Original paper

Influence of combined botanical extract preparation on body composition – results from double blind randomized clinical trial

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Submitted: 15 June 2006
Accepted: 30 July 2006

Arch Med Sci 2006; 2, 3: 171-178
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Abstract

Introduction: Obesity is becoming a great cause of concern in many countries. To shift the energy balance towards expenditure, dietary supplements should be designed to increase thermogenesis, lipolysis, loss of body water, and activation of digestive enzymes.
Material and methods: Double blind randomized placebo-controlled clinical trial to evaluate a botanical water extract composed of green tea extract, bean peel and asparagus. During 56 days of the study body composition, anthropometric measurements and biochemical parameters were estimated in fifty-one healthy, moderately obese subjects.
Results: Forty-two subjects completed the study according to the protocol. In the active preparation group, weight, BMI, percent of body fat, waist, hip and waist-to-hip ratio were not statistically different compared to placebo. The sum of skinfolds differed significantly. When selecting a subgroup of patients with hypercholesterolaemia (n=21), in the active extract group the change in body composition index (BCI) and fat mass (FM) were significant (p=0.037 and p=0.019 respectively) in patients with hypercholesterolaemia when compared to normocholesterolaemic patients. Fat-free mass (FFM) did not change significantly in the active extract group (p=0.083) when hypercholesterolaemic and normocholesterolaemic patients were compared. None of the parallel parameters (FM and FFM change, BCI) changed significantly in the placebo group when compared to hypercholesterolaemic and normocholesterolaemic subjects.
Conclusions: There was no statistically significant change in weight, BMI or percent of body fat measured by bioimpedance in the active extract and placebo groups. Obese patients with hypercholesterolaemia benefited from the active extract, with reduced total fat mass and a positive influence on the body composition improvement index.

Key words: obesity, herbal extracts, body fat, lipid profile, body composition.

Introduction

Obesity is becoming a great cause of concern in many countries. The problem is also associated with possible complications such as hyperlipidaemia, hypertension, coronary heart disease and diabetes [1-3]. Obesity has been characterized as a long-term energy imbalance. Energy balance is defined as the difference between total energy or caloric intake and energy expenditure. If food energy intake is greater than energy expenditure, the body will store the excess energy as fat [4]. Thus body composition could be changed either

by modifing food intake or expenditure [5]. The diet could be modified, but also research into dietary supplements is being performed worldwide.

A desirable dietary supplement should be simultaneously designed to increase thermogenesis, lipolysis, loss of body water, and activity of digestive enzymes. Single agents, mostly obtained from herbal sources, have been ineffective or moderately effective. Therefore finding a combination of more than one agent seems to be appropriate. Such a complex agent could act in many directions. Components should be sought among digestive enzymes, such as lipases through the catechins of tea extracts, and alpha-amylase through kidney bean extract. These same components may also improve the blood lipid profile. Other extracts may stimulate oxidation of fatty acids through the activity of caffeine from guarana and tea extracts.

The aim of this study was to evaluate the influence of a composite herbal extract called Nutrifin support on selected anthropometric measurements and body composition change in relation to lipid profile.

Material and methods

The study was performed between 2 October and 29 November 2003 at the Eugeniusz Piasecki University School of Physical Education. Forty-nine patients aged 25 to 64 (47.1±10.0) were scheduled for visit 1 (V1, screening and start visit) before randomization. They signed a written consent form and the study was approved by the local bioethics committee. The inclusion criteria were body mass index 25-35 kg/m^2 and no chronic disease. All subjects had anthropometric measurements taken including: four skinfolds (SKF, data presented as sum of 4 skinfolds), weight, height, waist and hip circumference, percentage of body fat (% body fat) estimated by bioimpedance method (Spectrum Lightweight, Italy). All patients were asked to fast at during visits and blood was collected for biochemical estimations. Total cholesterol, LDL, HDL, triglycerides, glucose and insulin were measured in sera from all subjects (Cormay Elisa kit, Poland). Prestudy patient characteristics are presented in Table I.

