REVIEW ARTICLES

The cholesterol-raising factor from coffee beans

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SUMMARY

Coffee beans and some types of coffee brew—not the regular types of coffee prepared with a paper filter or with soluble coffee granules—contain the diterpenes cafestol and kahweol. Cafestol and kahweol raise the serum concentration of cholesterol and triglycerides in humans, and they also appear mildly to affect the integrity of liver cells. Both effects are transient after withdrawal of the diterpenes, and it is as yet unsure whether these effects are associated. Patients at increased risk of heart disease who drink large amounts of coffee should be advised to select brews low in diterpenes.

INTRODUCTION

About three-quarters of the world coffee production is of the *Coffea arabica* species[1]. Arabica beans are composed of 55–66% carbohydrate, 15–18% lipids, 8–11% acids and phenols, 11–15% nitrogen compounds among which is the alkaloid caffeine and 3–5% minerals[2]. The other major commercial species is *Coffea canephora* var *robusta*, yielding 'robusta beans'. Robusta beans contain more caffeine and acids and less lipid and carbohydrate than arabica.

COFFEE AND CORONARY HEART DISEASE RISK

As early as 1963, it was suggested that coffee drinking might predispose to myocardial infarction[3]. This association was not confirmed in the majority of epidemiological investigations that followed, although some found a link (for reviews, see Tuomilehto and Pietinen[4], and Thelle[5]; for meta-analyses, see Myers and Basinski[6], and Greenland[7]). A complicating factor in these studies was that the effect of coffee drinking on coronary risk is hard to disentangle from the effect of smoking, as coffee drinkers smoke more than coffee abstainers[4]. The suspected higher risk was clearly not mediated through effects of coffee drinking on blood pressure, since the impact of chronic consumption of coffee or of caffeine on blood pressure is small[4,8].

COFFEE AND SERUM CHOLESTEROL

In the early eighties, Thelle *et al.*[9] cross-sectionally examined 14 000 subjects in Northern Norway and found that those reported to drink nine or more cups of coffee per day had significantly higher serum cholesterol levels than those drinking less than one cup per day. The differences were 0.67 mmol/L or 12% for men, and 0.60 mmol/L or 11% for women. Thelle and co-workers confirmed their finding in two experiments: withdrawal of coffee reduced serum cholesterol by 10% in both normocholesterolaemic[10] and hypercholesterolaemic subjects[11].

However, the relation as found in Norway was highly inconsistent in other populations (for reviews, see Aro[12], Thelle *et al.*[13], Kokjohn *et al.*[14]). The method of coffee brewing appeared to be crucial. Traditionally, Scandinavians prepare their coffee by boiling coarsely ground coffee beans with water and decanting the brew into the cup without the use of a filter. Aro *et al.*[15] showed in an experiment that eight cups per day of such 'boiled' coffee relative to filtered coffee increased serum cholesterol by 0.79 mmol/L or 10%. Bak and Grobbee[16] found that simply incubating the coffee grounds with water at 93°C before consumption produced the same effect. Later experiments showed that boiled or incubated coffee lost its cholesterol-raising potency when it was poured through a paper filter[17,18], indicating that the filter retained the active compounds(s) from the brew.

The epidemiological data also became unambiguous now that the type of coffee was specified: serum cholesterol levels increased markedly with the amount of boiled coffee consumed per day, and much less or not at all with intake of paper-filtered coffee[19–22].

THE CHOLESTEROL-RAISING FACTOR: COFFEE DITERPENES

Chemical analyses showed that boiled coffee as prepared in Scandinavia contains 1–2 g of oil per litre, whereas the lipid content of paper-filtered coffee is negligible[17,23]. Zock *et al.*[24] gave a daily dose of 1.3 g of such coffee lipids to 10 volunteers for 6 weeks, and found that serum cholesterol concentrations increased by 1.06 mmol/L or 23%. The

