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### Mate Tea (*Ilex paraguariensis*) Improves Glycemic and Lipid Profiles of Type 2 Diabetes and Pre-Diabetes Individuals: A Pilot Study

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# Mate Tea (*Ilex paraguariensis*) Improves Glycemic and Lipid Profiles of Type 2 Diabetes and Pre-Diabetes Individuals: A Pilot Study

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**Key words:** diabetes mellitus, *Ilex paraguariensis*, mate tea, glycemic control, lipid profile, dietary counseling

**Objectives:** Yerba mate (*Ilex paraguariensis*) infusions have been shown to reduce plasma glucose in animals and serum lipids in humans. The aim of this study was to evaluate the effects of roasted mate tea consumption, with or without dietary counseling, on the glycemic and lipid profiles of individuals with type 2 diabetes mellitus (T2DM) or pre-diabetes.

**Methods:** Twenty-nine T2DM and 29 pre-diabetes subjects were divided into 3 groups: mate tea, dietary intervention, and mate tea and dietary intervention. Individuals drank 330 mL of roasted mate tea 3 times a day and/or received nutritional counseling over 60 days. Blood samples were collected and food intake was assessed at baseline and after 20, 40, and 60 days of treatments.

**Results:** Mate tea consumption decreased significantly the levels of fasting glucose (25.0 mg/dL), glycated hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) (0.85%), and low-density lipoprotein cholesterol (LDL-c) (13.5 mg/dL) of T2DM subjects ( $p < 0.05$ ); however, it did not change the intake of total energy, protein, carbohydrate, cholesterol, and fiber. In pre-diabetes individuals, mate tea consumption combined with nutritional counseling diminished significantly the levels of LDL-c (11 mg/dL), non-high-density lipoprotein cholesterol (HDL-c) (21.5 mg/dL), and triglycerides (53.0 mg/dL) ( $p < 0.05$ ). Individuals of this group decreased significantly their consumption of total fat (14%), cholesterol (28%), and saturated (23.8%) and monounsaturated (28.0%) fatty acids, and increased their fiber intake by 35% ( $p < 0.05$ ).

**Conclusions:** Mate tea consumption improved the glycemic control and lipid profile of T2DM subjects, and mate tea consumption combined with nutritional intervention was highly effective in decreasing serum lipid parameters of pre-diabetes individuals, which may reduce their risk of developing coronary disease.

## INTRODUCTION

The incidence of diabetes mellitus (DM) has been progressively increasing worldwide, particularly in developing countries [1]. Type 2 diabetes mellitus (T2DM) is the most common form of diabetes, and patients with T2DM are at

increased risk of developing microvascular disorders and cardiovascular diseases (CVD), which are considered the most important long-term complications and the main cause of death in adult diabetic subjects [2,3]. Elevated CVD risk in T2DM subjects is a consequence of hyperglycemia status and the presence of additional risk factors such as dyslipidemia,

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Abbreviations: ADA = American Diabetes Association, AGEs = advanced glycation end-products, CHO = carbohydrates, Cholest = cholesterol, CVD = cardiovascular disease, DI = dietary intervention, DM = diabetes mellitus, MT = mate tea, MT-DI = mate tea and dietary intervention, MUFA = monounsaturated fatty acids, PUFA = polyunsaturated fatty acids, SFA = saturated fatty acids, T2DM = type 2 diabetes mellitus, UKPDS = United Kingdom Prospective Diabetes Study.

obesity, and hypertension. Randomized controlled clinical trials have shown that increases in glycated hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels are related to increased risk of microvascular complications and CVD [4,5], and therefore require treatments to decrease plasma glucose levels. Additionally, T2DM subjects have increased concentrations of advanced glycation end-products (AGEs), which have proinflammatory and pro-oxidant effects and play an important role in the development of chronic complications associated with diabetes [6]. Individuals with altered fasting glucose levels and/or impaired glucose tolerance have been referred to as having pre-diabetes, to indicate the relatively high risk of the development of diabetes and CVD [2]. Moreover, dyslipidemia, obesity, and hypertension have been associated with the pre-diabetes condition.

To decrease the rate of onset of DM in high-risk individuals and/or to prevent chronic complications in T2DM patients, the American Diabetes Association (ADA) recommends a reduction in calorie intake, including reduced intake of dietary saturated fatty acids (SFA) and carbohydrates, and increased consumption of dietary fiber, unsaturated fats, especially monounsaturated fatty acids (MUFA), and foods containing whole grains [2]. Although evidence is insufficient to conclude that low-glycemic load diets reduce the risk of developing diabetes, diets with a low glycemic index can be recommended to control postprandial glycemia in T2DM subjects [7]. Furthermore, therapies with certain oral hypoglycemic drugs in combination with lifestyle changes, such as diet and physical activity, have been used in T2DM and pre-diabetes subjects to control glycemic and lipid profiles and changes in body weight [2,8,9]. Therefore, alternative dietary antidiabetes therapies have gained attention, and many studies have been performed to identify dietary plant species with hypoglycemic and/or antihyperglycemic properties that may prevent and/or reduce diabetes complications [10].

Among the plants studied, yerba mate (*Ilex paraguariensis*, Aquifoliaceae, St. Hil.), a plant species found in the subtropical region of South America, is thought to have antidiabetes properties. Dried and ground leaves of *Ilex paraguariensis* are commonly used to prepare beverages, regionally known as *chimarrão*, *tererê*, or *maté*, which are appreciated for their stimulating properties and bitter taste. It is estimated that millions of people drink 1 to 2 L of yerba mate infusion daily; it is the main alternative to coffee or black tea in various South American countries, including Uruguay, Argentina, Paraguay, and the southeast region of Brazil [11,12]. Yerba mate consumed in the form of tea, known as mate in Brazil, is prepared with dried, ground, and roasted leaves of *Ilex paraguariensis*. Mate tea is a beverage of soft and pleasant aroma that is consumed in southern and southeastern Brazil and Argentina typically as a hot tea or in the form of a refreshing ready-to-drink iced mate tea.

Yerba mate contains various bioactive substances, such as phenolic compounds, saponins, methylxanthines (caffeine and

