Prospective Double-Blind Crossover Study of *Camellia Sinensis* (Green Tea) in Dyslipidemias

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Summary

Background: Epidemiological studies have established an association between dyslipidemias and atherosclerosis. Nutritional therapy is a key point in the prevention strategy for individuals who present with risk factors for atherosclerotic disease.

Objectives: To investigate the effects of green tea *(Camellia sinensis)* in patients with dyslipidemias.

Methods: The study included 33 patients aged between 21 and 71 years who had a low-fat diet (25-35% of total calories and 200 mg of cholesterol per day). They were randomized for two sequential treatments: 250 mg capsules of green tea dry extract or placebo for a total period of 16 weeks; each patient received green tea *(Camellia sinensis)* for eight weeks and placebo for another eight weeks.

Results: Baseline lipid values (mg/dL) were: HDL-cholesterol 60.7 ± 7.3; total cholesterol 255 ± 30.9; LDL–cholesterol 158.8 ± 29.0; triglycerides 169.0 ± 61.3 and Apo-B 120.2 ± 18.9. Mean lipid variations induced by the use of green tea *(Camellia sinensis)* showed a 3.9% reduction (p = 0.006) in total cholesterol concentrations and a 4.5% reduction (p = 0.026) in LDL-cholesterol. The intake of green tea did not significantly influence HDL-cholesterol, triglyceride, and Apo-B levels. Non-significant results were found in the assessment of blood lipids (total cholesterol and LDL-cholesterol) with the use of placebo.

Conclusion: A beneficial effect of green tea *(Camellia sinensis)* was demonstrated, with a significant reduction of total cholesterol and LDL-cholesterol levels in eight weeks, in the patients studied. (Arq Bras Cardiol 2009; 93(2):121-127)

Key Words: Epidemiologic studies; case-control studies; thea sinensis; *Camellia sinensis*; phytotherapy; dyslipidemias.

Introduction

Green tea (*Camellia sinensis*) is one of the oldest beverages in the world. Reports on the habit of drinking tea date back to ancient times, when plants were used as medicines both in the prevention and the treatment of disorders, dysfunctions or diseases in humans and other animals[1-3]. In the past years, growing attention has been given to the use of green tea in human health promotion. Reduction of blood levels of total cholesterol and LDL-cholesterol with the use of this tea has been repeatedly demonstrated in several studies[4-6]. The green tea compounds responsible for these changes have not yet been determined. Recently, some studies have postulated that, thanks to their high concentration of antioxidant polyphenols, green tea flavonoids (catechins), especially epigallocatekin gallate (EGCG), may be responsible for the beneficial effects of green tea[7-12]. Tea flavonoids are believed to be effective antioxidants that can protect against several chronic diseases, especially cardiovascular diseases. Based on the observation that the consumption of flavonoid-rich food contributes to a cardiovascular risk reduction, the objective of this study design was to evaluate green tea as a diet component and its relation with blood lipid profiles in the primary prevention treatment of patients with dyslipidemias.

Green tea originated in southern China and is cultivated in Asia and in Central African countries. It has been consumed for more than 3,000 years in China, which is its major producer. In Japan, it started to be consumed by Buddhist monks in the 9th century a.D.[13] Tea extract is a water-soluble product obtained by infusion. The three major types of tea are black, oolong and green tea. Non-fermented green tea is produced from fresh leaves of *Camellia sinensis*, a plant that contains water, protein, carbohydrates, minerals, vitamins, and flavonoid-like polyphenols. The major green tea flavonoids are the catechins epigallocatechin gallate (EGCG), which comprise one third of its total dry weight. Green tea is weakly aromatic; its taste is bitter, and the infusion is green. It is also known as Thea sinensis. Black tea is fully fermented. Its manufacturing includes an enzymatic oxidation in which most of the catechins (polyphenols) are converted into complex condensation products (theaflavins / thearubigins). Oloong tea is semi-fermented and elaborated mainly in China and Taiwan[14].

