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Original article

Effect of a combined mulberry-sage dietary supplement on food craving and body weight: a pilot clinical trial

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Abstract. *Background and aim:* Overweight and obesity are largely prevalent in developed and developing countries, being risk factors for type 2 diabetes, cardiovascular disease and all-causes mortality. The aim of this pilot study was to test the effect of a combined mulberry-sage dietary supplement on food craving and body weight in healthy overweight subjects. *Methods:* This is a randomized, single-blind, clinical trial, involving 40 overweight healthy subjects randomized to assume a combined dietary supplement containing mulberry and sage extracts vs. standard diet. The volunteers were visited after 14, 28 and 56 days, sampling anthropometric data and the scores of the Food Cravings Questionnaire–Trait (FCQ–T) and the Short Form Health Survey 36 (SF-36). *Results:* The active treatment was well-tolerated and all patients completed the study. After 56 days of intake, the subjects treated with the tested dietary supplement on top of a standard diet experienced a significant improvement in FCQ-T, SF-36 and percentage fat mass versus standard diet only treated ones ($p<0.05$). FCQ-T improved just after 14 days versus placebo in the dietary supplement treated subjects, only. *Conclusions:* In conclusion, the tested dietary supplement seemed to mildly but significantly support body weight loss by decreasing food craving in healthy overweight subjects.

Key words: food craving, weight loss, dietary supplement, mulberry, sage, clinical trial

Introduction

Data from World Health Organization (WHO) show that in 2016, more than 1.9 billion adults were overweight and of these over 650 million were obese. In particular, overweight is considered when Body Mass Index (BMI) is greater than or equal to 25 and obesity is greater than or equal to 30 (1).

As known, overweight and obesity are important risk factors of cardiovascular diseases (CVD) so the maintenance of an optimum body weight is of paramount importance in reducing CVD or other pathologies like type 2 diabetes (2).

Controlled body weight and a healthy lifestyle which include physical activity, limited alcohol intake and no smoking, are essential parameters to reduce CVD risk, so diet represents an efficient prevention strategy (3).

One of the main problems of diet regimen is linked to patient compliance, which could often be tough.

Among the main reasons, there is food craving that can be defined as a strong desire of food. It seems food craving can occur in response to food cues, even though they are external (e.g., food pictures, smell of food, advertisements…) or internal (e.g. stress, hormones change…) (4).

Other physiological mechanisms of food craving stimulus activation are linked to hormones release. For example, antagonists of melanin-concentrating

hormone (MCH) receptor have important role in appetite control (5), or cholecystokinin (CCK) is one of the best-known gastrointestinal hormones that induce satiety and plays a key role in food intake regulation (6).

Flavonoids are known to have a role in regulating such pathways, with an interesting appetite-control activity (7).

In order to help patients adhering properly to a diet, a food supplement rich in flavonoids could represent a safe strategy to counteract food craving, beyond synergising the slimming activity.

The aim of this pilot study was to test the effect of a combined mulberry-sage dietary supplement on food craving and body weight in healthy overweight subjects.

Material and methods

This was a randomized, single-blind, monocentric, pilot clinical trial. For the purpose of this study, 40 overweight healthy subjects were consecutive enrolled in the lipid outpatient clinic of the University of Bologna (Italy). The main inclusion criteria were: age between 18 and 65 years, body mass index (BMI) between 25 and 29.9kg/m2, self-perception of excessive food craving reducing the ability to follow a low-energy diet. Patients assuming any kind of drug were excluded from the trial, as well as patient with newly diagnosed type 2 diabetes, LDL-Cholesterol >190mg/dL and/or triglycerides >500 mg/dL, known active liver or renal disease.

The test was carried out in the context of standard clinical practice. All involved subjects signed an informed consent form. The test was carried out in agreement with the Declaration of Helsinki and the Good Clinical Practice (GCP) rules.

All enrolled subjects were suggested a low-energy Mediterranean diet (-10% of baseline energy intake). The enrolled subjects were randomized to assume 1 capsule a day each morning of a combined dietary supplement containing 500 mg of a purified white mulberry and sage extract (SelectSIEVE® Libra) standardized in hydroxycinnamic acids (≥1%) and deoxynojirimycin (≥ 0.4%) kindly supplied by ROELMI HPC, Origgio (VA), Italy. An age- and BMI matched group was managed with the prescribed diet only.

