Invited commentary

Parsley, polyphenols and nutritional antioxidants

Readers of this journal will be well aware of the strong evidence that diets rich in fruit and vegetables inhibit the development of major diseases such as CHD and certain cancers (Block *et al*. 1992; Ness & Powles, 1997). This beneficial effect is ascribed, in part, to the antioxidants in such foods which protect biomolecules in our cells, such as lipids, proteins and DNA, from oxidative damage by reactive free radicals; such damage is implicated in the pathogenesis of many clinical conditions. Until recently, most attention has focused on the role of the well-recognized nutritional antioxidants, vitamin E, vitamin C and carotenoids, in the prevention of these potentially deleterious reactions. However, since the publication of an epidemiological study suggesting that low dietary intakes of flavonoids were associated with increased CHD in Zutphen in the Netherlands (Hertog *et al*. 1993), there has be a veritable explosion of research into the antioxidant possibilities of a diverse range of plant polyphenols. Perhaps now is the time to review whether all this activity is really justified.

Plant polyphenols are products of the phenylpropanoid biosynthetic pathway and include ellagic acids, chalcones, flavonoids including the anthocyanins, coumarins and hydroxycinnamic and hydroxybenzoic acids. They are present in a wide range of fruits, vegetables, nuts, and beverages including wine and tea, and there is no doubt that many have the potential to act chemically as antioxidants as their extensive conjugated π-electron systems allow ready donation of electrons or H atoms from the hydroxyl moieties to free radicals (see, for example, Gardner *et al*. 1997). However, there is an important distinction between the *in vitro* antioxidant effectiveness of a substance and its ability to prevent oxidation *in vivo*; this is also dependent on low toxicity, absorption, transportation and incorporation into appropriate cellular sites. For example, although the process of absorption of all the eight vitamin E homologues in our diet is similar, the α-form predominates in blood and tissue despite some of the other forms being more potent antioxidants in chemical systems. This is due to the action of binding proteins which preferentially select the α-form over the others (Dutta-Roy *et al*. 1994). This important distinction between the *in vitro* antioxidant effectiveness of a substance in the stabilization of, for example, a food product and its *in vivo* potency as an antioxidant appears at times to be overlooked when speculating on the nutritional importance of polyphenols such as flavonoids.

Early animal studies aimed at elucidating the degree and mechanism of flavonoid absorption indicate that many common flavonoid glycosides and aglycones in the diet are absorbed only to a limited degree because gut micro-organisms preferentially destroy the heterocyclic rings of the compounds before any absorption takes place in the small intestine (Nakagawa *et al*. 1965; Das, 1969; Kuhnau, 1976). In addition, any flavonoids subsequently crossing the intestinal wall are quickly bound in the liver and excreted into the bile (Barrow & Griffiths, 1971). To achieve significant plasma and tissue concentrations appears to require the feeding of huge doses of the compounds which far exceed what may be achievable from diet alone (Manach *et al*. 1994, 1996).

In contrast, although it has been generally considered that absorption of β-glycosidic flavonoids does not occur in man, recent evidence indicates that conjugation with glucose enhances absorption of some flavonoids (Hollman *et al*. 1997; Manach *et al*. 1998), possibly mediated through specific transport systems (Noteborn *et al*. 1997). Moreover, recent improvements in analytical methods have resulted in an increasing number of studies (such as that of Nielsen *et al*. (1999) in this volume who gave volunteers apigenin-rich parsley) where increases in various polyphenolics and related metabolites are detected in plasma and urine following the consumption of polyphenol-rich vegetables and beverages such as wine, whisky and tea (see, for example, Duthie *et al*. 1998). This does not, of course, necessarily mean that plant polyphenols are important nutritional antioxidants. Whether the absorption of such compounds results in marked antioxidant effectiveness *in vivo* will remain unclear until there is a better understanding of their biological effects such as the ability to moderate markers of oxidative damage to lipids, DNA and proteins and to be transported to lipid and aqueous cellular sites where they may function as antioxidants.

In the headlong quest for healthy ageing, the consumer is now confronted with a huge range of concoctions and capsules available from commercial outlets. Many contain plant-derived polyphenols from diverse sources which have undergone little, if any, rigorous nutritional or clinical assessment. Before consuming such products it is worth bearing in mind that many natural phenolics function in plants to discourage attack by fungal parasites, herbivorous grazers and pathogens. Many are also toxic and mutagenic in cell culture systems and their consumption to excess by mammals could cause adverse metabolic reactions. For example, the unexpected increase in antioxidant enzymes detected by Nielsen *et al*. (1999) may reflect an adaptive response by the endogenous antioxidant defence system in the face of an imposed stress incurred by the consumption of apigenin-rich parsley. Equally, in view of the unexpected adverse effects that were apparent in recent intervention trials with supplements of some of the well-recognized antioxidant nutrients (Omenn *et al*. 1996; Rappola *et al*. 1997), it may be unwise at present to

contemplate similar studies with the less-well-understood plant polyphenols.

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