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Randomized double-blind controlled clinical trial of the blood pressure–lowering effect of fermented milk with *Lactococcus lactis*: A pilot study[1,2]

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ABSTRACT

The blood pressure–lowering effect of fermented milk with *Lactococcus lactis* NRRL B-50571 was evaluated in a double-blind randomized controlled clinical trial with prehypertensive subjects. Participants were randomized into 2 groups (n = 18 each group): one group treated with fermented milk with *Lactococcus lactis* NRRL B-50571 and a control group treated with artificially acidified milk. Results revealed that during daily consumption of fermented milk for 5 wk, systolic [(116.55 ± 12.26 mmHg vs. 124.77 ± 11.04 mmHg) and diastolic blood pressure (80.7 ± 9 vs. 84.5 ± 8.5 mmHg)] from the fermented milk group was lower than the control group. Additionally, triglyceride, total cholesterol, and low-density lipoprotein in blood serum were lower in the fermented milk group than in the control group. Results demonstrated that daily consumption of fermented milk with *Lactococcus lactis* (NRRL B-50571) had a blood pressure–lowering effect on prehypertensive subjects. Regular consumption of this product may be used as a potential functional food.
Key words: hypertension, *Lactococcus lactis*, fermented milk, clinical study, functional food

INTRODUCTION

Hypertension is a chronic degenerative disease that affects 1 billion people over the world and is a leading cause of death worldwide (WHO, 2013). Uncontrolled hypertension promotes chronic damage of the vascular system, myocardial strokes, and cerebrovascular insufficiency, among other cardiovascular diseases. However, with the objective of reducing the incidence of this disease, several pharmacological and nonpharmacological strategies have been implemented to prevent, treat, and reduce hypertension (Hernández and Anderson, 2012).

In this last respect, several foods have been identified that may help to reduce diseases, with milk and dairy products being the most widely studied (Shiby and Mishra, 2013). Furthermore, over the last 3 decades, milk-derived peptides have been identified with potential antihypertensive effect. These peptides may inhibit the angiotensin-converting enzyme (**ACE**), which prevents the formation of angiotensin II, a potent vasoconstrictor.

Several lactic acid bacteria have been reported to release potential antihypertensive peptides by the process of milk fermentation (Korhonen and Pihlanto, 2006). For instance, Rodríguez-Figueroa et al. (2010, 2012) fermented milk with specific strains of *Lactococcus lactis* and evaluated the ACE inhibitory activity in vitro. Results demonstrated that fermentation conditions and proteolytic activity of *L. lactis* for the production of ACE inhibitory peptides were strain dependent. Moreover, fermented milk with *L. lactis* NRRL-B50571 reduced systolic blood pressure (**SBP**) and diastolic blood pressure (**DBP**), heart rate, and had a hypolypidemic effect on spontaneously hypertensive rats (Rodríguez-Figueroa et al., 2013a,b). According to this, fermented milk with *L. lactis* NRRL B-50571 might have a hypotensive effect on hypertensive patients. Therefore, the aim of this work was to evaluate, in a randomized, placebo-controlled, double-blind study, the blood pressure–lowering effect of fermented milk with NRRL B-50571 on prehypertensive subjects.

MATERIALS AND METHODS

Subjects

A total of 60 volunteers aged from 25 to 55 yr were screened for enrollment at the Research Center for Food

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and Development (Spanish acronym: **CIAD**), Unilíder University, Caffenio Co., and Camino Nuevo School. A total of 36 subjects (20 men and 16 women) fulfilled the eligible criteria to participate (see Figure 1 for participant flowchart). Before screening, volunteers were given detailed information about the clinical study, and those willing to participate gave their voluntary written consent. Participant screening was performed at CIAD; and tests included medical clinical history, weight and height, laboratory tests on blood and urine, and blood pressure measurements. Blood pressure was measured in 3 separate visits. Inclusion criteria were both sexes, with SBP 120 to 139 mmHg and 80 to 85 mmHg for DBP (prehypertensive, JNC 8; Bell et al., 2015). Exclusion criteria were pregnancy, cardiovascular diseases, diabetes, cancer, dairy allergy, or lactose intolerance, and patients receiving ACE inhibitor pharmacological therapy. Nine volunteers were treated with antihypertensive medicines and were randomly allocated in both groups; their dosage did not change during this trial. Volunteers were asked not to make diet and lifestyle changes.

