Original Research

Green Tea Reduces LDL Oxidability and Improves Vascular Function

F. J. Tinahones, MD, PhD, M. A. Rubio, MD, PhD, L. Garrido-Sánchez, PhD, C. Ruiz, BSc, E. Gordillo, BSc, L. Cabrerizo, MD, PhD, F. Cardona, BSc, PhD

Servicio de Endocrinología, Hospital Clinico Virgen de la Victoria de Málaga (F.J.T.), Fundación IMABIS (Instituto Mediterráneo para el Avance de la Biotecnología y la Investigación Sanitaria) de Málaga (L.G.-S., F.C.), Málaga, Servicio de Endocrinología y Nutrición, Hospital Clínico San Carlos de Madrid (M.A.R., C.R., E.G., L.C.), Ciber Fisio Patologia de la Obesidad y Nutricion, CB06/03, ISCIII (F.J.T., L.G.-S., F.C.), Madrid, SPAIN

Key words: LDL, oxidized LDL, anti-oxidized LDL IgG antibodies, anti-oxidized LDL IgM antibodies, green tea

Objective: Several different epidemiological studies have examined the association between the consumption of tea and coronary heart disease. Some, though not all, support the view that tea or flavonoids reduce the risk of cardiovascular heart disease. The aim of this study was to determine the short-to medium-term effect of a green tea extract on vascular function and lipid peroxidation as compared with placebo.

Methods: The study was undertaken with 14 healthy women, none of whom were receiving any medical treatment. Measurements were made of antibodies and immune complexes by ELISA, endothelial dependent vascular function by Doppler ultrasound, and the concentration of oxidized LDL by TBARS.

Results: The mean diameter of the brachial artery following the post-compression hyperaemia phase rose significantly ($p < 0.0001$) after treatment with green tea extract. Flow-mediated brachial artery vasodilation ranged from 5.68% for the placebo phase to 11.98% after the green tea extract ($p = 0.02$). The consumption of green tea extract was associated with a significant 37.4% reduction in the concentration of oxidized LDL (TBARS) ($p = 0.017$). The levels of anti-oxidized LDL IgM antibodies fell significantly after treatment ($p = 0.002$).

Conclusion: This study found that consumption of green tea extract by women for five weeks produced modifications in vascular function and an important decrease in serum oxidizability.

INTRODUCTION

Tea, prepared from the leaves of Camellia sinensis, is the most popular beverage in the world, except for water. Tea contains a high amount of flavonoids. Epidemiological studies have been undertaken to determine the association between the consumption of tea and coronary heart disease. Some [1,2], though not all [3], support the view that tea or flavonoids reduce the risk of cardiovascular heart disease (CHD). If the association between consumption of tea and a reduction in CHD is confirmed, one reason could be that flavonoids may be antioxidants by virtue of the number and arrangement of their phenolic hydroxyl groups [4].

Oxidized LDL play a key role in the development of atherosclerosis [5,6]. Oxidative modification of LDL may be the prior step for their binding and accumulation by macrophages and later transformation into foam cells. In vitro studies have shown that oxidized LDL can be found in extracts from atherosclerotic lesions [7]. Indirect evidence for the in vivo oxidization of LDL is the rise in anti-oxidized LDL antibodies [8]. However, debate exists as to whether these anti-oxidized LDL antibodies are protective [9] or promote [10] atherosclerosis.

In vitro addition of purified tea catechins reduces the susceptibility of LDL to undergo oxidative modification [11]. In vivo studies, however, have produced differing results; whereas one study found that a cup of tea increased the plasma antioxidant potential by 40–50% [12], other studies found little or no increase in the plasma antioxidant potential [13,14]. These diverging experimental and epidemiological results emphasize the need for specially designed, well-controlled studies of tea or

Address reprint requests to: Francisco José Tinahones, c/ Manuel Vazquez Montalban n° 1, Rincón de la Victoria. Málaga, 29720, SPAIN. E-mail: fjtinahones@terra.es
The research group belongs to the Ciber Fisio Patologia de la Obesidad y Nutricion, CB06/03 of the "Instituto de Salud Carlos III", Madrid, Spain.

Journal of the American College of Nutrition, Vol. 27, No. 2, 209–213 (2008)
Published by the American College of Nutrition

tea flavonoids using early markers of CHD, such as endothelial dysfunction [15].