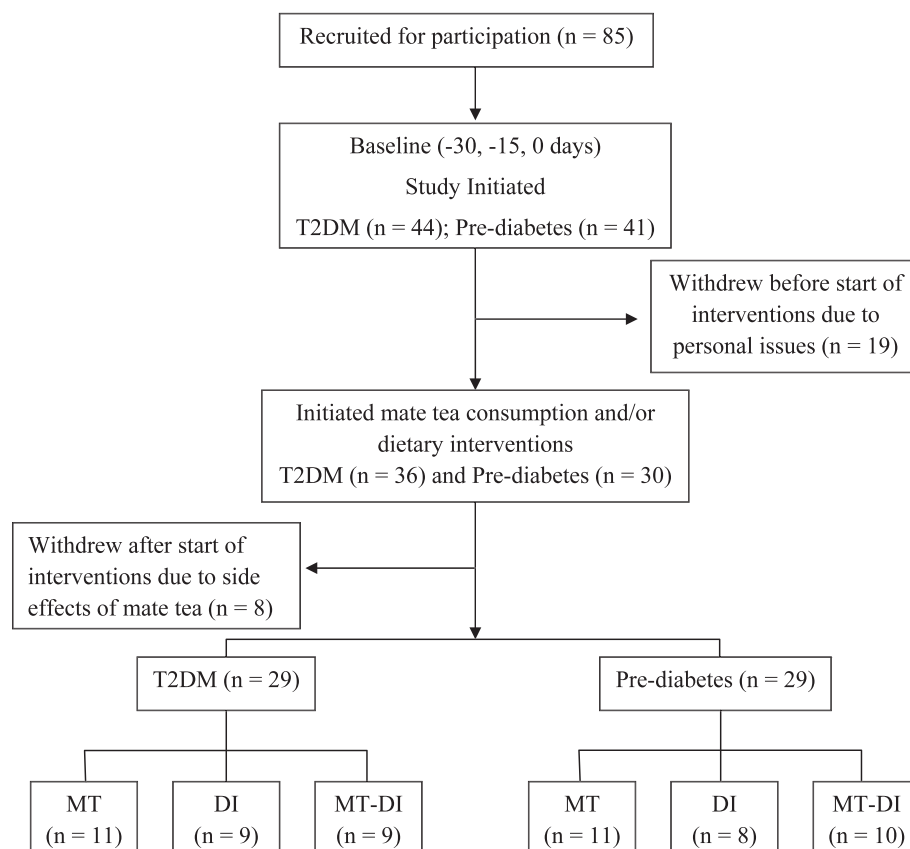
theobromine), flavonoids, amino acids, minerals, and vitamins. The major phenolic compounds in mate beverages are chlorogenic and gallic acids, as well as a few catechins [13], which reflect in their excellent antioxidant ability [11,12]. Ours and other research groups have shown that in humans, the consumption of yerba mate infusion can protect plasma and low-density lipoprotein (LDL) particles against oxidative stress [14,15], increase the total antioxidant status and gene expression of antioxidant enzymes [16], improve the serum lipid profile of normolipidemic and hypercholesterolemic individuals, mainly reducing LDL-cholesterol (LDL-c) levels [13], and decrease body weight and abdominal fat [17].

The potential antidiabetes effect of yerba mate has been reported by Sotillo and Hadley [18], who showed an improvement in the glucose tolerance of obese rats after administration of yerba mate aqueous extract. More recently, other authors have reported that yerba mate lowered serum levels of glucose in rats [19]. Although no serum glucose decrease was found, Oliveira et al. [20] reported that administration of roasted mate tea to diabetic rats reduced the gene expression of glucose intestinal transporter. Furthermore, aqueous extract of *Ilex paraguariensis* inhibited the *in vitro* formation of AGEs, suggesting a possible beneficial effect in decreasing the chronic complications of diabetes [21]. Overall, the potential for suppression of hyperglycemia and dyslipidemia through consumption of yerba mate-based beverages could be exploited as a strategy to prevent or delay the development of DM and/or its complications. Therefore, the aim of this pilot study was to verify the effects of daily consumption of roasted mate tea or dietary intervention on glycemic and lipid profiles and on serum AGEs of T2DM and pre-diabetes individuals. The effect of mate tea intake in combination with the dietary intervention was also evaluated.

## MATERIALS AND METHODS

### Population of Study

Twenty-nine free-living individuals with T2DM (7 male and 22 female) and 29 subjects with pre-diabetes (5 male and 24 female) participated in this single-blind, controlled, and randomized clinical intervention trial (Fig. 1). The average time that subjects had suffered from diabetes was  $7.4 \pm 1.8$  years, and all T2DM individuals were taking oral hypoglycemic medicine (i.e., metformin and sulphonylureas), but no lipid-lowering drugs. The pre-diabetes condition was characterized as altered fasting plasma glucose levels (100–125 mg/dL) [2]. Exclusion criteria included the presence of hepatic, gastrointestinal, or renal disease, cancer, thyroid disorder, alcoholism, morbid obesity, or pregnancy, and age younger than 18 years. Furthermore, potential volunteers who had routine laboratory results out of the reference ranges, except for glucose, HbA<sub>1c</sub>, and the lipid parameters, were also excluded. Participants who



**Fig. 1.** Flow diagram of subject screening process in this study. DI = dietary intervention, MT = mate tea, MT-DI = mate tea and dietary intervention, T2DM = type 2 diabetes mellitus.

had recently taken medications affecting glucose and/or lipid metabolism were not included in the study. Also, subjects who had altered the dose of a drug, changed their level of physical activity, showed intolerance to mate tea, or discontinued mate tea consumption for 3 or more consecutive days during treatment were excluded from the study.

Throughout the study period, participants were advised to maintain their regular lifestyle, such as the practice of moderate physical activity, and to follow their normal diet, except those who had received nutritional counseling. Participants who received nutritional counseling but not mate tea refrained from consuming any yerba mate-based beverages or products during the study. All participants gave written, informed consent, and the Human Studies Committee of the Federal University of Santa Catarina approved the study.

## Experimental Design

Eligible T2DM or pre-diabetes volunteers were distributed into three groups: (1) mate tea (MT;  $n = 11$  T2DM and  $n = 11$  pre-diabetes); (2) dietary intervention (DI;  $n = 9$  T2DM and  $n = 8$  pre-diabetes); and (3) mate tea and dietary intervention (MT-DI;  $n = 9$  T2DM and  $n = 10$  pre-diabetes). All participants remained for 30 days (baseline period) following their normal

lifestyle (diet and physical activity). However, at least 2 weeks before the initial visit and throughout the baseline period, T2DM and pre-diabetes subjects had to discontinue consuming yerba mate-containing beverages. To verify the effects of prolonged intake of yerba mate infusions on plasma glucose and serum lipid parameters, subjects in the MT and MT-DI groups were instructed to prepare the mate infusion daily, with no sugar or sugar-like substances, and to consume 330 mL of mate tea, 3 times/d for 60 days, immediately before or during breakfast, lunch, and dinner. Volunteers in the MT and MT-DI groups received 180 plastic bags, each containing 6.6 g of dried and minced leaves of commercial roasted yerba mate. Mate tea was prepared by mixing 330 mL of boiling water and 6.6 g of yerba mate leaves (i.e., 20 mg/mL), representing the amount normally consumed by the population. After 10 minutes of extraction, the mixture was filtered and was consumed immediately by volunteers. The roasted yerba mate used here was taken from the same batch used in our previous study [13]. T2DM and pre-diabetes subjects in the MT group followed a free diet throughout the study, but they did not consume additional yerba mate other than the amount provided. Participants in the DI and MT-DI groups received nutritional counseling to improve glycemic and lipid profiles based on Brazilian and

American Diabetic Associations guidelines [22,23]. For this purpose, volunteers were encouraged to increase their consumption of whole wheat cereals, fruits, vegetables, and legumes, and to reduce their intake of foods rich in simple sugars, cholesterol, and saturated or *trans* fatty acids.

Blood samples were collected before (baseline period and days -30, -15, and 0) and after 20, 40, and 60 days of treatment, after 12 to 14 hours of fasting, by venipuncture with a vacuum system (Vacutainer, BD, Franklin Lakes, NJ) in (1) tubes without additives but with serum separator to obtain serum for biochemical analysis; (2) tubes without separator but with ethylenediaminetetraacetic acid (EDTA) for hematologic analysis; and (3) tubes without separator but with NaF<sub>2</sub>-EDTA for plasma glucose measurement. All tubes were immediately centrifuged (1000 g, 15 minutes) to obtain plasma and serum for measurement of biochemical and hematologic parameters.

Participants served as their own controls, in that we compared all data obtained during the mate tea consumption or nutritional counseling periods versus average baseline values of 3 determinations. During each visit, blood pressure, body weight, and abdominal circumference were recorded using standard procedures, and dietary habits were verified by dietary records. Body mass index (BMI) was calculated as body weight (kg) divided by the squared body height (m), which was recorded during the first visit.

