengths in their paper to show the efficacy and safety data related to plant sterol use. Oat β -glucan and psyllium have both been formally assessed using these criteria and approved for cholesterol lowering in foods. Soy protein has now received similar approval. Internationally, there is considerable regulatory interest in facilitating this process, since in most jurisdictions only drug manufacturers can make a health claim or disease risk reduction claim. By opening up this process, it is hoped to encourage the food industry to develop products with specific health attributes. In the case of foods or food components which may lower serum cholesterol, official recognition draws attention to the validated components of a possible dietary cholesterol lowering portfolio. Where drug therapy is lifelong, it is important first to make maximum use of dietary approaches [23].

Product-Specific Claims

Williams and colleagues used a stanol (sitostanol) enriched margarine which appeared to change the total fat intake and PS ratio of the diet remarkably little, despite providing three eight-gram portions of spread containing one gram of stanol per eight grams of spread. The question therefore arises as to whether the fatty acid composition of the dietary vehicle for the stanol influences the action of the stanol together with the method of incorporation of the stanol into the fat. There is considerable variation in the literature on the effect of stanols on serum

cholesterol, with some studies showing just over 7% to others showing over 30% for 1.5 g stanol per day [11,27]. Product-specific health claims are therefore essential which encourage companies to explore the optimal method of incorporation of the active ingredient into the ideal vehicle to maximize its effect. They will give a measure of protection to the company from competitors who will have to demonstrate efficacy of a look-alike product before being allowed to make a claim. They will also provide the public with tested functional food products.

These concerns are equally valid for viscous fiber claims where destruction of viscosity by, for example, partial hydrolysis of oat β -glucan reduces physiological effectiveness [28,29] while potentially enhancing palatability. In the future, removal of potentially active ingredients, such as isoflavones or saponins from soy, to improve flavor, may also reduce the effectiveness of manufactured soy products [30–33].

The product-specific approach to health claims is not meant to replace generic health claims, but to augment them with special relevance to functional food products, including stanol margarines, which have been specifically designed to fulfill a physiological function.

Conclusion

It goes without saying that the drive to identify potentially active food components and produce functional manufactured foods should not eclipse the continued need to promote healthy diets and lifestyles with increased dependence on plant foods, whole grain cereals, legumes, fresh vegetables and fruit, all of which are likely to have multiple benefits [34–36]. Furthermore, the exact functional components of these foods have often not been defined. For example, insoluble cereal fiber consumption relates to freedom from diabetes and cardiovascular disease in cohort studies [37–40], despite the fact that increased fecal bulk is the only clear physiological effect of wheat fiber. Fresh vegetables and fruit may have many varied effects including lipid lowering, antioxidant protection and homocysteine reduction. Nevertheless, the specific focus on plant stanols and other functional dietary components provides data necessary to build an effective lipid-lowering portfolio. This approach to diet therapy may go some way towards bridging the gap between a conventional “good diet” and drug therapy.

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Received October 1999.