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Methods

This study was conducted in the Dyslipidemia Outpatient Service of *Hospital das Clínicas da Universidade Federal do Paraná (UFPR)*. A total of 38 hypercholesterolemic patients aged between 21 and 71 years participated in the study. The research was approved by the Ethics Committee on Human Research of *Hospital de Clínicas da UFPR*, and a written informed consent was obtained from all participants.

Patient selection

The following criteria were used for patient inclusion in the study: men and women older than 20 years of age, with no evidence of coronary artery disease, with total cholesterol (TC) > 200 mg/ml and LDL-cholesterol > 130 mg/dl. Patients with renal or hepatic failure, hypothyroidism and diabetes were excluded from the study. All participants included in the study underwent clinical examination and nutritional assessment. Blood pressure was measured using the palpatory and auscultatory methods with a mercury sphygmomanometer, according to instructions of the V Brazilian Guidelines on Hypertension[15], 2006.

Assessments

For the nutritional assessment, conventional methods such as anthropometry, clinical, family and diet history were used. Weight, height, body mass index (BMI), body composition using bioelectrical impedance analysis (BIA) and waist circumference were assessed. Eating habits were assessed by means of food frequency, 24-hour dietary recalls, and three-day dietary records. Based on these data, customized nutrition prescriptions were elaborated for all patients, and were monthly monitored for a 16-week period.

Table 1 – Anthropometric characteristics of the study group

Indicators	(Mean ± SD)	Values (n = 33)
Age (years)	55.4 ± 10.1	(21.0 - 71.0)
Baseline weight (kg)	72.0 ± 15.9	(45.0 - 108.0)
Height (m)	1.57 ± 0.07	(1.45 - 1.73)
BMI (kg/m²)	29.0 ± 5.7	(19.2 - 41.4)
Systolic blood pressure (mmHg)	135.7 ± 23.9	(100.0 - 190.0)
Diastolic blood pressure (mmHg)	85.2 ± 13.6	(60.0 - 110.0)
Waist circumference (cm)	97.0 ± 15.1	(62.0 - 124.0)
BIA (n = 27)		
BFM (%)	34.5 ± 10.4	(12.6 - 49.3)
LBM (kg)	65.5 ± 10.4	(50.7 - 87.4)

BMI - body mass index; BIA - bioelectrical impedance analysis; BFM - body fat mass; LBM - lean body mass. Values are expressed as mean ± standard deviation, with minimum and maximum values in parentheses.

Diet design

The diet prescription consisted of an intake of less than 35% of the total kilocalories from total fat, with less than 7% of saturated fat, 10% or less of polyunsaturated fat, and up to 20% of monounsaturated fat. The amount of cholesterol recommended was less than 200 mg/day, in conformity with the guidelines of the III National Cholesterol Education Program – NCEP[16]. All patients followed this baseline diet for 16 weeks, during which they were randomized to receive one of the treatments, including daily doses of capsules containing 250 mg of dry green tea extract (*Camellia sinensis*) or placebo every eight weeks. Because this was a double-blind crossover study, both the participants and the researchers were not aware of the sequence in which the substances would be administered. After eight weeks of treatment, the order was inverted: the group which was receiving green tea would now start to receive placebo and vice-versa for eight more weeks. The patients were also advised not to use any vitamin supplement during the investigation period. They were also informed of the importance of diet compliance and of the need for a change in lifestyle (weight control, physical activity, smoking and alcohol cessation). Levels of lipids, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides and apolipoprotein B (Apo-B), as well as of lifestyle changes were monitored.

Evaluation of data

The patients had their lipid profile determined after a 12 to 14-hour period of fasting. Serum levels of triglyceride and cholesterol fractions were quantified using the homogeneous colorimetric enzymatic method; LDL-cholesterol was estimated by the Friedewald formula[17], and apolipoprotein B (Apo-B) was determined using the Dade Behring kit. The Bayer alkaline picrate method was used for glucose determination, and an ion-selective electrode was used for sodium and potassium determination.

