Cholesterol-lowering effect of spreads enriched with microcrystalline plant sterols in hypercholesterolemic subjects

Summary Background Plant sterols have been shown to reduce serum lipid concentrations. The effectiveness is highly dependent on the physical state of the plant sterols. By means of a new crystallizing method, plant sterols can be added into dietary fats and oils homogeneously. In this fat ingredient, plant sterols are in a microcrystalline form. Aims of the study We investigated the cholesterol-lowering effect and possible side effects of vegetable oil-based spreads fortified with two different doses of microcrystalline plant sterols.

Methods: This double-blind randomized, placebo-controlled study consisted of a 6-wk run-in and a 6-month experimental period. During the run-in period, all 155 hypercholesterolemic subjects received rapeseed oil-based control spread. In the beginning of the experimental period subjects were randomly assigned into one of three experimental groups. The control group continued to use control spread, and the two test groups used spreads with added plant sterols of either 1.5 g/d or 3.0 g/d. The subjects consumed test spreads as a part of their normal diet without any restrictions in lifestyle and diet. Results Plasma total- and LDL-cholesterol concentrations were significantly reduced by 7.5–11.6% (0.46–0.62 mmol/l) in groups consuming margarine enriched with free plant sterols, compared with the control group. The effects were similar between the two groups consuming either 1.5 g or 3.0 g plant sterols per day. No effect on HDL-cholesterol or triacylglycerol concentrations occurred. The test spreads did not induce any adverse effects in blood clinical chemistry, hematology or decreases in serum concentrations of lipid soluble vitamins. Conclusions Microcrystalline plant sterols are effective in lowering serum total- and LDL-cholesterol concentrations without obvious side effects. The daily dose of 1.5 g plant sterols is enough to reach the maximum effect.

Key words Plant sterols – Cholesterol – LDL-cholesterol – Crystalline form – Clinical study

Introduction

Plant sterols are naturally occurring components of plants. They reduce serum cholesterol levels by inhibiting cholesterol absorption in the small intestine. In the lumen of the intestine, dietary fat including sterols is distributed between the oil and micellar phases [1]. When the solubility of sterols is exceeded, sterols may also occur as solid sterol monohydrated crystals [2]. The solubilities of cholesterol and plant sterols are not independent, but are mutually limiting [3, 4]. The presence of plant sterols decreases the solubility of cholesterol in the oil phase with the consequent precipitation of solid cholesterol monohydrate, which is not absorbed. According to the mechanism presented by Mattson et al [2] the absorptibility of cholesterol is determined by the total sterol concentration (cholesterol + plant sterols) in the...
fat. Similarly, large cholesterol doses are known to reduce the percent of cholesterol absorption [5]. It is likely that the effective form of plant sterols is the free form, not the ester form, as the free form will predominate in the intestinal lumen [1].

The maximum effectiveness of the plant sterols can be obtained only if they are present in the intestine simultaneously with the cholesterol [6]. The preferred carrier for plant sterols would be dietary fat, which is also a carrier of dietary cholesterol. Enrichment of food products with plant sterols is difficult from a production technology and food quality point of view since plant sterols are insoluble in water and only poorly soluble in dietary fats. Esterification of the plant sterols and stanols with fatty acids increases their lipid solubility and thus facilitates their incorporation into fat containing foods [4].

By means of a new crystallizing method, up to 30% of plant sterols can be added to food fats and oils without any chemical reactions or additives such as emulsifying agents. The resulting fat ingredient is homogeneous and stable, and plant sterols exist as the free sterols in both the dissolved and microcrystalline form.

The purpose of the present study was to investigate the cholesterol-lowering effect of the microcrystalline plant sterol ingredient in hypercholesterolemic subjects as a part of a normal Finnish diet. In addition the effect of 6 months consumption of the ingredient on serum concentrations of plant sterols, lipid soluble vitamins, clinical chemistry and hematological parameters were measured.

Subjects and methods

The study protocol was approved by the Human Ethical Committee of the Faculty of Agriculture and Forestry, University of Helsinki and by the Ethical Committee of the Oulu Deaconess Institute, in Finland.

Subjects

Subjects were recruited through advertising in the local newspaper. Altogether, 270 volunteers were screened for the study. To be included in the study, subjects had to have a total serum cholesterol concentration $\geq 5.8$ mmol/l, to have serum triacylglycerol concentration $< 3$ mmol/l, to be aged 25–64 y, to be willing to participate and not to be an abuser of alcohol. The following subjects were excluded: persons with a diagnosis of type 1 diabetes mellitus, myocardial infarction within the previous 3 months, malignancy, psychosis, malabsorption, chronic liver or renal disease or homozygous familiar hypercholesterolemia; subjects receiving lipid-lowering drugs or dietary regimen or using cortico-

steroids, oral anticoagulants, immunosuppressants; pregnant women, women who were breast feeding and women of child-bearing potential who were not using chemical or mechanical contraception. Subjects who had stable medication for hypothyreosis, type II diabetes, hypertension or other CVD were included. A total of 155 subjects participated in the study. All subjects received both written and oral information regarding the trial and gave written consent.

Study design

During the pre-screening visit medical history, alcohol consumption and use of drugs, including lipid-lowering therapy, were recorded. Weight and height were measured and recorded. The first blood samples were drawn for cholesterol and triacylglycerol concentration screening. The pre-screening visit also included a routine physical examination. Subjects were asked to confirm their agreement by signing a consent form and they were told that they could withdraw from the study at any time.

This double-blind randomized, placebo-controlled study consisted of a 6-wk run-in period and a 6-month experimental period. All subjects received a control spread during the run-in period. At the end of the 6-wk run-in period, the subjects were randomly assigned to one of three groups: the control group continued to use the control margarine, the second group used the margarine with 1.5 g/d added plant sterols and the third group used margarine with 3.0 g/d added plant sterols. The double-blind dietary testing period lasted for 6 months and there were three control visits during that period (0, 3 and 6 month's visits). Six weeks after subjects had finished the margarine-eating study and had returned to their habitual diet, the subjects were invited to attend the last control visit.

Test spreads and diet

The subject consumed test spreads as a part of their normal diet and they were advised not to make any dietary changes during the study. Subjects received 25 g per day of the test-spread and were advised to replace 25 g of their normal dietary fat by the test spread. The subjects were advised to use the daily margarine in at least two doses.

The three different spreads included a control spread (rapeseed oil based margarine) and two test spreads fortified with two different concentrations of ingredient-containing plant sterols. These test spreads provided 1.5 g/d and 3.0 g/d of plant sterols. The plant sterol-containing ingredient was a microcrystalline suspension of plant sterols in rapeseed oil. Wood-based plant sterols