### Dietary Record

The nutrient composition of the dietary intake of each individual was calculated from 3-day dietary records (1 day at the weekend and 2 nonconsecutive days during the week). Food intake during baseline and study periods was calculated as the mean value of the 3-day dietary records evaluated in the first and fourth weeks of the baseline period, and after 20, 40, and 60 days of mate tea consumption and/or dietary intervention. Food records were checked by a nutritionist with volunteers at each visit and were analyzed using Avanutri software, version 3.1.4 (Rio de Janeiro, Brazil). Dietary variables considered in this analysis included intake of energy, carbohydrates, proteins, total fat, SFA, polyunsaturated fatty acids (PUFA), and MUFA as a percentage of energy intake, as well as absolute amounts of cholesterol (g), fiber (mg), and mate tea (mL).

### Analytical Methods

The plasma level of glucose was determined by enzymatic methods, using the enzymes glucose-oxidase/peroxidase in automated equipment (Dimension RXL, Siemens Healthcare Diagnostics Inc, Deerfield, IL). Quantification of HbA<sub>1c</sub> was performed by ion-exchange high-performance liquid chromatography (Variant II, BIO-RAD Laboratories, Hercules, CA). Serum levels of AGEs were measured by fluorimetry using the characteristic fluorescence spectrum [24]. Serum concentra-

tions of total cholesterol and triglycerides were determined by colorimetric methods, using the cholesterol-oxidase and glycerol-oxidase enzymes, respectively, and LDL-c and high-density lipoprotein (HDL) cholesterol (HDL-c) were measured by homogenous methods (Dimension RXL). Non-HDL cholesterol (non-HDL-c) was calculated by the difference between total cholesterol and HDL-c.

Additional biochemical tests for determination of urea, creatinine, uric acid, and the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyltransferase (GGT) enzymes, as well as hematologic parameters (including complete blood count), were carried out using automated equipment (Dimension RXL; Sysmex Xe-2100D, Sysmex, Kobe, Japan), according to the manufacturers' instructions, to monitor potential side effects of mate tea intake.

### Statistical Analysis

Descriptive statistics were presented as mean and standard error of the mean (SEM) for continuous data, and as absolute and relative frequencies for categorical data. Baseline categorical and continuous variables of T2DM or pre-diabetes groups were analyzed by the chi-square test ( $\chi^2$ ) and 1-way analysis of variance (ANOVA), respectively. The Shapiro-Wilk test was applied to verify the normality of continuous variables. When necessary, logarithmic transformation of data was used. Repeated measures ANOVA or the paired Student's *t*-test was applied to verify the effects of mate tea consumption and/or the nutritional intervention within each group; ANOVA and Tukey's post hoc test were used to detect intergroup treatment differences [25]. All baseline values represent the mean of 3 determinations with 15-day intervals. The association between changes in biochemical parameters and changes in food intake variables and body weight was evaluated by the Pearson or Spearman correlation. Values of  $p \leq 0.05$  were considered significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 15.0 (SPSS Inc, Chicago, IL).

## RESULTS

### Chemical Characteristics of Roasted Mate Tea

As we have previously described [13], the average contents of total saponins and total phenols in mate tea used in the present study were 0.132 mg/mL and 1.74 mg/mL, respectively. Therefore, daily consumption of saponins and total phenols by participants was approximately 130 mg and 1.7 g, respectively. The main phenolic compound in the mate tea was chlorogenic acid (221.8  $\mu$ g/mL), followed by gallic acid (59.1  $\mu$ g/mL), protocatechuic acid (9.3  $\mu$ g/mL), and caffeic acid (4.8  $\mu$ g/mL). Gallocatechin (47.4  $\mu$ g/mL) and catechin



**Table 1.** Baseline Characteristics of Subjects at the Beginning of the Study<sup>a,b</sup>

	Type 2 Diabetes Mellitus (n = 29)			Pre-Diabetes (n = 29)		
	MT	DI	MT-DI	MT	DI	MT-DI
No. of subjects, M/F	1/10	4/5	2/7	1/10	2/6	2/8
Age, y	54.3 ± 6.9	60 ± 6.7	49.3 ± 6.5	58.5 ± 11.6	59.1 ± 10.1	59.2 ± 7.5
Weight, kg	79.6 ± 11.9	78.5 ± 13.2	76.3 ± 7.5	73.2 ± 13.1	76.0 ± 11.1	75.1 ± 10.8
BMI, kg/m <sup>2</sup>	32.1 ± 3.7	29.8 ± 3.8	30.6 ± 3.4	29.4 ± 4.0	29.5 ± 2.5	29.4 ± 4.0
AC, cm	103.0 ± 11.9	99.0 ± 13.0	98.0 ± 8.8	99.0 ± 11.0	97.0 ± 9.0	100.0 ± 12.0
SBP, mmHg	121.0 ± 12.1	129.0 ± 13.2	119.0 ± 10.8	120.0 ± 13.9	128.0 ± 20.5	137.0 ± 23.6
DBP, mmHg	74.0 ± 6.8	80.0 ± 3.7	76.0 ± 8.0	74.0 ± 10.0	78.0 ± 5.2	80.0 ± 7.5
Cigarette smoking, n (%)	1 (9.0)	0 (0)	0 (0)	1 (9.0)	0 (0)	0 (0)
DM diagnosed, y	7.1 ± 9.1	8.7 ± 7.0	6.5 ± 5.4	—	—	—
Family history of DM, n (%)	8 (72.7)	7 (77.7)	8 (88.8)	7 (63.6)	4 (50.0)	4 (40.0)
Family history of CVD, n (%)	10 (90.9)	6 (66.6)	6 (66.6)	8 (72.7)	6 (75.0)	7 (70.0)
Physical inactivity, n (%)	7 (63.3)	2 (22.2)	5 (55.5)	4 (36.3)	2 (25.0)	5 (50.0)

AC = abdominal circumference, BMI = body mass index, CVD = cardiovascular disease, DBP = diastolic blood pressure, DI = dietary intervention, DM = diabetes mellitus, M/F = male/female, MT = mate tea, MT-DI = mate tea and dietary intervention, SBP = systolic blood pressure.

<sup>a</sup> Data are expressed as means ± SEM.

<sup>b</sup> No significant differences were noted between variables of type 2 diabetes and pre-diabetes groups.

(34.1 µg/mL) were also identified. Caffeine was the major methylxanthine present in the mate tea (109.9 µg/mL), followed by theobromine (27.0 µg/mL); theophylline was not detected.

### Biodemographic and Clinical Characteristics of Participants

Eighty-five eligible volunteers (26 men and 59 women) were recruited to participate in this study. After the experimental protocol began, 19 volunteers interrupted their participation in the study owing to personal reasons. Eight additional individuals had an adverse reaction to mate tea, such as insomnia, heartburn, and tachycardia. Therefore, 58 subjects (13 men and 45 women) effectively participated in the study (29 T2DM and 29 pre-diabetes subjects; Fig. 1), with average age of 56.8 ± 9.1 years and BMI of 30.0 ± 3.7 kg/m<sup>2</sup>. For these volunteers, no additional evidence of adverse reactions or side effects was reported following consumption of mate tea, including absence of biochemical or hematologic changes (data not shown). Baseline clinical and biodemographic characteristics of all individuals are shown in Table 1. No significant differences were noted between baseline variables of the 3 groups of T2DM or pre-diabetes individuals.

