Influence of Tea Catechins on Lipid Metabolism

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Influence of Tea Catechins on Lipid Metabolism

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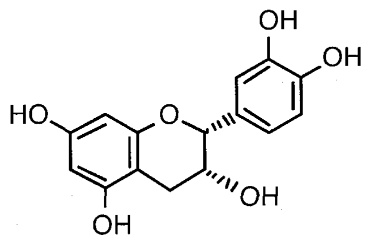
Summary

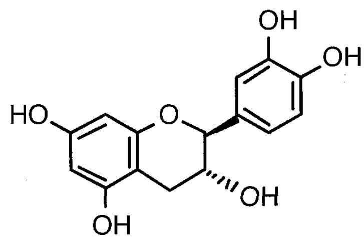
Tea catechins reduce serum cholesterol concentration and suppress postprandial hypertriacylglycerolemia in experimental animals and humans. These effects are mainly ascribed to gallate esters of catechins, (-)-epicatechin gallate (ECG) and (-)-epigallocatechin gallate (EGCG). During heat treatment for pasteurization, tea catechins are epimerized to so-called heat-treated tea catechins such as (-)-catechin gallate (CG) and (-)-gallocatechin gallate (GCG). We showed that both tea catechins and heat-treated tea catechins with galloyl moiety lower intestinal absorption of cholesterol by inhibiting micellar solubility of cholesterol. Since they inhibited pancreatic lipase *in vitro* and slowed down lymphatic absorption of triacylglycerol, we think that delayed intestinal absorption of triacylglycerol in the feeding of the catechin preparations causes suppression of postprandial hypertriacylglycerolemia. It has been reported that tea catechins and heat-treated tea catechins with galloyl moiety suppress deposition of visceral fat in experimental animals and humans. Some studies suggested that stimulation of hepatic β-oxidation might be a cause of reduced deposition of visceral fat. However, our study did not show any acceleration of β-oxidation in rat liver. Although there are some controversial observations, results obtained suggest a possibility that tea catechins and heat-treated tea catechins with galloyl moiety improve lipid metabolism and contribute to prevention of life-style related diseases.

Key words : catechins, cholesterol, triacylglycerol

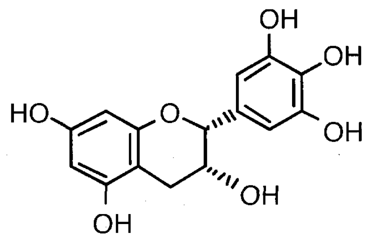
Tea catechins extracted from tea leaves consist mainly of (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG) and (-)-epigallocatechin gallate (EGCG) (Fig. 1). These catechins have been shown to have various physiological functions, such as antiatherogenic, antiobesity, antioxidative and anticacinogenic activities mainly in experimental animals and *in vitro* studies (Ikeda et al. 2003 and 2005). During heat treatment for sterilization to produce canned and bottled beverages, about a half of tea catechins is epimerized to (-)-catechin (C), (-)-gallocatechin (GC), (-)-catechin gallate (CG) and (-)-gallocatechin gallate (GCG) (Fig. 1). Although the consumption of canned and



