Nutrition 30 (2014) 116–119

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Brief report

Effect of buttermilk consumption on blood pressure in moderately hypercholesterolemic men and women

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ARTICLE INFO

Article history:
Received 19 April 2013
Accepted 24 July 2013

Keywords:
Buttermilk bioactive peptides
Blood pressure
Renin–angiotensin–aldosterone system
Milk fat globule membrane

ABSTRACT

Objectives: Milk fat globule membrane (MFGM) found in buttermilk is rich in unique bioactive proteins. Several studies suggest that MFGM proteins possess biological activities such as cholesterol-lowering, antiviral, antibacterial, and anticancer properties, but data in humans are lacking. Furthermore, to our knowledge, no study has yet investigated the antihypertensive potential of MFGM proteins from buttermilk. The aim of this study was to investigate the effects of buttermilk consumption on blood pressure and on markers of the renin–angiotensin–aldosterone (RAS) system in humans.

Methods: Men and women (N = 34) with plasma low-density lipoprotein cholesterol < 5 mmol/L and normal blood pressure (< 140 mm Hg) were recruited in this randomized, double-blind, placebo-controlled, crossover study. Their diets were supplemented with 45 g/d of buttermilk and with 45 g/d of a macro-/micronutrient-matched placebo in random order (4 wk for each diet).

Results: Buttermilk consumption significantly reduced systolic blood pressure (−2.6 mm Hg; $P = 0.009$), mean arterial blood pressure (−1.7 mm Hg; $P = 0.015$), and plasma levels of the angiotensin I-converting enzyme (−10.9%; $P = 0.003$) compared with the placebo, but had no effect on plasma concentrations of angiotensin II and aldosterone.

Conclusion: Short-term buttermilk consumption reduces blood pressure in normotensive individuals.

Introduction

Hypertension is a major risk factor for cardiovascular disease (CVD) and renal dysfunction, and as a leading cause of death worldwide, is associated with 7.1 million deaths per year [1]. A healthy diet is an important element in the primary prevention and management of hypertension [2]. The development of dairy-based functional foods for blood pressure (BP) management has been of major interest in the past years. Milk peptides have been shown to lower BP in many clinical trials, and have been extensively reviewed [3–6]. Indeed, small milk peptides with hydrophobic and aromatic amino acid residues have been targeted for the development of functional foods inhibiting angiotensin-converting enzyme (ACE) activity—a key enzyme involved in BP regulation. Milk fat globule membrane (MFGM) components, found in large quantities in buttermilk, have been of growing interest over the past years because of their unique nutritional properties [7]. However, no study has yet investigated the antihypertensive potential of MFGM proteins from buttermilk. The aim of this study was to investigate for the first time the effects of buttermilk consumption on BP and on the markers of the renin–angiotensin–aldosterone (RAS) system in normotensive patients.

Materials and methods

Participants

White men and women were recruited in Quebec City at the Institute of Nutrition and Functional Foods between January and April 2011. Participants' group age was between 18 and 65 y, with body mass index (BMI) ≤ 35 kg/m^2, plasma low-density lipoprotein cholesterol concentrations < 5 mmol/L, a 10-y

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0899-9007
http://dx.doi.org/10.1016/j.nut.2013.07.021

calculated Framingham risk < 10% [8], normal BP (< 140/90 mm Hg) [1], and with a stable weight. Participants with a previous history of CVD, type 2 diabetes, monogenic dyslipidemia, endocrine disorders, using medications for hyperlipidemia or hypertension, practicing extreme nutritional habits (i.e., vegetarianism, alcohol consumption > 2 drinks/d), and elite athletes were not eligible.

Study design

We used a randomized, double-blind, placebo-controlled, crossover study design, according to which participants were randomly subjected to two consecutive 4-wk treatments with buttermilk or placebo [9]. During the study period, participants were instructed to maintain their usual diet, medication, weight, alcohol consumption, tea/coffee consumption (with a limit of 2 cups/d), and smoking habits. The use of vitamins and natural health product supplements was strictly forbidden throughout the trial. Any deviation from those recommendations would lead to exclusion from the study.

The study protocol was approved by The Clinical Research Ethics Committee of Laval University, and informed consent was obtained from all participants included (registered at clinicaltrials.gov as NCT01248026).

Study products and diet instructions

The buttermilk and placebo formulations were artificially flavored with chocolate, and provided in amounts equal to two servings of low-fat milk (45 g/d of skim milk solids). Sucralose was added to both formulations to improve taste and acceptability. The placebo product was formulated using dairy ingredients to match the buttermilk composition, with the exception of the presumed active components (i.e., MFGM components). The presence of MFGM components in buttermilk was confirmed by sodium dodecyl sulphate–polyacrylamide gel electrophoresis (SDS-PAGE) and high-performance liquid chromatograph for minor proteins and phospholipids, respectively. The general composition of the test products is presented in Table 1. The major difference between test products pertained to their content in polar lipids. Indeed, the buttermilk product contained more than 440% more polar lipids than the placebo. The SDS-PAGE profile also revealed a higher MFGM protein content in the buttermilk product versus placebo [9].

