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A randomized, double-blind, placebo-controlled study of a once daily blend of herbal extracts for weight loss

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Abstract

A blend of herbal extracts (Weighlevel® One; a mixture of extracts from the leaves of *Alchemilla vulgaris*, *Olea europaea*, *Mentha longifolia* and from the seeds of *Cuminum cyminum*) taken once per day has previously been shown to be effective in producing weight loss in healthy volunteers. The aim of the present study was to confirm if the effects previously observed are reproducible in a second cohort of healthy volunteers. Thirty adult subjects were randomized to consume the herbal blend (n = 15) or placebo (n = 15) once per day for 8 weeks. Weight and waist circumference were assessed weekly. The primary endpoint was the change from baseline in body weight for the herbal blend group compared with placebo. Secondary assessments included waist circumference, appetite, craving, bowel health, and safety and tolerability. Treatment with the herbal blend for 8 weeks produced progressive and significant reductions in weight. Corresponding statistically significant reductions in body mass index and waist circumference were also observed. Weight loss with this herbal extract was similar to that observed in previous studies thus demonstrating a reproducible effect. Daily administration of this blend of herbal extracts supports weight loss.

Keywords: *Alchemilla vulgaris*, *Olea europaea*, *Mentha longifolia*, *Cuminum cyminum*, overweight, obesity, slow release

1. Introduction

The number of people living with overweight or obesity has risen to nearly 2 billion adults worldwide [1]. Obesity increases the risk of other serious comorbidities such as cardiovascular disease and type 2 diabetes. Weight loss is a key part of managing health as sustained weight loss of as little as 3% to 5% can produce clinically meaningful reductions in cardio-metabolic risk factors such as blood glucose and lipids, with larger weight losses producing greater benefits [2]. There is great interest in the use of dietary supplements for weight loss since many people are unsuccessful in their attempts to lose weight through diet and exercise alone. It is estimated that between 15 and 34% of adults have used a dietary supplement for weight loss at some point in their lives [3, 4]. Dietary supplement users are more likely to be concerned about their health and weight, and they are more likely to have attempted to lose weight multiple times with various products and methods [4]. People seek dietary supplements for weight loss for various reasons including frustrations with previous attempts at dieting and/or exercise, desire for a “magic bullet” for weight loss, ease of availability, appeal of a “natural” remedy, and belief that supplements are safer than over-the-counter or prescription medications [5]. Dietary supplements are one of the most common over-the-counter products on the market; however, the majority of dietary supplements lack any clinical evidence of efficacy or safety [6, 7].

The aim of the present study was to confirm the efficacy of a slow-release formulation of a blend of herbal extracts (Weighlevel® One) taken once per day in a randomized, double-blind, placebo-controlled study. We previously demonstrated that this blend of herbal extracts from plants traditionally used in Greco-Arab and Islamic medicine (Leaves of *Alchemilla vulgaris*, *Olea europaea*, and *Mentha longifolia* and the seeds of *Cuminum cyminum*) produced significant weight loss in healthy adults [8-10]. This clinical trial was conducted to determine if the effects seen could be reproduced in a second cohort of volunteers.

2. Methods

2.1 Ethical considerations

All experiments were examined and approved by the appropriate ethics committee represented by Dr. Steen Lindkær-Jensen (Aarhus University, Aarhus, Denmark and Imperial College, London, UK), and were performed in accordance with the ethical requirements and current scientific standards as indicated by European Good Clinical Practice Guidelines and the 1964

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Declaration of Helsinki.

Informed and written consent was obtained from all participants prior to participation in the study.

2.2 Participants

Participants were recruited from the Copenhagen area in Denmark via discussions with a specially trained qualified nurse (Erla Øregaard, who is recognized as a specialist in patient safety by the Danish Health Authority). Eligible participants were generally healthy, not pregnant, unsatisfied with their current weight, interested in losing weight, and agreed to follow study protocol. The study was performed at health clinics in Copenhagen, Denmark (Well-Come Fitness & Health Center, Strandvejen 203, DK 2900 Hellerup) between January 19, 2017 and March 30, 2017.

2.3 Study design

This study was a randomized, double-blind, placebo-controlled trial lasting 8 weeks. Participants were randomized 1:1 to the herbal blend or placebo treatment group. The herbal blend (Weighlevel®One) is a mixture of extracts from the leaves of *Alchemilla vulgaris*, *Olea europaea*, *Mentha longifolia* and from the seeds of *Cuminum cyminum* and a patented slow release component (Propol®). These ingredients are Generally Regarded as Safe (GRAS). The herbal blend and matching placebo each had a net weight of 0.88 grams and were manufactured by Propharma (Copenhagen).

