ELSEVIER

Nutrition 23 (2007) 625–633

NUTRITION

www.elsevier.com/locate/nut

Applied nutritional investigation

Examination of encapsulated phytosterol ester supplementation on lipid indices associated with cardiovascular disease

Conrad P. Earnest, Ph.D.[a,*], Catherine R. Mikus, M.S.[a], Isabelle Lemieux, Ph.D.[b], Benoit J. Arsenault, M.S.[b,c], and Timothy S. Church, M.D., Ph.D.[a]

[a] *Pennington Biomedical Research Center, Preventive Medicine Laboratory, Baton Rouge, Louisiana, USA*
[b] *Québec Heart Institute, Hôpital Laval Research Centre, Québec, Québec, Canada*
[c] *Department of Anatomy and Physiology, Faculty of Medicine, Université Laval, Québec, Québec, Canada*

Manuscript received March 21, 2007; accepted June 5, 2007.

Abstract

Objective: As opposed to traditional food based delivery we examined the efficacy of ingesting encapsulated phytosterol esters on indices of lipid health in hypercholesterolemic adults.

Methods: We performed a randomized, double-blinded, parallel-group, placebo-controlled, clinical intervention examining 54 men and women (20–70 y of age) with a low-density lipoprotein cholesterol (LDL-C) level ≥3.33 mmol/L. Participants were not taking cholesterol-lowering medications. Treatment consisted of ingesting 2.6 g of encapsulated phytosterol esters ($n = 25$) or a matching placebo ($n = 29$) for 12 wk.

Results: Total cholesterol (TC) levels at baseline (mean ± SD) were 6.29 ± 0.7 mmol/L in the phytosterol group and 6.00 ± 0.7 mmol/L in the placebo group. Baseline LDL-C levels were 4.27 ± 0.7 mmol/L in the treatment group and 4.00 ± 0.8 mmol/L in the placebo group. Analysis of variance and Tukey's least significant difference post hoc analyses revealed a significant within-group reduction in TC (−0.23 ± 0.4 mmol/L, $P < 0.05$) and LDL-C (−0.22 ± 0.5 mmol/L, $P < 0.05$) for the phytosterol treatment group. Mean reductions in TC and LDL-C were greater than placebo ($P < 0.05$). Percentages of change from baseline for TC were −3.52% (95% confidence interval −6.44 to −0.40) for phytosterol treatment and 2.64% (95% confidence interval 0.30–5.60) for placebo. Those for LDL-C were −5.00% (95% confidence interval −9.92 to −0.08) for phytosterol and 4.89 (95% confidence interval 0.24–9.5) for placebo. No other significant effects were observed.

Conclusion: Encapsulated phytosterol ester ingestion appears to positively modulate LDL-C. Given that the reduction in LDL-C was not as extensive as in food-based trials, future investigations should examine potential timing and dose issues relative to encapsulated delivery.

Keywords: Phytosterol ester; Cholesterol; Lipid dietary supplement

Introduction

Coronary heart disease (CHD) remains the leading cause of death in industrialized nations [1]. Elevated low-density lipoprotein cholesterol (LDL-C) is a hallmark risk factor for CHD and a primary target for lipid-lowering therapy [1]. Although pharmaceutical interventions are readily available to lower LDL-C, many patients still prefer to seek alternative remedies given concerns about adverse drug reactions to lipid-altering medications [2,3]. One such alternative is the ingestion of plant-derived phytonutrients known as phytosterols.

A phytosterol is a naturally occurring sterol compound (e.g., sitosterol, campesterol, Brassica sterol, and stigmasterol) derived from plants that resembles mammalian cholesterol and steroid hormones. Typically obtained from vegetable oils, nuts, soy, corn, woods, and beans, phytosterols compete with dietary cholesterol for absorption in the in-

* Corresponding author. Tel.: 225-763-2923.
E-mail address: conrad.earnest@pbrc.edu (C. P. Earnest).