Data were expressed as mean ± standard deviation of the mean. The parametric paired Student's t test and the non-parametric paired-sample Wilcoxon test were used to test the variables (by means of the Primer of Biostatistics software). The level of significance (significance probability) was set at lower than 5% ($p<0.05$).

Results

Demographic data

A total of 33 patients participated in the study. The predominant level of regular education was elementary school, with family income between one and two minimum wages. Most of the patients were women (84.8%); 15.2% were men. The mean age of the patients was 55.4 ± 10.1 years (ranging from 21 to 71 years). Anthropometric characteristics of the study group are shown in Table 1.

In relation to the anthropometric parameters, weight change was observed in the overall assessment of the group. In the pre-green tea period (71.4 ± 15.8 kg) and in the post-tea period (70.2 ± 15.4 kg), a 1.7% ($p=0.002$) weight

loss and 1.7% (p=0.002) BMI reduction were observed while the patients were using green tea. In comparison with the pre-placebo (70.6 ± 15.5 kg) and post-placebo (69.9 ± 14.9) periods, there was also weight loss although with a lower statistical significance: the weight loss was of 1.1% (p=0.041) and BMI reduction of 1.1% (p=0.047). Data regarding systolic and diastolic blood pressures showed no significant changes.

During the eight weeks when capsules containing dry green tea extracts (250 mg) were administered, we observed a significant change in blood lipid levels, especially a plasma LDL-c reduction. The assessment of the lipid profile (Table 2) pre and post-tea and pre and post-placebo showed that with tea intake there was a reduction in total cholesterol (3.9%) (p=0.006) and in LDL (4.5%) (p=0.026). A non-significant reduction in HDL (2.1%) (p=0.218) and non-significant increase in TG (7.5%) (p=0.807) and Apo-B (4.4%) (p=0.180) were also observed. With placebo, there was a non-significant reduction in total cholesterol (2.6%) (p=0.168), LDL (1.8%) (p=0.396), HDL (4.2%) (p=0.080) and Apo-B (0.8%) (p=0.677), and a non-significant increase in TG (1.9%) (p=0.733).

As regards the effects of diet intervention, after 16 weeks of treatment the nutritional needs were adequate to the recommendations and the eating changes obtained when under diet had an influence on the consumption of fats, especially on a significant reduction of saturated fatty acids. These values are shown in Table 3.

Table 2 – Comparison of the lipid profile pre and post-tea and pre and post-placebo

DATA	Mean ± SD	(Minimum - Maximum)	p
Total Cholesterol			
Pre Tea	246.5 ± 35.5	(177.0 - 327.0)	0.006
Post Tea	235.3 ± 28.9	(181.0 - 299.0)	
Pre Placebo	245.6 ± 26.4	(181.0 - 299.0)	0.168
Post Placebo	237.5 ± 27.8	(170.0 - 281.0)	
LDL–cholesterol			
Pre Tea	155.0 ± 31.4	(89.2 - 235.0)	0.026
Post Tea	145.7 ± 25.6	(90.0 - 190.2)	
Pre Placebo	151.2 ± 22.1	(97.6 - 193.0)	0.396
Post Placebo	147.1 ± 26.1	(73.2 - 188.2)	
HDL–cholesterol			
Pre Tea	57.6 ± 7.1	(36.0 - 67.0)	0.218
Post Tea	56.1 ± 8.4	(40.0 - 77.0)	
Pre Placebo	59.1 ± 8.2	(47.0 - 85.0)	0.080
Post Placebo	56.1 ± 8.5	(36.0 - 85.0)	
Triglycerides			
Pre Tea	165.8 ± 66.6	(84.0 - 342.0)	0.807
Post Tea	168.2 ± 61.4	(69.0 - 327.0)	
Pre Placebo	172.4 ± 61.5	(72.0 - 327.0)	0.733
Post Placebo	168.8 ± 67.5	(58.0 - 294.0)	
APO-B			
Pre Tea	116.0 ± 23.2	(73.0 - 152.0)	0.180
Post Tea	119.7 ± 21.9	(81.3 - 159.0)	
Pre Placebo	123.9 ± 17.2	(92.5 - 159.0)	0.677
Post Placebo	122.3 ± 21.8	(73.0 - 152.0)	

(1) Student's t test – paired data, and non-parametric Wilcoxon test for triglycerides.

