Nutrition xxx (2013) 1–5

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: A clinical trial

Telma A.F. Corrêa Ph.D. [a], Marcelo M. Rogero Ph.D. [a], Bruno M. Mioto B.D. [b], Daniela Tarasoutchi B.S. [b], Vera L. Tuda B.S. [b], Luiz A.M. César Ph.D. [b], Elizabeth A.F.S. Torres Ph.D. [a,*]

[a] Department of Nutrition, School of Public Health, University of São Paulo, São Paulo, Brazil
[b] The Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 6 September 2012
Accepted 6 January 2013

Keywords:
Antioxidants
Cardiovascular disease
Cholesterol
Coffee
Endothelial dysfunction
Inflammation
Risk factors

ABSTRACT

Objective: The aim of this study was to compare the effects of medium light roast (MLR) and medium roast (MR) paper-filtered coffee on cardiovascular risk factors in healthy volunteers.
Methods: This randomized crossover trial compared the effects of consuming three or four cups (150 mL) of MLR or MR coffee per day for 4 wk in 20 healthy volunteers. Plasma lipids, lipoprotein(a) (Lp[a]), total homocysteine, and endothelial dysfunction–related inflammation biomarkers, serum glycemic biomarkers, and blood pressure were measured at baseline and after each intervention.
Results: Both roasts increased plasma total cholesterol, low-density lipoprotein-cholesterol, and soluble vascular cell adhesion molecule-1 (sVCAM-1) concentrations (10%, 12%, and 18% for MLR; 12%, 14%, and 14% for MR, respectively) ($P < 0.05$). MR also increased high-density lipoportein-cholesterol concentration by 7% ($P = 0.003$). Plasma fibrinogen concentration increased 8% after MR intake ($P = 0.01$), and soluble E-selectin increased 12% after MLR intake ($P = 0.02$). No changes were observed for Lp(a), total homocysteine, glycemic biomarkers, and blood pressure.
Conclusion: Moderate paper-filtered coffee consumption may have an undesirable effect on plasma cholesterol and inflammation biomarkers in healthy individuals regardless of its antioxidant content.

© 2013 Elsevier Inc. All rights reserved.

Introduction

Dyslipidemia, hypertension, diabetes or glucose intolerance, and obesity are associated with a marked increase in vascular reactive oxygen species (ROS) production, which play important roles in atherosclerosis, diabetes, and cardiovascular diseases (CVD). It should be highlighted that ROS are involved in endothelial dysfunction, monocyte migration, low-density lipoprotein-cholesterol (LDL-C) oxidation, and vascular smooth muscle cell growth. ROS induce the expression of vascular cell adhesion molecule-1 (VCAM-1) and monocyte chemoattractant protein-1 (MCP-1) on the endothelial cell surface.

Coffee is consumed as a beverage worldwide; however, its effect as a cardiovascular risk factor is still controversial [1–3]. Roasted coffee contains naturally present antioxidants and others that are formed during the roasting process [4]. Chlorogenic acids (CGA) and caffeine have been extensively studied because they may play a role in the inhibition of lipid peroxidation, free radical scavenging, metal chelation, and anti-inflammatory activity. They also may reduce the risk for development and progression of atherosclerosis [5] and insulin resistance [6,7], and they may decrease blood pressure (BP) [8,9]. Coffee contains diterpenes, cafestol, and kahweol, which have a cholesterol-raising effect. However, most of them are retained by the paper filter, which substantially reduces the cholesterol-raising effects potentially associated with coffee [10,11].

Epidemiologic studies have indicated that regular coffee consumption is associated with a lower risk for CVD [3,12,13]. However, the coffee compounds responsible for the suggestive

TAFC contributed to the study design, data collection, analysis, and interpretation, and wrote the manuscript. MMR contributed to study design, data analysis, and interpretation. BMM, DT, and VLT contributed to the study design and data collection. LAMC and EAFST contributed to study design, data analysis, and interpretation. All authors read and approved the final manuscript and none of the authors have a conflict of interest.

* Corresponding author. Tel.: 55-11-3061-7857; fax: 55-11-3061-7130.
E-mail address: eatorres@usp.br (E. A. F. S. Torres).

