ABSTRACT  Evidence indicates that green tea consumption lowers the serum level of cholesterol (CH). This study was conducted to determine whether green tea lowers the intestinal absorption of CH and other lipids in ovariectomized (OX) rats. OX rats with lymph duct cannulae were infused at 3.0 mL/h for 8 h via an intraduodenal catheter with a lipid emulsion containing $^{14}$C-CH and $^{a}$-tocopherol ($^{a}$TP) without (GT0) or with green tea extract standardized to 42.9 mg (GT1) or 120.5 mg (GT2) of total catechins in PBS (pH 6.5). Green tea extracts dose-dependently reduced ($^{P} < 0.05$) the lymphatic absorption of $^{14}$C-CH. The cumulative absorptions of $^{14}$C-CH in rats infused with GT0, GT1 and GT2 were 36.3 ± 1.1, 20.7 ± 4.3 and 4.8 ± 4.1% dose, respectively. The percentage distribution of esterified CH did not differ between rats infused with GT0 and GT1 (80.2 ± 2.3% vs. 79.0 ± 1.7%), but was significantly lower in those given GT2 (69.1 ± 6.8%). The absorption of $^{a}$TP also was significantly reduced by GT1 (736.5 ± 204.9 nmol, 20.8 ± 5.8% dose) and GT2 (281.0 ± 190.8 nmol, 7.9 ± 5.4% dose) compared with GT0 (1048.8 ± 174.9 nmol, 29.6 ± 4.9% dose). The absorption of fat was significantly increased by GT1 (862.6 ± 151.1 μmol) but lowered by GT2 (557.9 ± 252.2 μmol) relative to GT0 (717.7 ± 39.1 μmol). The findings provide direct evidence that green tea has a profound inhibitory effect on the intestinal absorption of CH and $^{a}$TP in OX rats. Whether the inhibitory effect of green tea extract is attributable to a specific catechin(s) and other components in green tea remains to be determined. J. Nutr. 132: 1282–1288. 2002.

KEY WORDS:  green tea • catechins • cholesterol • absorption • rats • $^{a}$-tocopherol

Green tea (GT) is produced from freshly harvested leaves of the tea plant, Camellia sinensis. Exposure of fresh tea leaves to hot steam and air inactivates polyphenol oxidase and results in a peculiar green color, which yields polyphenol-rich green tea (1). The major polyphenols in GT are catechins (flavanols), which constitute about one third of its total dry weight. The major catechins present in GT (Fig. 1) are (-)-epigallocatechin gallate (EGCG), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG), and (-)-epicatechin (EC) (2).

Increasing evidence from animal studies indicates that GT or its catechins lower the blood levels of cholesterol (CH) in CH-fed male rats (3,4), mice (5) and hamsters (6), and retard the development or progression of atherosclerosis in apolipoprotein E–deficient mice (7) and hypercholesterolemic hamsters (8). These studies, along with the epidemiologic finding of an inverse association between coronary heart disease (CHD) risk and GT consumption in humans (9–13), strongly suggest that GT and its constituents may be used as an effective means of lowering blood CH levels and hence reducing the risk of CHD.

At present, the precise mechanism(s) by which GT or its catechins influence the blood levels of CH are unknown. In attempting to understand the mechanisms underlying the antiatherogenic effect of GT, much attention has been directed toward the antioxidant properties of its constituent catechins. Tea catechins are absorbed into the circulation in a dose-dependent manner and contribute significantly to the total antioxidant capacity of blood plasma (14,15). Numerous studies have shown that catechins bind to lipoproteins and possess antioxidant activities greater than $^{a}$-tocopherol ($^{a}$TP), effectively inhibiting LDL oxidation and lipid peroxidation in vitro (16–20). Among the tea catechins, EGCG is the most effective in inhibiting LDL oxidation (21). The inhibition of LDL oxidation by tea catechins may play a role in preventing or slowing the development of CHD (16–21). However, a recent study reported that in humans drinking eight cups of GT (0.5 g tea solids/cup) per day for 3 d, the amount of tea catechins associated with plasma LDL was <10% of the total amount in plasma, which was not sufficient to increase the resistance to LDL oxidation ex vivo in adults (22). The GT catechins

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2 Supported by the Kansas Agricultural Experiment Station, Kansas State University. Contribution no. 02–306-J.