Table I. Patient characteristics

Prestudy patient characteristics	Group A (combined botanical extract supplement)	Group B (*placebo*)
Weight (kg)	87.7±13.7	83.9±10.3
BMI (kg/m^2)	30.9±3.7	30.1±2.8
Sum of SKF (cm)	95.5±16.2	93.4±13.6
% body fat (%)	37.4±6.1	36.6±6.3
Waist (cm)	95.0±10.9	94.6±10.7
Hip (cm)	112.4±7.8	111.4±6.4
WHR (1/1)	0.85±0.08	0.85±0.09
Systolic pressure (mmHg)	129.3±12.8	128.8±21.0
Diastolic pressure (mmHg)	80.9±10.3	81.9±12.0
Cholesterol (mg/dl)	201.0±28.1	205.1±20.7
LDL (mg/dl)	124.2±27.1	117.5±30.0
HDL (mg/dl)	57.4±9.5	64.8±19.3
HDL/LDL (1/1)	0.49±0.15	0.70±0.69
Triglycerides (mg/dl)	96.7±42.2	114.0±40.3
Lp(a) (mg/dl)	10.7±12.6	12.6±13.4
Homocysteine (mmol/l)	12.5±4.4	8.6±2.5
Leptin (ng/ml)	22.4±12.6	20.7±11.3
Glucose (mg/dl)	100.6±17.2	95.0±16.3
Insulin (µIU/ml)	8.3±3.0	8.7±3.2

After visit 1 patients were randomized in a double-blind manner. Patients in group A received an active preparation in tablet form of Nutrifin support, which is a botanical water extract composed of green tea extract, bean peel and asparagus. Two coated tablets were dispensed daily, each containing 900 mg of active ingredients: asparagus extract 500 mg, green tea extract 300 mg, bean pod extract 100 mg. Group B received a placebo, which was identical in size, colour and taste. Both groups received 4 tablets per day. Patients were then scheduled for visit 2 (V2, 28 days after start point) and end visit 3 (V3, 56 days after start of the study). On each visit all above-mentioned procedures were repeated, on visits 1 and 2 a new part of the active preparation or placebo was dispensed, and on visits 2 and 3 remaining tablets were collected.

Additionally some anthropometric parameters were calculated: waist-to-hip ratio (WHR), fat mass (FM) as FM=weight (kg) x % body fat (%) and fat-free mass (FFM) as FFM=weight (kg) – FM (kg). The body composition improvement index (BCI) was calculated as the sum of positive changes (decrease in FM and increase in FFM, positive values) or the sum of negative changes (increase in FM and decrease in FFM, negative values).

Data were stored in Excel files and analysed with SigmaStat v3.1 software (Systat Software Inc, 2004, USA). Values are presented as means ±SD (standard deviation). The normal distribution was checked with the Kolgomorov-Smirnof test. Because only some subgroups of data were normally distributed, all data were analysed with distribution-free tests. In the comparisons between the same parameters measured during visits 1 and 3, Wilcoxon rank sum test was used. The difference in changing anthropological and biochemical parameters during visits (paired) was estimated using Friedman repeated measures analysis of variance on ranks with pairwise multiple comparison Tukey test. Correlations were estimated by Spearman's test (Rs). Differences

between groups A and B concerning change of parameters during the study were analysed with Mann-Whitney test, when not otherwise specified. A p value less than 0.05 was considered significant.

Results

Of 51 patients only 42 completed the study according to the protocol. Nine patients did not show up on scheduled visits (6 from group A and 3 from group B) or resigned from the study. Mean BMI in group A was 30.9±3.7 kg/m^2, in group B 30.1±2.8 kg/m^2 at first visit. Changes in outcome measures in groups A and B are presented in Tables II and III. In the active preparation and placebo groups a significant reduction in sum of skinfolds was noticed. This measurement is more dependent on the observer and probably represents measurement error.

