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Randomized control trials

Consuming a mixed diet enriched with lupin protein beneficially affects plasma lipids in hypercholesterolemic subjects: A randomized controlled trial

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SUMMARY

Background & aims: The objectives of this study were to assess whether 25 g/d lupin protein, integrated into a mixed diet, might affect cardiovascular risk factors and whether L-arginine was responsible for these effects.

Methods: Seventy-two hypercholesterolemic subjects participated in the randomized, controlled, double-blind three-phase crossover study. They were assigned to three diets with 25 g/d lupin protein (LP), milk protein (MP) or milk protein plus 1.6 g/d arginine (MPA) each for 28 d in a random order interrupted by 6-week washout periods. Lupin protein and the comparator milk protein were incorporated into complex food products (bread, roll, sausage, and vegetarian spread). Arginine was administered via capsules. Sixty-eight subjects were included in final analyses.

Results: Compared with MP, LDL cholesterol was significantly lower after LP. Compared with MP and MPA, homocysteine was significantly lower after LP. Compared with baseline, concentrations of total, LDL, and HDL cholesterol significantly decreased after LP and MPA. Triacylglycerols and uric acid significantly decreased after LP. The relative changes in total and LDL cholesterol were significantly greater for subjects with severe hypercholesterolemia (>6.6 mmol/L) than those with moderate hypercholesterolemia (5.2–6.6 mmol/L).

Conclusions: The present study showed for the first time that incorporation of 25 g/d of lupin protein into a variety of complex food products lowers total and LDL cholesterol, triacylglycerols, homocysteine, and uric acid in hypercholesterolemic subjects. The hypocholesterolemic effect is stronger in subjects with severe hypercholesterolemia. Arginine might be responsible for some, but not all of the beneficial effects of lupin protein.

This trial was registered at http://clinicaltrials.gov (study ID number NCT01598649).

1. Introduction

The potential of lupin protein to beneficially affect blood lipids and blood pressure has been investigated only in a few human intervention studies.[1–4] In all these studies, lupin protein was provided additionally to the normal diet in the form of a protein drink[1,4] or a dietary bar.[2,3] In all but one study, high daily doses of approximately 35 g lupin protein were given. So far, lupin protein has not been tested within a mixed diet by incorporating a modest amount (25 g/d) into a variety of well-designed food products with a complex composition and improved sensory properties. Moreover, the underlying mechanisms that are responsible for the lipid- and blood pressure-lowering activities of lupin protein have not yet been elucidated.[5] Accounting for more than 10% of total amino acids, L-arginine is abundant in lupin protein and thus suspected to be one of its bioactive compounds. Administration of additional arginine in amounts of 3 g/d up to 17 g/d was found to lower blood pressure[6] and total[7,8] as well as LDL cholesterol[8] in humans.

Thus, the objective of the present study was twofold: (1) to investigate the effect of 25 g/d lupin protein on blood lipids, the

Abbreviations: LP intervention, intervention with lupin protein; MP intervention, intervention with milk protein; MPA intervention, intervention with milk protein plus arginine; FFP, 3-d Food Frequency Protocol; hs-CRP, high-sensitivity C-reactive protein.

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amino acid profile, homocysteine, uric acid, high-sensitivity C-reactive protein (hs-CRP), as well as on blood pressure, incorporated into a variety of complex food products (bread, roll, sausage, and vegetarian spread), as part of a mixed diet; and (2) to test the effects of an arginine-supplemented milk protein diet in comparison with two diets enriched with lupin protein and milk protein. Therefore, a randomized, double-blind crossover intervention study was conducted in hypercholesterolemic subjects consuming three different intervention diets for 28 d each: (i) a diet with 25 g/d of lupin protein or (ii) milk protein, or (iii) the milk protein diet supplemented with 1.6 g/d arginine.

2. Materials and methods

2.1. Subjects

In and around Jena, 132 volunteers between 18 and 80 years of age were recruited. Eligibility criterion was a total cholesterol concentration of $\geq$5.2 mmol/L at screening. Exclusion criteria were the intake of lipid-lowering drugs or nutritional supplements that might potentially influence lipid metabolism and intolerance, an allergy, or strong aversion to any food ingredient used in the study products. In addition, breast-feeding mothers and pregnant females were excluded. Thus, 72 eligible participants (41 females, 31 males) were invited to an in-person meeting. Here, participants were offered essential study-relevant information in oral and written forms. Written informed consent was obtained from all subjects before the start of the study. The study was registered at ClinicalTrials.gov as NCT01598649 (National Institutes of Health) and approved by the Ethics Committee of the Medical Faculty of the Friedrich Schiller University, Jena (no.: 2607-07/09).