The herbal blend (60 tablets) or matching placebo (60 tablets) was supplied in coded containers. The sealed list of container numbers and corresponding contents was kept by an independent auditor until the end of the study. Participants were randomly assigned a coded container by the recruiting nurse. The participants, recruiting nurse, and investigators remained blinded during the study.

Treatment allocation was concealed, and blinding was maintained by administering the herbal blend or matching placebo in coded containers.

Participants were instructed to take 1 tablet with lunch each day and continue with their normal daily activities for the 8-week study. In person examinations were conducted at baseline and at Weeks 4 and 8. Weekly follow-up reports were conducted online. Adverse events were assessed throughout the study. The primary endpoint was the change from baseline in body weight for the herbal blend group compared with placebo. Secondary assessments included waist circumference, appetite, craving, bowel health, and safety and tolerability.

2.4 Visual analog scale assessments

Appetite, craving, and bowel health were assessed using visual analog scales (VAS) that have been reported to be reliable in appetite research [11]. Each VAS consisted of a clear unmarked plastic strip. Participants were asked to place their finger on the strip in response to the following questions: How hungry are you today? (Appetite), How much have you been craving sugar/sweets today? (Craving), and Are you

having bowel movements daily/how does your bowel feel? (Bowel health). Each plastic strip was then given a numerical rating from 1 to 5 by the investigator in which higher numbers indicated an improvement: Appetite (1 = hungry, 5 = low appetite), Craving (1 = craving sugar, 5 = no craving), Bowel Health (1 = infrequent bowel movements, uncomfortable bowel, 5 = bowel ok).

2.5 Statistical analysis

Analyses were conducted on the intent-to-treat population. A two-sample t-test was used to compare changes from baseline in treatment and control groups. No sample size calculations were conducted for this study.

3. Results

3.1 Participants

A total of 50 volunteers were assessed for eligibility. Reasons for exclusion from the study were: Did not meet inclusion criteria (n = 16) and declined to participate (n = 4). Thirty participants were randomized to receive the herbal blend (n = 15) or placebo (n = 15) once per day for 8 weeks. All participants completed the study according to the protocol and were included in final analyses.

Demographics and baseline characteristics were generally similar across treatment groups, although body weight and waist circumferences were slightly greater in the group that received the herbal blend (Table 1).

Table 1: Demographics and baseline characteristics

	Placebo (N = 15)	Herbal blend (N = 15)
Age (years)	45.3 ± 12.4	45.6 ± 13.8
Sex, Female	12 (80.0%)	11 (73.3%)
Weight (kg)	77.3 ± 7.9	83.6 ± 15.3
Height (cm)	173.7 ± 8.4	177.1 ± 10.3
BMI (kg/m ²)	25.6 ± 1.1	26.5 ± 2.1
Waist circumference (cm)	85.4 ± 6.4	92.5 ± 11.3

Data are mean ± SD or n (%)

3.2 Body weight and waist circumference

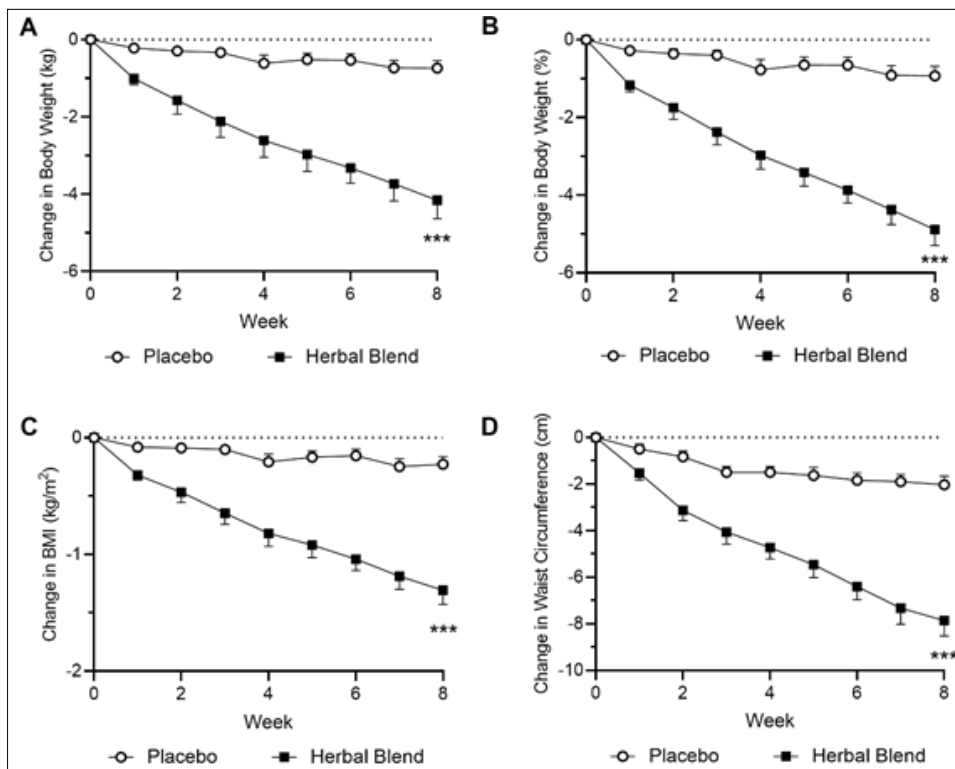
Over the course of the 8-week study, progressive weight loss of approximately 0.5 kg/week was observed in the herbal blend treatment group (Figure 1A). By week 8, the herbal blend group lost an average of 4.2 kg (95% CI: -5.2 to -3.1 kg; $P < 0.0001$) compared with 0.7 kg (95% CI: -1.2 to -0.3kg) weight loss for the placebo group (Table 2). This is equivalent to a 4.9% (95% CI: -5.8 to -4.0%; $P < 0.0001$) reduction in weight in the group that received the herbal blend, compared to a 0.9% (95% CI: -1.5 to -0.4%) reduction in the placebo group (Figure 1B, Table 2). Similarly, weight loss also resulted in a statistically significant reduction from baseline in BMI in the herbal blend group from 26.5 ± 2.1 kg/m² to 25.2 ± 1.9 kg/m² (Figure 1C and Table 2, $P < 0.0001$). Waist circumference was reduced by 7.9 cm in the herbal blend group (mean ± SE at Week 8: 84.6 ± 9.6 cm) compared with 2.0 cm in the placebo group (Week 8: 83.4 ± 6.2 cm) (Figure 1D and Table 2, $P < 0.0001$).

