

## Invited Commentary

# Soluble fibre oat and barley $\beta$ -glucan enriched products: can we predict cholesterol-lowering effects?

Amelioration of cardiovascular risk through a high intake of dietary fibre was originally highlighted by Ancel Keys and colleagues in the *Journal of Nutrition* in 1960 (Keys *et al.* 1960). More than 45 years later there is a growing body of evidence supporting the association between intake of whole grains and decreased incidence of fatal and nonfatal CHD (Liu *et al.* 1999; Steffen *et al.* 2003; Jensen *et al.* 2004), attributed to the hypocholesterolaemic effects of the viscous soluble fibre component of whole-grain foods such as oat and barley cereals (Ripsin *et al.* 1992; Brown *et al.* 1999) rather than the insoluble fibre component of whole-grain foods such as wheat and rice. However, it is notable that not all published studies of high soluble fibre oat and barley products show cholesterol-lowering effects and there is a growing body of thought that it may be more difficult to predict the cholesterol-lowering effects of products enriched with extracts of oats and barley (Keogh *et al.* 2003; Naumann *et al.* 2006).

As well as cereals, soluble fibre is found in many legumes (including peas, beans), some fruits (including apples, pears) and the plaintain seed husk psyllium (*Plantago psyllium*). However it is the  $\beta$ -glucan soluble fibre of cereals, which consists of linear unbranched polysaccharides of linked  $\beta$ -(1  $\rightarrow$  3)-(1  $\rightarrow$  4)-D glucopyranose units, that has been shown to be an important component in cholesterol-lowering properties of viscous soluble fibre.  $\beta$ -glucan occurs naturally in the bran of grasses (*Gramineae*) such as barley, oats and rye at about 7%, 5% and 2% (w/w) respectively.

Evidence for cholesterol-lowering effects of viscous soluble fibre  $\beta$ -glucan came originally from feeding trials of oats with fewer trials investigating barley fibre despite the naturally high  $\beta$ -glucan content, since barley is less palatable than oats and a less common dietary component. Many (Ripsin *et al.* 1992; Brown *et al.* 1999; Behall *et al.* 2004) but certainly not all (Leadbetter *et al.* 1991; Törrönen *et al.* 1992; Beer *et al.* 1995; Lovegrove *et al.* 2000; Keogh *et al.* 2003; Kerckhoffs *et al.* 2003) trials investigating oat and barley  $\beta$ -glucan have shown significant hypocholesterolaemic effects of supplementation, and it is differences in factors such as solubility, viscosity and molecular weight (MW) of  $\beta$ -glucans which may be the reason for conflicting outcomes.

Difficulty in interpretation of these studies is compounded by poor understanding of mechanisms by which  $\beta$ -glucan may lead to cholesterol-lowering. A  $\beta$ -glucan enriched meal is thought to increase intestinal viscosity and/or bile acid binding which in turn may (i) decrease reabsorption of bile acids and drive bile acid synthesis from hepatic cholesterol, hence depleting the body's cholesterol pool and/or (ii) decrease absorption of intestinal cholesterol (Mälkki *et al.* 1992;

Marlett *et al.* 1994; Lia *et al.* 1995; Naumann *et al.* 2006). Solubility and MW of  $\beta$ -glucan are also of import since both alter intestinal viscosity, although there is evidence that MW alone also does not provide a good prediction of efficacy (Frank *et al.* 2004; Naumann *et al.* 2006).

In this issue, Keenan *et al.* (2007) report a 9–15% decrease in LDL-cholesterol concentration achieved through a 6 week administration of a concentrated low and high MW barley  $\beta$ -glucan extract when given at doses of 3 and 5 g/day in a parallel study design of 155 hypercholesterolaemic men and women. Interestingly, whilst there was a clear improvement in serum cholesterol concentration, there were no differential effects of either increased dose or MW of the concentrated barley  $\beta$ -glucan. These findings are in contrast to an earlier trial of an enriched extract of  $\beta$ -glucan from barley from our laboratory found no significant total or LDL cholesterol-lowering (Keogh *et al.* 2003). This was a cross-over trial where eighteen hypercholesterolaemic men were given an enriched extracted form of barley  $\beta$ -glucan at a high dose of 10 g/d for 3 weeks in a carefully controlled residential setting in which only the soluble fibre component of the diet was altered. Of the seven studies which had previously administered enriched forms of oat  $\beta$ -glucan (10–80%), three also reported no significant cholesterol-lowering (see Keogh *et al.* 2003 for details) which raised further issues as to whether the process of enrichment may directly affect efficacy. Unfavourable structural changes during commercial purification such as depolymerisation of the linear structure may decrease MW and viscosity (Wursch & Pi-Sunyer, 1997); mild extraction conditions may not deactivate endogenous  $\beta$ -glucanases and hence increase depolymerisation (McLeary, 2001); cooking processes may decrease peak MW, and freezing and storage may reduce extractability of  $\beta$ -glucan in the intestine (Beer *et al.* 1997). It is likely that a combination of these factors including depolymerisation of  $\beta$ -glucan accounted for the poor efficacy observed in our trial (Keogh *et al.* 2003).

Based upon the majority of observational studies, in 1997 the US Food and Drug Administration (FDA) endorsed the relationship between inclusion of soluble fibre  $\beta$ -glucan in the diet and a decrease in serum cholesterol concentration by ratifying health claims for oat fibre and, more recently in May 2006, also for barley fibre (Food and Drug Administration, 2006). The FDA concluded that  $\beta$ -glucan soluble fibre (3 g/d) from oat bran and rolled oats or from whole-grain barley and dry-milled barley products are efficacious in lowering total and LDL-cholesterol concentrations. Whilst there is little doubt that a high soluble fibre diet should be strongly advocated, in the current climate of emergence of

highly enriched  $\beta$ -glucan products this may be an oversimplification since quantity of  $\beta$ -glucan ingested accounts only in part for hypocholesterolaemic effects, and intestinal viscosity, MW and other as yet undetermined factors which may be altered during extraction and processing may be equally important in determining cholesterol-lowering effects of enriched  $\beta$ -glucan cereal products. Whether  $\beta$ -glucan extracts can generate improvements in CVD comparable with that of whole grains has yet to be demonstrated.

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