

SYNOPSIS

Name of Sponsor <i>Nutritech International AB</i>	
Title of trial: Effects of boiled, flaked, milled barley powder product (<i>Aktiv</i>) on LDL-, HDL- and total cholesterol, triglycerides, glucose, insulin and HS-CRP levels in healthy hypercholesterolemic men and women.	
Study responsible: Johan Olsson, PhD	Project manager: Birgitta Sundberg, PhD
Trial centre: Centre for Human Studies of Foodstuffs, Uppsala University, Uppsala, Sweden	
Trial period: March – June 2005	
Objectives: <i>Primary Objectives:</i> To determine the effects of soluble fibers (mainly β -glucans) in <i>Aktiv</i> on LDL-cholesterol after 4 weeks of consumption in comparison to instant flour with cellulose as placebo, in mildly hypercholesterolemic men and women (LDL-cholesterol levels $>3,0$ mmol/l). <i>Secondary Objectives:</i> To determine the effects of <i>Aktiv</i> on HDL-, total cholesterol, triglycerides and HS-CRP, after 4 weeks consumption in comparison to placebo in healthy mildly hypercholesterolemic men and women. To determine the effects of <i>Aktiv</i> on glucose- and insulin levels, after 4 weeks consumption in comparison to placebo in healthy mildly hypercholesterolemic men and women. To evaluate the safety of <i>Aktiv</i> on gastrointestinal adverse events, ASAT, ALAT, TSH, creatinin and Hb in comparison to placebo in healthy hypercholesterolemic men and women.	
Methodology: Cross-over design, single-blind, randomised, placebo-controlled study.	

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Number of subjects (planned and analysed): The planned number of subjects to be included in this study was 46. Forty-nine subjects entered the study (20 males 29 females). Eight subjects discontinued the study, thus a total of 41 subjects completed the study period. Due to laboratory failure 39 subjects were analysed for efficacy.

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Summary

The compliance for the study was around 95 %. The back-ground diets were registered for two week days and one week-end day during each consumption period. The results from the intake of the back-ground diets showed only small differences between treatments.

Efficacy Results:

Primary endpoint

The mean change in LDL-cholesterol level between *Aktiv* and placebo after 4 weeks consumption showed statistical significance (estimate -0.21, p-value 0.0031). This change corresponds to a reduction of approximately 5 %.

Secondary endpoints

Total cholesterol and triglyceride levels were also significantly lower after consumption of *Aktiv* compared to placebo. Furthermore, no statistically significant differences between *Aktiv* and placebo were shown in HDL-cholesterol, HS-CRP, (High Sensitive C-reactive Protein), plasma-glucose and serum insulin levels.

Safety Results:

Only adverse events connected to gastro-intestinal events were registered. These events were evenly distributed between the treatments. At screening as well as at visit 4 clinical chemistry and haematology parameters were analysed. No differences between *Aktiv* and placebo were found. The BMI (body mass index) was measured at baseline and at the end of the study periods. These measurements showed no differences between treatments and no differences compared to baseline.

Conclusion:

The studied population was likely to achieve health benefits by reducing their cholesterol levels (LDL- and total cholesterol levels) when consuming *Aktiv* in comparison to placebo. By reducing the LDL-cholesterol levels, people might reduce their risk of coronary heart disease (CHD) and other major vascular events.

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Inclusion criteria:

- Healthy was assessed by the inclusion and exclusion criteria and the results of the screening laboratory tests.
- Signed written informed consent.
- Body Mass Index (BMI) ≥ 20 to ≤ 31 kg/m².
- LDL >3.0 mmol/l.
- Hb 120 g/l for women and 130 g/l for men.
- Age ≥ 20 and ≤ 75 years at visit 1.

Exclusion criteria:

- Participation in a clinical trial including blood sampling and/or administration of substances within 90 days prior to visit 1.
- Consumption of cholesterol lowering medication.
- Consumption of products or supplements fortified with plant sterols or omega-3 or omega-6 fatty acids within 3 weeks prior to the study and no consumption during the study.
- Consumption of glucosamine two months prior screening visit and throughout the study.
- Slimming or medically prescribed diet or medication or a special diet (i.e. vegetarian, vegan, gluten-free).
- Changed body weight more than 10 % six months prior to the study.
- Pregnant or lactating or wish to become pregnant during the period of the study.
- Lack of suitability for participation in the trial, for any reason, as judged by the personnel at KPL.

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Test products, doses and mode of administration:

Three separated times a day, the subjects were obliged to stir carefully one serving of the investigational products (20 g) into a cold non-alcoholic beverage (i.e. water, juice, milk, yoghurt etc) and to drink immediately thereafter. The subjects were asked to fill in date and sign every day they consumed 60 g of the investigational products. They were also asked to comment any failure in their obligations and to give a reason for not consuming the total amount of investigational products.