### Effects of Mate Tea and/or Dietary Intervention on Glycemic Profile and AGEs

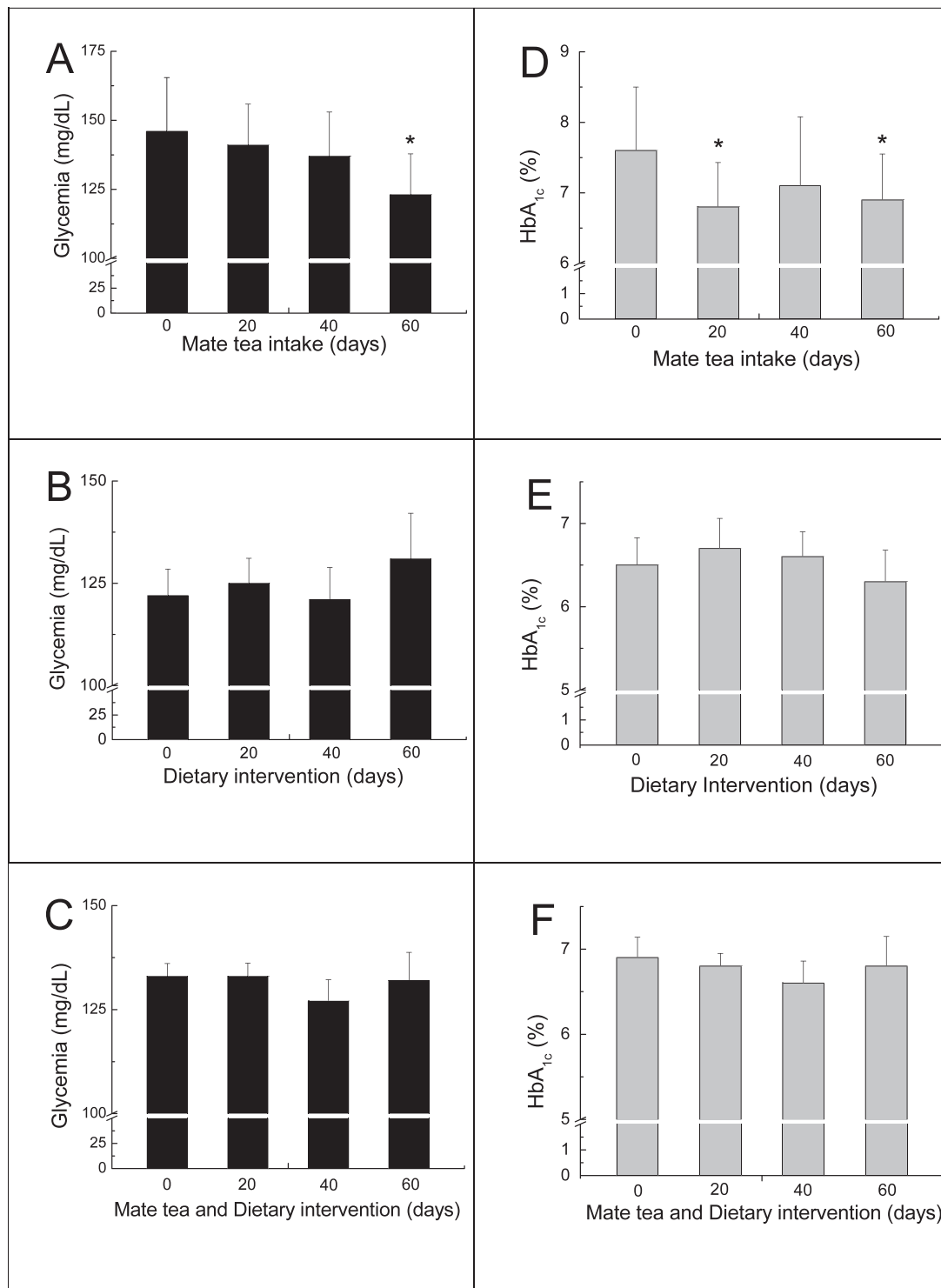
T2DM subjects in the MT group had a significant reduction in fasting plasma glucose (25.0 mg/dL or 17%) after 60 days of mate tea consumption when compared with baseline levels ( $p < 0.05$ ; Fig. 2). A statistical difference was also detected in comparison with data for the DI (7.4%) or MT-DI (−0.75%) group after 60 days. Additionally, HbA<sub>1c</sub> level decreased by around 0.85% after 20 and 60 days of mate tea intake ( $p =$

0.05; Fig. 2); this was also statistically different from corresponding reductions observed for the DI (0.1%, average) or MT-DI (0.2%, average) group ( $p < 0.05$ ). However, no significant variation was observed in plasma glucose or HbA<sub>1c</sub> levels of T2DM individuals in the DI and MT-DI groups compared with respective baselines values (Fig. 2). In addition, serum levels of AGEs did not change during treatments (results not shown).

Among pre-diabetes individuals, mate tea consumption, dietary intervention, or both treatments combined did not promote a significant decrease in fasting plasma glucose or AGE values (results not shown). Nevertheless, pre-diabetes subjects in the MT and MT-DI groups had significant lowering of HbA<sub>1c</sub> concentration (by 0.4%) after 40 days of treatment ( $p = 0.01$ ) (MT group: baseline 6.1 ± 0.24% versus 5.7 ± 0.26%; MT-DI group: baseline 5.7 ± 0.15% versus 5.3 ± 0.13%).

### Effects of Mate Tea and/or Dietary Intervention on Serum Lipid Profile

Table 2 shows the results for lipid parameters in the serum of individuals with T2DM according to treatments. Mate tea intake promoted a significant decrease in levels of LDL-c after 20 days (13.5 mg/dL, or 12.4%;  $p < 0.05$ ) and after 60 days (8.1 mg/dL;  $p < 0.05$ ). Despite nonexistent significant LDL-c lowering after 40 days of mate consumption, 7 of 11 T2DM individuals showed a reduction in LDL-c of 11.5 mg/dL (96.8 mg/dL versus 85.3 mg/dL;  $p < 0.05$ ). T2DM subjects in the DI group did not show significant reductions in lipid parameters. Furthermore, mate tea intake combined with dietary intervention did not promote additional improvement in the serum lipid profile, except for an increase in HDL-c levels (by 5.2 mg/dL) after 60 days of treatment ( $p < 0.05$ ) (Table 2).



**Fig. 2.** Mean values ( $\pm$ SEM) of glycemia and glycated hemoglobin (HbA<sub>1c</sub>) concentrations in T2DM individuals in the mate tea (A and D), dietary intervention (B and E), and mate tea plus dietary intervention (C and F) groups. \* Significantly different from baseline values (0 day) for the same group ( $p < 0.05$ ) and from 60-day values for the DI and MT-DI groups ( $p < 0.05$ ). DI = dietary intervention, MT-DI = mate tea and dietary intervention.

