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Efficacy of a Traditional Herbal Mixture as an Anti-Obesity Supplement in Obese Individuals: A Randomized Controlled Trial

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Background: Obesity and overweight are critical public health concerns characterized by excessive body fat. Worldwide, many natural products have been used for treating obesity. It seems that natural supplements based on traditional medicinal plants are safe options for treating obesity. Recent experiments have revealed many herbal medicinal products as useful treatments for obesity.

Methods: In this study, we used an herbal formulation consisting of four traditional medicinal plants including Origanum vulgare, Carum carvi, Trachyspermum copticum, and Ruta graveolens as an anti-obesity supplement for obese adults. An 8-week double-blind randomized placebo-controlled clinical trial was conducted in obese adults. Sixty-eight subjects were randomly assigned to two groups of control (n = 34) and intervention (n = 34). Anthropometric indices and biochemical parameters were measured at baseline and after the intervention.

Results: Body weight, body mass index, and percent body fat were significantly lower in the intervention group than in the control group (p=0.046 and p = 0.02, respectively). Moreover, there were significant reductions in total cholesterol, low-density lipoprotein cholesterol, and triglyceride in the intervention group in comparison with the control group. The supplement was generally well tolerated and no remarkable adverse side effects were reported.

Conclusion: This herbal mixture effectively reduced body weight and fat mass in obese subjects. It also showed potential efficacy in controlling lipid profile and blood glucose.

Introduction

Obesity and overweight, characterized by excess body fat, are critical public health problems [1]. In 2012, 1 billion adults were overweight, and approximately 500 million were obese throughout the world [2]. It was projected that, by 2050, 60% of men and 50% of women [in the UK] could be obese [3]. Body mass index (BMI), waist to hip ratio (WHR), and waist to height ratio (WHtR) are helpful measures for diagnosing obesity [4]. Obesity is closely associated with various pathological disorders such as diabetes [5], hypertension and coronary heart disease [6], hyperlipidemia [7], liver disease [8], and cancer [9]. Globally, prevention and treatment of obesity and related complications are the main concern of many studies [10]. Changes in human behavior and lifestyle and medical or surgical interventions are the most common treatments for obesity [11]. Several drugs are currently used for managing obesity through mechanisms such as blocking fat absorption in the intestines, suppressing appetite, and altering metabolism [12]. Many prescription drugs cause unfavorable side effects including intestine problems [13], mutagenic effects [14], neuropsychiatric diseases [15], cardiovascular disorders [16], and interaction with other drugs [17]. Therefore, there is a tendency for using alternative treatment methods with less adverse side effects and better results [18]. Worldwide,

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natural products are used for treating obesity and weight loss [19]. It seems that the use of natural supplements obtained from traditional medicinal plants is the safest approach to treating obesity [20], and recent experiments have revealed many useful herbal products for treating obesity [21]. In this study, we used an herbal formulation consisting of four traditional medicinal plants including Origanum vulgare, Carum carvi, Trachyspermum copticum, and Ruta Graveolens. These traditional medicinal plants have been shown to possess many health-improving effects including antioxidant [22], antidiabetic [23], anti-inflammatory [24], and antihyperlipidemic [25] effects. Since regulation of glucose utilization [26], lipid mobilization [27], and inflammation mechanisms [28] can lead to obesity and weight gain, we designed a placebo-controlled study to evaluate the effect of a mixture of these four herbs on weight loss, anthropometric parameters, and serum lipid profile in obese adults consuming a typical Iranian diet.