Table 2: Change from baseline to week 8 in weight, BMI, waist circumference, and patient-reported outcomes

Change in	Placebo (N = 15)	Herbal blend (N = 15)	LS Mean difference	P-value
Body weight (kg)	-0.7 (0.2)	-4.2 (0.5)	-3.4 (0.5)	<0.0001
95% CI	[-1.2, -0.3]	[-5.2, -3.1]	[-4.5, -2.3]	
Body weight (%)	-0.9 (0.2)	-4.9 (0.4)	-4.0 (0.5)	<0.0001
95% CI	[-1.5, -0.4]	[-5.8, -4.0]	[-4.9, -3.0]	
BMI (kg/m ²)	-0.2 (0.1)	-1.3 (0.1)	-1.1 (0.1)	<0.0001

95% CI	[-0.4, -0.1]	[-1.6, -1.0]	[-1.4, -0.8]	
Waist circumference (cm)	-2.0 (0.4)	-7.9 (0.7)	-5.8 (0.7)	<0.0001
95% CI	[-2.8, -1.2]	[-9.3, -6.5]	[-7.4, -4.3]	
VAS appetite	-0.3 (0.1)	0.5 (0.2)	0.9 (0.3)	0.004
95% CI	[-0.6, -0.1]	[0.0, 1.0]	[0.3, 1.4]	
VAS cravings	-0.1 (0.2)	0.6 (0.2)	0.7 (0.3)	0.03
95% CI	[-0.6, 0.3]	[0.1, 1.1]	[0.1, 1.4]	
VAS bowel	0.0 (0.1)	0.1 (0.2)	0.1 (0.3)	0.61
95% CI	[-0.2, 0.2]	[-0.4, 0.6]	[-0.4, 0.7]	

Data are mean ± SD and 95% confidence interval. BMI: Body mass index; VAS: Visual analog scale.



Data are mean ± SE (n = 15). *** $P < 0.001$ compared to placebo.

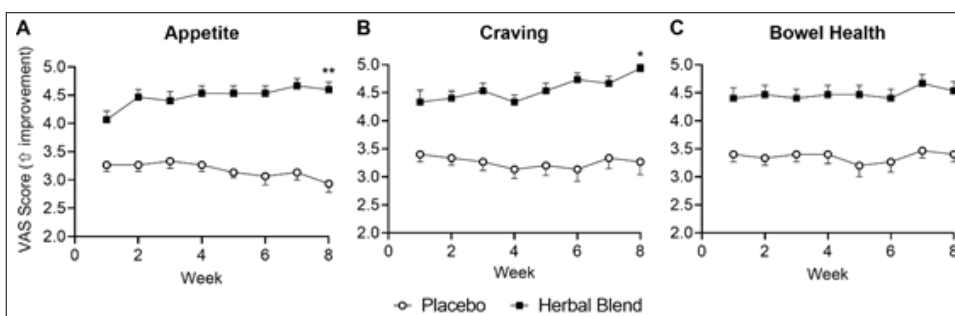
Fig 1: Herbal blend reduces body weight, BMI, and waist circumference.

A) Change in body weight, B) Change in percent body weight, C) Change in BMI, D) Change in waist circumference.