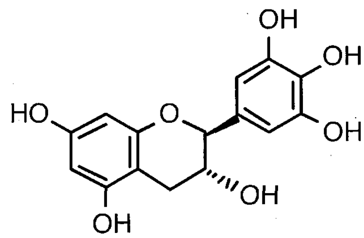
(-)-Epicatechin



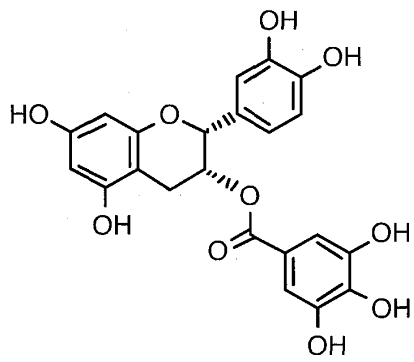
(-)-Catechin



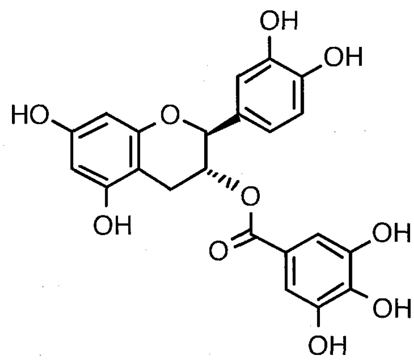
(-)-Epicatechin gallate



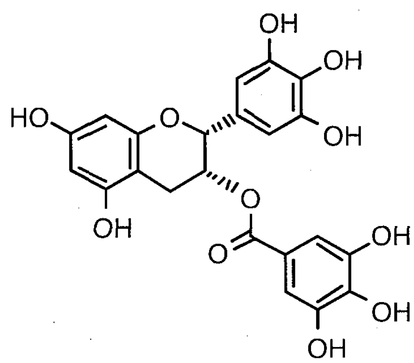
(-)-Gallocatechin



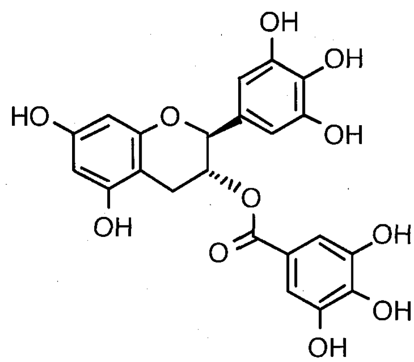
(-)-Epigallocatechin



(-)-Catechin gallate



(-)-Epigallocatechin gallate



(-)-Gallocatechin gallate

FIG. 1.

bottled tea drinks is huge in Japan, studies on heat-treated tea catechins are scarce. In this review, effects of tea catechins and heat-treated tea catechins on lipid metabolism are summarized.

Hypocholesterolemic activity of tea catechins and heat-treated tea catechins

Hypercholesterolemia is known to be a major risk factor for coronary heart disease. Matsuda et al. (1986) observed that 50% methanol extracts from green tea leaves lowered serum cholesterol concentration in mice fed a high-cholesterol diet. They also showed that fractions containing ECG or EGCG, but not those containing EC or EGC, caused the reduction of serum and liver cholesterol concentrations in mice. Muramatsu et al. (1986) reported that a crude catechin mixture added at 1% and 2% in diets containing 1% cholesterol reduced plasma and liver cholesterol concentrations in rats. The feeding of the catechin mixture increased fecal excretion of cholesterol. Fukuyo et al. (1986) showed that EGCG caused a similar effect to a crude catechin mixture. These observations strongly suggest that tea catechins, in particular, their gallate esters, exert a hypocholesterolemic activity by increasing fecal output of cholesterol.

To investigate effect of catechin mixtures on intestinal absorption of cholesterol, rats were cannulated in the thoracic duct and given an emulsion containing ^{14}C-cholesterol with a mixture of catechins to the stomach (Ikeda et al. 1992). Lymphatic recovery of the radioactivity was significantly lower in the administration of mixtures of catechins. A mixture of ECG and EGCG was more effective in reducing cholesterol absorption than the EC and EGC mixture. The results strongly suggest that tea catechins inhibit cholesterol absorption in the intestine.