**Table 2.** Effects of Mate Tea and Dietary Intervention Treatments on Serum Lipid Parameters of Individuals with T2DM<sup>a</sup>

	Cholesterol, mg/dL				Triglycerides, mg/dL
	Total	LDL	HDL	Non-HDL	
Mate tea (n = 11)					
Baseline	185.7 ± 34.0	109.0 ± 29.7	45.0 ± 7.3	140.0 ± 39.7	167.2 ± 73.0
Δ 20 d, mg/dL	-8.9 ± 18.6	-13.5 ± 19.4*	0.2 ± 5.1	-8.9 ± 19.7	2.6 ± 40.8
Δ 40 d, mg/dL	-1.0 ± 22.2	-0.8 ± 15.6	-1.0 ± 6.1	0.4 ± 18.5	-12.5 ± 35.2
Δ 60 d, mg/dL	-4.8 ± 18.5	-8.1 ± 11.5*	1.5 ± 6.9	-6.3 ± 21.2	-9.2 ± 92.6
Dietary intervention (n = 9)					
Baseline	186.0 ± 47.6	103.0 ± 36.5	49.0 ± 12.0	136.0 ± 44.6	167.0 ± 65.9
Δ 20 d, mg/dL	-8.3 ± 20.7	-7.1 ± 10.3	-0.6 ± 4.2	-7.4 ± 18.7	-2.5 ± 52.9
Δ 40 d, mg/dL	-10.6 ± 19.4	-8.1 ± 21.1	2.1 ± 4.9	-12.2 ± 18.8	-21.6 ± 61.0
Δ 60 d, mg/dL	-8.2 ± 33.3	-6.6 ± 27.6	3.7 ± 7.8	-11.4 ± 38.3	9.8 ± 89.8
Mate tea and dietary intervention (n = 9)					
Baseline	197.0 ± 42.9	119.0 ± 37.0	49.0 ± 7.7	147.0 ± 44.0	145.0 ± 75.5
Δ 20 d, mg/dL	-4.2 ± 23.5	-4.5 ± 25.2	0.4 ± 4.8	-4.3 ± 22.7	-5.1 ± 41.8
Δ 40 d, mg/dL	-9.3 ± 44.2	-4.2 ± 35.5	-0.2 ± 3.8	-8.5 ± 43.7	-21.0 ± 33.3
Δ 60 d, mg/dL	24.8 ± 44.8	9.6 ± 25.0	5.2 ± 4.9*	20.2 ± 43.2	-6.4 ± 40.6

HDL = high-density lipoprotein; LDL = low-density lipoprotein; T2DM = type 2 diabetes mellitus.

<sup>a</sup> Data are expressed as means ± SEM.\* Significantly different from baseline values of the same group:  $p < 0.05$ .

For pre-diabetes subjects, consumption of mate tea or the dietary intervention for 20, 40, and 60 days did not improve significantly the lipid parameters (Table 3). However, pre-diabetes subjects in the MT-DI group showed significant lowering of LDL-c (11.0 mg/dL;  $p = 0.05$ ), non-HDL-c (22.0 mg/dL;  $p = 0.05$ ), and triglycerides (53.0 mg/dL, or 20%;  $p < 0.01$ ) after 60 days of treatment compared with baseline levels (Table 3).

Effects of treatments on the lipid parameters of T2DM or pre-diabetes subjects, when calculated as relative (percentage)

changes after 20, 40, and 60 days for the MT, DI, and MT-DI groups, did not show statistical intergroup differences, probably owing to high variation in results and/or to the small number of individuals studied.

### Intake of Macronutrients, Cholesterol, Saturated and Unsaturated Fatty Acids, and Fiber

Tables 4 and 5 show the dietary food records of T2DM and pre-diabetes subjects during baseline, mate tea consumption,

**Table 3.** Effects of Mate Tea and Dietary Intervention Treatments on Serum Lipid Parameters of Individuals with Pre-Diabetes<sup>a</sup>

	Cholesterol, mg/dL				Triglycerides, mg/dL
	Total	LDL	HDL	non-HDL	
Mate tea (n = 11)					
Baseline	234.0 ± 28.4	150.0 ± 28.8	50.0 ± 9.4	184.0 ± 27.9	185.0 ± 123.0
Δ 20 d, mg/dL	4.9 ± 16.7	6.6 ± 19.8	1.9 ± 12.1	3.0 ± 19.0	0.5 ± 35.1
Δ 40 d, mg/dL	-3.5 ± 21.1	-8.2 ± 15.4	3.1 ± 8.0	-6.6 ± 19.1	-0.07 ± 35.4
Δ 60 d, mg/dL	-7.7 ± 14.6	-9.4 ± 18.6	4.2 ± 6.0	-12.0 ± 18.5	-12.4 ± 13.3
Dietary intervention (n = 8)					
Baseline	228.0 ± 16.8	134.0 ± 23.7	49.0 ± 9.4	179.0 ± 23.9	263.0 ± 211.0
Δ 20 d, mg/dL	2.0 ± 22.4	-3.2 ± 17.1	-0.7 ± 6.7	2.8 ± 21.6	11.0 ± 67.1
Δ 40 d, mg/dL	-16.7 ± 28.2	-13.5 ± 30.5	-2.6 ± 5.6	-14.0 ± 28.4	-12.0 ± 81.1
Δ 60 d, mg/dL	-3.3 ± 28.2	3.7 ± 27.4	4.5 ± 8.5	-7.9 ± 34.2	-19.0 ± 51.0
Mate tea and dietary intervention (n = 9)					
Baseline	246.0 ± 34.1	151.0 ± 30.9	52.9 ± 9.0	197.0 ± 37.5	249.0 ± 178.0
Δ 20 d, mg/dL	-10.8 ± 26.9	-14.0 ± 22.3	-1.0 ± 4.9	-13.0 ± 28.5	-22.1 ± 42.2
Δ 40 d, mg/dL	-19.0 ± 28.7	-16.5 ± 24.3	0.7 ± 9.1	-23.3 ± 32.5	-45.4 ± 72.7
Δ 60 d, mg/dL	-19.0 ± 27.9	-11.0 ± 14.8*	-0.6 ± 5.3	-21.5 ± 29.0*	-53.0 ± 62.7†

HDL = high-density lipoprotein; LDL = low-density lipoprotein.

<sup>a</sup> Data are expressed as means ± SEM.Significantly different from baseline values of the same group: \*  $p = 0.05$ ; †  $p < 0.01$ .



**Table 4.** Effects of Mate Tea and Dietary Intervention Treatments on Dietary Composition of Individuals with T2DM<sup>a</sup>