The volunteers were visited after 14, 28 and 56 days, sampling blood pressure, anthropometric data and the scores of the Food Cravings Questionnaire–Trait (FCQ–T) (8) and the Short Form Health Survey 36 (SF-36) (9). Body fat percentage refers to the amount of body fat mass as part of the total body weight described as a percentage, estimated by the Omron HBF-306C Handheld Body Fat Loss Monitor.

Data were analysed with the support of the Statistical Package for Social Sciences (SPSS) 23.0, version for Windows. Visit-by-visit data were compared with ANOVA or Kruskal-Wallys non-parametric analysis of variance for repeated measures, while ANCOVA was used to compare parameters between treatment groups. A “p” level less than 0.05 was considered significant for all tests.

Results

The active treatment was well-tolerated and no adverse events have been registered during the study. In the nutraceutical treated group, the compliance to the treatment was 92%. After 56 days of intake, the subjects treated with the tested dietary supplement experienced a significant improvement in FCQ-T, SF-36 and percentage fat mass versus the diet-alone treated ones ($p<0.05$). FCQ-T improved just after 14 days versus placebo in the dietary supplement treated subjects (Table 1).

Discussion

Obesity represents a major risk for the development of a large number of chronic diseases. Diet and a healthy lifestyle can be a basic treatment for overweight people, in order to prevent obesity (10). The most part of dietary supplements suggested to support weight loss have limited efficacy and/or a questionable safety profile. Pharmacological treatments are usually very expensive and not always well-tolerated, as well. (10)

White mulberry (*Morus alba*) extract, rich in flavonoids, represent an eligible ingredient to counteract

Table 1. Effect of the tested dietary supplements versus diet only on anthropometric data, and perceived craving and quality of life during reduced-energy diet (data are reported as mean±standard deviation, beyond SF-36 score reported as median and 95% confidence intervals).

	Diet-only (M: 10; F: 10)				**Diet + Tested supplement (M: 9; F= 11)**			
	T0	T14	T28	T56	T0	T14	T28	T56
Age (years)	45±4				46±5			
SBP (mmHg)	132±3	132±4	131±4	130±3	134±5	132±6	132±5	131±5
DBP (mmHg)	83±2	82±3	82±2	81±3	84±3	84±2	82±3	80±4
BMI (kg/m^2)	27.3±2.4	27.3±2.3	27.2±2.1	27.0±2,3	27.5±2.1	27.4±2.0	27.1±1.9	26.7±1.7*
FCQ-T-Reduced	38±3	37±4	38±4	39±4	38±4	36±2*	36±3*	35±2*°
SF-36	516 (397–627)		515 (456–678)	517 (482–697)	532 (366–661)		557 (463–688)*	587 (425–700)*°
Free Fat Mass (%)	51.6±5.5		50.4±4.9	50.1±5.7	51.0±6.0		51.0±6.0	49.6±5.9
Fat Mass (%)	32.7±4.4		32.1±5.5	30.1±5.2*	33.7±4.2		32.2±4.8	29.0±4.7*°
Total Body Water (%)	45.5±3.8		45.1±3.9	44.9±4.7	45.6±4.5		45.9±4.4	44.6±4.8

* p<0,05 vs. baseline; ° p<0.05 vs. diet-only.

food craving with a hormonal-like activity (11). Sage (*Salvia officinalis* L.) has a wide range of biological activities, such as anti-oxidative properties, glucose-lowering and anti-inflammatory, that could be involved in the development of type 2 diabetes (12).

The main limitations of our trial are intrinsic in its preliminary pilot nature. In fact, the sample size is relatively small as well as the observation period. Then the anthropometric changes observed have not been related with changes in laboratory parameters.

Based on our preliminary observation, the tested food supplement, containing 500 mg of a purified white mulberry and sage extract, seemed to mildly but significantly support body weight loss by decreasing food craving in healthy overweight subjects, with an optimal tolerability profile. These results represent an interesting starting point to develop a new tolerable tool to support weight management diets.

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Conflict of Interest: No one of the authors has a direct conflict of interest in the publication of this paper.

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