3 To whom correspondence should be addressed.

E-mail: koo@humec.ksu.edu

4 Abbreviations used: ACAT, acyl CoA:cholesterol acyltransferase; $^{a}$TP, $^{a}$-tocopherol; BBM, brush border membrane; $^{14}$C-CH, $^{14}$C-cholesterol; CH, cholesterol; CHD, coronary heart disease; EC, (-)-epicatechin; EGC, (-)-epicatechin gallate; EGGC, (-)-epigallocatechin gallate; GC, gas chromatography; GT, green tea; GT0, a dose of 0.0 mg catechins; GT1, a dose of 42.9 mg catechins; GT2, a dose of 120.5 mg catechins; GTE, green tea extract; LPC, lysophosphatidylcholine; MDR, multidrug resistance; OX, ovariectomized; pPLA$_{2}$, pancreatic phospholipase A$_{2}$; PC, phosphatidylcholine; PL, phospholipid; TAG, triacylglycerol; UWL, unstirred water layer.


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MATERIALS AND METHODS

Animals and diet. Female Sprague-Dawley rats (n = 15; Harlan Sprague Dawley, Indianapolis, IN) weighing 228.2 ± 4.6 g were individually housed in plastic cages with stainless steel wired floors in a windowless room. All rats were subjected to a daily 12-h light:dark cycle with the dark period from 0330 to 1530 h, and had free access to deionized water prepared from a water purification system (Millipore, Malboro, MA). The rats consumed ad libitum a nutritionally adequate diet (Table 1) containing soybean oil as the fat source and egg white as the protein source for 8 wk. The diet was formulated according to the AIN-93G recommendations (30, 31). Rats were cared for in an animal facility accredited by the American Association for the Accreditation of Laboratory Animal Care, and the animal care protocols were approved by the Kansas State University Institutional Animal Care and Use Committee. At 14 wk of age, the rats were ovariectomized (32) while under halothane anesthesia.

Mesenteric lymph duct cannulation. Rats were deprived of food overnight (16 h) 5 wk after ovariectomy and anesthetized with halothane (2.0% halothane in 2.0 L O2/min) before and during cannulation of the mesenteric lymph duct. The superior mesenteric lymph duct was cannulated and an infusion catheter was placed via the gastric fundus into the proximal duodenum and secured by purse-string suture, as previously described in detail (33). After the abdominal incision was closed by suture, the rats were placed in restraining cages and housed in a recovery chamber controlled at 30°C for 20 h. During the postoperative recovery period, a maintenance solution [277.0 mmol/L glucose in PBS containing 6.8 mmol/L Na2HPO4, 16.5 mmol/L NaH2PO4, 115 mmol/L NaCl and 5 mmol/L KCl, pH 6.6] was infused at 3.0 mL/h through the intraduodenal catheter by an infusion pump (Harvard Apparatus, Model 935, South Natick, MA).

Preparation of GTE and lipid emulsion. GTE was prepared by soaking 4 g (GT1) or 20 g GT leaves (GT2) (Salada Foods Division, Redco Foods, Little Falls, NY) in 200 mL deionized water (97°C) for 5 min. The extracts were filtered (0.45 μm Mixed Cellulose Ester filter, Millipore, Bedford, MA). The volume was adjusted to 200 mL in a volumetric flask with deionized water. The extracts were diluted with deionized water (1:10 for GT1 and 1:48 for GT2); 10 μL of these diluted extracts was analyzed for catechin content by HPLC (Beckman Instruments, System Gold Nouveau software, Fullerton, CA) with a C18 reverse-phase column (Alltima C18, 5 μm, 4.6 × 150 mm, Alltech Associates, Deerfield, IL). The method used was adapted from an Alltech bulletin (CHROM 8825, Catechins in GT) and Dalluge et al. (34). Catechins were detected at 210 nm and eluted within 20 min at a flow rate of 1 mL/min of mobile phase (83% water/17% acetonitrile/0.05% trifluoroacetic acid). GT1 and GT2, as prepared above, yielded 42.9 mg/24 mL and 120.5 mg/24 mL GTE, respectively. The relative (%) distributions of individual catechins between GT1 and GT2 were very similar, although the efficiency of total catechin extraction decreased with increasing GT as shown in Table 2.