Table 3 – **Diet changes obtained after nutrition advice.**

Food consumption	Mean ± SD	(Minimum-Maximum)	p
Calories (cal)			
Pre Advice	2010.1 ± 315.8	(1469.5 - 2621.3)	< 0.0001
Post Advice	1502.5 ± 133.3	(1231.3 - 1796.4)	
Carbohydrates (CH) (%)			
Pre Advice	44.0 ± 7.3	(25.8 - 57.4)	0.039
Post Advice	47.7 ± 7.5	(32.3 - 59.0)	
Proteins (PTN) (%)			
Pre Advice	15.2 ± 3.7	(6.8 - 25.6)	< 0.0001
Post Advice	23.5 ± 5.5	(15.0 - 35.0)	
Total Fat (%)			
Pre Advice	40.9 ± 10.1	(21.8 - 62.3)	< 0.0001
Post Advice	28.8 ± 9.4	(18.2 - 52.3)	
Monounsaturated Fatty Acids (%)			
Pre Advice	12.5 ± 4.0	(5.9 - 21.5)	< 0.0001
Post Advice	8.0 ± 2.8	(4.7 - 15.8)	
Polyunsaturated Fatty Acids (%)			
Pre Advice	17.5 ± 5.2	(7.1 - 29.3)	0.148
Post Advice	15.8 ± 5.1	(10.4 - 26.4)	
Saturated Fatty Acids (%)			
Pre Advice	10.8 ± 5.4	(3.7 - 24.9)	< 0.0001
Post Advice	5.0 ± 1.8	(2.9 - 10.1)	
Cholesterol (mg)			
Pre Advice	247.3 ± 174.4	(63.8 - 581.7)	< 0.0001
Post Advice	107.1 ± 27.7	(44.4 - 174.2)	
Fibers (g)			

Discussion

Dyslipidemias are among the major risk factors for atherosclerotic cardiovascular diseases. Several studies have shown that the fight against dyslipidemias brings benefits to patients at different cardiovascular risks, and that by reducing hypercholesterolemia increasingly more beneficial effects on the reduction of coronary events are provided[17-27]. With these studies, significant advances were obtained concerning the knowledge and control of dyslipidemias.

The treatment program recommended for dyslipidemias is based on blood lipid level monitoring and on the adoption of interventions on lifestyle, which include healthy eating habits, maintenance of the ideal weight, regular physical activity, and fight against cigarette smoking. Diet intervention is the first approach in the treatment of dyslipidemias, and should be maintained even when drug therapy is required[28-30].

The American Heart Association stresses the use of a diet including a variety of fruits, vegetables and grains, because these foods may reduce the risk of cardiovascular diseases by providing the vitamins, antioxidant nutrients (flavonoids), phytochemicals and fibers they contain[16].

In the present study, with the diet intervention adopted we could evaluate the effects of green tea together with a diet following the recommendations of the American Heart Association and of the National Program of Education on Cholesterol[30], without the interference from the variation of other diet nutrients or components.

In order to include green tea in the diet as a double-blind intervention, we could not introduce it as a beverage, because of the difficulty in monitoring its preparation and the amount ingested. Thus, it was necessary to administer it in the form of capsules, in an amount equivalent to four tea cups (150mL) per day.