Solubilization of cholesterol in the bile salt micelle is essential for intestinal absorption of cholesterol. Dietary and biliary cholesterol is emulsified and then solubilized in micelles with bile salt and hydrolyzed products of triacylglycerol and phospholipids. We measured effect of catechin mixtures on micellar solubility of cholesterol *in vitro* (Ikeda et al. 1992). Catechin mixtures were added to the bile salt micelle containing cholesterol. Immediately after the addition of catechin mixtures, the micellar solution got turbid and precipitates were formed. Then, we centrifuged the solution and the concentration of cholesterol in the clear supernatant (micellar solution) was measured. The addition of catechin mixtures dose-dependently reduced the concentration of cholesterol in the micellar solution. Again, a mixture of ECG and EGCG was more effective than the EC and EGC mixture. When purified catechins were used, EGCG and ECG were more effective to precipitate micellar cholesterol than free catechins, EC and EGC. When EGCG and ECG were compared, the former was more effective than the latter. The concentration of EGCG in the bile salt micelle was paralleled with the concentration of cholesterol. The results suggest that EGCG co-precipitates with cholesterol and therefore, micellar solubility of cholesterol is reduced. This may be the reason why tea catechins, especially the gallate esters, inhibit cholesterol absorption in the intestine. Since bile salt concentration in the micelle was not influenced by the addition of tea catechins, it is not thought that tea catechins reduce micellar solubility of cholesterol by decreasing availability of bile salt.

We compared effect of heat-treated tea catechins rich in CG and GCG and tea catechins rich in ECG and EGCG on cholesterol absorption in rats cannulated in the thoracic duct (Ikeda et al. 2003). Heat-treated tea catechins were more effective to reduce lymphatic recovery of cholesterol than tea catechins. CG and GCG were more effectively reduced micellar solubility of cholesterol *in vitro* than their epimers, ECG and EGCG, respectively.

Kobayashi et al. (2005) compared hypocholesterolemic effect of heat-treated tea catechins with that of tea catechins in rats. Rats were fed on a 0.5% cholesterol diet with 1% of one of the catechin preparations for 3 weeks. The concentrations of serum and liver cholesterol were significantly lower in the feeding of both catechin preparations. The excretion of fecal neutral steroids originated from cholesterol was significantly higher in the feeding of the catechin preparations. Although heat-treated tea catechins tended to be more effective than tea catechins, significant difference was not observed. Differential effect might be obtained in more prolonged feeding.

In a human study, Kajimoto et al. (2003) examined effect of heat-treated tea catechins on serum cholesterol levels in a placebo-controlled double-blind study in which a beverage containing 197 mg of heat-treated tea catechins was given twice a day for 12 weeks. The subjects were adult male and female having mild and borderline hypercholesterolemia. Average serum cholesterol concentration was 222 mg/dl and the range was 180–259 mg/dl. Serum cholesterol concentration was significantly reduced from 229 mg/dl to 218 mg/dl at 8 weeks after the start of the intake of the catechin preparation in male subjects. The effect was maintained until 12 weeks. In placebo beverage group, serum cholesterol was increased from 226 mg/dl to 231 mg/dl. The similar results were also obtained in female subjects (Kajimoto et al. 2006).

Suppression of postprandial hypertriacylglycerolemia by tea catechins and heat-treated tea catechins

Postprandial hypertriacylglycerolemia has been recognized to be an independent risk factor for coronary heart disease. We showed that tea catechins and heat-epimerized tea catechins suppressed postprandial hypertriacylglycerolemia in rats given a fat emulsion in the stomach (Ikeda et al. 2005). Our previous study suggested a possibility that lymphatic absorption of triacylglycerol is slowed or inhibited by the co-administration of tea catechins (Ikeda et al. 1992). In the study, coconut and palm olein oils were used to examine effect of tea catechins on fatty acid absorption. Since endogenous fatty acids existed in the lymph, reliability of the results was low. Recently, we used radioactive trioleoylglycerol instead of vegetable oils and estimated effect of tea catechins and heat-treated tea catechins on lymphatic absorption of triacylglycerol (Ikeda et al. 2005). Both of these catechin preparations lowered lymphatic recovery of the radioactivity at an early time (0–1 hr after the administration). The recovery of the radioactivity at 24 hr was the same as the control group (catechin-free group). The result strongly suggests that tea catechins and heat-treated tea catechins delay intestinal absorption of triacylglycerol. This may be a major reason why tea catechins suppress postprandial hypertriacylglycerolemia.

