Assessment of a food supplement for weight management in overweight volunteers

FINAL REPORT

Introduction

Recent *in vitro* studies suggest that *Lippia citriodora* (LC) and *Hibiscus sabdariffa* (HS) polyphenolic extracts have favorable effects on reducing the accumulation of intracellular lipids and to decrease high glucose-induced oxidative stress and inflammation in adipose tissue through the regulation of different metabolic pathways (Fernández-Arroyo et al., 2011; Herranz-Lopez et al., 2015; Herranz-Lopez et al., 2012; Joven et al., 2012; Joven et al., 2014). These include the energy sensing metabolic pathway governed by the AMP-activated protein kinase (AMPK), through the activation of nuclear receptors such as PPAR-gamma and the adipokine adiponectin.

Most of these effects have been corroborated in animal hyperlipidemic models in which the continuous consumption of polyphenols from these extracts prevented fatty liver disease (FLD) and improved lipid metabolism.

Study Objectives

The objective of this study was to evaluate the efficacy of the food supplement MetabolAid® (*Lippia citriodora* extract + *Hibiscus sabdariffa* extract) on body weight as well as on several metabolic and hematological parameters associated with metabolic syndrome on overweight volunteers.

Methods

Study population

Participants for the study were recruited from the city of Elche, Alicante, Spain. Fifty-five healthy women, aged 36-69 years old, with a body mass index (BMI) from 24 to 34 kg/m^2 were recruited into the study. During enrollment period in pharmacy, 74 prospective volunteers responded to recruitment. Fifty-five passed a telephone-based health screening and interview as well as the biochemical and anthropometrical evaluation (Table 1). Exclusion criteria included total cholesterol lower than 200 mg/dL, presence of any obesity-related pathology, use of prescription medication for cholesterol or hypertension, consumption of antioxidant supplements/drugs, alcohol addicts and women who were pregnant or lactating. After recruitment, the subjects were randomly assigned into the placebo or experimental group.

Prior to participate in the study, subjects were informed by the investigators about the product and the study procedures. Informed consent form (ICF) was obtained before the subject entered the study. Based on the above criteria, 55 consenting volunteers were selected to participate in the study. Nine subjects dropped out during the study and forty-six subjects completed the study. All subjects provided written ICF and the Ethical Committee of the Miguel Hernández University of Elche approved the study protocol (reference IB.ER.01.15). The study was conducted in accord with the Helsinki Declaration (1983 version).