In this study, after the interventions, the mean lipid changes induced by the use of green tea (*Camellia sinensis*) showed a reduction by 3.9% (p=0.006) in total cholesterol concentrations and a reduction by 4.5% (p=0.026) in LDL-cholesterol. This amount of green tea consumed did not significantly influence the levels of HDL-c, triglycerides and Apo-B. The absence of a significant change in Apo-B, which did not follow the LDL-c reduction, was particularly noteworthy. We believe that this can be explained by the small number of patients and the short follow-up period; this difference could not be observed with a sample of this size. From the biochemical point of view, a hypothesis to justify the absence of a significant change in Apo-B levels could be the fact that the Apo-B percentage in low-density lipoproteins is lower than that of LDL-cholesterol, so the change was not significant in this small sample. No significant differences were found in lipid levels with the use of placebo.

Although this study included a relatively small number of volunteers, our results corroborate those of the first clinical experiment in humans conducted by Maron et al in 2003[13], which assessed 240 hospitalized individuals with dyslipidemias in China. The researchers demonstrated in a double-blind, placebo-controlled study that the patients who had taken capsules containing tea extract for 12 weeks showed a reduction by 11.3% in total cholesterol levels and by 16% in LDL-cholesterol levels.

In another study similar to ours, Davies et al[31] assessed the effect of green tea on 15 adult volunteers with mild hypercholesterolemia, who also received a step I-type diet, as described by the American Heart Association and by the National Cholesterol Education Program. After three weeks of treatment, the investigators found that five cups of tea per day reduced total cholesterol by 6.5% and LDL-cholesterol by 11.1% in comparison to placebo beverages. These findings were similar to those verified in our study.

In another double-blind study conducted in 2003, Kajimoto et al[32] showed that treatment with an intake of 395 mg/day of green tea significantly reduced total cholesterol levels after eight weeks of treatment in patients with moderate hypercholesterolemia: this was not observed in the placebo group. More recently, in a study with a different design also conducted by Kajimoto[33], the treatment with higher tea doses (666 mg/day) produced additional reductions in total cholesterol in comparison to the group consuming 444 mg/day, but both groups showed significant reductions in total cholesterol and LDL-cholesterol.

In Tokunga et al's study[4] conducted in 2002 with 13,916 Japanese individuals, green tea consumption was associated with a reduction in serum cholesterol levels when the total intake was higher than 10 cups per day. However, when correlated with lifestyle aspects of the population (smoking, use of coffee and alcohol), BMI and age, reduction in cholesterol had already been observed with the ingestion of only one cup of tea per day.

Other studies showed the beneficial effect of tea on reducing the incidence of cardiovascular diseases[32,34].

Although our results showed that green tea intake as part of the diet contributed to a reduction in blood lipids, it was not possible to evaluate the mechanisms through which flavonoids produce this effect. However, this was not the objective of our research.

Also, another benefit attributed to tea consumption was related to the anthropometric parameters: weight loss by 1.7% (p=0.002) and BMI reduction by 1.7% (p=0.002) were observed. In the placebo group, the variation was significant, although smaller: weight loss by 1.1% (p=0.041) and BMI reduction by 1.1% (p=0.047).

Weight control is an important factor especially in patients with cardiovascular risks. Two important studies evaluated the thermogenic effect of tea in humans. In 1999, Dulloo et al[35] reported the effect of green tea extract containing caffeine and polyphenols, showing an increased 24-hour energy expenditure and fat oxidation in healthy young people. An equivalent dose of caffeine did not produce the same effect, and the researchers suggested that tea polyphenols were accountable for that effect.

In another study, Chantre and Lairon[36] also demonstrated that green tea caused weight loss and attributed this effect to increased thermogenesis. After a 3-month intervention, a reduction of waist circumference by 4.48% and of weight by 4.6% was observed.

Regarding the other diet components, after 16 weeks of treatment, the nutritional requirements were adequate to the NCEP – ATP III recommendations[15]. Eating changes obtained with diet had an influence on fat consumption, especially regarding the reduction of saturated fatty acids. There was a very significant reduction of total calorie intake (p=0.0001), reduction in the consumption of total fat, saturated fat, and cholesterol (p=0.0001), and increase in fiber consumption (p=0.0001). We also observed increased protein consumption (p=0.0001). These changes could be explained by the restriction in fatty foods (beef and derivatives, trans fat and fried food in general), which were replaced by other sources including the group of milk and skim milk products, as well as soy protein.

