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Letter to the Editor: Chlorogenic Acids—Confounders of Coffee-Serum Cholesterol Relationships

Dear Sir,

The epidemiological evidence linking higher coffee consumption with elevated serum LDL cholesterol concentration has been inconsistent, the results of small studies generally suggesting such a relationship, and the results of larger studies generally suggesting no such effect (Friedman, 1984). However the results from a recent intervention study in which coffee type and brewing method were controlled strongly suggest that consumption of black boiled coffee can elevate serum cholesterol levels and that this relationship can be modified by altering the brewing method (Førde *et al.*, 1985).

The composition of coffee beverage is incompletely defined, chemically complex and known to vary with the choice of green bean, preroasting treatments, severity of roasting, post-roasting processing and brewing method (Maier, 1981; Clifford, 1985; Clarke & Macrae, 1985). It is suggested that the results of previous epidemiological studies could have been confounded by variations in beverage composition. At this stage it would be foolish to attempt to predict unequivocally which constituents of the beverage might be of particular importance and it would be very foolish to focus blindly upon a single component. However there is evidence to suggest that variations in the chlorogenic acids (CGA) content could be one such confounding factor and this evidence is summarised below to illustrate that in future epidemiological studies it will be essential to control, and preferably define, the beverage composition.

The CGA are a group of widely occurring plant phenols, of which the commonest are mono or di-esters of caffeic acid and/or ferulic acid, conjugated with quinic acid. (It should be noted that caffeic acid is not related structurally or pharmacologically to caffeine.) For many people coffee beverage will be the major dietary source but depending upon the

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variables referred to above coffee beverage (200 ml) prepared from roast and ground coffee could supply less than 20 mg or as much as 675 mg CGA. Beverage prepared from soluble powders (2 g per cup) sold in the U.K. could supply between 70 mg and 220 mg (Maier & Grimsehl, 1982; Clifford, 1985; Clarke & Macrae, 1985). Studies in this laboratory (Clifford, unpublished data) indicate that brewing with hard, as opposed to soft, water has no effect upon beverage CGA content but it is clear that other brewing variables can have small effects (Maier & Grimsehl, 1982).

Mammalian studies on CGA have established very low oral toxicity (Preziosi & Loscalzo, 1958; Marmo & Miele, 1962; and Lietti, 1977) rapid metabolism (hydrolysis and methylation) yielding quinic acid (which is pharmacologically inactive), ferulic acid and isoferulic acid which are choleretic (Michaud *et al.*, 1971; Czok & Schulze, 1973; Czok *et al.*, 1974; Westendorf & Czok, 1978, 1983).

These metabolites are thought to be responsible for the choleretic and hypolipaemic action of CGA in animal (Preziosi *et al.*, 1960; Marmo & Miele, 1962; Frohlich & Mayr, 1973; Lietti, 1977; Szwed, 1977; Wojcicki, 1978; Kimura *et al.*, 1984) and human studies (Mancini *et al.*, 1961; Schreiber *et al.*, 1970; Cairella & Volpari, 1971; Hammerl *et al.*, 1973; Marler, 1973; Wojcicki & Kadykow, 1974; Montini *et al.*, 1975; Heckers *et al.*, 1977; Martindale, 1982; Wojcicki *et al.*, 1982; Marler, 1983), and one such CGA, cynarin, has been marketed (Marler, 1973; Reynolds and Prasad, 1982; Marler, 1983) (e.g. Anghirol®, Cinarcef®, Listrocol®, Nivellipid®) for these purposes. There is one report of clinical studies with hyperlipaemic patients in which cynarin produced no hypolipaemic effect (Heckers *et al.*, 1977). However, in the majority of such studies cynarin regularly produced reductions in total serum cholesterol (−13 to −31%) (Cairella & Volpari, 1971; Hammerl *et al.*, 1973; Wojcicki & Kadykow, 1974; Montini *et al.*, 1975), β-lipoproteins (−12 to −28%) (Mancini *et al.*, 1961; Wojcicki & Kadykow, 1974; Montini *et al.*, 1975), the β/α lipoprotein ratio (Mancini *et al.*, 1961; Caruzzo *et al.*, 1969; Montini *et al.*, 1975), serum triglycerides (−11 to −30%) (Hammerl *et al.*, 1973; Wojcicki & Kadykow, 1974; Montini *et al.*, 1975; Wojcicki *et al.*, 1982), serum FFA (−29%) and serum glycerol (−24%) (Hammerl *et al.*, 1973) and increased (× 3) the elimination of bile acids in the faeces (Schreiber *et al.*, 1970). Doses were generally between 500 mg and 1500 mg per day but as low as 60 mg per day in one study (Hammerl *et al.*, 1973).

The data for coffee beverage composition given above indicate clearly that some coffee drinkers could receive levels of CGA shown to be hypolipaemic, whereas others may not. This variation, coupled with a possibility of a rebound effect, which was noted in one clinical study (Caruzzo *et al.*, 1969) using cynarin, clearly has the potential to confound epidemiological studies into the possible role of coffee in hyperlipaemias.

That there might be some dietary merit in high CGA coffee beverage to combat the hyperlipaemic effect of other dietary components is an intriguing possibility, but one that requires much careful study since the possibility that coffee beverage might also contain a hyperlipaemic agent cannot be excluded.

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