0899-9007/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.nut.2013.01.003

Please cite this article in press as: Corrêa TA, et al., Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: A clinical trial, Nutrition (2013), http://dx.doi.org/10.1016/j.nut.2013.01.003

ARTICLE IN PRESS

protective effects are still unknown [1]. The data related to the effect of coffee on inflammation are conflicting, showing that coffee consumption by healthy individuals can be either directly [14], inversely [4], or not associated with proinflammatory biomarkers [15]. Therefore, we compared the effects of ingesting medium light roast (MLR) or medium roast (MR) filtered coffee in plasma lipids, total homocysteine (tHcy), endothelial dysfunction–related inflammation biomarkers, glycemic biomarkers, and BP in healthy volunteers.

Participants and methods

Participants

Twenty-two healthy and habitual coffee drinkers were recruited and gave informed consent. This study was approved by the School of Public Health of São Paulo University Review Board and registered as a clinical trial (ACTRN12609001064291). Eligibility criteria were age 20 y to 65 y, plasma cholesterol <6.21 mmol/L, blood glucose <5.56 mmol/L, nonsmoker or former smoker (>2 y), alcohol consumption less than one drink per day, absence of chronic diseases, and no use of regular medication. Two subjects declined participation, one could not attend the meetings, and one consumed coffee during the washout period. Twenty healthy participants (14 women) were evaluated (Fig. 1).

Study design

This randomized, crossover clinical trial lasted 9 wk. After a 1-week run-in, participants consumed MLR or MR paper-filtered coffee for 4 wk and then switched to the other roast for an additional 4 wk.

Participants were asked to make no changes in their diet or lifestyle. We questioned physical activity of the participants in the baseline interview and after each intervention period. A 3-d food diary (2 d during the week and 1 d on the weekend) was collected before baseline and during each intervention to control for possible confounding factors and check for compliance with dietary instructions.

Coffee samples and beverage preparation

Two commercially available blends (80% *Coffea arabica* L. cv. Bourbon and 20% *C. canephora* cv. Robusta) of caffeinated, roasted, ground coffee were used in the study. Both coffees were cultivated in the same geographic region. They were vacuum packed in 500-g aluminized bags. Roasting degree classification was done according to the "Roast Color Classification System" (Agtron/SCAA, Reno, NV, 1995). Coffee packages and paper filters (Classic n° 102) were provided by Melitta do Brasil Indústria e Comércio Ltda, São Paulo, Brazil. Coffee was distributed to participants in 500-g packages at the beginning of each intervention period. Subjects were instructed on how to prepare the beverage (15 g of coffee/150 mL cup) in a household coffee maker by filtering through paper, and to consume the total daily amount in three of four separate cups without a fixed schedule.

Coffee beverages were prepared as instructed to the participants for the analysis of the antioxidant content and diterpenes. CGA and caffeine were determined by high-performance liquid chromatography (HPLC) with diode-array detector (DAD) and mass spectrometer [16]. Cafestol and kahweol were determined in the unsaponified matter by HPLC with DAD [17].

Blood collection and biomarker assessment

At baseline, and at the end of each intervention, venous blood samples were taken after a 12-h overnight fast and centrifuged for plasma separation. Plasma samples were stored at −80°C for inflammation biomarker analyses.

Plasma concentrations of total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), and triacylglycerol were measured by enzymatic assays on a Dimension RXL (Siemens Healthcare Diagnostics Deerfield, IL, USA). LDL-C was calculated according to the Friedewald formula [18]. Plasma lipoprotein(a) (Lp[a]) concentration was assessed by immunonephelometric assay on a BN II analyzer (Siemens Healthcare Diagnostics, Marburg, Germany). Plasma tHcy concentration was measured by a chemiluminescence immunoassay on an Immulite 2000 Analyzer (Diagnostic Products Corporation, Los Angeles, CA, USA).

Fasting serum glucose concentration was determined by a commercial kit (Siemens Healthcare Diagnostics, Marburg, Germany). Blood-glycated hemoglobin and frutosamine were measured by immunoturbidimetric and colorimetric assays, respectively. Fasting serum insulin concentration was determined by a chemiluminescence assay. These analyses were performed by use of an automated analyzer (Dimension RXL, Siemens Healthcare Diagnostics, Llanberis, Gwynedd, UK). Insulin resistance was estimated by Homeostasis Model Assessment for insulin resistance [19,20].