The potential of flavonoids in the prevention of cardiovascular diseases has become increasingly clearer. Their biologically active substances have a reductant effect on LDL-cholesterol, comparable to or greater than that obtained with low saturated fat and cholesterol diets. Although there are no randomized clinical trials demonstrating that these vegetable substances reduce cardiovascular morbidity and mortality, it is believed that these foods could be regularly included in a cardioprotective diet.

Conclusion

These findings show benefits of green tea (*Camellia Sinensis*), in concordance with previous studies of the literature. However, further investigations with a greater number of patients and longer follow-up periods are necessary to validate our initial observations.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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References

1. Korolkovas A. A riqueza potencial de nossa flora. Rev Bras Farmacognosia. 1996; 1: 1-7.
2. Rates SMK. Plants as source of drugs. Toxicon. 2001; 39: 603-13.
3. Maron DJ, Sibilo GL, Sheng CN, Swu ZG, Li YH, Chen H, et al. Cholesterol-lowering effect of a theaflavin-enriched green tea extract: a randomized controlled trial. Arch Intern Med. 2003; 163: 1448-53.
4. Tokunaga S, White IR, Frost C, Tanaka K, Kono S. Green tea consumption and serum lipids and lipoproteins in a population of healthy workers in Japan. Ann Epidemiol. 2002; 12: 157-65.
5. Hertog MG, Kromhout D, Aravanis C, Blackburn H, Buzina R, Fidanza F, et al. Flavonoid intake and long-term risk of coronary heart disease and cancer in the seven countries study. Arch Intern Med. 1995; 155 (4): 381-6.
6. Mukamal KJ, Maclure M, Muller JE. Tea consumption and mortality after acute myocardial infarction. Circulation. 2002; 105: 2476-81.
7. Hodgson JM, Puddey IB, Croft KD. Acute effects of ingestion of black and green tea on lipoprotein oxidation. Am J Clin Nutr. 2000; 71 (5): 1103-7.
8. Leung LK, Su RCY, Zesheng Z, Huang Y, Chen ZY. Theaflavins in black and catechins in green tea are equally effective antioxidants. J Nutr. 2001; 131: 2248-51.
9. Hodgson JM, Croft KD, Mori TA, Burke V, Beilin LJ, Puddley IB. Regular ingestion of tea does not inhibit in vivo lipid peroxidation in humans. J Nutr. 2002; 132: 55-8.
10. Duffy SJ, Vita JA, Holbrook M, Swerdloff PL, Keaney JF Jr. Effect of acute and chronic tea consumption on platelet aggregation in patients with coronary artery disease. Arterioscler Thromb Vasc Biol. 2001; 21 (6): 1084-9.
11. Simin L, Manson JAE, Lee IM, Cole SR, Hennekens CH, Willett WC, et al. Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. Am J Clin Nutr. 2000; 72: 922-8.
12. Siddiqui IA, Afaq F, Adhami VM, Ahmad N, Mukhtar H. Antioxidants of the beverage tea in promotion of human health. Antioxid Redox Signal. 2004; 6 (3): 571-82.
13. Chopra D. The Chopra Center Herbal Handbook. USA: Three Rivers Press; 2000.
14. Ody P. The Herb Society's complete medicinal herbal. London: Dorling Kindersley; 1993.
15. Sociedade Brasileira de Cardiologia. Sociedade Brasileira de Hipertensão. V Diretrizes Brasileiras de Hipertensão arterial. 2006. (on line). [acesso em 2007 setembro 10]. Disponível em: http://publicacoes.cardiol.br/consenso/2006/VDiretriz-HA.pdf
16. Third Report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) National Cholesterol Education Program (NCEP). Expert panel on Detection, Evaluation and Treatment of High Blood Cholesterol in adults. Circulation. 2002; 106 (25): 3143-421.
17. Santos RD, Spósito AC, Santos JE, Fonseca FH, Moriguchi EH, Martinez TLR, et al. Programa de avaliação nacional do conhecimento sobre prevenção da aterosclerose (PANDORA): como tem sido feito o tratamento das dislipidemias pelos médicos brasileiros. Arq Bras Cardiol. 2000; 75: 289-95.
18. Santos Filho RD, Martinez TLR. Fatores de risco para doença cardiovascular: velhos e novos fatores de risco, velhos problemas! Arq Bras Endocrinol Metab. 2002; 46 (3): 212-4.
19. Castelli WP. Cholesterol and lipids in the risk of coronary artery disease: the Framingham Heart Study. Can J Cardiol. 1998; 4 (Suppl A): 5A-10A.
20. Server PS, Dahlof B, Poulter NR, Wedel H, Beevers G, Caulfield M, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. Lancet. 2003; 361: 1149-58.
21. Kannel WB, Castelli WP, Gordon T. Serum cholesterol lipoproteins and of coronary heart disease: the Framinghan study. Ann Int Med. 1971; 74: 1-12.
22. Assmann G, Schulte H. Results and conclusions of the Prospective Cardiovascular Münster (PROCAM) Study. In: Assmann G. (ed). Lipid metabolism disorders and coronary heart disease. 2nd. ed. Stuttgart: FK Schattauer; 1993.
23. Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, et al. For the AFCAPS/TexCAPS Research Group. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. JAMA. 1998; 279: 1615-22.
24. The Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4,444 patients with coronary heart disease: the Scandinavian Simvatatin Survival Study (4S). Lancet. 1994; 344: 1383-9.
25. Shepherd J, Blauw GJ, Murphy MB. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. PROspective Study of Pravastatin in the Elderly at Risk. Lancet. 2002; 360: 1623-30.
26. MRC/BHF heart protection study of cholesterol lowering with sinvastatin in 20536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 2002; 360: 7-22.
27. Grundy SM. Slide Atlas of lipid disorders. 3rd. ed. New York: Gower Medical Publishing; 1990.
28. Kannel WB, Wilson PW, Nam BH, D'Agostino RB. Risk stratification of obesity as a coronary risk factor. Am J Cardiol. 2002; 90: 697-701.
29. Scott M, Grundy SM. Obesity, metabolic syndrome, and coronary atherosclerosis. Circulation. 2002; 105 (23): 2696-8.
30. Krause MV, Mahan LK. (eds.). Alimentos, nutrição e dietoterapia. 10ª ed. São Paulo: Roca; 2002.