In view of this situation, we studied the effect of an extract of green tea in order to standardize the dose and determine the effect of this extract on vascular function and lipid peroxidation in a group of healthy women.

SUBJECTS AND METHODS

The study was undertaken in 14 healthy women with a mean age of 34.9 years. They were not taking any medication at the time of the study. Table 1 shows their clinical characteristics. All participated voluntarily in the study after giving their informed consent. The study was approved by the Ethics Committee of San Carlos Clinical Hospital. The participants were evaluated at baseline after taking a placebo for seven days. For five weeks they then took AR25 Catechol, after which they were again evaluated. During the whole study (i.e., from the start of the placebo period until the end of the five-week period) the patients followed a controlled diet of 1800 Kcal daily. Neither the participants nor the person measuring vascular function were aware of what the participant was taking. All the capsules, whether they contained AR25 Catechol or placebo, were provided by the same laboratory (Laboratories Farmacéuticos Arkochim, Madrid, Spain), and were the same size, colour, and shape. The treatment consisted of the daily intake of four capsules (two before breakfast and two before lunch), taken with water a few minutes before the meal. The intake of the capsules was the equivalent of a daily dose of 150 mg of caffeine and 375 mg of catechols (270 mg as epigallocatechin gallate). The daily intake of 350 mg catechols is the equivalent of 8.43 gr of green tea.

Measurements were also made of total cholesterol, triglycerides and HDL cholesterol by enzymatic methods, and LDL cholesterol was calculated from the Friedewald equation.

Characteristics of the Study Product

AR25 Catechol (a standardized, dry ethanol extract of *Camellia sinensis*) was produced from dried, crushed leaves of the plant. The extract was later concentrated by distillation under pressure and dried by atomization. Maltodextrin was added, the amount depending on the dosification of the extract obtained, and which enables the concentration of polyphenols to be standardized. HPLC analysis of the product confirmed that it contained 25% catechols, mainly epigallocatechin gallate (EGCG) and about 5–10% caffeine. In this study EGCG, the main component responsible for the pharmacological activity of green tea, represented 72% of the total amount of catechols. Smaller amounts of epigallocatechol, epicatechol and epicatechol gallate were also present. The product was packaged in capsules to facilitate administration and ensure the correct bioavailability in each participant.

Table 1. Baseline Anthropometric Characteristics of the Study Subjects (n = 14 women)

	Mean (SD)	95% CI
Age (years)	34.9 (9.7)	30.0–39.7
Weight (Kg)	74.7 (7.7)	70.8–78.5
Height (cm)	159.6 (7.1)	156.0–163.1
BMI (Kg/m^2)	29.3 (1.9)	28.3–30.2
Waist circumference (cm)	88.7 (7.1)	85.2–92.3
Hip circumference (cm)	108.9 (5.2)	106.4–111.5
Fat-free mass (Kg)	42.0 (5.3)	39.4–44.6
Fat mass (Kg)	32.5 (4.7)	30.2–34.8

Vascular Function

Endothelial-dependent vascular function was measured by Doppler ultrasound. Measurement was made of the post-ischaemic vasodilation produced by occlusion of the arm for 5 minutes with a blood pressure cuff. The vasodilator response was measured twice, once at baseline and once five weeks later after finishing the AR25 Catechol treatment, using a variable frequency (7–11 MHz) HP Sonos 4500 device. Four consecutive readings were made of the diameter of the brachial artery, measured at rest and after compression of the artery with a blood pressure cuff on the forearm, keeping the pressure above 200 mm Hg for four minutes. The ultrasound images were obtained by the same observer blinded to the characteristics of the participants and whether they had received placebo or AR25 Catechol.

LDL Isolation

LDL was isolated from a pool of human fasting plasma from blood donors by density gradient ultracentrifugation at 65000 rpm (BECKMAN Optima XL-100K ultracentrifuge. USA, vertical rotor VTI65.2) for 35 minutes at 4°C. This was then further purified with a second ultracentrifugation at 49000 rpm (fixed angle rotor TY65) for 18 hours at 4°C. The LDL was then dialyzed against PBS (4°C for 30 hours) (0.14 M NaCl/0.01 M phosphate buffer).