	Energy, kcal	Proteins, %	CHO, %	Fat, %	Chol, mg	SFA, %	PUFA, %	MUFA, %	Fiber, g
Mate tea (n = 11)									
Baseline	1688.0 ± 561.0	18.9 ± 4.5	50.9 ± 5.6	30.2 ± 4.3	212.0 ± 85.0	8.6 ± 1.3	5.3 ± 2.1	7.9 ± 1.4	12.5 ± 5.8
20 days	1570.0 ± 398.0	18.1 ± 4.5	55.5 ± 5.6§	26.4 ± 3.6‡	235.0 ± 148.0	7.4 ± 1.5‡	4.8 ± 1.5	6.9 ± 1.8‡	13.0 ± 5.8
40 days	1634.0 ± 397.0	18.6 ± 5.6	54.1 ± 5.5	26.1 ± 5.6‡	248.0 ± 138.0	7.1 ± 2.0‡	5.7 ± 1.7	6.7 ± 2.2‡	11.9 ± 4.4
60 days	1566.0 ± 462.0	19.1 ± 3.8	50.0 ± 4.6	30.9 ± 5.1	259.0 ± 152.0	8.2 ± 1.9	7.4 ± 3.7	7.7 ± 1.8	12.8 ± 4.9
Dietary intervention (n = 9)									
Baseline	1631.0 ± 462.0	19.1 ± 4.7	53.7 ± 5.3	27.1 ± 4.8	195.0 ± 62.0	8.2 ± 4.9	3.9 ± 1.7	7.9 ± 5.0	14.3 ± 4.2
20 days	1615.0 ± 444.0	20.1 ± 4.8	49.8 ± 4.0§	30.1 ± 5.8	200.0 ± 35.0	7.5 ± 3.3	3.6 ± 1.8	8.0 ± 3.7	14.0 ± 7.6
40 days	1504.0 ± 247.0	21.3 ± 4.2	51.8 ± 6.6	26.8 ± 6.3	254.0 ± 150.0	7.1 ± 2.1	4.2 ± 2.6	8.3 ± 5.1	11.4 ± 2.5
60 days	1336.0 ± 165.0	21.6 ± 3.4	51.9 ± 4.5	26.4 ± 4.8	154.0 ± 50.9	8.1 ± 1.3	4.8 ± 1.1	7.7 ± 3.3	10.6 ± 1.4
Mate tea and dietary intervention (n = 9)									
Baseline	1793.0 ± 474.0	17.3 ± 4.3	54.5 ± 10.2	28.2 ± 6.6	201.0 ± 92.0	7.8 ± 2.2	5.1 ± 2.4	7.6 ± 3.0	14.2 ± 3.9
20 days	1664.0 ± 635.0	19.6 ± 3.9	56.0 ± 6.6	24.3 ± 6.1	172.0 ± 67.0	6.3 ± 1.8	4.2 ± 2.3	6.3 ± 2.9	16.0 ± 4.2
40 days	1336.0 ± 454.0§	21.9 ± 4.1	53.8 ± 6.2	23.6 ± 7.3‡	172.0 ± 61.7	7.6 ± 1.7	3.6 ± 1.9‡	6.5 ± 2.2	12.6 ± 4.1
60 days	1503.0 ± 572.0*	20.7 ± 2.2	53.2 ± 5.0	25.8 ± 6.8	208.0 ± 75.2	5.7 ± 2.3	3.8 ± 2.2	5.9 ± 2.8	14.0 ± 5.5

CHO = carbohydrates, Chol = cholesterol, MUFA = monounsaturated fatty acids, PUFA = polyunsaturated fatty acids, SFA = saturated fatty acids, T2DM = type 2 diabetes mellitus.

<sup>a</sup> Data are expressed as means ± SEM.Significantly different from baseline values of respective group: \*  $p < 0.05$ ; †  $p < 0.01$ ; ‡  $p < 0.01$ ; §  $p < 0.05$ .**Table 5.** Effects of Mate Tea and Dietary Intervention Treatments on Dietary Composition of Individuals with Pre-Diabetes<sup>a</sup>

	Energy, kcal	Proteins, %	CHO, %	Fat, %	Chol, mg	SFA, %	PUFA, %	MUFA, %	Fiber, g
Mate tea (n = 11)									
Baseline	1932.0 ± 460.0	17.3 ± 2.3	51.9 ± 4.5	30.7 ± 4.6	240.0 ± 55.0	9.0 ± 2.5	5.9 ± 1.9	8.7 ± 2.0	9.3 ± 1.7
20 days	1769.0 ± 474.0	17.3 ± 4.0	54.7 ± 5.7	27.5 ± 6.4	199.0 ± 85.0	8.1 ± 3.1	5.3 ± 2.5	7.6 ± 2.3	9.8 ± 2.4
40 days	1700.0 ± 427.0	16.3 ± 4.7	53.9 ± 5.6	29.8 ± 3.9	211.0 ± 91.0	9.1 ± 2.6	6.0 ± 2.2	8.1 ± 2.5	8.7 ± 3.0
60 days	2189.0 ± 787.0	17.1 ± 5.8	51.4 ± 8.4	31.5 ± 4.8	225.0 ± 102.0	8.5 ± 2.7	6.5 ± 2.5	8.8 ± 1.0	9.9 ± 5.6
Dietary intervention (n = 8)									
Baseline	1630.0 ± 367.0	15.7 ± 3.4	52.7 ± 6.6	31.4 ± 4.5	166.0 ± 106.0	8.3 ± 2.9	5.3 ± 2.2	8.0 ± 3.9	13.8 ± 6.0§
20 days	1465.0 ± 346.0	17.2 ± 6.0	60.0 ± 7.0	22.8 ± 6.9‡	145.0 ± 61.0	5.0 ± 1.8	4.8 ± 1.6	5.6 ± 1.9	14.0 ± 5.9
40 days	1239.0 ± 205.0*	16.3 ± 4.2	57.4 ± 6.4	25.4 ± 1.8	122.0 ± 34.0	6.0 ± 1.5*	4.4 ± 1.5	6.4 ± 1.1	10.0 ± 4.4
60 days	1575.0 ± 368.0	16.7 ± 2.5	54.4 ± 5.7	29.0 ± 2.7	220.0 ± 138.0	8.2 ± 2.5	5.8 ± 1.0	7.8 ± 2.3	12.0 ± 4.7
Mate tea and dietary intervention (n = 9)									
Baseline	1818.0 ± 447.0	17.7 ± 4.5	48.8 ± 5.2	33.4 ± 5.1	261.0 ± 117.0	9.7 ± 3.3	6.2 ± 2.0	8.9 ± 2.6	9.6 ± 2.1
20 days	1829.0 ± 523.0	15.9 ± 3.3	53.4 ± 5.5	30.6 ± 3.8	188.0 ± 79.0*	7.9 ± 2.4	5.2 ± 2.4	8.7 ± 4.5	12.0 ± 5.9
40 days	1678.0 ± 319.0	17.1 ± 3.7	53.1 ± 4.0	29.8 ± 4.8	230.0 ± 80.0	7.5 ± 2.9	5.9 ± 2.9	8.8 ± 4.3	12.2 ± 3.4‡
60 days	1729.0 ± 375.0	18.5 ± 4.7	55.6 ± 8.1	25.8 ± 8.1*	188.0 ± 112.0*	6.7 ± 2.9‡	5.6 ± 2.6	6.4 ± 3.3‡	13.0 ± 5.3‡

CHO = carbohydrates, Chol = cholesterol, MUFA = monounsaturated fatty acids, PUFA = polyunsaturated fatty acids, SFA = saturated fatty acids.

<sup>a</sup> Data are expressed as means ± SEM.Significantly different from baseline values of respective group: \*  $p \leq 0.05$ ; ‡  $p = 0.01$ .Significantly different from baseline values of mate tea + nutritional intervention groups: §  $p < 0.05$ .

## Mate Tea Improves Glycemic and Lipid Profiles

and/or nutritional intervention periods. At the beginning of the study, T2DM individuals of different groups had comparable dietary patterns (Table 4). Pre-diabetes participants of different groups also had similar nutrient intake profiles in the baseline period, except for fiber intake, which was lower in individuals in the DI group compared with individuals in the MT and MT-DI groups ( $p < 0.05$ ; Table 5).

During the treatment period, T2DM subjects in the MT group did not show significant changes in energy intake or consumption of proteins, cholesterol, PUFA, or fiber. However, significant reductions of around 13.1% for total fat ( $p = 0.01$ ), 15.7% for SFA ( $p = 0.01$ ), and 13.9% for MUFA intake ( $p = 0.01$ ) were observed after 20 and 40 days of mate tea consumption (Table 4).

T2DM subjects in the DI group reduced their carbohydrate consumption significantly (by around 7.3%) but temporarily after 20 days of nutritional counseling ( $p < 0.05$ ; Table 4). However, significant variations were not observed for other macronutrients, or for SFA, PUFA, MUFA, and fiber. Individuals with T2DM in the MT-DI group showed an important decrease in fat intake (12.6%, average of period), SFA (16%), PUFA (23%), and MUFA (18.4%), which resulted in reduced energy intake (16.3%;  $p < 0.05$ ; Table 4).