2.2. Study design

The randomized, double-blind crossover study consisted of three intervention periods of 28 d each, separated by 6-week washout periods. During the intervention periods, subjects received either: (i) lupin protein (LP intervention); (ii) milk protein (MP intervention); or (iii) milk protein plus arginine (MPA intervention) in a random order. Before commencement, subjects were randomly assigned to one of the three randomization groups, A, B, or C using computer-generated random numbers (Fig. 1). The research assistants who performed the randomization did not have access to any information regarding demographic or laboratory characteristics of the subjects. Moreover, all study products were labeled with numeric codes and all research assistants as well as the participants were blinded to group assignments. The study was conducted between June and December 2012 at the Friedrich Schiller University Jena (Institute of Nutrition, Department of Nutritional Physiology, Jena, Germany).

2.3. Study products and capsules

In the present study, 25 g lupin protein isolate was incorporated into complex study products and administered as part of a mixed diet for 28 d. The amount of protein and intervention time were based on the results of a previous study of our work group,[4] where

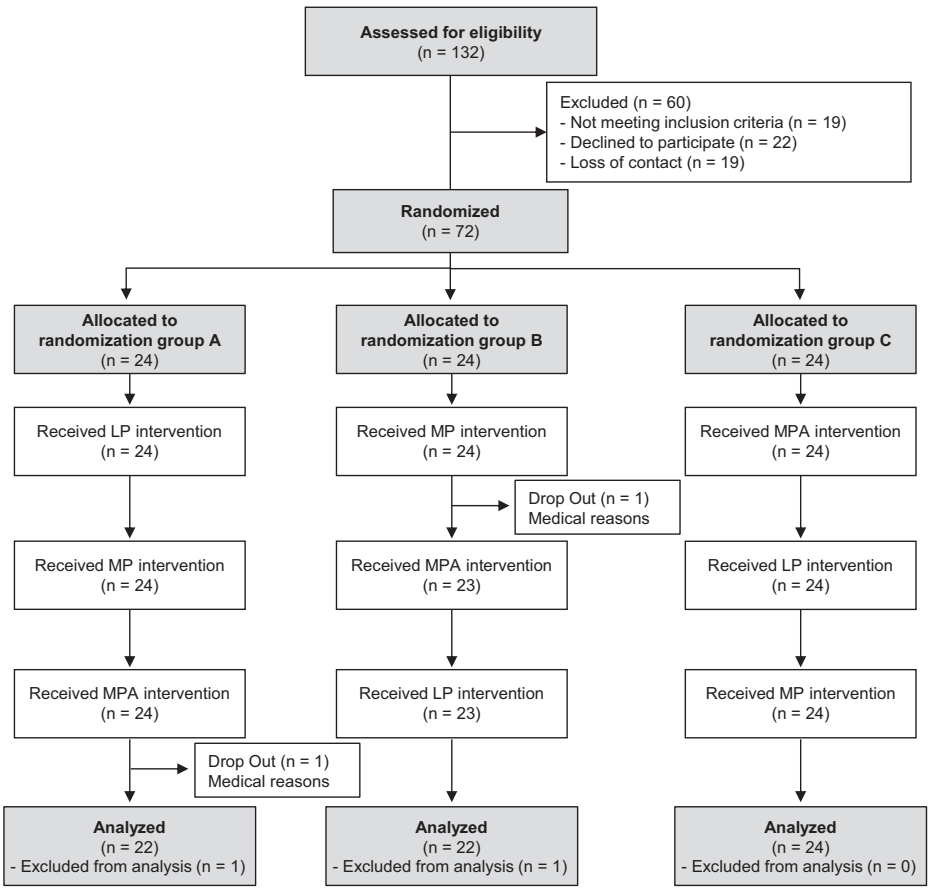

Fig. 1. CONSORT 2010 flow diagram of the study participants. LP intervention, intervention with lupin protein; MP intervention, intervention with milk protein; MPA intervention, intervention with milk protein plus arginine.

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