

## Review Article

# Multifunctional effects of green tea catechins on prevention of the metabolic syndrome

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Tea catechins reduce serum cholesterol concentrations and suppress postprandial hypertriacylglycerolemia in experimental animals and humans. These effects are mainly ascribed to the gallate esters of catechins, (-)-epicatechin gallate (ECG) and (-)-epigallocatechin gallate (EGCG). During pasteurization of tea drinks, 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 the galloyl moiety lowered intestinal absorption of cholesterol by inhibiting micellar solubility of cholesterol. Since they inhibited pancreatic lipase *in vitro* and slowed down lymphatic absorption of triacylglycerols, it is suggested that delayed intestinal absorption of triacylglycerols after the feeding of catechin preparations causes suppression of postprandial hypertriacylglycerolemia. It has been reported that tea catechins and heat-treated tea catechins with the galloyl moiety suppress deposition of visceral fat in experimental animals and humans. Some studies suggest that the stimulation of hepatic  $\beta$ -oxidation might be a cause for reduced deposition of visceral fat. However, our study did not show any acceleration of  $\beta$ -oxidation in rat livers. Although there are some controversial observations, results obtained suggest a possibility that tea catechins and heat-treated tea catechins with the galloyl moiety improve lipid metabolism and contribute to the prevention of the metabolic syndrome.

**Key Words:** epigallocatechin gallate, gallocatechin gallate, cholesterol, triacylglycerol, visceral fat

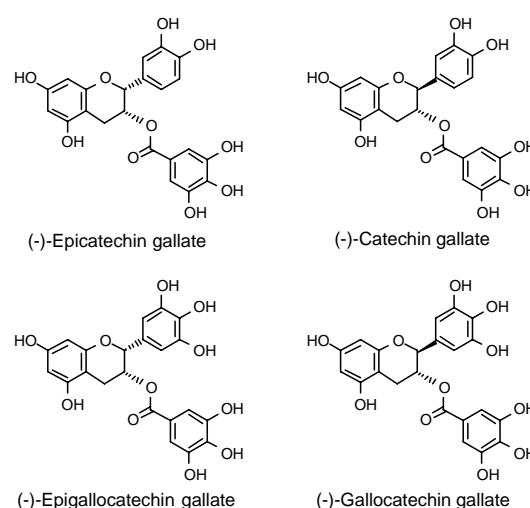
## INTRODUCTION

Tea catechins, contained in green and oolong tea, consist mainly of epicatechin, epigallocatechin, epicatechin gallate (ECG) and epigallocatechin gallate (EGCG). Various physiological functions of tea catechins have been reported, such as antiatherogenic, antiobesity, antioxidation and anticarcinogenic activities. It is known that about half of the catechins are epimerized to catechin, gallocatechin, catechin gallate (CG) and gallocatechin gallate (GCG) during heat treatment for sterilization. Although the consumption of canned and bottled tea drinks growing in Japan, studies on physiological functions of these 'heat-treated tea catechins' are scarce. We investigated functions of tea catechins and heat-treated tea catechins on lipid metabolism in rats and *in vitro*. Physiological functions of tea catechins are mainly ascribed to the gallate esters of catechins. Therefore, we used tea catechins rich in gallate esters, ECG and EGCG. In heat-treated tea catechins, about 50% of ECG and EGCG are epimerized to CG and GCG, respectively. Chemical structure of these gallate esters are shown in Fig. 1.

## CHOLESTEROL-LOWERING ACTIVITY

Hypercholesterolemia is a major risk factor for atherosclerosis. We investigated effects of tea catechins and heat-treated tea catechins rich in gallate esters on cholesterol metabolism in rats. Rats were fed a 0.5% cholesterol diet with 1% catechin preparations for 3 weeks.<sup>1</sup> Both catechin preparations significantly lowered serum and liver choles-

terol concentrations. Fecal excretion of neutral steroids originated from cholesterol was significantly higher in rats fed a catechin preparation. Although these effects tended



**Figure 1.** Chemical structure of catechins with galloyl moiety

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to be more effective in heat-treated tea catechins than in tea catechins, significant difference was not observed. When lymphatic absorption of cholesterol was investigated in thoracic duct lymph cannulated rats, administration of a catechin preparation (100 mg as catechins) to the stomach with radiolabeled cholesterol (25 mg) reduced lymphatic recovery of the radioactivity.<sup>2</sup> Heat-treated tea catechins were more effective in the reduction of cholesterol absorption than untreated catechins. These results suggest that both catechin preparations inhibit intestinal cholesterol absorption and therefore, reduce serum cholesterol concentrations.