TABLE 1

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Diet composition1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g/kg</td>
</tr>
<tr>
<td>Egg white</td>
<td>200.0</td>
</tr>
<tr>
<td>Cornstarch</td>
<td>396.5</td>
</tr>
<tr>
<td>Dextrose</td>
<td>132.0</td>
</tr>
<tr>
<td>Cellulose</td>
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<tr>
<td>Soybean oil2</td>
<td>70.0</td>
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<tr>
<td>Mineral mix</td>
<td>35.0</td>
</tr>
<tr>
<td>Vitamin mix</td>
<td>10.0</td>
</tr>
<tr>
<td>Biotin (1 mg/g biotin succrose mix)</td>
<td>4.0</td>
</tr>
<tr>
<td>Choline bitartrate</td>
<td>2.5</td>
</tr>
</tbody>
</table>

1 Formulated and supplied from Dyets, Bethlehem, PA, according to the recommendations of the AIN (30, 31).
2 Contained 0.02% tert-butylhydroquinone.
TABLE 2

Catechin content in green tea (GT) extracts

<table>
<thead>
<tr>
<th>GT catechins</th>
<th>GT1</th>
<th>GT2</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg µmol (mol/100 mol)</td>
<td>mg µmol (mol/100 mol)</td>
<td></td>
</tr>
<tr>
<td>EGC2</td>
<td>23.8</td>
<td>141.4</td>
</tr>
<tr>
<td>EGG</td>
<td>39.6</td>
<td>51.9</td>
</tr>
<tr>
<td>EGC</td>
<td>36.5</td>
<td>48.4</td>
</tr>
<tr>
<td>EC</td>
<td>10.4</td>
<td>23.5</td>
</tr>
<tr>
<td>Total</td>
<td>120.5</td>
<td>314.4</td>
</tr>
</tbody>
</table>

1 GT1 yielded 42.9 mg total catechins; GT2 yielded 120.5 mg total catechins.
2 EGG, epigallocatechin gallate; EGC, epigallocatechin; EGC, epicatechin gallate; and EC, epicatechin.

Lipid emulsions were prepared under a gentle N2 stream and subdued light for 50 min using a microprocessor-controlled ultrasonicator equipped with a microtip (XL-2020 Ultrasonic Liquid Processor, Misonix, Farmingdale, NY). The lipid emulsions contained 451.8 µmol triolein (95%, Sigma Chemical, St. Louis, MO), 20.7 µmol CH, 27.8 kBq [14C-CH] (specific activity, 1.9 GBq/µmol, DuPont-NEN, Boston, MA), 3.6 µmol αTP (all-α αTP, 97%, Aldrich Chemical, Milwaukee, WI), and 396 µmol Na+ -taurocholate in 24 mL PBS (pH 6.5) containing GTE (GT1 or GT2) or no GTE (GT0). The amount of triolein provided for 8 h was ~29% of the daily fat intake of a rat consuming 20.0 g/d of the AIN-93G diet that contains 7.0% fat (30), representing a moderate fat intake, whereas the amount of CH represented a moderately high intake in proportion to the total amount of fat given. The amount of αTP was set at 100% of the daily intake of the vitamin as recommended (30).

Determination of 14C-cholesterol (14C-CH) absorption. After postoperative recovery, rats were infused with the lipid emulsions at 3.0 mL/h via the intraduodenal catheter and lymph was collected via the lymph cannula at hourly intervals for 8 h under subdued light into preweighed, ice-chilled plastic tubes containing 4 mg Na3-EDTA and 30 µg n-propyl gallate as antioxidants. Fresh lymph samples (100 µL) were mixed with 10 mL scintillation fluid (Scinti Verse, Fisher Scientific, Fair Lawn, NJ) and the 14C-activity was counted using a scintillation counter (Beckman LS-6500, Beckman Instruments, Fullerton, CA). The 14C-activity in hourly lymph volume was expressed as a percentage of the total radioactivity infused (% dose). Specific activity was calculated by dividing total dpm by the amount of CH in lymph (dpm/µmol CH).