Plasma fibrinogen concentrations were measured by the Clauss method [21] on a Destiny Max (MedLab) and high-sensitivity C-reactive protein (hs-CRP) concentration by use of a high-sensitivity latex-enhanced immunonephelometric assay on BN II analyzer (Siemens Diagnostics). Interleukin (IL)-1β, IL-6, tumor necrosis factor (TNF)-α, MCP-1, soluble E-selectin (sE-selectin), sVCAM-1, soluble intercellular adhesion molecule-1 (sICAM-1), and tissue-type plasminogen activator inhibitor-1 (PAI-1) were quantified by bead-based multiplex Luminex xMAP technology assays (Millipore, Missouri, USA) on a Luminex 200 analyzer (Luminex Corporation, Austin, TX, USA).

Assessment of other measurements

Weight, height, abdominal circumference, and body fat were measured after the washout period and after each intervention. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). Body fat percentage was measured by bipolar impedance on a portable electronic scale (Plenna, São Paulo, Brazil).

BP was measured by ambulatory BP monitoring, using a 90207 portable monitor (Spacelabs Healthcare, Washington, USA), scheduled for six measurements during the day (between 0700 and 2200) and three at night (between 2200 and 0700).

Statistical analysis

The results are expressed as means ± SD. CGA, caffeine, and diterpenes content of the two coffee beverages were compared by *t* test for independent samples. Differences in biomarker concentrations were analyzed by paired *t* test (glucose biomarkers) or by repeated-measures analysis of variance (ANOVA) for comparisons of MLR coffee intake with MR and of each roast with the baseline. Variables that were not normally distributed (Lp[a], fasting glucose, diastolic BP and heart rate) were submitted to the logarithmic transformation and analyzed by repeated-measures ANOVA. Evaluation of the two groups' mean profile was carried out to measure the effects of the MLR and MR order of consumption and possible carryover effect. All analyses were performed using SPSS 18.0 (SPSS Inc., Chicago, IL, USA). A two-tailed $P < 0.05$ was considered significant.

Results

Participants

Twenty healthy individuals (49 ± 9 y, range 37–63 y) were evaluated. Table 1 shows their baseline characteristics. Most participants were women (70%) and overweight (76%).

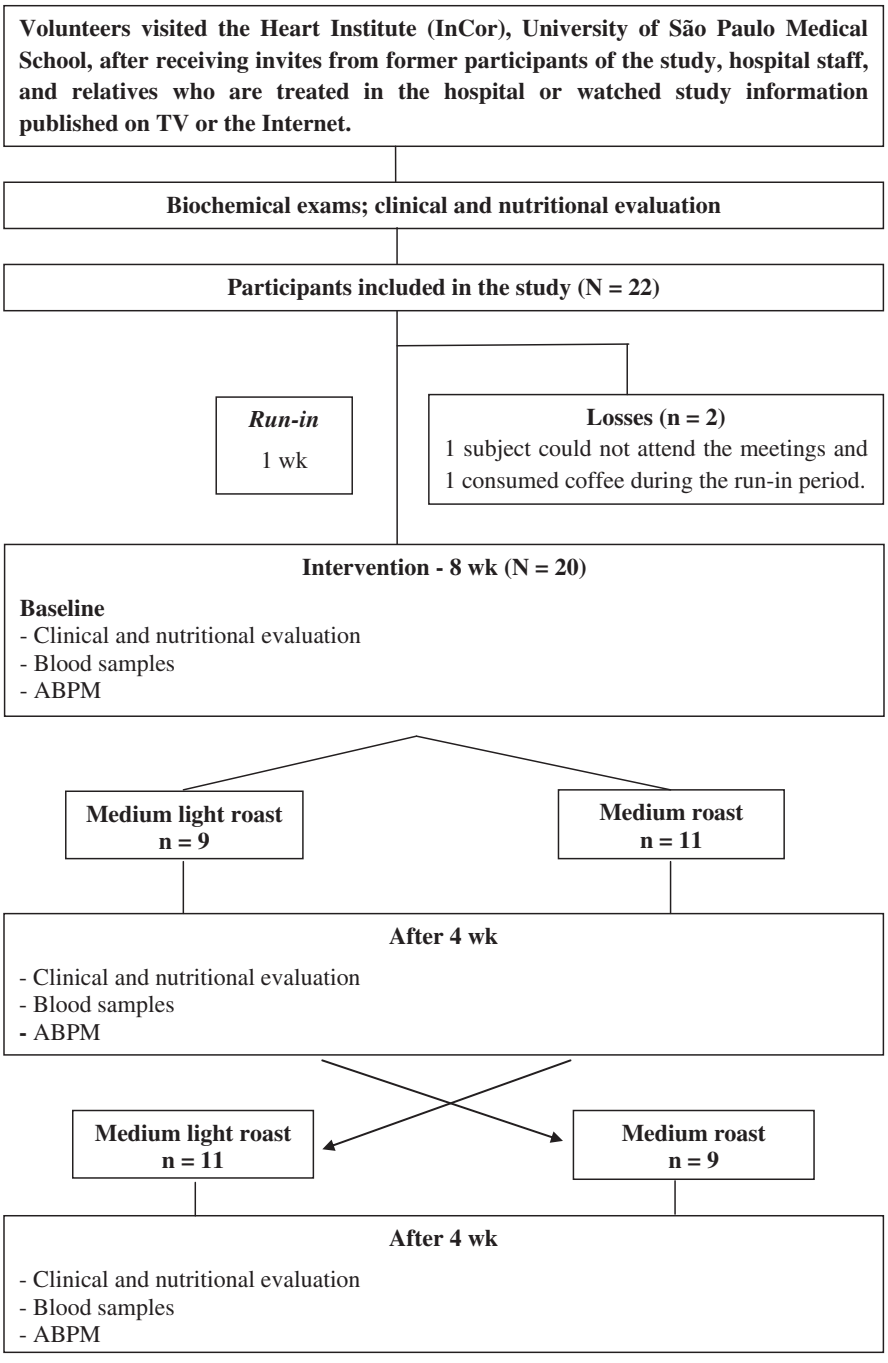
During the first 4-wk intervention period, 45% of the participants (55.6% women) ingested MLR coffee and 55% (81.8% women) MR coffee. In the next 4-wk period, they switched to the opposite roast coffee. Coffee consumption was 482 ± 61 mL/d throughout the study. Coffee provided 334 mg of CGA per cup in MLR and 210 mg per cup in MR ($P < 0.001$) and 231 mg of caffeine per cup in MLR and 244 mg per cup in MR ($P = 0.003$). The mean concentrations of cafestol and kahweol were 5.36 mg and 0.79 mg per cup in MLR and 6.30 mg and 0.51 mg per cup in MR, respectively. MLR provided more CGA and kahweol and less caffeine, cafestol, and melanoidins ($P < 0.001$) than MR.