Study Design

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki (1975) as revised in 1983, and the protocol was approved by the Bioethics Committee of CIAD, Hermosillo, Sonora, Mexico (CE/003/2013).

This study was designed as a randomized, placebo-controlled, double-blind study. Personnel unaware of the treatment assignments performed all procedures (blood and urine samples and blood pressure measurements). A run-in period before the study started took place for baseline measurements and for randomization. Measurements included: blood pressure, total cholesterol, low-density lipoproteins (**LDL**), high-density lipoproteins (**HDL**), and triglycerides (**TG**). Based on

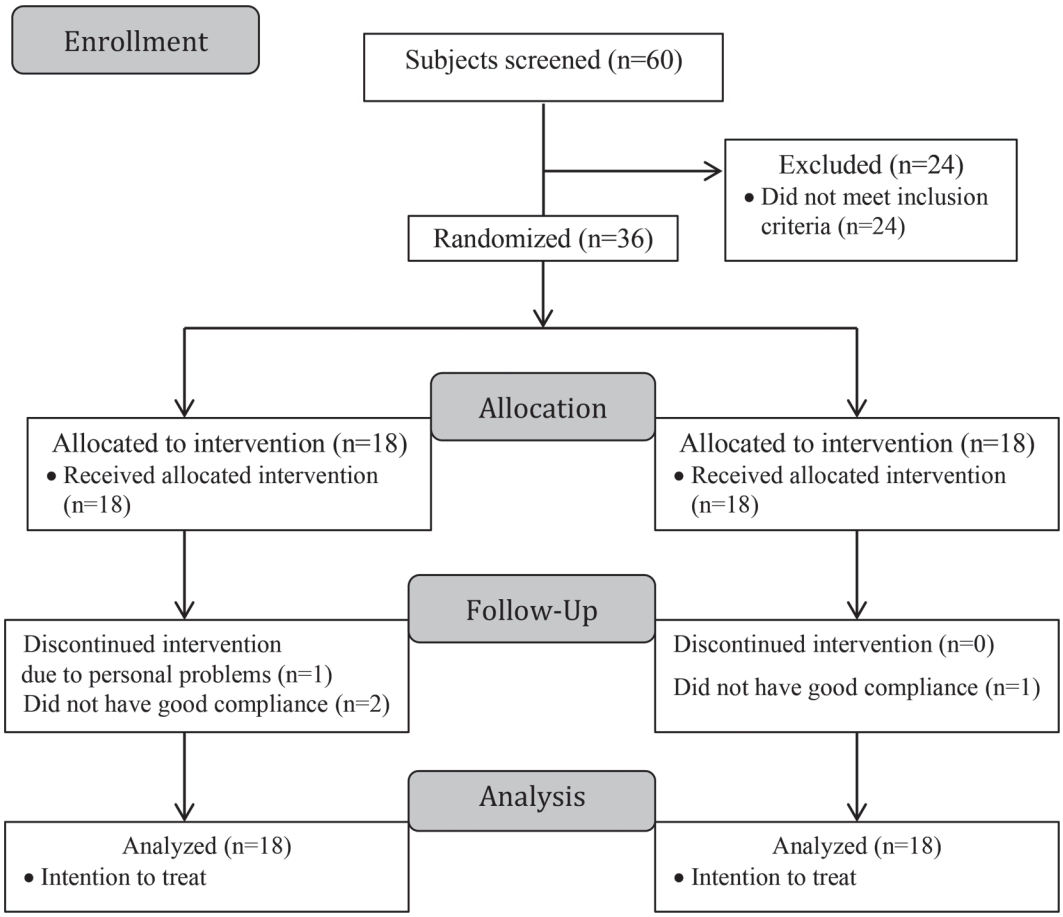

Figure 1. Participant inclusion flow chart.