Subjects and methods

Study design

An 8-week double-blind randomized placebo-controlled clinical trial was conducted in obese subjects. Sixty-eight subjects were randomly assigned to two groups of control (n = 34) or intervention (n = 34). Randomization was accomplished using computer-generated numbers and stratified based on age, sex, and BMI. The intervention group received 3 capsules per day, each capsule containing 1 gram of powder of dried O. vulgare, C. carvi, T. copticum, and R. Graveolens obtained from Booali Daroo Company, while the control group received 3 identical-looking capsules per day containing corn starch at the same dose as the intervention group. Participants were blinded to the type of capsules they took. The daily caloric requirement was calculated by using the Mifflin equation. Total energy expenditure was calculated according to physical activity level, and, finally, a reduction of 600 kcal/d was applied for all the estimated caloric requirements. The diet contained 55%, 15%, and 30% carbohydrate, protein, and fat, respectively. Possible side effects were evaluated during the intervention.

Ethical consideration

All participants provided informed written consent. The trial was conducted according to the guidelines established in the Declaration of Helsinki. The study was approved by the Ethics Committee of Tabriz University of Medical Sciences (REC number: 1424/4/5) and registered with the Iranian registry of clinical trials (www.irct.ir/, IRCT201307272017N17).

Participants

The study participants were recruited from among patients visiting Sheykholrais Medical Clinic, Tabriz, Iran. Inclusion criteria were having a BMI of >30 kg/m2, being between 20 and 50 years old, willing to participate in the study, being able to attend the clinic three times in the next two months to receive drugs and undergo laboratory examination, and, finally, having a waist circumference of >102 cm (men) or >88 cm (women). Exclusion criteria included smoking (more than twenty cigarettes daily) or drinking; being pregnant; having cardiovascular disease, diabetes mellitus, diagnosed malignancy, asthma, chronic cough, lung diseases, inflammatory bowel disease, fever of unknown origin, a history of chronic kidney or liver disease, allergies, skin problems, occasional gastroesophageal disease, irritable bowel syndrome, obesity due to endocrine disorders such as hypothyroidism, or genetic obesity syndrome; taking medications affecting appetite or body weight; being on a weight loss diet in the last three months; having psychological problems including depression, bipolar disorder, or anxiety determined by a self-report questionnaire during screening; taking corticosteroid or immunosuppressive medications.

Measurements

The participants' demographic data (age, sex, and literacy) and medical, body weight, and physical activity history were obtained at baseline. Dietary intake was assessed using a 72-hour dietary recall for two weekdays and one weekend day at baseline and at the end of the intervention. The Nutritionist 4 software was used for analyzing macronutrient and micronutrient intake. Anthropometric measurements were made at the beginning and end of the study. Patients were weighed on a balance scale with 0.1-kg precision (Seca, Birmingham, UK), and height was measured to the nearest 0.1 cm using a stadiometer. BMI was calculated by dividing weight (kg) by the square of height (m2). Waist circumference was measured in standing position at the midpoint between the lower rib margin and the iliac crest using a fiberglass tape. Hip circumference was measured at the widest point over the buttocks by a non-stretchable plastic tape measure. Body composition was evaluated by a

bioelectric impedance analyzer (QuadScan 4000, Bodystat, UK), and total body water (TBW), lean mass (LM), and total body fat (TBF) were determined for all subjects.

Blood sampling and laboratory procedures

Blood samples were obtained after 10-12 hours of overnight fasting at baseline and at the end of the intervention. After centrifugation of blood samples at 3000 rpm at 4°C for 10 minutes, serum aliquots were prepared and stored at -80°C. Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglyceride were determined by enzymatic colorimetric methods using commercial kits (Pars Azmoon, Tehran, Iran) and an automatic analyzer (Abbott, model Alcyon 300, USA), and low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula. For the evaluation of liver function, serum levels of aspartate transaminase (AST), alanine transaminase (ALT), and bilirubin were measured, and renal function was assessed by measuring creatinine and uric acid.

Sample size

Based on the study by Mansour et al [29], considering 90% power, a 95% confidence interval, and a 20% dropout rate throughout the study, 34 subjects were selected for each group.

Statistical analysis

The normality of the data distribution was controlled by the Kolmogorov-Smirnov test. An unpaired t test was used for comparing differences between the groups. For non-normal distribution, the Mann-Whitney U test was used. Comparison of baseline and postintervention values was performed using a paired t test or the Wilcoxon test. P values less than 0.05 were considered statistically significant. Data are reported as mean ± standard deviation. All statistical analyses were carried out using SPSS 20.