Self-reported diets showed that none of the participants consumed a significant amount of polyphenol-rich foods other than coffee during the study and the nutritional intake was similar before and after each intervention period for all participants ($P > 0.05$). Additionally, we found no significant differences in physical activity, body composition, and BP throughout the study (data not shown).

Cardiovascular risk biomarkers

Table 2 shows a significant increase in TC and LDL-C after intake of each coffee roast compared with the baseline. TC concentrations increased 0.46 mmol/L after MLR ($P < 0.01$) and 0.59 mmol/L after MR ($P < 0.001$). LDL-C increased 0.36 mmol/L

Please cite this article in press as: Corrêa TA, et al., Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: A clinical trial, Nutrition (2013), http://dx.doi.org/10.1016/j.nut.2013.01.003



ABPM, ambulatory blood pressure monitoring

Fig. 1. Flowchart of the study. The flowchart shows a randomized crossover clinical trial.

and 0.44 mmol/L after MLR ($P < 0.01$) and MR ($P < 0.001$), respectively. HDL-C increased 0.09 mmol/L after MR intake ($P < 0.01$). We observed no difference in TC and LDL-C between the two intervention periods. However, there was an increase of 0.04 mmol/L in HDL-C after MR intake in relation to MLR ($P = 0.04$). Plasma triacylglycerols increased, but not significantly.

No significant effect of the two coffee roasts was observed on plasma Lp(a), tHcy, or serum glycemic biomarkers (data not shown).

We observed an 8% increase in plasma fibrinogen concentration after MR intake ($P < 0.01$) and 12% in sE-selectin after consumption of MLR ($P < 0.05$). Fibrinogen increased after MLR and sE-selectin increased after MR, but these were not significant. Fibrinogen concentration also increased 6.5% after MR in relation to MLR ($P = 0.02$). Plasma sVCAM-1 increased 18% and 14% after MLR ($P < 0.001$) and MR ($P < 0.05$), respectively (Table 2). No significant changes were found for hs-CRP, IL-1β, IL-6, TNF-α, MCP-1, sICAM-1, and tPAI-1.