Thiobarbituric Acid-Reactive Substances (TBARS)

The LDL samples isolated from the serum of each participant (100μl) were incubated with 0.5 ml acetic acid at 20% and pH of 3.5, and with 0.5 ml of thiobarbituric acid in an aqueous solution at 0.78%. After heating the mixture to 95°C for 45 minutes, the samples were centrifuged at 4000 rpm for 4 minutes. The red supernatant was measured at 532 nm with a Versamax plate spectrophotometer. A standard curve with malonyldialdehyde (MDA) was prepared. The results were expressed as nmol of MDA per mg of LDL protein.

LDL Oxidation

Oxidized LDL was prepared by incubating the LDL for 3 hours at 37°C with 0.5 M MDA at a constant ratio of 100 μl/mg

of LDL. MDA was prepared fresh by acid hydrolysis of MDA-bis-dimethyl acetal; 88μl of MDA-bis-dimethyl acetal was incubated with 12μl of HCl 4M and 400μl of distilled water at 37°C for 10 minutes. The reaction was stopped by adjusting the pH to 7.4 with 1M NaOH. After conjugation, MDA-LDL was extensively dialyzed against PBS.

Anti-oxidized LDL Antibodies

Microtitre plates for determination of anti-oxidized LDL antibodies were coated with either native- or MDA-LDL according to the technique of Tinahones et al. [16,17].

Detection of Immune Complexes with Oxidized LDL

Measurement of the LDL immune complexes in serum was done with a sandwich type ELISA using a human anti-apoB100 antibody described by Wu et al. [18].

Statistical Study

The biological variables were analysed by Student *t* test, with means ± standard deviation in the tables. In all cases the rejection level for a null hypothesis was a $p < 0.05$ for two tails. Statistical analyses were performed with SPSS 6.0 for Windows.

RESULTS

No significant change was detected over the study period in any anthropometric variable, nor were any adverse events noted.

Effect of AR 25 Catechol® on Vascular Function

The mean diameter of the brachial artery at rest was no different between the phases with and without AR25 Catechol. Following post-compression hyperaemia, the brachial artery diameter was significantly increased after treatment ($p < 0.0001$). The percent increase in the brachial artery diameter, also known as flow-mediated brachial artery vasodilation, ranged from 5.68% for the placebo phase to 11.98% after taking the green tea extract ($p = 0.02$) (Table 2).

Table 2. Variation in the Brachial Artery Diameter after 5 Weeks Treatment with AR25 Catechol

	Placebo	Treatment[3]
Brachial artery diameter at rest (nm)	3.52 (0.38)	3.59 (0.32)
Brachial artery diameter after hyperaemia (nm)	3.72 (0.33)	4.02 (0.42)[1]
FMV (%)	5.68 (3.8)	11.98 (6.0)[2]

FMV = flow-mediated brachial artery vasodilation.

[1] $P < 0.0001$, [2] $P = 0.02$.

[3] Treatment: chronic treatment with AR25 Catechol for 5 weeks.

Influence on Lipid Profile

There was a significant reduction in the concentrations of triglycerides ($p = 0.04$), whereas no significant changes were noted in the concentrations of total cholesterol, high density lipoprotein cholesterol (HDL cholesterol) or LDL cholesterol (Table 3).

Influence on Lipoprotein Oxidation

Prolonged administration of AR25 Catechol led to a significant 37.4% reduction in the concentrations of oxidized LDL (TBARS) ($p = 0.017$). No significant differences were found for the concentrations of anti-oxidized LDL IgG antibodies or anti-LDL IgG or IgM immune complexes between the periods with and without treatment, though the anti-oxidized LDL IgM antibodies decreased significantly after treatment ($p = 0.002$) (Table 3).

DISCUSSION

This study found that administration of an extract of green tea produced a marked change in the response of the brachial artery to compression. Others have detected the effect of green tea on vascular function [19,20]. The ability of green tea to inhibit human vascular smooth muscle cell proliferation stimulated by native LDL had already been demonstrated [15]. This is further supported by the observation that treatment with antioxidants interferes with vascular smooth muscle cell proliferation, at least in certain species [21,22]. In rat aortic vascular smooth muscle cells, DNA synthesis stimulated by platelet-derived growth factor or serum is inhibited by green tea constituents [23].