Measurement of depression

Hospital Anxiety and Depression Scale (HADS) were used to measure the depression and anxiety levels [17]. This scale consists of a 7-item anxiety subscale and a 7-item depression subscale to assess the anxiety and depressive symptoms during the preceding week in medically ill patients. Each item is rated on a scale of 0–7, with higher scores denoting a greater mood disturbance. HADS questionnaire was completed by each subject at baseline, fourth and eighth weeks of the trial. In addition, the correlation of anxiety and depression with different educational and occupational levels was assessed.

Statistical Analysis

Data were analyzed by two-way ANOVA for repeated measurement using SPSS 16.0 for Windows (SPSS Inc. Chicago, IL, USA) and is presented as mean ± SD. For treatments showing a main effect by ANOVA, means were compared using LSD Pairwise Comparisons test. $P<0.05$ was considered as significant differences between treatments.

Results

Baseline characteristics

Of the 92 potentially eligible participants, 68 were selected based on the inclusion criteria. Three participants in the treatment group and 1 in the placebo group were excluded from the study for non-availability during the study. The baseline characteristics of the participants are summarized in (Table 1). Participants in the intervention group ($n = 31$) and control group ($n = 33$) were similar with respect to sex, age, level of education, marital status, body weight, BMI, and waist and hip circumference at baseline. In addition, there was no statistically significant difference in dietary intake at baseline.

Clinical efficacy

Body weight, BMI, and percent body fat

Implementing the hypocaloric diet for 8 weeks significantly reduced body weight and BMI in both groups ($p < 0.001$). However, body weight and BMI reductions were significantly greater in the intervention group than in the control group ($p = 0.02$ and $p = 0.046$, respectively). Significant difference of reductions in percent body fat were observed in both study groups (p 0.02) (Table 2).

Waist and hip circumference

Significant decreases in waist and hip circumference from baseline to postintervention were observed in both groups. However, there was no statistically significant difference in the amount of reduction in waist and hip circumference between the two groups after 8 weeks of treatment (Table 2).

Plasma parameters

At the beginning of the study, no statistically significant differences were observed in any of the serum variables. Table 3 presents between- and within-group comparisons of values for serum variables. Serum levels of TC $p = 0.04$, LDL-C $p = 0.04$, and TG ($p = 0.02$) significantly decreased in the intervention group compared with the control group. There was no significant

difference in plasma HDL-C levels between the groups. After 8 weeks of dietary intervention, a significant decrease in fasting blood sugar (FBS) from baseline to intervention was observed in the intervention group ($p = 0.04$) but not in the control group. However, the mean changes in the FBS level were not significantly different between the groups. Also, there were no differences in ALT and AST levels between the groups. Statistical analysis of kidney function biomarkers (creatinine, blood urea, nitrogen, and uric acid) are presented in (Table 3).

Adverse events

The supplement was generally well tolerated, and no remarkable adverse side effects were reported.

Table 1. Demographic data and baseline characteristics of the study participants

Variable	Intervention	Control	P value
Gender, n (%)			0.87
Female	21 (67.7)	23 (69.7)	
Male	10 (32.3)	10 (30.3)	
Age, y, mean	38.77	39.33	0.63
Education, n (%)			0.95
Lower diploma	11(35.5)	13 (39.4)	
Diploma	12 (38.7)	12 (36.4)	
BS or upper	8 (25.8)	8 (24.2)	
Marital status, n (%)			0.78
Single	13 (41.9)	15 (45.5)	
Married	18 (58.1)	18 (54.5)	
Weight, kg, mean ± SD	101.20 ± 16.90	100.50 ± 9.60	0.53
BMI, kg/m2, men ± SD	39.90 ± 9.60	39.80 ± 5.30	0.25