The group receiving combined botanical extract and that receiving placebo were compared. Changes in anthropometric measurements from both groups between start and end visit are presented in Table IV. They were not statistically significant except for sum of skinfolds, which probably represents measurement

Table II. Changes of main parameters during 3 visits in group A, in [ ] parenthesis – Tukey contrast test to indicate visits with statistical difference

Parameter group A	Visit 1 (V1)	Visit 2 (V2)	Visit 3 (V3)	Friedman test p [Tukey test]
Weight (kg)	87.7±13.7	87.3±13.33	87.2±13.33	0.85
BMI (kg/m^2)	30.9±3.7	0.8±3.79	0.8±3.7	0.75
Sum of SKF (cm)	95.5±16.2	2.8±14.7	91.7±14.7	**<0.001**
% body fat (%)	37.4±6.1	37.7±6.2	36.9±6.4	**[V1:V2, V1:V3] 0.029 (0.045)* [V2:V3]**
Waist (cm)	95.0±10.9	94.8±11.1	95.6±11.0	0.67
Hip (cm)	112.4±7.8	111.0±8.6	111.8±8.3	0.41
WHR (1/1)	0.85±0.08	0.85±0.08	0.86±0.09	0.25

Table III. Changes of main parameters during 3 visits in group B, in [ ] parenthesis – Tukey contrast test to indicate visits with statistical difference

Parameter group A	Visit 1 (V1)	Visit 2 (V2)	Visit 3 (V3)	Friedman test p [Tukey test]
Weight (kg)	83.9±10.3	83.7±10.6	83.8±10.6	0.46
BMI (kg/m^2)	30.1±2.8	30.1±2.9	30.1±3.0	0.86
Sum of SKF (cm)	93.4±13.6	89.1±13.4	87.5±13.1	**<0.001 [V1:V2, V1:V3, V2:V3]**
% body fat (%)	36.6±6.3	37.0±6.8	36.5±6.8	0.11
Waist (cm)	94.6±10.7	93.4±10.7	93.2±11.4	0.18
Hip (cm)	111.4±6.4	111.0±5.9	110.9±7.3	0.42
WHR (1/1)	0.85±0.09	0.84±0.08	0.84±0.08	0.64

Table IV. Changes in main outcome measures between visit 3 and visit 1 in combined botanical extract supplement group (A) and placebo (B)

Parameter	Change in group A between V3 and V1	Change in group B between V3 and V1	Mann-Whitney test p
Weight (kg)	-0.43±1.09	-0.09±1.49	0.65
BMI (kg/m^2)	-0.14±0.38	0.02±0.57	0.52
sum of SKF (cm)	-3.8±3.2	-5.9±2.8	**0.049**
% body fat (%)	-0.54±1.55	-0.09±1.9	0.37
Waist (cm)	0.6±2.7	-1.4±4.7	0.096
Hip (cm)	-0.6±1.9	0.5±2.8	0.96
WHR (1/1)	0.01±0.03	-0.01±0.04	0.16

Table V. Changes in FM, FFM and BCI in groups A and B. In [] parenthesis: difference between visits 1 and 3 in Mann-Whitney test, p value

Parameter (kg)	Group A [Mann-Whitney test]	Group B [Mann-Whitney test]	p (Mann-Whitney test)
FM visit 1	32.85±8.13	30.88±7.33	0.46
FM visit 3]	32.15±7.78	30.80±7.91	0.64
FM V1 vs V3	[0.06]	[0.87]	
FFM visit 1	54.81±10.18	53.05±7.83	0.91
FFM visit 3	55.09±10.63	53.04±8.06	0.95
FFM V1 vs V3	[0.34]	[0.98]	
Change FM	-0.70±1.56	-0.08±2.10	0.37
Change FFM	0.28±1.28	-0.01±1.62	0.70
BCI	0.98±2.64	0.06±3.43	0.36

Table VI. Correlations between start parameters (visit 1) and changes in anthropologic and biochemical parameter in group A (active preparation)