Table 3. Evolution of the Lipid Profile and of the Oxidation of Lipoproteins during Treatment with AR 25 Catechol

	Placebo	Treatment[4]
Total cholesterol (mg/dl)	176.7 (26.2)	168.3 (27.1)
HDL cholesterol (mg/dl)	57.9 (18.6)	54.9 (14.3)
LDL cholesterol (mg/dl)	104.5 (23.1)	101.7 (24.0)
Triglycerides (mg/dl)	71.9 (21.9)	58.1 (20.6)[1]
Oxidized LDL (TBARS) (nmol MDA/mg LDL protein)	14.8 (5.6)	9.2 (6.5)[2]
Anti-oxidized LDL IgG antibodies (O.D.)	0.41 (0.2)	0.39 (0.2)
Anti-oxidized LDL IgG immune complexes (O.D.)	0.33 (0.1)	0.34 (0.1)
Anti-oxidized LDL IgM antibodies (O.D.)	0.16 (0.05)	0.12 (0.05)[3]
Anti-oxidized LDL IgM immune complexes	0.20 (0.03)	0.21 (0.02)

O.D. = optic density

[1] $P = 0.04$, [2] $P = 0.017$, [3] $P = 0.002$.

[4] Treatment: chronic treatment with AR25 Catechol for 5 weeks.

Our results also show that green tea extract can reduce LDL oxidizability. Other controlled, intervention studies, however, found that the intake of tea did not effect LDL oxidation in vivo [11,13,14,24]. The absence of effects on LDL oxidizability in vivo may be related to the method used to assess LDL oxidizability. The standard method requires prior isolation of the LDL particles by ultracentrifugation of the aqueous phase of the serum. Following LDL isolation, its resistance to oxidation is verified with different pro-oxidants. In one study, most of the catechins were associated with the water-soluble fraction and it was concluded that there was insufficient accumulation of catechins in LDL to improve resistance to LDL oxidation in vivo after its isolation [25]. It was suggested that flavonoids act in the aqueous phase [26], perhaps at the surface of lipoprotein particles. Therefore, the isolation of LDL from antioxidant flavonoids in the water-soluble fraction of serum may be inappropriate. The assay used in the present study to assess in vivo lipoprotein oxidation does not involve isolation of lipoproteins. Employing the same methodology as us, other authors recently found a decrease in TBARS after 12 weeks treatment with an extract of green tea that contained 690 mg of catechins [27]. We detected this effect with just 375 mg of catechins and in as few as five weeks. Caffeine may also contribute to this effect, as it has been suggested to be an antioxidant at millimolar concentrations [28].

The role of anti-oxidized LDL antibodies is controversial. Small changes in the LDL particle make it highly immunogenic, inducing immunogenic epitopes that lead to the formation of antibodies against these [29]. However, the clinical relevance of these antibodies is currently under debate [30]. Early studies detected these antibodies in most patients with advanced atherosclerotic lesions [31]. Recent studies, however, failed to find a connection between the levels of antibodies against free oxidized LDL and coronary heart disease [32]. Other authors even found an inverse association between anti-oxidized LDL IgM antibodies and carotid artery atherosclerosis [9]. Additionally, an inverse association exists between the levels of cholesterol and the levels of anti-oxidized LDL IgG antibodies in the general population, as well as a decrease in the levels of anti-oxidized LDL IgG antibodies with age [16,17]. No association has been found between these antibodies and the degree of oxidizability of the serum [33]. In our study, the green tea extract failed to modify either the levels of anti-oxidized LDL IgG antibodies or the LDL immune complexes, although it significantly reduced the levels of anti-oxidized LDL IgM antibodies. This great diversity of results concerning the clinical importance of the anti-modified LDL antibodies may be related with the differences in the methodological determination of these antibodies.

A Japanese study found green tea consumption was associated with decreased concentrations of cholesterol and triglycerides and an increased proportion of HDL [34]. Experimental animal models have determined that the plasma lipid profile is significantly improved by the two types of tea included in the study as compared with controls [35]. In our study there was a significant decrease in the concentration of triglycerides.

In summary, this study found that intake by women of a green tea extract for five weeks resulted in changes in vascular function and a marked decrease in the oxidizability of the serum.

ACKNOWLEDGMENTS

The authors wish to thank Juan Miguel Gómez-Zumaquero for excellent laboratory technical assistance, all the patients for their collaboration, and IMABIS. We also gratefully acknowledge the help of Ian Johnstone for his expertise in preparing this manuscript.