3.3 Visual analog scale ratings

Patient-reported ratings of appetite and cravings for sweets improved significantly in the herbal blend group compared

with the placebo group after 8 weeks ($P < 0.05$, Table 2 and Figure 2). No significant changes in ratings of bowel health were observed.



Data are mean ± SE (n = 15). * $P < 0.05$, ** $P < 0.01$ compared to placebo.

Fig 2: Subjective ratings of appetite, craving, and bowel health

A) Visual analog scale rating of appetite (1 = hungry, 5 = no appetite). B) Visual analog scale rating of craving for sweets (1 = craving sugar, 5 = no craving). C) Visual analog scale rating of bowel health (1 = infrequent bowel movements, uncomfortable bowel, 5 = bowel ok).

3.4 Safety

No adverse events were reported, and the herbal blend was well tolerated.

4. Discussions

In this randomized, double-blind, placebo-controlled, 8-week

study, daily administration of the herbal blend resulted in progressive and statistically significant weight loss in healthy adults. At the end of the study, individuals in the herbal blend group lost an average of 4.2 kg (4.9% of baseline body weight) while individuals in the placebo group lost an average of 0.7 kg (0.9% of body weight).

The herbal blend was well tolerated with no adverse events were reported. These results are similar to what we observed in a previous 8-week study where participants taking the once daily herbal blend lost an average of 4.7% of their baseline body compared with 0.2% weight loss in the placebo group [10]. Although these studies were only 8 weeks in duration, weight loss approached the clinically meaningful 5% reduction from baseline that is expected to produce improvements in cardio-metabolic markers [12]. In both studies, weight loss continued for the duration of the study without evidence of a plateau, thus additional weight loss may be possible with continued administration of the herbal blend beyond 8 weeks. In previous studies with a 3 times per day formulation of the herbal blend, weight loss continued over the 3 month duration of the study for a final weight loss of 10-13% of baseline body weight [8, 9]. All trials of the herbal blend conducted to date consistently demonstrate statistically significant and clinically meaningful weight loss.

In conjunction with meaningful weight loss, BMI and waist circumference also decreased significantly. Elevated BMI and/or waist circumference are components of metabolic syndrome, a cluster of risk factors that promotes the development of cardiovascular disease [13]. Treatment with the herbal blend decreased BMI by an average of 1.3 kg/m² compared with a decrease of 0.2 kg/m² in the placebo group. Waist circumference decreased an average of 7.9 cm in the herbal blend group compared with a decrease of 2.0 cm in the placebo group. These changes suggest a decrease in adiposity, especially central adiposity, with the herbal blend. Reductions in waist circumference have also been associated with improvements in lipids and blood pressure [14, 15]. Further research is needed to directly confirm if the herbal blend caused any change in fat mass or other cardio-metabolic markers such as blood pressure, lipids, and blood glucose.

While the herbal blend appears effective in producing weight loss, the exact mechanisms behind its effects are unknown. Our previous study had suggested that reduced caloric intake may play a role due to reductions in appetite and craving as measured by VAS [10]. In the present study, similar significant changes in appetite or craving were also observed, suggesting that the reductions in appetite and craving observed with the herbal blend are reproducible. These changes in subjective measures of appetite and craving may translate into reduced caloric intake and warrants further study.

The plants used in the herbal blend are expected to contribute to weight loss and produce improvements in cardiovascular and metabolic measures through several potential mechanisms. We previously demonstrated that treatment with the herbal blend increases brown adipose tissue thermogenesis in rats [9]. *Alchemilla vulgaris* (Lady's mantle) is used in traditional Arabic medicine for weight loss [16], and extracts of *Alchemilla vulgaris* and *Olea europaea* (olive) stimulate metabolic rate in rats [17, 18]. Olive leaf extracts have been shown to inhibit intestinal glucose absorption and improve blood pressure, lipids, and markers of inflammation [19-21] while *Cuminum cyminum* (cumin) has been demonstrated to reduce elevated blood glucose by improving glucose utilization [22]. *Mentha longifolia* (wild mint) is traditionally used to treat gastrointestinal disorders, as it increases gastric emptying and passage of food through the gastrointestinal tract [23], and a potential benefit on blood pressure has also been suggested [24].

Limitations of the current study include a relatively small sample size and brief study duration. Additionally, the study was conducted in healthy adults who were mostly overweight

(BMI ≥ 25.0 and < 30.0), and the effects might differ in a population with a higher BMI as well as other obesity-related comorbidities. Further research is needed to determine potential cardio-metabolic benefits of the herbal blend.

5. Conclusions

In conclusion, the herbal blend produced significant weight loss of 4.9% that is highly consistent with a similar study [10] and which would be expected to improve markers of cardio-metabolic risk [2].

6. Data availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

7. Conflicts of interest

The authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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