Results for the dietary intake of pre-diabetes individuals can be found in Table 5. No significant variations in intake of energy, macronutrients, SFA, PUFA, MUFA, cholesterol, or fiber were noted among subjects in the MT group. Pre-diabetes individuals in the DI group did not modify their consumption of protein, carbohydrates, cholesterol, PUFA, MUFA, or fiber. On the other hand, a significant reduction in intake of energy (24%, average;  $p < 0.05$ ), fat (23.2%;  $p = 0.01$ ), and SFA (34%;  $p < 0.05$ ) was detected after 20 and 40 days. Pre-diabetes subjects in the MT-DI group decreased significantly their consumption of total fat (14%, average), cholesterol (28%), SFA (23.8%), and MUFA (28.0%) after 60 days of treatment ( $p < 0.05$ ), and increased their fiber intake by approximately 30% ( $p < 0.01$ ; Table 5).

Based on the dietary records, adherence of T2DM and pre-diabetes subjects to mate tea intake was satisfactory. All volunteers reported having drunk 330 mL of mate tea 3 times a day, except 1 T2DM and 2 pre-diabetes individuals in the MT group, who reported having drunk 330 mL 2 times a day on 8 different days during a treatment period of 60 days.

### Association of Dietary Intake and Body Weight with Glycemic Profile

Correlations between dietary intake or body weight and the glycemic profile were examined to search for a potential influence of nutrients on levels of glucose and HbA<sub>1c</sub> (Table 6). In spite of the absence of significant differences in the average intake of carbohydrates or in the body weight of T2DM volunteers who had drank mate tea, correlation coefficients showed that carbohydrate consumption and body

**Table 6.** Relationships between Changes ( $\Delta$ ) in Plasma Glucose Levels and Changes in Carbohydrate, PUFA, MUFA, and Fiber Intake and Body Weight (Pearson's Correlation)

	Type 2		Pre-Diabetes	
	Diabetes Mellitus		$\Delta$ Glycemia	
	$r$	$p$	$r$	$p$
Mate tea				
$\Delta$ Carbohydrate	0.470	0.018	0.036	0.868
$\Delta$ PUFA	-0.393	0.050	-0.051	0.813
$\Delta$ MUFA	-0.500	0.010	0.042	0.846
$\Delta$ Fiber	-0.222	0.284	-0.167	0.434
$\Delta$ Body weight	0.399	0.050	-0.032	0.881
Dietary intervention				
$\Delta$ Carbohydrate	0.164	0.467	0.123	0.637
$\Delta$ PUFA	-0.495	0.031	-0.474	0.050
$\Delta$ MUFA	-0.379	0.082	-0.632	0.008
$\Delta$ Fiber	-0.325	0.139	-0.569	0.017
$\Delta$ Body weight	-0.408	0.159	0.486	0.047
Mate tea and dietary intervention				
$\Delta$ Carbohydrate	-0.302	0.184	-0.151	0.463
$\Delta$ PUFA	-0.056	0.809	0.146	0.475
$\Delta$ MUFA	0.193	0.402	0.333	0.096
$\Delta$ Fiber	-0.027	0.909	-0.252	0.213
$\Delta$ Body weight	-0.358	0.144	0.165	0.420

MUFA = monounsaturated fatty acids, PUFA = polyunsaturated fatty acids.

weight were directly associated with fasting plasma glucose levels ( $r = 0.470$  and  $r = 0.399$ , respectively;  $p \leq 0.05$ ). On the other hand, increased consumption of PUFA and MUFA was found to be associated with reductions in plasma glucose ( $r = -0.393$  and  $-0.500$ , respectively;  $p \leq 0.05$ ). For T2DM subjects in the DI group, PUFA intake was also inversely correlated with levels of glucose ( $r = -0.495$ ;  $p < 0.05$ ). In contrast, T2DM individuals in the MT-DI group did not show significant correlations between dietary intake or body weight and glycemia or HbA<sub>1c</sub> (results not shown). Moreover, nonsignificant associations between other nutrients and glycemia or HbA<sub>1c</sub> were also observed for the MT and DI groups (results not shown).

For pre-diabetes individuals in the DI group, fiber intake was inversely correlated with changes in the plasma levels of glucose ( $r = -0.632$ ;  $p = 0.017$ ) and HbA<sub>1c</sub> ( $r = -0.483$ ;  $p = 0.05$ ). In addition, the consumption of MUFA and PUFA was inversely associated with glycemia ( $r = -0.632$  and  $r = -0.474$ , respectively;  $p \leq 0.05$ ). Intake of other dietary components was not correlated with plasma glucose or HbA<sub>1c</sub> (data not shown). Improvement in body weight was directly associated with changes in glucose levels ( $r = 0.486$ ;  $p < 0.05$ ; Table 6). In contrast, pre-diabetes individuals in the MT or MT-DI group did not show significant correlations between dietary consumption and glycemia or HbA<sub>1c</sub> (results not shown).

## Effects of Mate Tea and/or Dietary Intervention on Body Weight, BMI, Abdominal Circumference, and Blood Pressure

Throughout the study, T2DM subjects did not show significant variations in body weight, BMI, abdominal circumference, or blood pressure (data not shown). However, individuals with pre-diabetes in the MT group had a significant reduction in body weight (baseline,  $73.2 \pm 3.1$  kg versus  $71.6 \pm 13.5$  kg) and BMI (baseline,  $29.4 \pm 4.0$  kg/m<sup>2</sup> versus  $28.7 \pm 3.4$  kg/m<sup>2</sup>) after 60 days' consumption of mate tea ( $p < 0.05$ ). After 20 days of intervention, pre-diabetes individuals in the MT-DI group experienced significant lowering of systolic blood pressure (baseline,  $137.6 \pm 23.6$  mmHg versus  $130.3 \pm 19.7$  mmHg;  $p < 0.05$ ) and diastolic blood pressure (baseline,  $80.5 \pm 7.5$  mmHg versus  $76.1 \pm 7.7$  mmHg;  $p < 0.05$ ).

## DISCUSSION

The present study demonstrated that daily consumption of approximately 1 L of roasted mate tea, rich in phenolic compounds and saponins, by individuals with T2DM lowered the fasting plasma glucose level by 25 mg/dL after 60 days of consumption. Additionally, mate tea intake reduced the concentration of HbA<sub>1c</sub> by 0.85% after 20 and 60 days of treatment. It has been shown that a decrease in blood glucose and HbA<sub>1c</sub> levels is associated with a reduction in diabetes complications [2]. The United Kingdom Prospective Diabetes Study (UKPDS) Group has stated that for every 1% reduction in HbA<sub>1c</sub>, relative risks of acute myocardial infarction and of microvascular complications are lowered by approximately 14% and 37%, respectively [4]. It should be noted that T2DM subjects who had consumed mate tea did not diminish their carbohydrate intake or increase considerably their consumption of fiber, both of which can favorably affect plasma glucose levels [2,26]. However, the glycemia was inversely associated with PUFA and MUFA intake ( $r = -0.393$  and  $-0.500$ , respectively;  $p < 0.05$ ) and directly related to the variation in carbohydrate consumption ( $r = 0.470$ ;  $p = 0.018$ ) and body weight ( $r = 0.399$ ;  $p < 0.05$ ), consistent with previous reports [27]. Therefore, additional studies should clarify whether mate tea possesses a glycemia-lowering effect *per se*, or whether this result was due to increased consumption of PUFA and MUFA and/or to weight loss, which could be caused by intake of mate tea, particularly owing to its thermogenic effect [28].