31. Davies MJ, Judd JT, Baer DJ, Clevidence BA, Paul DR, Edwards AJ, et al. Black tea consumption reduces total and LDL cholesterol in mildly hypercholesterolemic adults. J Nutr. 2003; 133: 3298S-3302S.

32. Kajimoto O, Kajimoto Y, Yabune M, Nozawa A, Nagata K, Kakuda T. Tea catechins reduce serum cholesterol levels in mild borderline hypercholesterolemic patients. J Clin Biochem Nutr. 2003; 33: 101-11.

33. Kajimoto O, Kajimoto Y, Yabune M, Nakamura T, Kotani K, Suzuki Y, et al. Tea catechins with a galloyl moiety reduce body weight and fat. J Health Sci. 2005; 51: 161-71.

34. Geleijnse JM, Launer LJ, Van der Kuip DA, Hofman A, Witteman JC. Inverse association of tea and flavonoid intakes with incident myocardial infarction: the Rotterdam Study. Am J Clin Nutr. 2002; 75 (5): 880-6.

35. Dulloo AG, Duret C, Rohrer D, Girardier L, Mensi N, Fathi M, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. Am J Clin Nutr. 1999; 70: 1040-5.

36. Chantre P, Lairon D. Recent findings of green tea extract AR25 (Exolise) and its activity for the treatment of obesity. Phytomedicine. 2002; 9 (1): 3-8.