Parameter group A	Change in weight	Change in BMI	Change in SKF sum	Change in % fat	Change in cholesterol	Change in LDL	Change in HDL	Change in HDL/LDL	Change triglycerides
VISIT 1 Age	NS	NS	NS	NS	NS	NS	NS	NS	NS
Weight	NS	NS	NS	NS	NS	NS	NS	NS	NS
BMI	NS	NS	NS	-0.52 (0.027)	NS	NS	NS	NS	NS
SKF sum	NS	NS	-0.54 (0.02)	NS	0.70 (0.001)	0.70 (0.001)	NS	-0.74 (<0.001)	NS
% fat	NS	NS	NS	NS	0.48 (0.045)	NS	NS	NS	NS
Waist	NS	NS	NS	NS	NS	NS	NS	NS	NS
Hip	NS	NS	NS	NS	NS	NS	NS	NS	NS
WHR	NS	NS	NS	NS	-0.53 (0.02)	-0.48 (0.04)	NS	NS	NS
Cholesterol	NS	NS	NS	-0.56 (0.016)	-0.92 (<0.001)	-0.88 (<0.001)	NS	0.55 (0.02)	NS
LDL	NS	NS	NS	-0.52 (0.027)	-0.86 (<0.001)	-0.91 (<0.001)	NS	0.63 (0.005)	NS
HDL	NS	NS	NS	NS	NS	NS	NS	NS	NS
HDL/LDL	NS	NS	NS	NS	0.65 (0.002)	0.74 (<0.001)	NS	-0.59 (0.009)	NS
Triglycerides	NS	NS	NS	NS	NS	NS	NS	NS	NS

variability rather than higher reduction of this parameter in the placebo group. We also calculated fat mass, fat-free mass and body composition improvement index (during visits 1 to 3). Differences in observation in each group and comparison between groups are presented in Table V.

To search for additional relationships between values, correlations were estimated. They are presented in Table VI for group A (combined botanical extract supplement) and Table VII for group B (placebo). All anthropometric measurements (main outcome measure) and lipid profile were correlated

Table VII. Correlations between start parameters (visit 1) and changes in anthropologic and biochemical parameter in group B (*placebo*)

Parameter group B	Change in weight	Change in BMI	Change in SKF sum	Change in % fat	Change in cholesterol	Change in LDL	Change in HDL	Change in HDL/LDL	Change triglycerides
VISIT 1 Age	NS	NS	NS	NS	NS	NS	NS	NS	NS
Weight	NS	NS	NS	NS	NS	NS	NS	NS	NS
BMI	NS	NS	NS	NS	NS	NS	NS	NS	NS
SKF sum	NS	NS	NS	0.68 (0.001)	NS	NS	NS	NS	NS
% fat	NS	NS	NS	NS	NS	NS	NS	NS	NS
Waist	NS	NS	-0.54 (0.018)	NS	NS	NS	NS	NS	NS
Hip	NS	NS	NS	NS	NS	NS	NS	NS	NS
WHR	NS	NS	-0.52 (0.022)	NS	NS	NS	NS	NS	NS
Cholesterol	NS	NS	NS	NS	-0.54 (0.016)	NS	NS	NS	NS
LDL	NS	NS	NS	NS	NS	NS	NS	NS	NS
HDL	NS	NS	NS	NS	NS	NS	-0.64 (0.003)	NS	-0.47 (0.041)
HDL/LDL	NS	NS	NS	NS	NS	NS	-0.57 (0.01)	NS	-0.48 (0.037)
Triglycerides	NS	NS	NS	NS	NS	NS	NS	NS	-0.71 (<0.001)

with change from baseline of selected parameters. Lipid profile and its change were not the main outcome measure, but the lipid status could be of importance in separating patients with potential influence of the researched botanical extract. We selected a subgroup of hypercholesterolaemic patients (the inclusion criterion was total cholesterol >200 mg/dl on visit 1) and analysed some anthropometric measurements once again. The results are presented in Table VIII. Changes in fat mass, fat free mass and body composition improvement index dependent on hypercholesterolaemia in both gro-ups A and B are presented in Figure 1. In the combined botanical extract supplement group the change in BCI and FM was significant (p=0.037 and p=0.019 respectively) in patients with hypercholesterolaemia when compared to normocholesterolaemic patients. Fat-free mass did not change significantly in the active extract group (p=0.083) when hypercholesterolaemic and normocholesterolaemic patients were compared. None of the parallel parameters (FM and FFM change, BCI) changed significantly in the placebo group when comparing hypercholesterolaemic and normocholesterolaemic subjects.