Discussion

We observed an increase in HDL-C after MR consumption, which is of great relevance, as this particle has been recognized as an anti-atherogenic. Some proposed mechanisms for this

Please cite this article in press as: Corrêa TA, et al., Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: A clinical trial, Nutrition (2013), http://dx.doi.org/10.1016/j.nut.2013.01.003

Table 1
Baseline characteristics of the participants (N = 20)

Gender (male/female, n)	6/14
Age (y)	49.5 ± 8.9
BMI (kg/m^2)	27.0 ± 3.8
Body fat (male/female, %)	29.1 ± 3.0/37.5 ± 4.2
Abdominal circumference (male/female, cm)	98.7 ± 4.9/92.8± 9.0
Lipoprotein(a) (mg/dL)	21.6 ± 26.5
Total homocysteine (μmol/L)	9.2 ± 3.0
Fasting glucose (mmol/L)	4.8 ± 0.6
Glycated hemoglobin (%)	5.5 ± 0.3
Frutosamine (μmol/L)	226.6 ± 12.7
Fasting insulin (μU/mL)	3.6 ± 3.4
HOMA-IR	0.8 ± 0.8
24-h blood pressure averages (mm Hg)	
Systolic	110.2 ± 9.7
Diastolic	70.5 ± 6.9
24-h heart rate averages (beats/min)	77.2 ± 10.1
Habitual coffee consumption (mL/d)	307 ± 110
Energy intake (kcal/d)	1831 ± 535
Carbohydrate (% energy)	52.2 ± 9.2
Protein (% energy)	19.9 ± 6.3
Total fat (% energy)	27.8 ± 8.5.9
Cholesterol (mg/d)	157.3 ± 71
Family history of CVDs (%)	30

BMI, body mass index; CVD, cardiovascular disease; HOMA-IR, Homeostasis Model Assessment for insulin resistance
Data expressed as mean ± standard deviation, numbers or %

protective action are reverse cholesterol transport, inhibition of LDL-C oxidation, blood viscosity reduction, regulation of prostaglandins and thromboxane synthesis, activation of fibrinolysis, inhibition of adhesion molecules and monocytes to endothelium, and stimulation of nitric oxide release [22].

TC and LDL-C concentrations increased after consumption of each coffee roast compared with baseline. However, there was no significant change in these lipids between the coffee roasts, indicating that the roasting degree is not related to an increase in these lipid concentrations. Data on the effects of filtered coffee intake on plasma lipids are still limited and contradictory [23]. Increased plasma TC and LDL-C are more pronounced with unfiltered coffee, whereas paper-filtered coffee has been less frequently reported to raise these lipids [6].

Table 2
Lipid profile and inflammation biomarkers at baseline and after intake of each roast of filtered coffee

Biomarkers	Baseline	MLR	MR
Lipids			
TC (mmol/L)	4.8 ± 0.6	5.3 ± 0.9*	5.4 ± 0.8†
HDL-C (mmol/L)	1.2 ± 0.3	1.3 ± 0.3	1.3 ± 0.2*,§
LDL-C (mmol/L)	3.1 ± 0.5	3.4 ± 0.7*	3.5 ± 0.7†
Triacilglycerols (mmol/L)	1.1 ± 0.4	1.2 ± 0.5	1.2 ± 0.6
Inflammation biomarkers			
Fibrinogen (mg/dL)	357.1 ± 48.3	362.3 ± 67.8	385.8 ± 67.7*,§
sE-selectin (pg/mL)	33.6 ± 11.9	37.7 ± 14.8‡	34.4 ± 11.6
sVCAM-1 (pg/mL)	1049 ± 174	1235 ± 256†	1191 ± 299‡
hs-CRP (mg/L)	2.2 ± 2.1	2.1 ± 2.0	2.6 ± 2.2
IL-1β (pg/mL)	0.1 ± 0.2	0.1 ± 0.1	0.1 ± 0.2
IL-6 (pg/mL)	1.2 ± 0.8	1.7 ± 2.6	1.3 ± 1.2
TNF-α (pg/mL)	2.8 ± 1.4	3.3 ± 2.4	2.9 ± 2.0
MCP-1 (pg/mL)	75.4 ± 19.3	79.6 ± 15.7	80.1 ± 17.9
sICAM-1 (pg/mL)	220.5 ± 62.5	243.1 ± 91.7	237.6 ± 85.9
tPAI-1 (pg/mL)	54.6 ± 20.3	53.8 ± 20.1	54.1 ± 21.4