REFERENCES

1. Hertog MG, Feskens EJ, Kromhout D: Antioxidant flavonols and coronary heart disease risk. Lancet 349:699, 1997.
2. Sesso HD, Gaziano JM, Buring JE, Hennekens CH: Coffee and tea intake and the risk of myocardial infarction. Am J Epidemiol 1149:162–167, 1999.
3. Rimm EB, Katan MB, Ascherio A, Stampfer MJ, Willett WC: Relation between intake of flavonoids and risk for coronary heart disease in male health professionals. Ann Intern Med 125:384–389, 1996.
4. Rice-Evans CA, Miller NJ, Paganga G: Structure-antioxidant activity relationships of flavonoids and phenolic acids. Free Rad Biol Med 20:933–956, 1996.
5. Hamilton CA: Low-density lipoprotein and oxidised low-density lipoprotein: their role in the development of atherosclerosis. Pharmacol Ther 74:55–72, 1997.
6. Witztum JL, Steinberg D: Role of oxidized low density lipoprotein in atherogenesis. J Clin Invest 88:1785–1792, 1991.
7. Yla-Herttuala S, Palinski W, Rosenfeld ME, Parthasarathy S, Carew TE, Butler S, Witztum JL, Steinberg D: Evidence for the presence of oxidatively modified low density lipoprotein in atherosclerotic lesions of rabbit and man. J Clin Invest 84:1086–1095, 1989.
8. Radulescu L, Stancu C, Antohe F: Antibodies against human oxidized low-density lipoprotein (LDL) as markers for human plasma modified lipoproteins. Med Sci Monit 10:BR207–214, 2004.
9. Karvonen J, Paivansalo M, Kesaniemi YA, Horkko S: Immunoglobulin M type of autoantibodies to oxidized low-density lipoprotein has an inverse relation to carotid artery atherosclerosis. Circulation 108:2107–2112, 2003.
10. Salonen JT, Ylä-Herttuala S, Yamamoto R, Butler S, Korpela H, Salonen R, Nyyssönen K, Palinski W, Witztum J: Autoantibody against oxidized LDL and progression of carotid atherosclerosis. Lancet 339:883–887, 1992.
11. Ishikawa T, Suzukawa M, Ito T, Yoshida H, Ayaori M, Nishiwaki M, Yonemura A, Hara Y, Nakamura H: Effect of tea flavonoids supplementation on the susceptibility of low-density lipoprotein to oxidative modification. Am J Clin Nutr 66:261–266, 1997.