The study product, *Aktiv*, was a boiled flaked and milled barley powder. *Aktiv* was prepared by a patented process. The barley kernels were, before the patented process prepared by a process kept by the sponsor. *Aktiv* was distributed as a powder in 20 g serving packages. *Aktiv* used in the study contained per 100 g fresh weight:

Starch	57 %
Protein	11.2 %
Fat	2.6 %
Dietary fibre	11.2 %
Insoluble dietary fibre	6.2 %
β-glucan	1.3 %
Soluble dietary fibre	5 %
β-glucan	3.7 %
Water	10.2 %

The molecular weight measurements of the β-glucans in *Aktiv* was made at Swedish University of Agricultural Sciences in Uppsala, Sweden. The results showed an average molecular weight of 1.70×10^6 Daltons in *Aktiv*, which is considered to be a high molecular weight.

The reference product (placebo): Conventional instant wheat flour with an addition of cellulose. The placebo product was distributed as flour in 20 g serving packages. The placebo product contained per 100 g fresh weight:

Starch	65 %
Protein	8.5 %
Fat	1.3 %
Dietary fibre	11.2 %
Insoluble dietary fibre	9.7 %
Soluble dietary fibre	1.5 %
Water	10.6 %

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Duration of treatment:

The study was a randomised, placebo-controlled, single-blind, cross-over, intervention study with voluntary free-living subjects. A total of 49 healthy male and female subjects with elevated LDL-cholesterol levels (>3.0 mmol/l) were randomised. After a screening visit subjects with elevated levels of LDL-cholesterol were chosen to participate in the study. The subjects were randomised into one of two groups, starting to consume either *Aktiv* or placebo wheat for 4 weeks. After the first 4 weeks period, a 4 weeks wash-out period was followed. After the wash-out period the group that started consuming *Aktiv* was eating the placebo product and vice versa for 4 weeks.

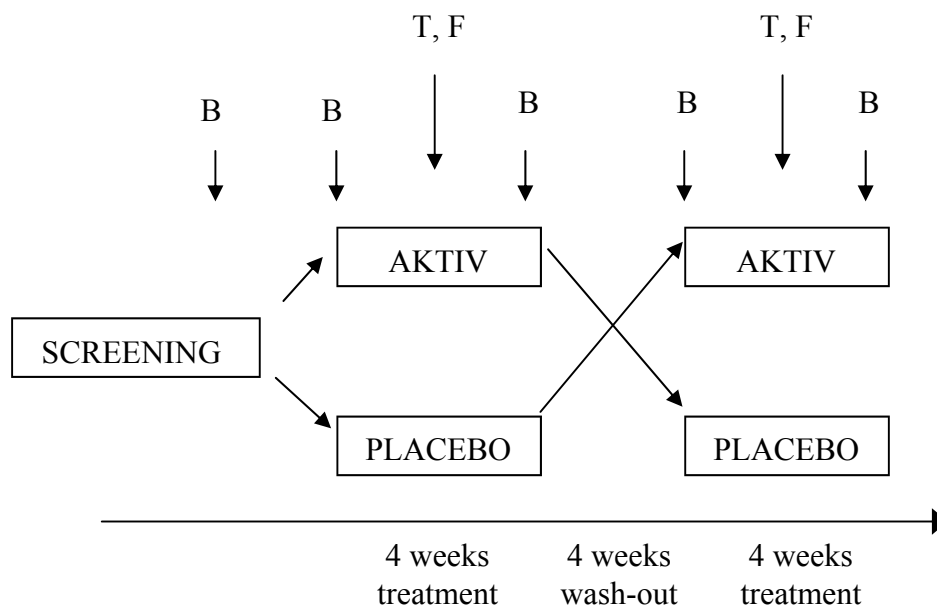


Figure 1. Cross-over design for the *Aktiv* study, B=blood samples, T=Telephone follow-up, F=food registration.

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Criteria for evaluation:

Efficacy:

Efficacy population – Subjects with no major protocol deviation and a compliance of at least 79.8 %.

Safety:

Safety population - Subjects with at least one intake of test substance.

Statistical methods:

The carry-over effect of the primary endpoint was evaluated by testing the mean sums of the levels of LDL-cholesterol between treatment sequences with the Student's t-test, this test is two-sided and performed at 10 % significant level. Since no significant carry-over effect was found, the treatment differences were analysed with a paired t-test.

The secondary efficacy endpoints were evaluated with similar methods as for the primary endpoint.

Date of report

Draft: September 2005

Final: October 2005