ANOVA, analysis of variance; hs-CRP, high-sensitivity C-reactive protein; IL-1β, interleukin-1 beta; IL-6, interleukin-6; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; MCP-1, monocyte chemoattractant protein-1; MLR, medium light roast; MR, medium roast; sICAM-1, soluble intercellular adhesion molecule-1; sVCAM-1, soluble vascular cell adhesion molecule-1; TC, total cholesterol; TNF-α, tumor necrosis factor-alpha; tPAI-1, total plasminogen activator inhibitor-1
Data expressed as means ± SD (n = 20).
* Significantly different from baseline (ANOVA of repeated measures): $P < 0.01$.
† Significantly different from baseline (ANOVA of repeated measures): $P < 0.001$.
‡ Significantly different from baseline (ANOVA of repeated measures): $P < 0.05$.
§ Significantly different from MLR (ANOVA of repeated measures): $P < 0.05$.

Cafestol levels obtained in this study were higher than those found for the paper-filtered coffee in other studies [17,24,25], which might explain the increase of plasma cholesterol concentrations observed. These findings are in agreement with studies that showed that diterpenes are only partly removed by the paper filter [10,11]. Several variables may influence the diterpenes content in the paper-filtered coffee such as coffee species, geographical distribution, roasting degree, grind sizes, extraction time and temperature, porosity of the paper filter, and coffee-to-water ratio [25,26]. An interesting fact that should be mentioned is that we did not find significant increase in triacylglycerols concentration, a cafestol consumption-related effect observed in some studies [25,27,28].

Cafestol has been reported to be the most potent cholesterol-raising compound of a coffee brew. The mechanism for the effect of cafestol on the increase of plasma cholesterol concentration remains unclear. However, Ricketts et al. [29] proposed a mechanism that could explain this effect. “Cafestol activates the nuclear hormone receptors pregnane X receptor (PXR) and farnesoid X receptor (FXR) in the small intestine. Then, PXR activates Cyp27A1 and ABCA1 expression, increasing the efflux of cholesterol to the liver. FXR activates the intestinal bile acid-binding protein (IBABP), a bile acid transporter, increasing the transportation of bile acids into the portal circulation. Both PXR and FXR induce fibroblast growth factor 15 (FGF15), which signals to the liver to inhibit bile acids synthesis. In the liver, FXR suppress the expression of Cyp7A1, Cyp8B1, and NTCP, reducing the synthesis of bile acids, increasing consequently the cholesterol concentrations.”

Previous studies [11,27] found significant increases in TC and LDL-C, but not in HDL-C, after coffee consumption. A few studies found a positive association between filtered coffee consumption and an increase in HDL-C concentration [4,30], as we did, which can counterbalance the deleterious effects of increased LDL-C.

We observed no significant change in glycemic biomarkers after the intervention periods. Another interventional trial [4] also observed no significant changes in these biomarkers after filtered coffee intake.

We observed a significant increase in plasma fibrinogen concentration after MR consumption. We also observed an increase in sE-selectin after MLR, and in sVCAM-1 after intake of each coffee roast, which suggests an inflammatory effect related to coffee consumption.

Several studies suggest that oxidized LDL stimulates the expression of adhesion molecules in endothelial cell surface [31]. However, in another study [32], we observed no significant changes in oxidized LDL after consumption of both coffee roasts. Fibrinogen concentration and adhesion molecule expression are positively correlated with TNF-α, hs-CRP, BMI, BP, and blood glucose [31,33]; however, these parameters did not change significantly in this study. To date, data on the relationship of coffee consumption and inflammation biomarkers are scarce and contrasting. One study found an increase [14] in inflammation biomarkers after coffee consumption for healthy individuals. Other studies have found no significant changes for the inflammation biomarkers evaluated in our study [4,15]. Coffee components responsible for the increase of these biomarkers are still unknown [4].

We observed no significant difference in lipid profile and inflammation biomarkers between 4 wk and 8 wk of coffee

Please cite this article in press as: Corrêa TA, et al., Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: A clinical trial, Nutrition (2013), http://dx.doi.org/10.1016/j.nut.2013.01.003

ARTICLE IN PRESS

consumption compared with the baseline. This finding suggests that the increase in lipids and inflammation biomarker concentration is an acute effect of coffee that is unrelated to a potential accumulative effect of longer periods of coffee consumption.

