Invited commentary

Functional foods: cholesterol-lowering benefits of plant sterols

Many workers believe that the association between serum cholesterol concentration and ischaemic heart disease is one of cause and effect and it is reported that a 10 % decrease in serum cholesterol is associated with a 27 % reduction in the risk of ischaemic heart disease (Law *et al.* 1994*b*) achieved after 5 or more years (Law *et al.* 1994*a*). The chief dietary determinants of plasma total cholesterol are saturated fat, polyunsaturated fat and cholesterol. Plasma cholesterol can also be reduced by low energy intakes, which result in weight loss, and possibly specific dietary supplements including fibre, garlic and fish oils (Tang *et al.* 1998). Studies done within the metabolic ward suggest that dietary change can reduce blood total cholesterol by up to 15 % (Clarke *et al.* 1997) but in free-living subjects the reductions achieved are more modest (around 3–6 %), and undoubtedly poor compliance with the dietary advice is a major factor (Tang *et al.* 1998). Surprisingly, compliance seemed no better, and reductions in cholesterol equally poor, in patients with a higher risk of cardiovascular disease (Tang *et al.* 1998). Therefore, in public health terms, achieving a reduction in cholesterol by dietary advice is of limited effectiveness (Davey Smith & Ebrahim, 1998).

It is not surprising, therefore, that many investigators have been exploring the possibility of increasing components in the diet which have hypocholesterolaemic effects. One particular group of substances which has attracted much attention has been plant sterols (phytosterols) (Ling & Jones, 1995). Phytosterols are structurally very similar to cholesterol except that they always contain some substitutions on the C_{24} position on the sterol side-chain. The dietary intake of phytosterols is almost equal to that of dietary cholesterol, approximately 160–360 mg/d, and since the 1950s large amounts of these sterols, mainly sitosterol, have been added to patients' diets in the treatment of hypercholesterolaemia (Miettinen *et al.* 1995). In the last decade, interest in the cholesterol-lowering properties of phytosterols has accelerated to such an extent that 1999 saw the launch of ®Benecol (a phytosterol-containing margarine), the first functional food registered in the UK.

The active ingredient in Benecol is sitostanol ester which is obtained by hydrogenation of sitosterol, obtained from pine-wood pulp, followed by *trans*-esterification with rapeseed oil (Miettinen *et al.* 1995). Studies with sitostanol-ester have shown it to be highly effective in reducing cholesterol. As little as 1·5 g/d reduced total cholesterol in hypercholesterolaemic patients by 10 and 15 % at 3 and 4 weeks respectively, the effect being entirely on LDL-cholesterol (Heinemann *et al.* 1986). Likewise, a study conducted for 1 year with sitostanol-ester at 1·8 and 2·6 g/d reduced LDL-cholesterol by 14 %. Sitostanol is tasteless and the mechanism of cholesterol reduction would appear to be one of competition with dietary cholesterol absorption by displacement from micelles. However, sitostanol itself was not absorbed and the authors also reported that it did not interfere detectably with absorption of fat-soluble vitamins (Miettinen *et al.* 1995). It is important to note that in both studies, cholesterol levels returned to pre-treatment levels quickly following cessation of treatment.

The paper by Sierksma *et al.* (1999) in this issue follows two other reports on the cholesterol-lowering properties of sitosterol obtained from soyabean oil (Weststrate & Meijer, 1998; Hendriks *et al.* 1999). The main sterols in soyabean oil are β-sitosterol, campesterol and stigmasterol with very small amounts of the corresponding stanols (Hendriks *et al.* 1999). Sierksma *et al.* (1999) report that they were interested to determine the cholesterol-lowering efficiency of non-esterified soyabean oil sterols (0·8 g/d) in comparison with that previously reported for the esterified forms fed either as 2·4 g/d (range 1·5–3·3) (Weststrate & Meijer, 1998) or as increasing amounts from 0·8 to 3·24 g/d (Hendriks *et al.* 1999). The authors were also interested to determine the effects of the non-esterified sterols on specific plasma carotenoids since their previous work had shown plasma lipid-standardized levels to be reduced by 15–19 %.

To compare the cholesterol- and carotenoid-lowering effects of the soyabean phytosterol in the three publications, I have calculated the approximate amounts of non-esterified sterol equivalent used in the three studies. Sierksma *et al.* (1999) used 0·8 g/d free sterol equivalents, Weststrate & Meijer (1998) used an average of 2·4 g/d partly-esterified sterols which is approximately equivalent to 1·7 g free sterol/d (assuming free sterol is 60 % of the ester) and the lowest dose used by Hendriks *et al.* (1999) was 0·83 g 82 % esterified phytosterols/d, which approximates to $< 0{\cdot}6$ g/d free sterols. The reductions in plasma total- and LDL-cholesterol were dose-responsive at 3·8 and 6 %, 8 and 13 % and 4·9 and 6·5 % respectively. All studies were done over 3·5 weeks and, while the lowest dose of sitosterol ester may be marginally more effective than the others, there is probably no statistical difference in cholesterol-lowering efficiency between free or esterified forms. Surprisingly, the influence of free sterol on carotenoid reduction was different to that of the esterified form. With respect to lipid-standardized lycopene, the papers report dose-responsive reductions of 10 % (Hendriks *et al.* 1999), 7 % (Sierksma *et al.* 1999) and 20 % (Weststrate & Meijer, 1998). However, following the use of the free sterol, the authors found no reduction in α- and β-carotene, while both previous studies using esterified sterol reported similar reductions in these carotenoids to that of lycopene.

Esterification of the phytosterols is needed to increase their solubility in fat (Sierksma *et al.* 1999) but at low doses, the most recent study suggests that free phytosterol is equally effective in lowering plasma total cholesterol by

4–5 % as 0·83 g/d of the esterified form (Hendriks *et al.* 1999). Such a reduction is similar to that achieved by dietary intervention following advice on health promotion (Tang *et al.* 1998). Poor compliance with dietary guidelines is the main reason why health promotion fails to achieve the potential reductions in cholesterol obtained by studies in the metabolic ward. Will adherence to a particular brand of margarine be more successful? The answer is probably yes, since the public will pay a premium on the functional food and this in turn will be used to support advertising and maintain public awareness. Additionally, the use of a functional food exerts little interference on overall dietary habits and therefore favours compliance, in contrast to the changes which must be introduced to follow healthy-eating guidelines.

So what are the disadvantages? There is a slight decrease in absorption of certain carotenoids. Consumption of dietary carotenoids is believed to reduce the risk of cancer, cardiovascular and macular diseases but the small effects of the phytosterol are probably in themselves of little importance and, using the lower dose of the free sterol forms, appears to reduce the risk of any detrimental effects still more. What tends to be overlooked, however, is the fact that predictions of the beneficial effects of cholesterol lowering are based on the assumption that persons with low cholesterol tend to be persons with healthier diets. Reducing cholesterol by phytosterols alone will not be associated with a reduction in dietary fat or energy and there will be no incentive to increase the intake of fibre, fruit and vegetables. Polyunsaturated fatty acid intakes may increase as spreads themselves tend to have higher levels than butter, but these changes alone may not be sufficient to have the predicted beneficial effects on health. Thus it is important that health professionals continue to advise the public on healthy diets and that the spreads themselves should also carry the same healthy-eating advice and/or a warning, that health benefits may not result if the overall diet does not improve at the same time as cholesterol is reduced!

David I. Thurnham
Northern Ireland Centre for Diet and Health
School of Biomedical Sciences
University of Ulster
Coleraine BT52 1SA, UK

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