These catechin preparations dose-dependently inhibited the activity of pancreatic lipase *in vitro* (Ikeda et al. 2005). These preparations had almost the same inhibitory activity. However, when purified catechins were used, GCG and CG rich in heat-treated tea catechins were more effective to inhibit pancreatic lipase than EGCG and ECG rich in tea catechins. Since purities of the catechin preparations were about 60% and the remaining parts contained polymerized products of catechins that were not identified, there is a possibility that components other than catechins also have an activity to inhibit pancreatic lipase.

Effect of heat-treated tea catechins on postprandial hypertriacylglycerolemia was examined in human subjects (Unno et al. 2005). Male subjects with mild or borderline hypertriacylglycerolemia were given a beverage containing 224 or 674 mg of heat-treated tea catechins with a meal consisted of a piece of bread and 20 g butter. Serum triacylglycerol concentration was continuously increased by the administration of a meal until 3 hr. The intake of heat-treated tea catechins dose-dependently lowered the increment of serum triacylglycerol. Significant difference was observed at 2 and 3 hr after a high dose of tea catechins.

Antiobesity Activity of Tea Catechins and Heat-treated Tea Catechins

Obesity is an important social issue in advanced countries. Obesity induces diabetes, hyperlipidemia and hypertension and hence, increases death by coronary heart disease. Meguro et al. (2001) for the first time showed that feeding for 4 weeks of a high fat diet containing 0.5% tea catechins mainly composed of EGCG and ECG reduced visceral fat weight in mice. In human study, Nagao et al. (2001) observed that the intake for 12 weeks of a beverage containing 600 mg/day heat-treated tea catechins significantly reduced visceral fat area compared with the control group. Kajimoto et al. (2005) also observed in healthy adults that the intake of 444 and 666 mg/day of heat-treated tea catechins given as beverages for 12 weeks significantly reduced body weight, body mass index and visceral fat area compared with the placebo beverage group.

It has been suggested that oxidation of dietary lipids (Onizawa et al. 2001) and energy expenditure (Osaki et al. 2001) was increased after a single dose of tea catechins in rats. Murase et al. (2002) reported that when mice were fed a high fat diet containing 0.5% tea catechins for 1 month, hepatic β-oxidation and mRNA expressions of hepatic acyl-CoA oxidase and medium chain acyl-CoA dehydrogenase, enzymes related to β-oxidation, were increased. They suggested that tea catechins increase energy expenditure by stimulating β-oxidation in the liver. It has been known that expression of enzymes related to β-oxidation in the liver is stimulated by peroxisome-proliferator activated receptor (PPAR)α. However, there is no evidence that tea catechins act as ligands for PPARα.

We also observed that the feeding of tea catechins and heat-treated tea catechins reduced visceral fat deposition in rats fed a normal fat diet (Ikeda et al. 2005). Rats were fed on a diet containing 1% tea catechins or heat-treated tea catechins for 3 weeks. The activities of hepatic carnitine palmitoyl transferase and acyl-CoA oxidase, the rate-limiting enzymes of mitochondrial and peroxisomal β-oxidations, respectively, were not influenced by the feeding of the catechin preparations. In contrast, the activities of fatty acid synthase and the malic enzyme, enzymes related to fatty acid synthesis, were lower in the two catechin groups than in the control group. The observation suggests that tea catechins do not stimulate lipid oxidation, but they lower fatty acid synthesis. Discrepancy between these studies cannot be explained at present. More studies are necessary to solve this issue.

Conclusion

Tea catechins with galloyl moiety lower serum cholesterol concentration and visceral fat deposition and suppress postprandial hypertriacylglycerolemia in experimental animals and humans. Heat-treated tea catechins, in which catechins are epimerized, are also as effective as tea catechins. Although there are some controversial results on mechanisms of antiobesity activity, it is strongly suggested that tea catechins and heat-treated tea catechins contribute to prevention of coronary heart disease.

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