Our study has some limitations. First, it comprised a small sample size, which may be explained by its considerable participation period (9 wk) and the large coffee intake. Second, the fact that roasting degrees were similar also might constitute a limitation, but it should be noted that their antioxidant composition is different and that HDL and fibrinogen concentration increased only after MR intake and sE-selectin increased only after MLR intake. Finally, the absence of a run-in period between the interventions was a potential limitation. However, the statistical analysis showed that there was no carryover effect.

As strengths, this is the first interventional trial to show an increase in inflammation biomarkers of healthy individuals after coffee consumption and to compare the effects of two different coffee roasts on inflammation. Previous studies of the effect of coffee on inflammation markers were generally observational or cross-sectional studies [14,15]. One study was an interventional trial, but the amount of coffee consumed was three times higher than the amount used in our study and fewer proinflammatory markers were analyzed [4]. Additionally, our study analyzed several cardiovascular risk biomarkers.

Moderate filtered coffee consumption has undesirable effects on cholesterol and inflammation biomarkers in healthy individuals, regardless of its antioxidant content. More interventional trials and the evaluation of other coffee components are needed to clarify its effects on cardiovascular risk factors and to identify the main players associated with these effects.

Acknowledgments

We thank the following volunteers for their participation: Dr. Geni Sampaio for technical support, Julia Fukushima, M.S. for statistical support; FAPESP for financial support (Process 2009/05792-7) and for the student fellowship of TAFC (Process 2008/10933-6); National Council for Scientific and Technological Development (CNPq) for the research fellowship to EAFST; and Melitta for providing the roasted ground coffees and paper filters.