Lipid analysis. CH was analyzed colorimetrically (35). The distribution of lymph 14C-radioactivity between free and esterified CH fractions was determined using digitonin (36). The digitonin precipitate (free CH fraction) was counted for 14C-radioactivity. The 14C-radioactivity of the esterified CH fraction was calculated by total 14C-radioactivity minus 14C-radioactivity in the free CH fraction.

Phospholipid (PL) was analyzed colorimetrically (37) from lipid extracts of the lymph samples (38). αTP was determined by a modification of an HPLC method (39), as described in detail in our recent study (33).

For fatty acid analysis, total lipids from lymph were extracted (38) with a chloroform/methanol mixture (2:1 v/v) containing BHT (151.3 µmol/L). Fatty acids were analyzed by gas chromatography (GC) (40). An internal standard (17:0) was added to each tube during lipid extraction. Lipids were saponified in methanolic sodium hydroxide (0.5 mol/L, methanolic NaOH) and methylated simultaneously with 12.1 mol/L boron trifluoride in methanol. The fatty acid methyl esters were redissolved in petroleum ether and analyzed by GC (Hewlett-Packard, model GC 6890, Palo Alto, CA) with an HP-INNOWax cross-linked polyethylene glycol column and flame ionization detector.

Statistics. Statistical analysis was performed with PC SAS (41). Repeated-measures ANOVA and the least significance difference test were used to compare multiple group means and time-dependent changes within groups. Differences were considered significant at P < 0.05. Values presented are means ± SD.

RESULTS

Lymph flow. The rate of lymph flow was increased in response to lipid infusion in all groups, peaking at 4 h. The rate of lymph flow did not differ between rats administered GT0 (2.3 ± 0.4 mL/h) and GT1 (2.6 ± 0.4 mL/h), but was significantly lower (P < 0.05) in those given GT2 (1.7 ± 0.4 mL/h). Total lymph volume for 8 h was significantly lower in rats infused with GT2 than in those infused with GT0 and GT1 (Table 3).

Lymphatic absorption of 14C-CH. The hourly rates of 14C-CH absorption were significantly lower in rats infused with GT1 and GT2 than in those given GT0 from 2 to 8 h (Fig. 2). The absorption of 14C-CH rose at a significantly slower rate in those infused with GT1 and GT2 than in those given GT0 (Table 3). Consequently, the cumulative lymphatic absorptions of 14C-CH over 8 h were markedly reduced in GT-treated groups compared with those given GT0 (Table 3). The percentage distribution of 14C-radioactivity in the esterified CH fraction did not differ between rats infused with GT0 (80.2%) and GT1 (79.0%), but was significantly lower in those given GT2 (69.1%) than in those given GT0 and GT1.

TABLE 3

Total lymphatic absorption of 14C-cholesterol (14C-CH), α-tocopherol (αTP) and outputs of total cholesterol (CH), phospholipid (PL), oleic acid (OA), total fatty acids and lymph fluid in rats infused with green tea (GT) extracts