Table 2. Changes in anthropometric parameters of the intervention and control groups

		Intervention	Control	P value[b]
Body weight (kg)	Baseline	101.20 ± 16.90	100.50 ± 9.60	
	Final	96.10 ± 16.96	97.60 ± 9.50	
	Change	-5.10 ± 0.06	-2.20 ± 2.90	0.02
	P value[a]	< 0.001	< 0.001	
Body mass index (kg/m2)	Baseline	39.90 ± 9.60	39.80 ± 5.30	
	Final	36.00 ± 9.9	38.30 ± 4.45	
	Change	-3.90 ± 1.4	-1.50 ± 0.84	0.046
	P value[a]	< 0.001	< 0.001	
Body fat (%)	Baseline	39.38 ± 12.40	41.58 ± 10.50	
	Final	35.04 ± 12.25	39.50 ± 2.40	
	Chang	-4.25 ± 0.20	-2.05 ± 0.30	0.04
	P value[a]	0.02	0.045	
Waist circumference (cm)	Baseline	116.25 ± 13.33	106.08 ± 8.82	
	Final	112.90 ± 11.71	102.53 ± 8.50	
	Change	-3.34 ± 5.82	-3.54 ± 2.82	0.86
	P value[a]	0.003	0.001	
Hip circumference (cm)	Baseline	124.35 ± 11.22	111.73 ± 7.19	
	Final	121.22 ± 11.92	109.80 ± 6.58	
	Change	-3.12 ± 3.56	-1.93 ± 2.57	0.14
	P value[a]	< 0.001	0.001	

a Within-group comparison.
b Between-group comparison.

Table 3. The effect of treatment on laboratory parameters

		Intervention	Control	P value[b]
TC (mg/dl)	Baseline	176.70 ± 35.04	187.60±33.20	
	Final	170.20 ± 34.60	181.20±36.00	
	Change	-6.50 ± 28.76	13.86±2.36	0.04
	P value[a]	0.02	0.07	
LDL-C (mg/dl)	Baseline	129.10 ± 32.30	119.20 ± 33.00	
	Final	119.50 ± 11.80	111.80 ± 40.90	
	Change	-9.60 ± 10.80	-7.40 ± 25.20	0.04
	P value[a]	0.02	0.40	
HDL-C (mg/dl)	Baseline	48.54 ± 9.28	45.06 ± 10.93	
	Final	45.67 ± 8.35	45.60 ± 10.47	0.09
	Change	-2.87 ± 9.79	0.54 ± 5.91	
	P value[a]	0.11	0.60	
TG (mg/dl)	Baseline	142.32 ± 81.93	127.24 ± 67.08	
	Final	154.48 ± 78.94	119.61 ± 50.86	
	Change	12.16 ± 62.62	-7.63 ± 29.06	0.02
	P value[a]	0.29	0.14	
FBS (mg/dl)	Baseline	96.82 ± 14.60	96.99 ± 6.52	
	Final	91.41 ± 11.92	95.57 ± 7.32	
	Change	-5.41 ± 14.24	-1.42 ± 4.88	0.15
	P value[a]	0.04	0.10	
Uric acid (mg/dl)	Baseline	6.13 ± 1.99	6.10 ± 2.30	
	Final	6.72 ± 1.72	6.21 ± 1.20	
	Change	0.59 ± 1.55	0.11 ± 1.55	0.86
	P value[a]	0.08	0.07	
Creatinine (mg/dl)	Baseline	0.77 ± 0.18	0.65 ± 0.20	
	Final	0.84 ± 0.24	0.72 ± 0.18	
	Change	0.07 ± 0.23	0.07 ± 0.67	0.46
	P value[a]	0.01	0.12	
Blood Urea Nitrogen (mg/dl)	Baseline	28.16 ± 9.14	26.16 ± 7.12	
	Final	26.90 ± 8.33	24.10 ± 9.33	
	Change	-1.25 ± 8.89	-2.06 ± 7.89	0.58
	P value[a]	0.44	0.55	
AST (U/L)	Baseline	28.45 ± 7.43	19.09 ± 4.31	
	Final	28.32 ± 7.16	18.42 ± 7.15	
	Change	-0.12 ± 6.90	-0.66 ± 5.80	0.74
	P value[a]	0.92	0.51	
ALT (U/L)	Baseline	17.45 ± 6.91	18.87 ± 5.86	
	Final	18.38 ± 9.84	19.63 ± 9.09	
	Change	-0.93 ± 7.63	-0.75 ± 8.64	0.29
	P value[a]	0.41	0.62	