Discussion

Treatment of obesity is complex and requires changes in eating habits and energy expenditure, but many other factors such as motivation, lifestyle, understanding, activity and pressure from the media are crucial to control body weight. Introducing herbal products which undergo microbiological and analytical tests seems to be reasonable to assess as adjuvant treatment of overweight subjects [6]. Many dietary supplements targeted at weight management are combination products rather than single agents. Thus it is difficult to evaluate the effectiveness of single agents when combination products are tested. Lenz et al. performed a meta-analysis of not numerous, but only single agents, tested in randomized, double blind, placebo-controlled clinical trials [7]. Chromium in a dose of 200 or 400 µg daily, as a single agent, failed to produce a statistically significant effect on body weight in all analysed trials [7-9]. Other studies

Table VIII. Changes in main outcome parameters in patients with hypercholesterolaemia (>200 mg/dl at the start of the study)

Parameter	Change in group A between V3 and V1 n=10	Change in group B between V3 and V1 n=11	Mann-Whitney test p
Weight (kg)	-0.88±1.13	-0.11±1.26	0.13
BMI (kg/m^2)	-0.30±0.40	0.04±0.48	0.078
sum of SKF (cm)	-2.8±3.4	-6.8±2.7	0.012
% body fat (%)	-1.1±1.54	-0.30±2.33	0.38

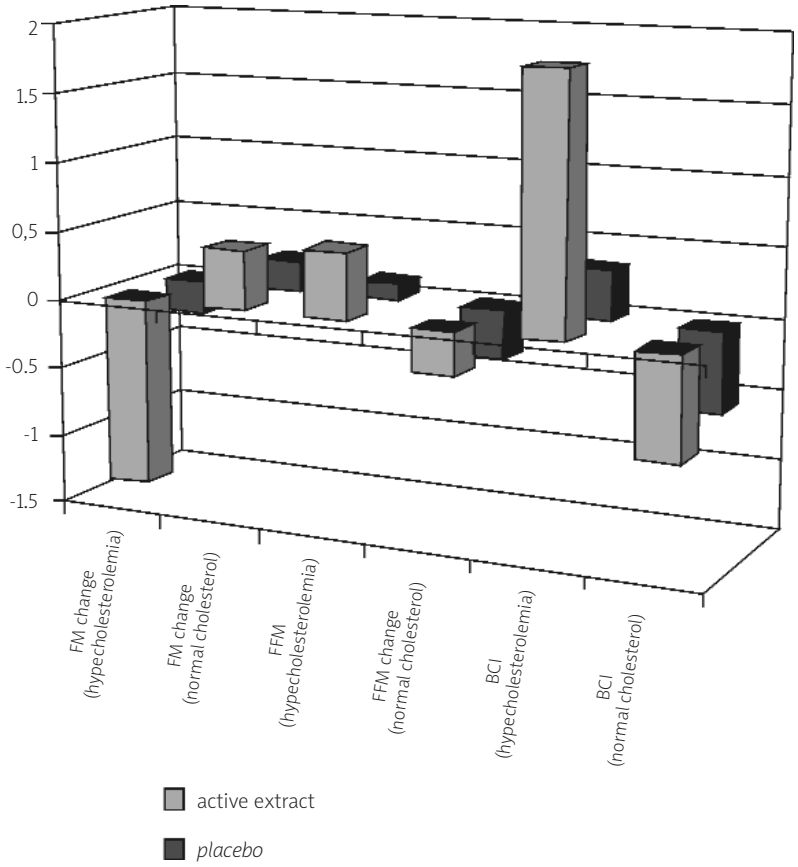

Figure 1. Changes in fat mass, fat-free mass and body composition improvement index dependent on hypercholesterolaemia in group A (active extract) and group B (*placebo*)

with hydroxycitric acid (HCA) obtained from Garcinia cambogia yielded inconsistent results in weight reduction [6, 7, 10-13]. Other factors to be discussed are ephedrine alkaloids and caffeine. Green tea extracts contain up to 25% of xanthine alkaloids including caffeine and theobromine; they also consist of up to 60% flavonols including the whole group of catechins, especially epigallocatechin gallate (EGCG), which inhibit lipase activity [14, 15]. Green tea extract (rich in catechin polyphenols and to a lesser extent in caffeine) stimulates the respiration rate of brown adipose tissue [16]. Numerous clinical studies on the slimming properties of green and black teas and their constituents such as EGCG have been performed and their efficacy has been shown. Extract from tea also increases thermogenesis and in consequence also energy expenditure. The energy balance could be shifted towards weight reduction [14-16]. If, as is generally accepted, thermogenesis contributes 8-10% of daily energy expenditure, the 4% increase in 24-h energy expenditure due to green tea extract in a study by Dulloo et al. would