<table>
<thead>
<tr>
<th></th>
<th>GT0</th>
<th>GT1</th>
<th>GT2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymph volume, mL</td>
<td>18.7 ± 3.1a</td>
<td>20.8 ± 5.5a</td>
<td>13.5 ± 3.8b</td>
</tr>
<tr>
<td>14C-CH, % dose</td>
<td>36.3 ± 1.1a</td>
<td>20.7 ± 4.3b</td>
<td>4.8 ± 4.1c</td>
</tr>
<tr>
<td>% dose/h</td>
<td>4.5 ± 2.4a</td>
<td>2.6 ± 1.6b</td>
<td>0.6 ± 0.4c</td>
</tr>
<tr>
<td>CH, µmol</td>
<td>15.0 ± 0.8a</td>
<td>10.0 ± 1.5b</td>
<td>5.0 ± 1.4c</td>
</tr>
<tr>
<td>µmol/h</td>
<td>1.9 ± 0.4a</td>
<td>1.3 ± 0.2b</td>
<td>0.6 ± 0.1c</td>
</tr>
<tr>
<td>PL, µmol</td>
<td>21.2 ± 1.5a</td>
<td>20.6 ± 1.5a</td>
<td>17.7 ± 5.0b</td>
</tr>
<tr>
<td>αTP, % dose</td>
<td>29.8 ± 4.9a</td>
<td>20.8 ± 5.8b</td>
<td>7.9 ± 5.4c</td>
</tr>
<tr>
<td>nmol</td>
<td>1048.8 ± 174.9a</td>
<td>736.5 ± 204.9b</td>
<td>281.0 ± 190.8c</td>
</tr>
<tr>
<td>nmol/h</td>
<td>131.1 ± 42.8a</td>
<td>92.1 ± 29.9b</td>
<td>35.1 ± 10.8c</td>
</tr>
<tr>
<td>OA, µmol</td>
<td>559.0 ± 25.2b</td>
<td>704.6 ± 135.7a</td>
<td>452.2 ± 210.4c</td>
</tr>
<tr>
<td>Total fatty acid, µmol</td>
<td>717.7 ± 39.1b</td>
<td>862.6 ± 151.1a</td>
<td>557.9 ± 252.2c</td>
</tr>
</tbody>
</table>

1 Values are mean ± SD; n = 5. Values in a row with different superscript letters differ, P < 0.05.
2 GT0, 0.0 mg GT catechins; GT1, 42.9 mg GT catechins; and GT2, 120.5 mg GT catechins.
The relative (%) distribution of 14C-radioactivity in the esterified CH fraction decreased significantly in those given GT2 between 1 and 3 h to 55.3 ± 9.9%, rose to 70.9 ± 7.8% at 5 h, and stabilized at 73.0% thereafter (Fig. 3). The specific activity of 14C-CH in all groups increased with time with no difference between those infused with GT0 and GT1. However, the 14C-CH specific activity was significantly lower in those given GT2, reflecting the decrease in 14C-CH absorption (Table 4).

**Lymphatic output of total CH.** The rates of total CH (exogenous and endogenous) output in rats infused with GT0, GT1, and GT2 were 1.9 ± 0.4, 1.3 ± 0.2 and 0.6 ± 0.1 μmol/h, respectively, with significant differences among all groups. The hourly rate of total CH output decreased significantly with GTE infusion in a dose-dependent fashion at 2 h and thereafter compared with control (GT0) (Fig. 4). The cumulative lymphatic outputs of total CH were significantly lower in rats infused with GT1 and GT2 than in those given GT0 (Table 3). The total lymphatic output in GT2-treated rats was also significantly lower than in those given GT1.

**Lymphatic outputs of αTP and other lipids.** In parallel with the decreases in the rate and the total amount of CH absorption, the hourly rates and the total amount of αTP absorbed also were markedly lowered by GTE in a dose-dependent manner (Fig. 5, Table 3). The total amounts of αTP absorbed in rats infused with GT1 and GT2 represented 70.2 and 26.8%, respectively, of the control (GT0).

Total PL outputs did not differ between rats infused with GT0 and GT1. However, the PL output was significantly lower in those infused with GT2 than in those given GT0 and GT1 (Table 3). The effect of GTE on the lymphatic output of fatty acids was biphasic, i.e., the output of total fatty acids was moderately increased at a low dose (GT1), but drastically lowered at a high dose (GT2). Similarly, the output of 18:1, which was infused as triolein, was increased by GT1 and lowered by GT2 compared with GT0. Rats administered GT0 and GT1 did not differ in total outputs of 16:0, 18:0, 18:2, 20:4 and 22:6, whereas the outputs of these fatty acids were significantly lower in those infused with GT2 than in those given GT0 and GT1 (data not shown). The cumulative outputs of 18:3 tended to be greater (P > 0.05) in rats infused with GT1.
FIGURE 5 Hourly rates of lymphatic absorption of α-tocopherol (αTP) in rats infused with green tea (GT) extracts (GTE) (GT0, 0.0 mg; GT1, 42.9 mg; and GT2, 120.5 mg GT catechins). Values are expressed as means ± SEM, n = 5. Means with different superscript letters at each time differ, *P < 0.05.