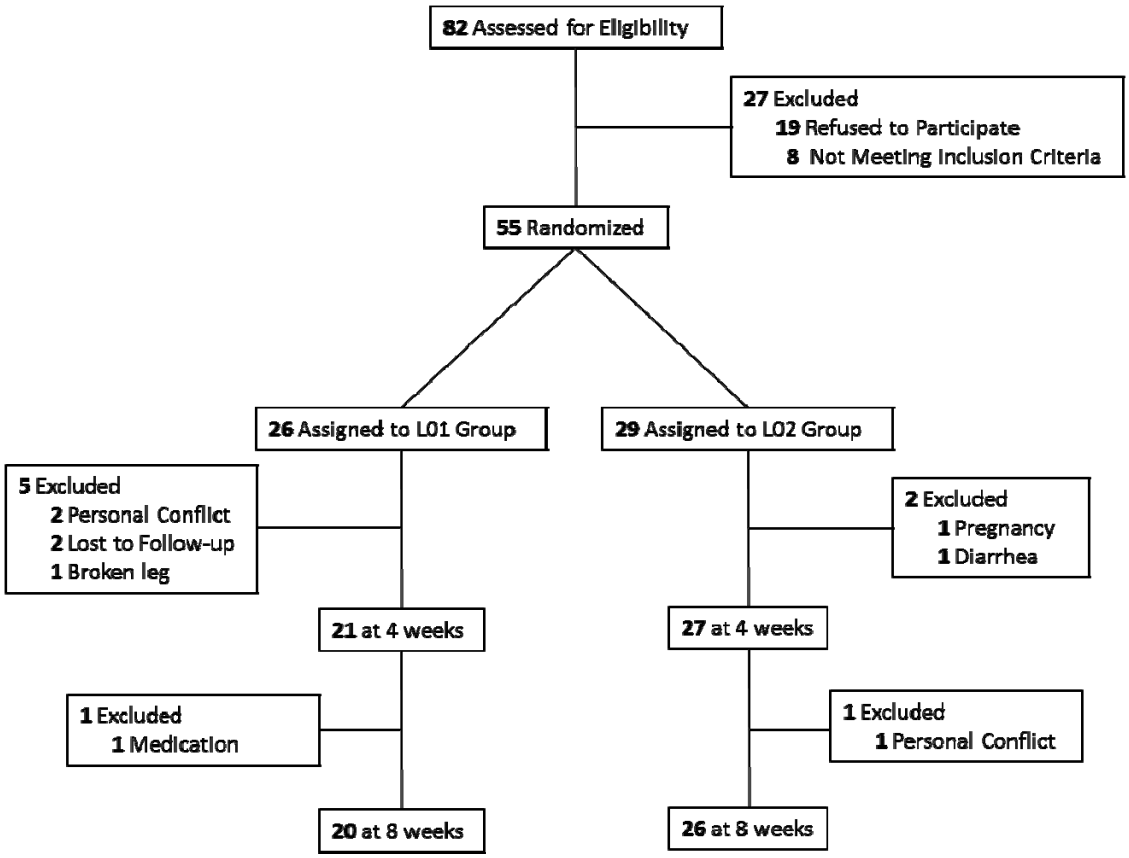

Table 1. Recruitment.

Study design

The study was a double blind, placebo controlled and randomized trial. The control group (L1) (mean age 51) received two capsules of placebo (250 mg of crystalline microcellulose) and treatment group (L2) (mean age 52) received two capsules, each one containing 250 mg MetabolAid® (*Lippia citriodora* extract + *Hibiscus sabdariffa* extract), 150 mg excipients (magnesium stearate) and coating (gelatin). The treatment group received a total of 500 mg of MetabolAid® per day. Volunteers were instructed to take two Metabolaid® capsules or two placebo capsules 20-30 minutes prior to breakfast every day during two months. Compliance of the subjects with the ingestion of capsules and diet was assessed at each clinic visit or by telephone interviews every week. Women were instructed by a qualified dietician to follow an isocaloric diet with a normal hydration and to walk for at least 30 minutes per day. The study

duration for each subject was 2 months. Measurements were taken after 30 and 60 days of the study and data were analyzed and compared to the start of the study.

Anthropometric and biochemical measurements

Anthropometric and biochemical measurements were taken at baseline, 30 and 60 days of the intervention period. Anthropometric measurements included body weight, height, triceps skinfold thickness and waist and hip circumference. Body weight and height were measured using a scale with height measuring rod. Body mass index (BMI) was derived from body weight and height by the equation BMI = Body weight (Kg) / height^2 (m). Triceps skinfold thickness was measured using a skinfold caliper and waist and hip circumference were measured using a tape measure. Percentage of body fat (% BF) was derived from waist (Pabd1) and hip (Pabd2) circumference by a Weltman equation.

Biochemical measurements determined in blood samples were glycosylated haemoglobin, blood glucose, triglycerides, total cholesterol, HDL and LDL-cholesterol, creatinine, urea, uric acid, glutamic-pyruvic transaminase (GPT) and glutamic-oxaloacetic transaminase (GOT).

Furthermore, systolic and diastolic blood pressure and heart beat were also measured at rest at the beginning, 30 and 60 days of the intervention using an Omron blood pressure monitor with large cuff.

Statistical analysis

Statistical analyses were performed by Student's unpaired t-test using Graphpad Prism software. Outcome variables were assessed for conformance to the normal distribution and transformed if necessary. Data were reported as mean ± SEM. Reported *p* -values were two-sided and a P-value of 0.05 or less was considered statistically significant for between-group comparisons. All comparisons reported in this study are established between the placebo and the MetabolAid® groups. *p <0.05; ** p <0.01, *** p <0.001.

Results

Body weight, waist size and body fat

Baseline characteristics of the two groups were well matched and no significant differences were found at baseline. The results showed an overall improvement of the anthropometric data in the group having MetabolAid® compared to placebo after two months, particularly in the body weight and abdominal parameter 1 (Pabd1). MetabolAid® group exhibited a higher decrease of body weight compared to the control group and significant differences were observed between the placebo and experimental intervention groups (2.04 ± 0.56 kg vs. 4.04 ± 0.33 kg, respectively, $p < 0.01$). Both abdominal perimeters were also reduced over the two months of treatment. The abdominal circumference 1 (Pabd1), which coincides with the waist circumference, was reduced 6.48 ± 0.71 cm in the group L2, whereas this parameter only decreased 2.44 ± 0.77 cm in the L1 group, $p < 0.001$. Consistently with this data, % Body

fat (BF) decreased over time in both groups but the experimental group lost significantly more body fat (2.04 ± 0.17 %) compared to the placebo group (1.15 ± 0.21%, p <0.01) (table 4).