Participants were instructed to mix 22.5g pouches of chocolate-flavored buttermilk or a placebo with 250 mL of water, which they consumed just before breakfast and dinner each day, for a total consumption of 45 g/d of buttermilk or a placebo. Participants also were required to restrain their dairy consumption to a maximum of two servings daily.

Biochemical assessments

Blood samples were taken at screening and on two consecutive days at the end of each 4-wk test period (i.e., wks 4 and 8). The average of the two post-treatment values was used in all analyses. Plasma levels of ACE were measured with enzyme-linked immunosorbent assay (ELISA) kits (Quantikine; R&D Systems, Inc., Minneapolis, MN; coefficient of variation [CV] < 10 %). Plasma concentrations of angiotensin II (ANG) and aldosterone (ALDOS) were assessed using ELISA kits (Enzo Life Sciences, Inc., Plymouth Meeting, PA; both CV ≤ 18 %).

Anthropometric and blood pressure assessments

Anthropometric measures were taken at the beginning and at the end of each test period according to standardized procedures. BP was measured on the right arm using an automated mercury sphygmomanometer after a 10-min rest in a seated position. Systolic BP (SBP) and diastolic BP (DBP) measures were analyzed using the mean of three readings at 3-min intervals. Mean arterial pressure (MAP) was calculated as:

$$MAP = [(2 \times DBP) + SBP]/3$$

Statistical analysis

Data are reported as mean (± SD). Mixed models for repeated measures in SAS 9.2 (SAS Institute Inc., Cary, NC, USA) were used to assess the effect of buttermilk on the study outcomes. Changes in the study outcomes (buttermilk versus placebo) were analyzed in models using treatment as a fixed effect and adjusting for sex and values on placebo. There was no treatment by sequence interaction on any of the outcomes assessed. Significance was accepted at $P < 0.05$.

Results

Participants

Of the 40 participants randomized, 6 did not complete the intervention and were excluded from statistical analysis. No change in body weight and in hip and waist circumferences was recorded during the duration of the trial, and there were no side effects associated with the consumption of buttermilk compared with a placebo. Self-reported compliance was > 97% for both treatments. There was no difference in sodium intake between the two dietary phases (not shown). As shown previously [9], buttermilk consumption in these participants reduced plasma cholesterol and triglycerides (TG) concentrations by −3.1% ($P = 0.019$) and −10.7% ($P = 0.007$), respectively, compared with placebo.

Table 1
Composition of the ready-to-use buttermilk and placebo products (for a daily dose of 45g) and data on blood pressure and biomarkers of the RAS system in 34 normotensive men and women

	Placebo*	Buttermilk*	Difference†	*P*‡
	Mean ± SD	Mean ± SD		
Composition (45 g of powder)§				
Energy (kcal)	179.2	177.8	−0.8%	
Lactose (g)	23.0 ± 1.0	22.8 ± 1.0	−0.9%	
Total proteins (g)	13.0 ± 0.8	12.8 ± 1.0	−1.5%	
Total fat (g)	4.0 ± 0.4	4.0 ± 0.4	0.0%	
SFA (g)	2.30	2.08	−9.6%	
MUFA (g)	0.98	0.84	−14.3%	
PUFA (g)	0.14	0.12	−14.3%	
Total phospholipids (mg)	34.6	187.5	+441.9%	
Ashes (g)	3.6 ± 0.4	4.0 ± 0.0	+11.1%	
Water (g)	1.4 ± 0.4	1.4 ± 0.0	0.0%	
Systolic blood pressure (mm Hg)	110.9 ± 11.2	108.3 ± 11.6	−2.3%	0.009
Diastolic blood pressure (mm Hg)	65.6 ± 8.6	64.4 ± 8.3	−1.8%	0.069
Mean arterial pressure (mm Hg)	80.7 ± 8.8	79.0 ± 8.9	−2.1%	0.015
ACE level (ng/mL)‖	157.5 ± 48.0	138.8 ± 42.1	−10.9%	0.003
ANG-II level (pg/mL)	29.3 ± 51.1	27.8 ± 46.5	−5.1%	0.126
ALDOS level (pg/mL)‖	224.6 ± 154.2	226.6 ± 129.0	+0.9%	0.780

ACE, angiotensin I converting enzyme; ALDOS, aldosterone; ANG, angiotensin; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; RAS, renin–angiotensin–aldosterone; SFA, saturated fatty acid

* Values are means ± SD.

† Values are expressed as percentages of change compared with placebo.

‡ *P*-values were obtained using the PROC MIXED procedure in SAS.

§ Lactose, total proteins, total fat, ashes, and water values are presented as means and SD (n = 3).

‖ Analyses were performed on log-transformed values.