References

[1] Bohn SK, Ward NC, Hodgson JM, Croft KD. Effects of tea and coffee on cardiovascular disease risk. Food Funct 2012;3:575–91.
[2] Mineharu Y, Koizumi A, Wada Y, Iso H, Watanabe Y, Date C, et al. Coffee, green tea, black tea and oolong tea consumption and risk of mortality from cardiovascular disease in Japanese men and women. J Epidemiol Community Health 2011;65:230–40.
[3] de Koning Gans JM, Uiterwaal CSPM, van der Schouw YT, Boer J, Grobbee DE, Verschuren WM, et al. Tea and coffee consumption and cardiovascular morbidity and mortality. Arterioscler Thromb Vasc Biol 2010;30:1665–71.
[4] Kempf K, Herder C, Erlund I, Kolb H, Martin S, Carstensen M, et al. Effects of coffee consumption on subclinical inflammation and other risk factors for type 2 diabetes: a clinical trial. Am J Clin Nutr 2010;91:950–7.
[5] Butt MS, Sultan MT. Coffee and its consumption: benefits and risks. Crit Rev Food Sci Nutr 2011;51:363–73.
[6] Ranheim T, Halvorsen B. Coffee consumption and human health—beneficial or detrimental?—Mechanisms for effects of coffee consumption on different risk factors for cardiovascular disease and type 2 diabetes mellitus. Mol Nutr Food Res 2005;49:274–84.
[7] Van Dieren S, Uiterwaal CSPM, Van der Schouw YT, van der ADL, Boer JMA, Spijkerman A, et al. Coffee and tea consumption and risk of type 2 diabetes. Diabetologia 2009;52:2561–9.
[8] Yamaguchi T, Chikama A, Mori K, Watanabe T, Shioya Y, Katsuragi Y, et al. Hydroxyhydroquinone-free coffee: a double-blind, randomized controlled dose-response study of blood pressure. Nutr Metabol Cardiovasc Dis 2008;18:408–14.
[9] Medina-Remón A, Zamora-Ros R, Rotchés-Ribalta M, Andres-Lacueva C, Martínez-González MA, Covas MI, et al. Total polyphenol excretion and blood pressure in subjects at high cardiovascular risk. Nutr Metabol Cardiovasc Dis 2010;21:323–31.
[10] Thelle DS, Strandhagen E. Coffee and disease: an overview with main emphasis on blood lipids and homocysteine. Scand J Food Nutr 2005;49:50–61.
[11] Strandhagen E, Thelle DS. Filtered coffee raises serum cholesterol: results from a controlled study. Eur J Clin Nutr 2003;57:1164–8.
[12] Andersen LF, Jacobs DR, Carlsen MH, Blomhoff R. Consumption of coffee is associated with reduced risk of death attributed to inflammatory and cardiovascular diseases in the Iowa Women's Health Study. Am J Clin Nutr 2006;83:1039–46.
[13] Freedman ND, Park Y, Abnet CC, Hollenbeck AR, Sinha R. Association of coffee drinking with total and cause-specific mortality. N Engl J Med 2012;366:1891–904.
[14] Zampelas A, Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C. Associations between coffee consumption and inflammatory markers in healthy persons: the ATTICA study. Am J Clin Nutr 2004;80:862–7.
[15] Lopez-Garcia E, van Dam RM, Qi L, Hu FB. Coffee consumption and markers of inflammation and endothelial dysfunction in healthy and diabetic women. Am J Clin Nutr 2006;84:888–93.
[16] Jaiswal R, Patras MA, Eravuchira PJ, Kuhnert N. Profile and characterization of the chlorogenic acids in green robusta coffee beans by LC-MSn: identification of seven new classes of compounds. J Agric Food Chem 2010;58:8722–37.
[17] Silva JA, Borges N, Santos A, Alves A. Method validation for cafestol and kahweol quantification in coffee brews by HPLC-DAD. Food Anal Methods 2012;5:1404–10.
[18] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502.
[19] Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412–9.
[20] Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes care 2004;27:1487–95.
[21] Clauss A. Rapid physiological coagulation method in determination of fibrinogen. Acta Haematol 1957;17:237–46.
[22] NCEP. 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) Final Report. Circulation 2002;106:3143–421.
[23] Burke MF, Khera AV, Rader DJ. Polyphenols and cholesterol efflux is coffee the next red wine? Circ Res 2010;106:627–9.
[24] Sridevi V, Giridhar P, Ravishankar GA. Evaluation of roasting and brewing effect on antinutritional diterpenes-cafestol and kaweol in coffee. Global J Med Res 2011;11:17–22.
[25] Naidoo N, Chen C, Rebello SA, Speer K, Tai ES, Lee J, et al. Cholesterol-raising diterpenes in types of coffee commonly consumed in Singapore, Indonesia and India and associations with blood lipids: a survey and cross sectional study. Nutr J 2011;10:48.
[26] Zhang C, Linforth R, Fisk ID. Cafestol extraction yield from different coffee brew mechanisms. Food Res Int 2012;49:27–31.
[27] Jee SH, He J, Appel LJ, Whelton PK, Suh II, Klag MJ. Coffee consumption and serum lipids: a meta-analysis of randomized controlled clinical trials. Am J Epidemiol 2001;153:353–62.
[28] Cai L, Ma D, Zhang Y, Liu Z, Wang P. The effect of coffee consumption on serum lipids: a meta-analysis of randomized controlled trials. Eur J Clin Nutr 2012;66:872–7.
[29] Ricketts ML, Boekschoten MV, Kreeft AJ, Hooiveld GJEJ, Moen CJA, Müller M, et al. The cholesterol-raising factor from coffee beans, cafestol, as an agonist ligand for the farnesoid and pregnane X receptors. Mol Endocrinol 2007;21:1603–16.
[30] Fried RE, Levine DM, Kwiterovich PO, Diamond EL, Wilder LB, Moy TF, et al. The effect of filtered-coffee consumption on plasma lipid levels. JAMA 1992;267:811–5.
[31] Galkina E, Ley K. Vascular adhesion molecules in atherosclerosis. Arterioscler Thromb Vasc Biol 2007;27:2292–301.
[32] Corrêa TAF, Monteiro MP, Mendes TM, Oliveira DM, Rogero MM, Benites CI, et al. Medium light and medium roast paper-filtered coffee increased antioxidant capacity in healthy volunteers: results of a randomized trial. Plant Foods Hum Nutr 2012;67:277–82.
[33] Kaptoge S, White IR, Thompson SG, Wood AM, Lewington S, Lowe GD, et al. Associations of plasma fibrinogen levels with established cardiovascular disease risk factors, inflammatory markers, and other characteristics: individual participant meta-analysis of 154,211 adults in 31 prospective studies: the fibrinogen studies collaboration. Am J Epidemiol 2007;166:867–79.

Please cite this article in press as: Corrêa TA, et al., Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: A clinical trial, Nutrition (2013), http://dx.doi.org/10.1016/j.nut.2013.01.003