

Letter to the Editor

Serum phytosterols not only from dietary intake

Phytosterols are common components of plant foods, especially vegetable oils, seeds, nuts and cereals. It is generally assumed that all serum and tissue phytosterols are derived exclusively by intestinal absorption and therefore that serum levels of phytosterols reflect dietary plant sterol intake and intestinal absorption (Miettinen *et al.* 1990).

We suggest that there is another route of intake of phytosterols which has not yet been considered: dermal absorption from cosmetics. Cosmetics such as body creams, soaps, sun creams, etc. contain a considerable quantity of phytosterols, from natural ingredients that often are not assessed for safety by the Cosmetic Ingredient Review board and that are considered safe on the basis of oral studies (Anon., 2004). Sitosterol is present in avocado oil (*Persea gratissima*) at a concentration of 0.4–0.9%, in rice bran oil (*Oryza sativa*) at 0.5–0.8%, in corn oil at 0.5–1.0% (Olivado Gourmet Foods New Zealand, 2006), and in sweet almond oil (*Prunus dulcis*), soyabean oil, shea butter (*Butyrospermum parkii*) and many other cosmetic ingredients. The use of these oils is quite widespread in moisturizers because of their relatively large amount of unsaponifiables and their capacity to penetrate the skin quickly and deeply without leaving a greasy residue. The physico-chemical properties of phytosterols are ideal for penetration into deeper skin layers owing to their affinity with lipids of cellular membranes (Sekiya *et al.* 1997; Marjukka Suhonen *et al.* 1999) and phytosterols and/or their metabolites can reach the systemic circulation as occurs for steroid hormones in transdermal delivery. Once they reach systemic circulation, skin-penetrated phytosterols and/or their metabolites enter a pool with dietary absorbed phytosterols and follow the same metabolic destiny.

This fact has hidden until now the dermal route of intake, but the recent finding of oxyphytosterols in the plasma of healthy human subjects (Grandgirard *et al.* 2004a) could represent an effect of such absorption. Oxyphytosterols are oxidized derivatives of phytosterols that have toxicity comparable to oxysterols (Adcox *et al.* 2001), to which have been ascribed a number of important roles in connection with cholesterol turnover, atherosclerosis, apoptosis, necrosis, carcinogenesis, inflammation, immunosuppression and the development of gallstones (Bjorkhem & Diczfalussy, 2002). Two possibilities have been suggested for the presence of oxyphytosterols in plasma: absorption of oxidized sterols present in food and 'in vivo' oxidation of phytosterols in plasma.

In patients with sitosterolaemia, who have elevated levels of plant sterols due to increased intestinal absorption and reduced biliary secretion of neutral sterols (Berge, 2003), the principal oxyphytosterols are 5 α ,6 α -epoxysitostanol, 3 β ,5 α ,6 β -sitostanetriol, 7-ketositosterol and 7 β -hydroxysitosterol (Plat *et al.* 2001). The same oxyphytosterols are found in two frequently used soya-based lipid emulsions. In healthy subjects Grandgirard

et al. (2004a) find noticeable quantities of 5 β ,6 β -epoxysitostanol and 3 β ,5 α ,6 β -sitostanetriol and minor levels of 5 α ,6 α -epoxysitostanol, 3 β ,5 α ,6 β -campestanetriol and 7-ketositosterol.

The different types and proportion of oxyphytosterols could indicate a different origin for these compounds in healthy subjects compared with sitosterolaemic patients, for whom absorption from food seems the main derivation.

Aringer & Eneroth (1974) showed that the epoxidation of cholesterol and sitosterol in rat liver cellular subfraction occurs only in connection with non-enzymatic tissue oxidation of sterols and that the β -epoxides are formed in three- to four-fold excess over the α -epoxides. An excess of 5 β ,6 β -epoxysitostanol over 5 α ,6 α -epoxysitostanol in healthy subjects could therefore derive from an 'in vivo' oxidation, but Grandgirard *et al.* (2004b) observe that sitostanetriol is not formed 'in vivo' from sitosterol in rats fed a high level of phytosterols, and they conclude that the oxidation of phytosterols in plasma is not probable.

The skin is a tissue exposed to sunlight and free radical reactions are common in it: UV radiation on skin causes the formation of vitamin D₂ and D₃ from ergosterol and 7-dehydrocholesterol in a free radical reaction. UV skin irradiation can cause non-enzymatic 'in vivo' oxidation of sterols in reactions that involve free radicals and reactive oxygen species (Black & Douglas, 1972; Datsenko *et al.* 1976; Smith, 1981). Oxyphytosterols in healthy subjects could derive from the oxidation catalysed by UV light of skin phytosterols absorbed from cosmetic products.

With the increasing consumption of cosmetics, a rising use and hence dermal absorption of phytosterols is expected. As nature has selected and conserved a mechanism to exclude phytosterols from dietary intake, we deem that the amount and effects of transdermal penetration of phytosterols should be seriously evaluated.

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