0899-9007/07/$ – see front matter
doi:10.1016/j.nut.2007.06.003

testines, resulting in lower blood cholesterol concentrations, specifically total cholesterol (TC) and LDL-C [4–9]. The effectiveness of phytosterols and phytostanols (the hydrogenated form of phytosterols) are endorsed by the United States National Cholesterol Education Program (NCEP) Adult Treatment Panel III at 2 g/d as an essential feature of therapeutic lifestyle changes along with diet modifications, weight reduction, intake of viscous fibers, and increased physical activity to reduce risk for CHD [10]. As part of a therapeutic lifestyle program, supplementing with phytosterols continues to be an effective means of reducing one's cholesterol. Further, phytosterols are also complementary to a cholesterol treatment program involving statins [11]. Indicative of the clinical evidence supporting phytosterols, the Food and Drug Administration (FDA) has authorized the use of a health claim for plant sterols and stanols recognizing that plant sterols may reduce the risk of CHD [12]. Although statin medications are highly effective in lowering TC and LDL-C, the authors of a recent report examining adherence to medication use in 31,750 patients with CHD contend that only 44% of patients reporting to take a lipid-lowering drug take it consistently [8].

Most studies showing a cholesterol reduction range from 7% to 15% and incorporate the phytosterols/stanols into margarine [4–7,9,13] or rapeseed-oil margarine [9,14,15]. Other dietary delivery vehicles include rapeseed-oil mayonnaise [16,17], reduced-fat spread and salad dressing [18], chocolate [19], butter [4], ground beef [20], low-fat yogurt [21], reduced-fat spread [22–24], and beverages [25,26]. Although reports do exist regarding the tablet administration form using phytostanols, the efficacy of encapsulated phytosterol ester administration is not as well established [27,28]. The aim of our present investigation was to examine the effects of ingesting 2.6 g/d of encapsulated phytosterols esters on indices of cholesterol metabolism in hypercholesterolemic adults.

Materials and methods

Study population

We examined 54 men and women 20–70 y of age who volunteered for this investigation. This study was performed at the Cooper Institute in Dallas, Texas and was approved by a human subjects review board for the same institution. All participants entered the trial with LDL-C concentrations ≥3.33 mmol/L. We recruited individuals by radio, television, and newspaper advertisements. All participants signed an informed written consent before entering into the investigative portion of the trial. Participants were excluded from the trial if their body mass index was <18.5 or >34.9, they had recently donated blood (<3 mo), or they did not agree to abstain from donating blood during the trial. Also excluded were participants with elevated blood pressure, TC, LDL-C, or fasting plasma glucose requiring immediate drug therapy as described by national guidelines (Joint National Committee VI, Adult Treatment Panel II, and American Diabetes Association) [29].

We also excluded those individuals who planned to move from the area during the trial, had taken lipid-altering medications in the previous 6 mo (inclusive of niacin), smoked, consumed alcoholic beverages exceeding an average of three drinks per day, consumed caffeinated coffee in excess of 710 mL/d, and women who were pregnant or lactating. We accepted those currently on standard medical therapy for conditions such as hypertension, arthritis, or other chronic diseases and postmenopausal women on and off hormone replacement therapy if they agreed to remain on their current therapy during the trial. All participants were informed of their baseline cholesterol concentrations so that they could make an informed decision as to whether to enter the trial or seek medical counsel. We advised participants with an LDL-C level ≥4.14 mmol/L of the risks associated with LDL-C concentrations of this nature and recommended they seek medical attention; however, we allowed those participants wishing to continue participation in the trial to do so.

Pretrial screening

As with previous trials from our group, we used a four-phase approach to implement the trial [30–32]. A schematic of the study timeline is presented in Figure 1. These phases included 1) a telephone screening procedure to determine potential eligibility, 2) an initial screening visit to examine fasting LDL-C, 3) two baseline visits inclusive of a second confirmatory LDL-C examination (visit 1) and a more thorough examination (visit 2), and 4) one post-test assessment at 12 wk. Continuation to the treatment portion of our study was predicated on participants having two screening LDL-C measurements differing by ≤10%. If the difference in LDL-C measurements between the two visits was >10%, the participant was asked to return for a third screening visit. The average of the two closest screening visit measurements was used for the criterion entry lipid variable. During the last baseline visit, participants also completed several questionnaires detailing their medical history and dietary habits. Once participants completed all of these forms, they became eligible for formal randomization into the treatment portion of the trial. If participants did not meet these conditions, they were not randomized into the treatment portion of the study. The time elapsed between the first run-in visit and the third baseline collection periods ranged from 10 to 14 d. Fifty-four participants were successfully randomized into the trial.

The rationale for using this type of enrollment procedure was to establish stable baseline entry criteria for LDL-C and to minimize dropouts and maximize protocol compliance by dissuading participants who were less likely to complete the trial given their willingness to adhere to the study procedure. During the treatment