(1.4 ± 0.3 μmol) than in those given GT0 (0.9 ± 0.4 μmol) and GT2 (1.0 ± 0.4 μmol).

**DISCUSSION**

This study, using OX rats with lymph cannulae, provides the first direct evidence that fresh GTE lowers the lymphatic absorption of 14C-labeled total CH in a dose-dependent manner, whereas it alters the absorption of fat (fatty acids) in a biphasic fashion, producing a moderate increase at a low dose (GT1) but a marked decrease at a higher dose (GT2). In addition, GTE has a profound inhibitory effect on αTP absorption, suggesting that GT consumption may adversely affect nutritional status of the vitamin.

At present, the precise mechanism governing the inhibitory effect of GTE on CH absorption is far from clear. Available evidence suggests that GTE may alter the following luminal and intracellular events that influence CH absorption: 1) hydrolysis of triacylglycerol (TAG) and PL; 2) formation and diffusion of mixed micelles through the unstirred water layer (UWL); 3) uptake of CH by the enterocyte via the brush border membrane (BBM); and 4) intracellular esterification and transport of CH via chylomicrons (42,43).

Previously, Juhel et al. (24) observed that a GTE significantly inhibited the activities of gastric and pancreatic lipases, as determined in vitro using a relatively high level of catechins. On the basis of their findings in vitro, Juhel et al. (24) suggested that GT catechins might interfere with lipid emulsification, thereby inhibiting fat digestion by pancreatic lipase in the intestinal lumen. In the present study, the emulsion, as prepared with much lower levels of catechins (5.4 and 15.1 mg/3 mL in GT1 and GT2, respectively), remained stable with no precipitation of lipids or phase separation. Under the present conditions, the effect of GTE on fat absorption was biphasic, i.e., the lymphatic output of 18:1, infused in the form of triolein, was significantly decreased at a high dose (GT2), whereas it was moderately increased at a low dose (GT1). Such a biphasic effect of GTE also was shown when the lymphatic outputs of total fatty acids were compared. Thus, our findings indicate that GTE affects the absorptions of CH and fatty acids (or TAG) via distinctly different mechanisms. The dose-dependent inhibition of CH absorption by GTE may not be explained entirely by an adverse effect of GTE on the hydrolysis of fat and subsequent solubilization of CH in mixed micelles.

In a recent study (44), we observed that GT catechins have a profound inhibitory effect on porcine pPLA2 in vitro. EGCG, a major catechin (flavanoid) present in GT, was most effective in inhibiting pPLA2. Under the in vitro conditions used, the percentage of inhibition of pPLA2 by EGCG at 4.0 mg (9.0 μmol)/3.0 mL was 65%, whereas inhibition by other catechins ranged from 23 to 40%. Also, when rats were infused intraduodenally with a triolein emulsion containing 14C-PC in the presence of EGCG (25.0 μmol/h), the luminal hydrolysis of PC was significantly inhibited, with a significant increase in unhydrolyzed PC in the lumen and a marked decrease in the lymphatic output of 14C-radioactivity (unpublished data). Previous studies showed that PC on the surface of lipid emulsions inhibits hydrolysis of the core TAG by pancreatic lipase, even in the presence of bile salts and colipase (45) and that the presence of unhydrolyzed PC in lipid emulsions or mixed micelles inhibits CH uptake by Caco-2 and IEC-6 intestinal cells in vitro, whereas the substitution of LPC for PC or addition of pPLA2 reversed the PC-induced inhibition of CH uptake (46–48). It is of particular interest that the presence of PC in mixed micelles had no effect on the cellular uptake of other lipids such as fatty acids, monosacylglycerol and retinol, which are less hydrophobic than CH (47,48). In the present study, the lymphatic absorptions of both CH and αTP were inhibited by GTE in a dose-dependent manner. Recently, we showed that addition of PC in a triolein emulsion increases the output of 18:1, whereas it markedly lowers the lymphatic absorption of both CH and αTP, and the substitution of LPC for PC in the triolein emulsion increases their absorptions (33). The above-cited studies strongly suggest that PC hydrolysis is an important determinant of the absorption of both CH and αTP. Thus, the dose-dependent inhibition of CH and αTP absorptions by GTE may be explained in part by the inhibition of pPLA2 by GT catechins such as EGCG (44) and interference with micellar solubilization of both CH and αTP, extremely hydrophobic lipids. It also has been shown that the size of mixed micelles increases in the presence of intact PC relative to LPC, resulting in delayed diffusion across the UWL and retarding uptake of micellar lipids by enterocytes (49,50). On the basis of the observation that micellar CH was coprecipitated with GT catechins in vitro, Ikeda et al. (26) postulated that GT catechins per se decrease the intestinal absorption of CH by decreasing the micellar solubility of CH. However, catechins did not precipitate micellar bile acids, suggesting that the inhibitory effect of GTE on CH absorption may not be directly attributable to the sequestration of bile acids from the micellar matrix by tea catechins.