To the best of our knowledge, yerba mate effects in diabetic individuals have not been studied previously. However, recent reports in animals have described that a mate tea-supplemented diet decreased the serum glucose level of obese rats [19] and diminished gene expression of the intestinal glucose transporter SGLT1 in diabetic rats [20], suggesting that mate tea could modulate glucose absorption. It was shown that chlorogenic acid, the major polyphenol constituent of mate tea, modulates

the enzyme glucose-6-phosphate translocase, reducing hepatic glucose release and, consequently, the concentration of plasma glucose [29]. In addition to chlorogenic acid, gallic and caffeic acids, which also are present in mate tea, may improve glycemic control by increasing glucose uptake in hepatocytes and 3T3-L1 cells [30,31]. Furthermore, evidence in humans and in laboratory animals indicates that caffeine can improve insulin sensitivity, resulting in amelioration of the glycemic profile [32,33].

The nutritional counseling performed herein, with or without mate tea intake, did not promote a significant and/or clinically relevant improvement in the glycemic control and lipid parameters of T2DM individuals. These negative results might be due to the absence of a significant decrease in carbohydrate consumption and/or an increase in fiber intake. In spite of the considerable decrease in SFA consumption by T2DM individuals in the DI and MT-DI groups (18% and 32.5%, respectively), which could improve insulin sensitivity and plasma glucose and lipid parameters [34], the dietary intervention promoted an important reduction in PUFA and MUFA intake, especially by T2DM subjects in the MT-DI group, minimizing the potentially favorable effects of both lower SFA intake and mate tea consumption. In fact, a reduction in PUFA intake was associated with increased levels of fasting plasma glucose ( $r = -0.495$ ;  $p < 0.05$ ) in T2DM individuals. Overall, our results confirmed previous reports that adherence of T2DM subjects to dietary recommendations is not completely satisfactory [8,34].

In pre-diabetes individuals, mate tea consumption, with or without nutritional counseling, did not promote a reduction in fasting plasma glucose, although a significant and temporary decrease in HbA<sub>1c</sub> levels was detected. Similar results were obtained in our previous study with healthy or euglycemic-dyslipidemic subjects [13]. Therefore, mate tea appears to have the property of decreasing fasting plasma glucose in T2DM subjects on antidiabetes therapy, but not in pre-diabetes or euglycemic individuals. Additional studies will be necessary to better address this question. The nutritional counseling applied in this study also did not improve the glycemic control of pre-diabetes individuals, probably owing to decreased fiber intake, which was negatively associated with enhancement of plasma glucose and HbA<sub>1c</sub> levels ( $r = -0.569$  and  $-0.483$ , respectively;  $p < 0.05$ ). Although the dietary intervention promoted a reduction in SFA intake by pre-diabetes individuals, their consumption of PUFA and MUFA decreased, resulting in the lack of a favorable effect on mean levels of glycemia or HbA<sub>1c</sub> [27,34]. Nevertheless, participants who increased their consumption of PUFA and MUFA showed lower levels of plasma glucose ( $r = -0.632$  and  $-0.474$ , respectively;  $p < 0.05$ ). In addition, pre-diabetes subjects who had lost body weight also presented a plasma glucose decrease ( $r = 0.486$ ;  $p < 0.05$ ), consistent with findings described by Norris et al. [35], indicating that modest weight loss improved insulin resistance in individuals with pre-diabetes or diabetes.

Available evidence shows the importance of lowering LDL-c in the prevention of CVD, especially in subjects with T2DM [1]. In this study, it was found that intake of roasted mate tea reduced LDL-c levels by approximately 13 mg/dL and 8 mg/dL in diabetic subjects after 20 and 60 days, and by 11.5 mg/dL after 40 days, for 7 of the 11 T2DM individuals. When mate tea was combined with dietary intervention, a hypolipidemic effect was detected to an even greater extent in pre-diabetes subjects. After 60 days of treatment, total lipids and LDL-c were reduced by 19.0 mg/dL and 11.0 mg/dL, respectively, and non-HDL-c and triglycerides decreased, respectively, by 21.5 mg/dL and 53.0 mg/dL. Considering that for every 30 mg/dL reduction in LDL-c, the relative risk of developing CVD is lowered by around 30% [2], the proportional decreases in the risk of CVD development in T2DM and pre-diabetes individuals would be 8% and 11%, respectively, consistent with our previous results on dyslipidemic subjects [13].

A possible mechanism for the LDL-c- and non-HDL-c-lowering ability of mate tea is the inhibition of cholesterol absorption and/or endogenous biosynthesis, which can be attributed to the saponins, phenolic compounds, and/or caffeine present in mate tea. Aqueous extracts of *Ilex paraguariensis*, or its isolated saponins, can form complexes with cholic acid *in vitro* [36], suggesting inhibition of cholesterol absorption. Moreover, catechins and caffeine have been found to inhibit the intestinal absorption of cholesterol in rats [37,38]. Phenolic compounds, such as chlorogenic [39] and caffeic acids [40], reportedly decrease cholesterol biosynthesis in cultured hepatocytes and in hypercholesterolemic rat liver, respectively, by inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase activity. In the case of pre-diabetes subjects who had drunk mate tea and simultaneously received nutritional counseling, the observed decrease in LDL-c and non-HDL-c levels may have been due to the reduction of 23% in total fat intake, particularly SFA (36%) and cholesterol (28%), and the concomitant enhancement of 35% fiber consumption. It has been shown that increasing fiber intake can improve the lipid profile and reduce the risk of CVD in T2DM patients [26,34].

We were surprised that we did not observe significant improvement in the lipid profiles of T2DM individuals who consumed mate tea and received nutritional counseling, except for the 5.2-mg/dL increase in HDL-c, which might be associated with weight loss (0.7 kg average), as reported by McLaughlin et al. [41]. A probable explanation for the lack of lipid lowering is that T2DM subjects reduced the intake of all fatty acids, not altering the PUFA/SFA and/or MUFA/SFA ratio.

It should be noted that inconsistent results were found at different periods of time for certain biochemical and dietary variables; this may be considered a limitation of the present pilot study. Such variations might be due to the small number of individuals studied and/or to differences in dietary intake,

which may indicate some difficulty encountered by a few subjects in maintaining the same dietary pattern throughout the study.

## CONCLUSIONS

Results of this pilot study show significant improvement in glycemic control and a reduction in LDL-c levels among individuals with T2DM after consumption of roasted mate tea for 60 days. Furthermore, for pre-diabetes subjects, the association of mate tea with dietary intervention, in the form of nutritional counseling, was more effective in improving the lipid profile than was each treatment alone. The dietary intervention, especially when associated with mate tea intake, promoted a decrease in total fat consumption, including SFA and cholesterol, and an increase in the fiber intake of pre-diabetes subjects. Based on these results, it is suggested that epidemiologic and/or long-term prospective studies should be carried out to investigate the antidiabetes and antiatherosclerosis properties of mate tea in both T2DM and pre-diabetes subjects.

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G.A.K., E.W., P.F.P., and E.L.S. participated in the design of the study and drafted the manuscript. G.A.K., A.S., B.C.B.B., and E.C.M. recruited subjects, randomized the experimental groups, and collected and recorded the data, including preparation and analysis of blood samples. E.W. and P.F.P. supervised and coordinated the dietary food record studies. L.S.C. and E.L.S. performed the statistical calculations. F.A. and M.M. performed the chemical analysis of mate tea. G.A.K. and E.L.S. wrote the manuscript and had primary responsibility for the final content. All authors read and approved the final manuscript.

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