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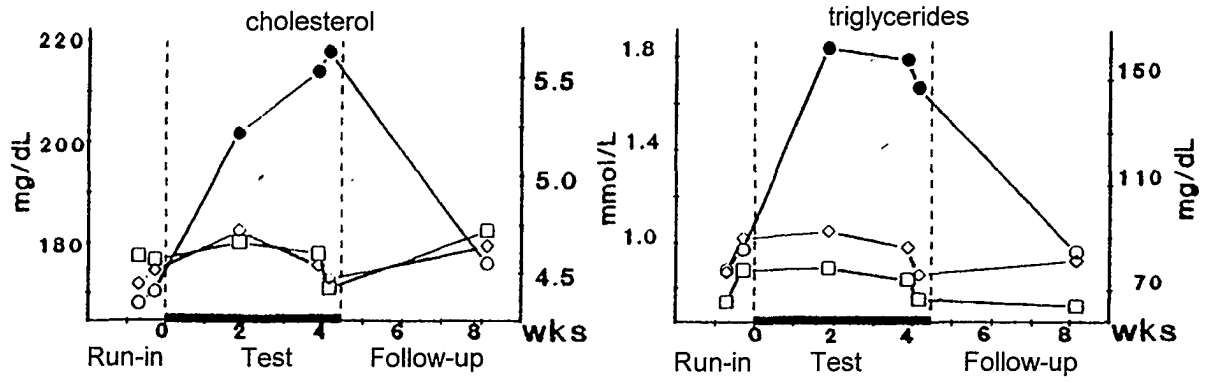

Figure 1 **The effect on serum levels of total cholesterol and triglycerides of consumption of 2 g of placebo oil (□), coffee oil (●) or coffee oil without cafestol and kahweol (◇) per day in healthy volunteers (n=12–16 per group). The test period is indicated by a horizontal black bar. During the run-in period the volunteers swallowed 2 g of placebo oil per day. No oil was given during the follow-up period[33]**

increase was mainly due to low-density-lipoprotein (LDL) cholesterol, which rose by 29%. In addition, all volunteers had sharply elevated levels of fasting triglycerides, and there was also a slight dip in serum concentrations of high-density-lipoprotein (HDL) cholesterol. Apparently, the putative factor from coffee beans was a lipid compound.

None of the models tested to study the effects of this factor in animals has proven effective. Sanders and Sandaradura[25] found that consumption of boiled coffee did increase serum cholesterol in Syrian hamsters, but attempts to verify this were unsuccessful[26,27]. In other experiments in gerbils[28], rats[26,29], rabbits[30], and cebus or rhesus monkeys[31], none of the animals responded to boiled coffee or to coffee oil, irrespective of the administered amount. The cholesterol-raising factor therefore appears to be specific for humans.

Coffee oil consists mainly of triglycerides, but it also contains unsaponifiable matter consisting of diterpenes, sterols, squalene, and other hydrocarbon compounds[2]. The cholesterol-raising factor is most likely to be found in this unsaponifiable fraction, since consumption of gram amounts of fatty acids hardly affects blood lipoprotein profile[32]. The main part of the unsaponifiable fraction of coffee oil is formed by the diterpenes[2]. In an experiment with 43 volunteers, Weusten-van der Wouw *et al.*[33] showed that coffee oil that had been stripped of such coffee diterpenes had entirely lost its cholesterol- and triglyceride-raising potential (Figure 1). They then tested the efficacy of cafestol and kahweol, the two main diterpenes in coffee oil. In three volunteers consumption of a mixture of 72 mg/day of cafestol and 53 mg/day of kahweol purified from coffee oil raised serum levels of cholesterol by 1.71 mmol/L and those of triglycerides by 1.83 mmol/L[33]. Heckers *et al.*[34] also reported that ingestion of cafestol and kahweol increased serum total cholesterol and triglyceride levels. It was now clear that the lipid-raising factor from coffee beans was either cafestol or kahweol, or both (Figure 2).

SEPARATE ACTIVITIES OF CAFESTOL AND KAHWEOL

The separate effects of cafestol and kahweol have been examined indirectly in two studies comparing the effects of robusta oil, which contains mainly cafestol, and arabica oil, which contains cafestol and kahweol. Van Rooij *et al.*[35] found that robusta oil increased serum cholesterol by 11%, whereas arabica oil that contained five times more diterpenes than robusta oil, mostly through a higher kahweol content, increased serum cholesterol by only 21%. Mensink *et al.*[36] found that serum cholesterol levels increased by 13% on either oil, whereas the intake of cafestol and kahweol with arabica oil