Dietary and biliary cholesterol is solubilized in the bile salt micelle and then, subjected to incorporation into intestinal epithelial cells through brush border membranes. We investigated the effect of purified ECG, EGCG, CG and GCG on micellar solubility of cholesterol *in vitro*.<sup>2</sup> The addition of these catechins to micellar solution formed precipitations. They reduced the concentration of micellar cholesterol and GCG and CG were more effective than EGCG and ECG with regard to this.

A placebo-controlled double-blind human study using heat-treated tea catechins was conducted. A drink containing 197 mg of the catechin preparation was given to mildly hypercholesterolemic subjects twice a day for 12 weeks. Serum cholesterol concentration was 5% lower in the experimental group than in the placebo control group.<sup>3</sup>

#### SUPPRESSION OF POSTPRANDIAL HYPERTRIACYLGLYCEROLEMIA

Postprandial hypertriacylglycerolemia may be a risk factor for coronary heart disease. When rats were orally given a fat emulsion with or without catechin preparations, increase in serum triacylglycerol was suppressed in rats given a catechin preparation at 1, 2 and 3 hours after administration.<sup>4</sup> Both tea catechins and heat-treated tea catechins have the same triacylglycerol lowering activity. When thoracic duct lymph cannulated rats were orally given a fat emulsion containing 200mg radiolabeled trioleoylglycerol with 100 mg of a catechin preparation, delayed absorption of the radioactivity in lymph was observed after the administration of catechin preparations.<sup>4</sup> We also measured the effect on pancreatic lipase activity of catechin preparations *in vitro*. Both preparations dose-dependently inhibited lipase activity. The results suggest that catechin preparations suppress postprandial hypertriacylglycerolemia through the inhibition of pancreatic lipase and therefore, delayed absorption of fat.<sup>4</sup>

Unno *et al.* reported that when male subjects with mild or borderline hypertriacylglycerolemia were given a beverage containing 224 or 674 mg heat-treated tea catechins with a meal that contained 20 g of butter, postprandial increase of serum triacylglycerol concentration was dose-dependently suppressed by the intake of heat-treated tea catechins.<sup>5</sup>

#### ANTIOBESITY ACTIVITY

Deposition of visceral fat induces diabetes, hyperlipidemia and hypertension and hence, increases the risk of death as a result of coronary heart disease. Kajimoto *et al.* observed in healthy adults that the intake of a beverage

that contained 444 mg of heat-treated tea catechins for 12 weeks significantly reduced body weight, body mass index and visceral fat area compared with the placebo beverage group.<sup>6</sup> We fed rats a diet containing 1% tea catechins or heat-treated tea catechins for 3 weeks and observed both catechin preparations reduced visceral fat deposition to the same extent.<sup>7</sup> The activities of hepatic 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. In contrast, the activities of hepatic carnitine palmitoyl transferase and acyl-CoA oxidase, the rate-limiting enzymes of mitochondrial and peroxisomal  $\beta$ -oxidation respectively, were not altered by the feeding of the catechin preparations. However, Murase *et al.* reported that hepatic  $\beta$ -oxidation and mRNA expressions of hepatic acyl-CoA oxidase and medium chain acyl-CoA dehydrogenase, enzymes related to  $\beta$ -oxidation, were increased in mice fed a high fat diet containing 0.5% tea catechins for 1 month.<sup>8</sup> Discrepancy between these studies cannot be explained at present.

#### AUTHOR DISCLOSURES

Ikuo Ikeda, no conflicts of interest.

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