[a] Within-group comparison.
[b] Between-group comparison.

Discussion

The present study showed that the combination of four traditional medicinal plants including Origanum vulgare, Carum carvi, Trachyspermum copticum, and Ruta graveolens significantly decreased body weight, BMI, and body fat mass. In recent years, the use of herbal supplements for treating obesity and losing weight has increased because of their low adverse effects and inexpensiveness. Many constituents of these plants, including fiber, unsaturated fatty acids, polyphenols, flavonoids, saponins, and terpenoids, have demonstrated anti-obesity effects [30-31]. Studies have indicated that herbal phytochemicals inhibit fat absorption through lipase suppression [32- 34]. Our results revealed a significant body fat mass reduction in the intervention group compared with the control group. It has been suggested that synergistic interactions between polyphenols and other compounds of herbal supplements may boost thermogenesis, contributing to metabolic activity of these supplements [35]. Mechanisms such as reducing appetite and influencing serotonin could be mentioned as other anti-obesity effects of herbal supplements [32].

In the present study, reductions in TC, LDL-C, and TG were in accordance with the weight loss observed after 8 weeks of intervention. The reduced level of these lipids may be the result of improved fat metabolism and reduced body fat

mass. In this regard, Haidari et al showed that C. carvi reduced TC and LDL-C levels in diabetic rats [25]. Also, R. graveolens extract significantly decreased TC and LDL-C levels in a dose-dependent manner. It has been claimed that 36 different active compounds, especially flavonoids, influence lipid profile. Flavonoids exert hypolipidemic effects through lipogenesis inhibition [37], fatty acid oxidation [38], and cholesterol synthesis [39]. Brusselmans el al showed that flavonoids act as potent inhibitors of lipogenesis by inhibiting fatty acid synthase [37].

Our results indicated that herbal supplementation significantly decreased FBS level compared with baseline after 8 weeks of treatment. Therefore, it seems that regulation of blood glucose with this herbal supplement could somewhat justify food intake during the study, although there was no significant difference in FBS level compared with the control group at the end of the study.

In recent years, the safety of herbal medicine has been a general concern in obesity management. Kidney failure due to herbal weight lose supplements has been reported in a few studies [40]. The results of the present study indicated no significant differences in kidney factors including creatinine and uric acid, and no adverse side effects were reported by the intervention group during the study.

In this study, there were limitations that should be addressed in future studies. First, we did not determine the mechanisms underlying the anti-obesity effects of these herbs, such as affecting lipase activity, appetite hormones, or insulin resistance. Second, although anti-obesity effect of the herbal mixture was confirmed in this study, we did not determine the main constituents of the herbs contributing to these properties. Third, this was a short-term interventional study for a duration of 8 weeks in obese individuals. Therefore, long-term follow-up studies with larger sample size are suggested.

Conclusion

The herbal mixture consisting of Origanum vulgare, Carum carvi, Trachyspermum copticum, and Ruta Graveolens effectively reduces body weight and fat mass in adults with obesity. It also has potential efficacy in controlling lipid profile and FBS level. In addition, the analysis of kidney and liver parameters provides evidence for the safety of this herbal mixture for human consumption. Further studies are needed to assess the active compounds of these herbs and evaluate the precise anti-obesity mechanisms of this supplement.

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Conflict of interest

None of authors have conflict of interests.

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