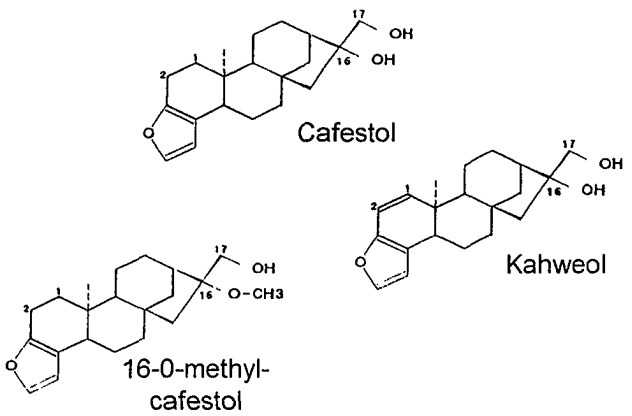

Figure 2 **Structure of the coffee diterpene alcohols cafestol, kahweol, and 16-o-methylcafestol. Compared to cafestol, kahweol has an additional double bond between the C1 and C2 carbon atoms. 16-o-methylcafestol contains a methyl group at the C16 carbon atom, and no extra double bond. Diterpenes occur in coffee beans either as free alcohols or esterified to fatty acids at the C17-position**

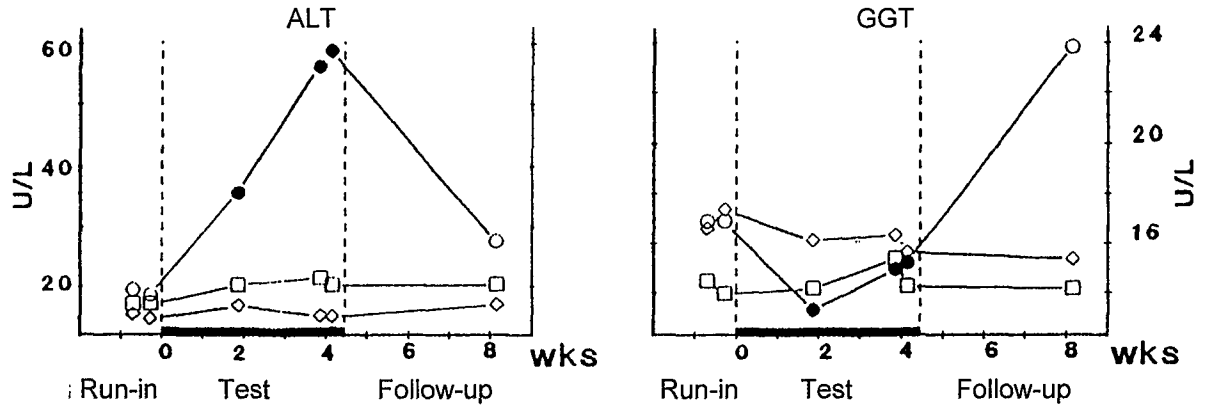

Figure 3 **The effect on serum activities of alanine aminotransferase (ALT) and γ-glutamyltransferase (GGT) of consumption of 2 g of placebo oil (□), coffee oil (●) or coffee oil without cafestol and kahweol (◇) per day in healthy volunteers (*n*=12–16 per group). The test period is indicated by a horizontal black bar. During the run-in period the volunteers swallowed 2 g of placebo oil per day. No oil was given during the follow-up period[33]**

was twice that with robusta oil. As robusta oil raised serum cholesterol levels, cafestol should have hypercholesterolaemic capacity, whereas the separate activity of kahweol could not be ascertained. Robusta beans also contain small amounts of 16-o-methylcafestol (Figure 2), of which the efficacy is also not known. However, as 16-o-methylcafestol accounts for only about 3% of the diterpenes present in commercial roast and ground coffees (see below), intakes of this diterpene are small.

DO CAFESTOL AND KAHWEOL INFLUENCE LIPOPROTEIN METABOLISM BY AFFECTING LIVER CELLS?

Weusten-van der Wouw *et al.*[33] observed in their experiments that coffee diterpenes also increased the serum activities of alanine aminotransferase and to a lesser extent aspartate aminotransferase, and reduced those of γ-glutamyltransferase. Elevations of liver transaminase activities in serum may be indicative of disturbed integrity of the liver cell[37]. Just as for serum lipids, serum activities of the transaminases returned to baseline after withdrawal of the diterpenes. However, the serum activity of γ-glutamyltransferase first showed a sharp rebound rise after withdrawal of the treatment (Figure 3) before eventually returning to baseline.