12. Serafini M, Ghiselli A, Ferro-Luzzi A: In vivo antioxidant effect of green and black tea in man. Eur J Clin Nutr 50:28–32, 1996.
13. Van het Hof KH, de Boer HS, Wiseman SA, Lien N, Westrate JA, Tijburg LB: Consumption of green or black tea does not increase resistance of low-density lipoprotein to oxidation in humans. Am J Clin Nutr 66:1125–1132, 1997.
14. McAnlis GT, McEneny J, Pearce J, Young IS: Black tea consumption does not protect low density lipoprotein from oxidative modification. Eur J Clin Nutr 52:202–206, 1998.
15. Locher R, Emmanuele L, Suter PM, Vetter W, Barton M: Green tea polyphenols inhibit human vascular smooth muscle cell proliferation stimulated by native low-density lipoprotein. Eur J Pharmacol 434:1–7, 2002.
16. Tinahones FJ, Gomez-Zumaquero JM, Rojo-Martinez G, Cardona F, Esteva de Antonio IE, Ruiz de Adana MS, Soriguer FJ: Increased levels of anti-oxidized low-density lipoprotein antibodies are associated with reduced levels of cholesterol in the general population. Metabolism 51:429–431, 2002.
17. Tinahones FJ, Gomez-Zumaquero JM, Garrido-Sanchez L, Garcia-Fuentes E, Rojo-Martinez G, Esteva I, Ruiz de Adana MS, Cardona F, Soriguer F: Influence of age and sex on levels of anti-oxidized LDL antibodies and immune complexes in the general population. J Lipid Res 46:452–457, 2005.
18. Wu R, de Faire U, Lemme C et al. Autoantibodies to OxLDL are decreased in individuals with borderline hypertension. Hipertensión 33:53–59, 1999.
19. Hodgson JM, Puddey IB, Burke V, Watts GF, Beilin LJ: Regular ingestion of black tea improves brachial artery vasodilator function. Clin Sci (Lond) 102:195–201, 2002.
20. Widlansky ME, Biegelsen ES, Hamburg NM, Duffy SJ, Keaney JF Jr, Vita JA: Coronary endothelial dysfunction is not rapidly reversible with ascorbic acid. Free Radic Biol Med 36:123–130, 2004.
21. Greene EL, Velarde V, Jaffa AA: Role of reactive oxygen species in bradykinin-induced mitogen-activated protein kinase and c-fos induction in vascular cells. Hypertension 35:942–947, 2000.
22. Ruef J, Rao GN, Li F, Bode C, Patterson C, Bhatnagar A, Runge MS: Induction of rat aortic smooth muscle cell growth by the lipid peroxidation product 4-hydroxy-2-nonenal. Circulation 97:1071–1078, 1998.
23. Ahn H.Y, Hadizadeh K.R, Seul C, Yun Y.P, Vetter H, Sachinidis A: Epigallocathechin-3-gallate selectively inhibits the PDGF-BB-induced intracellular signaling transduction pathway in vascular smooth muscle cells and inhibits transformation of sis-transfected NIH 3T3 fibroblasts and human glioblastoma cells (A172). Mol Biol Cell 10:1093–1104, 1999.
24. Princen HM, van Duyvenvoorde W, Buytenhek R, Blonk C, Tijburg LB, Langius JA, Meinders AE, Pijl H: No effect of consumption of green and black tea on plasma lipid and antioxidant levels and on LDL oxidation in smokers. Arterioscler Thromb Vasc Biol 18:833–841, 1998.
25. van het Hof KH, Wiseman SA, Yang CS, Tijburg LBM: Plasma and lipoprotein levels of tea catechins following repeated tea consumption. Proc Soc Exp Biol Med 220:203–209, 1999.
26. Carbonneau MA, Leger CL, Monnier L, Bonnet C, Michel F, Fouret G, Dedieu F, Descomps B: Supplementation with wine phenolic compounds increases the antioxidant capacity of plasma and vitamin E of low-density lipoprotein without changing the lipoprotein Cu(2+)-oxidizability: possible explanation by phenolic location. Eur J Clin Nutr 51:682–690, 1997.
27. Esterbauer H, Cheeseman KH: Determination of aldehydic lipid peroxidation products: malonaldehyde and 4-hydroxynonenal. Methods Enzymol 186:407–421, 1990.
28. Lee C: Antioxidant ability of caffeine and its metabolites based on the study of oxygen radical obsorbing capacity and inhibition of LDL peroxidation. Clin Chim Acta 295:141–154, 2000.
29. Palinski W, Rosenfeld ME, Yla-Herttuala S, Gurtner GC, Socher SS, Butler SW, Parthasarathy S, Carew TE, Steinberg D, Witztum JL: Low density lipoprotein undergoes oxidative modification in vivo. Proc Natl Acad Sci USA 86:1372–1376, 1989.
30. Shoenfeld Y, Wu R, Dearing LD, Matsuura E: Are anti-oxidized low-density lipoprotein antibodies pathogenic or protective? Circulation 110:2552–2558, 2004.
31. Inoue T, Uchida T, Kamishirado H, Takayanagi K, Hayashi T, Morooka S: Clinical significance of antibody against oxidized low density lipoprotein in patients with atherosclerotic coronary artery disease. J Am Coll Cardiol 37:775–779, 2001.
32. Rossi GP, Cesari M, De Toni R, Zanchetta M, Maiolino G, Pedon L, Ganzaroli C, Maiolino P, Pessina AC: Antibodies to oxidized low-density lipoproteins and angiographically assessed coronary artery disease in white patients. Circulation 108:2467–2472, 2003.
33. Craig WY, Poulin SE, Neveux LM, Palomaki GE, Dostal-Johnson DA, Ledue TB, Ritchie RF: Anti-oxidized LDL antibodies and antiphospholipid antibodies in healthy subjects: relationship with lipoprotein- and oxidation-related analytes. J Autoimmun 8:713–726, 1995.
34. Imai K, Nakachi K: Cross sectional study of effects of drinking green tea on cardiovascular and liver diseases. BMJ 310:693–696, 1995.
35. Vinson JA, Dabbagh YA: Effect of green and black tea supplementation on lipids, lipid oxidation and fibrinogen in the hamster: mechanisms for the epidemiological benefits of tea drinking. FEBS Lett 433:44–46, 1998.

Received June 6, 2006; revision accepted October 12, 2006.