extrapolate to a 35-43% increase in the thermogenesis compartment [16]. But how to translate this theoretical calculation into clinical evaluation? The results from controlled studies are optimistic, moderately influencing weight, body composition and blood lipids [16-19]. The currently studied composition contained 4 x 300 mg green tea extract daily, but failed to produce a significant effect in combination with asparagus and bean pods. The potential active ingredients in green tea extract are caffeine and catechins. In our study the dose of caffeine and epigallocatechin in green tea extract was 10% and 40% respectively. Particular interest should be focused on the effects of green tea extract in enhancing thermogenesis and fat oxidation, which could not be explained solely on the basis of its caffeine content. In a well designed study with green tea extract compared to caffeine and placebo, equivalent to that in the extract dose of caffeine solely failed to alter energy expenditure [16]. The dose of caffeine in this study as well as those by Dulloo et al. is far too low to produce a thermogenic effect. Doses of 600-1000 mg of caffeine daily are supposed to produce such an effect [8, 20]. But it was also reported that lower doses could be useful (55-87 mg) [6]. Other composite extracts (ephedrine alkaloids, caffeine, white willow bark) were evaluated in a randomized double-blind, placebo-controlled trail during 12 weeks among 102 subject with BMI 30-39.9 kg/m^2. Such composition revealed significant between-group difference in weight loss (-2.18 vs -0.53 kg), BMI (-0.87 vs -0.21 kg/m^2), but not in percent of body fat or fat mass [19]. In a randomized controlled trial among 288 subjects a dose of 200 mg of caffeine daily was evaluated as safe. The FDA allows up to 1600 mg daily caffeine as over-the-counter preparations [20].

The other group of herbal substances which act as appetite modulators comprises plants characterized by the presence of dietary fibre. Asparagus and bean pods contain soluble fibre. Among acting mechanisms the most important is to produce the satiety effect. Other mechanisms are a regulatory effect on intestinal functions common to both soluble and insoluble fibre and the barrier effect. Daily consumption of fibre should be about 40 grams, much more than in our study with combined botanical extract. Probably this is also a reason why most observations suggest that fibre intake does not result in a positive effect on body weight [6].

Asparagus and kidney bean pods are common food plants, and as with tea or extracts they have a long tradition of use as mild diuretics. Asparagus has been cultivated for over 2,000 years as a vegetable and medicinal herb. Both the roots and the shoots can be used medicinally; they have a restorative and cleansing effect on the bowels, kidneys and liver. The plant is an antispasmodic, aperient, cardiac, demulcent, diaphoretic, diuretic, sedative and tonic. Kidney bean (*Phaseolus vulgaris*) extract contains alpha amylase inhibitor [21, 22].

In this study no significant influence on body weight or anthropometric parameters was observed, except sum of skinfolds. Measuring skinfolds is an indirect method of estimating body composition, but the bioimpedance method is preferred. Interestingly, body composition changed when dividing patients into hypercholesterolaemic (>200 mg/dl) and normocholesterolaemic. The effect was composed of decreasing body fat, increasing fat-free mass, thus improving body composition. But also weight reduction and percentage of body fat was close to borderline significance. However, small groups make it difficult to draw conclusions.

In the current trial a composition of three herbal extracts was used, which theoretically should increase antiobesity potential. Unfortunately, within a combination it is difficult to estimate which herbal extract contributed significantly to the observed decreased body fat and improvement in body composition.

Conclusions

1. There was no statistically significant change in weight, BMI or percent of body fat measured by bioimpedance in the combined botanical extract supplement and placebo groups.
2. Changes in fat mass, fat-free mass and body composition improvement index were slightly more favourable for the active extract group compared to placebo, but did not reach statistical significance.
3. Obese patients with hypercholesterolaemia benefited from the active extract, with a reduction in total fat mass and a positive influence on the body composition improvement index.
4. Changes of anthropometric measurements in subjects with hypercholesterolaemia from the active extract group were more favourable than from the placebo group, but did not reach statistical significance.

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