Weusten-van der Wouw *et al.*[33] tried to confirm their findings in a cross-sectional study in Norway. Serum activities of γ-glutamyltransferase were slightly lower in 150 boiled-coffee drinkers when compared to 159 matched filtered-coffee drinkers, an observation that had been reported before in Norwegian boiled-coffee drinkers[38,39]. However, the differences in activities of alanine and aspartate aminotransferase between the two groups were negligible, indicating that the mild deleterious effect of cafestol and kahweol on the liver as seen in the experiments may be transient with prolonged consumption.

This finding is inconsistent with the hypothesis that the increase in serum LDL cholesterol and triglycerides is secondary to a more general hepatotoxic effect of the coffee diterpenes or any of their metabolites. As a matter of fact, serum cholesterol levels remain elevated with chronic consumption of boiled coffee[19–22,33]. The mechanism(s) by which coffee diterpenes affect cholesterol synthesis or breakdown in the human body are still largely unknown. There is some evidence from studies in human fibroblasts that cafestol increases serum cholesterol via downregulation of the LDL-receptor[40], but more studies are needed to confirm this.

DITERPENES IN ROAST AND GROUND COFFEES

As the commercially available *Coffea* strains differ in diterpene level and profile[41–43], intake levels of cafestol and kahweol will depend on the composition of the blends used. We examined diterpene levels in a range of commercial roast and ground coffees, and found that cafestol varied little[44] (Figure 4). Grounds with lower levels

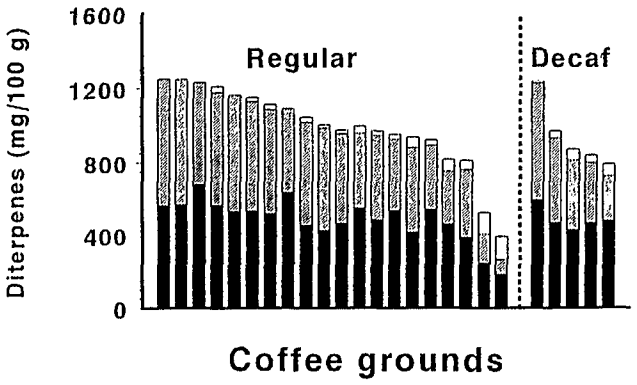

Figure 4 **Levels of cafestol (■), kahweol (▨) and 16-o-methylcafestol (□) in commercially available roast and ground coffees. Values are given in mg of free alcohols per 100 g of grounds. 'Regular' refers to caffeine-containing products, 'Decaf' refers to decaffeinated products[44]**

of cafestol were blends containing robusta beans, as indicated by concurrent higher levels of 16-o-methylcafestol[45] and lower levels of kahweol[41]. Higher proportions of robusta beans in commercial coffee blends may therefore reduce intake of coffee diterpenes. However, consumers in most European countries and in the USA prefer arabica[1].

It has been suggested that consumption of decaffeinated coffee may relate to increased serum cholesterol levels[46], or even to a higher risk of cardiovascular diseases[47]. We found similar diterpene concentrations in regular roast and ground coffees and in decaffeinated coffees (Figure 4).

PREDICTED EFFECTS OF VARIOUS COFFEE BREWS ON SERUM CHOLESTEROL LEVELS

From the results of their experiments with oily solutions of diterpenes, Weusten-van der Wouw *et al.*[33] estimated that daily ingestion of 10 mg of cafestol increases serum cholesterol by 5 mg/dL (0.13 mmol/L)[33]. However, with unfiltered coffee, up to 90% of the coffee diterpenes that are consumed with the brew may be carried by floating coffee bean particles[44]. To examine the availability of diterpenes from such coffee particles, we gave 18 g/day of spent coffee grounds providing 39 mg/day of cafestol and 49 mg/day of kahweol to 14 volunteers. After three weeks, serum cholesterol levels had increased by 0.65 mmol/L or 14% and the activity of alanine aminotransferase by 19 U/L[48]. As these increases were comparable to those with similar amounts of diterpenes in coffee oil, we concluded that the diterpenes are well absorbed from the grounds, and that diterpene measurements in coffee brews should include the contribution of grounds.

We then measured diterpene levels in various types of coffee brews (Table 1). Scandinavian boiled coffee provided on average 3 mg of cafestol and 4 mg of kahweol per cup of 150 mL[44]. Thus, five cups of boiled coffee per day will provide on average 15 mg of cafestol, an amount that theoretically raises serum cholesterol by 0.20 mmol/L. This figure is well in line with results from cross-sectional studies in Scandinavian boiled-coffee drinkers[19–22,33].