Increasing evidence suggests that CH uptake through the BBM of the enterocyte is protein mediated. GT catechins may interact with proteins implicated in the uptake and efflux of CH across the BBM such as multidrug resistance P-glycoprotein 1 (MDR1) (51,52), ATP-binding cassette proteins (53) and class B type-1 scavenger receptors (54–56). Flavonoids form complexes with proteins through hydrophobic interactions and hydrogen bonding (37,38). Evidence from recent studies indicates that certain flavonoids modulate the activities of MDR glycoproteins by interacting with the ATP-binding site and steroid-interacting region (59,60). Thus, flavonoids including GT catechins may influence the uptake of CH by enterocytes by interacting with CH carriers such as MDR1 and other CH transport protein(s) present in the BBM (59,60).

Once taken up by the enterocyte, CH is esterified by acyl CoA-cholesterol acyltransferase (ACAT) (61). We observed a significant decrease in the relative (%) amount of esterified
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14C-CH appearing in lymph when GTE was infused at a high dosage (GT2), whereas no such change was noted at a lower dosage (GT1). This finding suggests that a high intake of GTE may inhibit intestinal ACAT activity and hence CH absorption. It is not known whether GTE affects CH synthesis in the intestine. A previous study (6), however, showed that even a high GTE intake did not alter hepatic 3-hydroxy-3-methyl-glutaryl CoA reductase.

In this study, the dosages of GTE, standardized at 42.9 (GT1) and 120.5 mg (GT2) of total catechins, were equivalent to 0.13 and 0.36 mg/kg as estimated on the basis of the rat’s daily food intake of 20 g providing 334 kJ (AIN-93G diet). For a person consuming 8360 kJ/day, the amounts of GT catechins used in this study would be equivalent to daily intakes of 1.1 and 3.0 g catechins/d, which can be obtained from 6 cups (12.3 g tea leaves) and 16 cups (33.5 g tea leaves), respectively. The estimates are based on the catechin content in a cup of tea (188.0 mg catechins/2.1 g GT leaves) as determined by a new method of GTE preparation and analysis. The yield of catechins/g GT is in close agreement with that reported by others (54.9 mg catechins/g GT) (62). Studies indicate that an average tea drinker in Japan consumes 4–9 cups of GT (63) and that heavy tea drinkers consume >10 cups GT/d (63), with polyphenol intakes ranging from 180 to 240 mg/cup (64). Our findings suggest that GTE at normal intakes may significantly lower the intestinal absorption of CH. However, our data also suggest that GT intake might adversely affect aTP status due to inhibition of aTP absorption. It remains to be determined whether the failure of GT intake to inhibit LDL oxidation ex vivo (22) and lipid peroxidation in vivo (23) in adult humans is associated with decreased status of the vitamin.

In summary, this study provides the first evidence that freshly extracted GT has a profound inhibitory effect on the intestinal absorptions of CH and aTP in vivo. The benefits and safety of GT intake should be examined under chronic feeding conditions in view of the CH-lowering action of GTE and its potential adverse effect on vitamin E status. Whether adaptive responses to chronic green tea intake occur in intestinal lipid absorption is yet to be investigated. Further studies will be required to delineate the precise mechanisms underlying the effects of GT and to identify active constituents including catechins and caffeine in GT that influence the absorption of lipids.

LITERATURE CITED