High diterpene concentrations were also found in Turkish/Greek coffee, and in plunger pot coffee (Figure 5,

Table 1 **Preparation techniques of various coffee brews and levels of cafestol and kahweol in coffee brews collected in countries where specific types of coffee are popular, and predicted effects on serum cholesterol levels with chronic consumption of five cups per day[44]. Estimates are based on the observation of Weusten-van der Wouw *et al.*[33] that every 10 mg of cafestol plus a similar amount of kahweol raises serum cholesterol by 0.13 mmol/L**

Type of coffee	*Preparation technique*	*Diterpenes per cup*		*Predicted rise in serum cholesterol levels with consumption of five cups/day (mmol/L)*
		Cafestol (mg)	*Kahweol (mg)*	
Filtered	Boiled water is poured over finely ground roasted coffee beans in a paper filter, either by hand or by using an electric coffee maker	0.1	0.1	<0.01
Percolated	Coarsely ground roasted coffee beans are extracted by recirculating boiling water until the desired brew strength is reached	0.1	0.1	<0.01
Instant	2–3 g of soluble coffee granules are dissolved into 150–190 ml of hot water	0.2	0.2	0.01
Espresso	Hot water is forced under high pressure through a bed of finely ground, usually dark roasted, coffee beans	1.5	1.8	0.10
Mocha	Just overheated water is forced through a bed of finely ground, usually dark roasted, coffee beans	1.1	1.4	0.07
Boiled	Coarse grounds are boiled with water for 10 or more min, or infused with hot water ('infused' coffee), and the liquid is decanted without the use of a filter	3.0	3.9	0.19
Plunger pot	Hot water is poured onto coarse grounds, and after 2–5 min the metal screen strainer is pushed down to separate the grounds from the fluid	3.5	4.4	0.23
Turkish/Greek	Very fine/powdery grounds are brought to a boil once or repeatedly, or incubated with hot water ('mud' coffee), and the liquid is decanted without the use of a filter	3.9	3.9	0.25

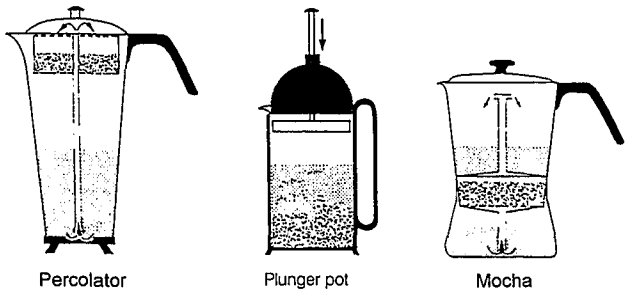

Figure 5 **Brewing principles for percolated, plunger pot (cafetière) and mocha coffee**

Table 1), also called cafetière coffee. Cross-sectional studies in Israel have indeed shown higher cholesterol levels in coffee drinkers[49–51], but to our knowledge this has not yet been confirmed experimentally. No data on effects of plunger pot coffee are available. However, as predictions of cholesterol responses based on diterpene levels of coffee brews appeared to be valid, people at increased risk of coronary heart disease should be advised not to drink more than a few cups of plunger pot coffee or Turkish/Greek coffee per day.

In Italy, the most popular coffee brews are espresso and mocha coffee (Figure 5, Table 1). Cross-sectional data from Italy have indicated higher serum lipid levels in mocha and espresso coffee drinkers[52–54], whereas intervention trials have refuted this association[55,56]. The procedure of brewing espresso efficiently extracts the oil from coffee grounds[23,44], but as espresso coffee is usually served in quantities as small as 25 mL per cup[57], diterpene contents on a *per cup* basis are low (Table 1). Moderate intakes of espresso or mocha coffee are therefore expected to have negligible effects on serum cholesterol and coronary heart disease risk.

Surprisingly, percolated coffee is almost devoid of cafestol and kahweol[44]. In the percolator pot (Figure 5, Table 1), coffee is constantly recirculated through a bed of coarsely ground coffee, which seems to function as a filter cake retaining the diterpenes from the brew. Percolators were the major type of coffee makers used in the USA until recently, but our data suggest that changes in coffee brewing practices have had little effect on coronary heart disease risk in the USA.

Finally, instant (soluble) coffee also contains negligible amounts of diterpenes[23,44]. Predicted effects of consumption of instant coffee on serum lipids through its diterpene content are minimal, which is in line with results of clinical trials[58–60].

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