Heart rate and blood pressure

On the other hand, a significant decrease was observed in the heart rate of the patients of the group consuming MetabolAid® after 60 days (80 to 71 beats per minute) (table 2). At two months, significant differences were observed for the change into heart rate when the two groups were compared (placebo: 0.25 ± 1.96 bpm vs. MetabolAid®: 8.43 ± 0.98 bpm, p < 0.001). The L2 group also showed a significant reduction in the systolic blood pressure, with figures of nearly 130 at the beginning of the treatment that dropped below 110 at the end of treatment. Whereas blood pressure dropped 18.74 mmHg in the MetabolAid® group, the same parameter decreased only 8.60 mmHg in the placebo group, p < 0.01 (table 4).

Biochemical measurements

Biochemical data also exhibited a global decrease of the blood sugar level, total cholesterol and LDL cholesterol in both groups, probably influenced by the isocaloric diet, but the decrease was stronger into the L2 group. Anyhow, the differences on these particular parameters were not statistically significant. Glycosylated hemoglobin was also determined at the beginning of the study but no abnormal values were detected on any of the individuals. Therefore measurements on this parameter were not taken throughout the study.

Adverse events

Treatment of overweight and obese subjects with MetabolAid® was well-tolerated. The incidence of a reported diarrhea case in the treated group was caused by a viral infection. No subjects had adverse side effects during intervention period, and so indicate hepatic hematological reference values (table 3).

Appetite assessment

Although appetite assessment was not strictly evaluated, monitoring of the volunteers throughout the study indicated that most individuals of the MetabolAid® group experienced a satiating effect.

Conclusions

1. The consumption of 500 mg per day of MetabolAid® for two months in overweight women exhibited higher reductions of body weight (4.04 Kg, p < 0.01), waist circumference (6.48 cm, p < 0.001) and percentage of body fat (2.04 %, p < 0.01) compared to the placebo group and showed differences statistically significant, both groups having an isocaloric diet.

2. The consumption of MetabolAid® also significantly decreased heart rate (80 to 71, p < 0.001) and systolic blood pressure (128.7 to 109.96 mm Hg, p < 0.01) compared to the placebo group.

3. The group having MetabolAid® exhibited a decrease of blood sugar level (93.3 to 90 mg/dl), total cholesterol (237.78 to 207.94 mg/dl) and LDL cholesterol (158.5 to 127.4 mg/dl) compared to the placebo group.

4. The results show that the consumption of MetabolAid® for two months in overweight women decreased weight, improved anthropometric parameters, decreased systolic blood pressure and heart beat and improved blood lipid profile. The satiating effect on appetite indicated by the volunteers may deserve further attention. Therefore the consumption of 500 mg/day of MetabolAid®, in combination to isocaloric diet, may be considered as a dietary supplement for weight management and the prevention of metabolic syndrome.

References

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	MetabolAid® (L2; N=26)			**Placebo** (L1; N=20)		
Anthropometric parameters	BASELINE	MONTH 1	MONTH 2	BASELINE	MONTH 1	MONTH 2
Body weight	75.12 ± 13.62	72.76 ± 13.51	71.08 ± 13.34***	75.16 ± 11.34	73.36 ± 11.24	73.12 ± 11.47**
Body mass index (BMI)	29.20 ± 4.76	28.26 ± 4.63	27.59 ± 4.44***	30.23 ± 4.41	29.52 ± 4.42	29.43 ± 4.58**
Hear rate (BPM)	79.43 ± 9.84	74.36 ± 9.03	71 ± 8.40***	75.75 ± 8.62	75.15 ± 11.86	75.50 ± 11.61
Pabd 1 (cm)	90.87 ± 10.81	86.59 ± 9.51	84.39 ± 9.91***	90.93 ± 13.12	89.21 ± 12.83	88.50 ± 11.65**
Pabd 2 (cm)	100.52 ± 9.10	97.10 ± 8.20	94.71 ± 8.94***	102.32 ± 11.59	99.87 ± 11.96	97.05 ± 10.66***
% Body fat (BF)	55.11 ± 3.92	53.80 ± 3.68	53.08 ± 3.82***	55.37 ± 4.11	54.65 ± 4.13	54.22 ± 3.88***
Systolic BP mm Hg	128.70 ± 12.74	118.43 ± 13.91	109.96 ± 9.09***	126.65 ± 19.06	120.70 ± 17.50	118.05 ± 15.64*
Diastolic BP mm Hg	77.62 ± 10.99	72.76 ± 10.54	67.05 ± 9.30***	78.30 ± 13.12	76.10 ± 8.16	71.10 ± 11.61*
Triceps skinfold thickness	28.36 ± 7.57	26.08 ± 6.95	24.67 ± 7.42***	30.13 ± 5.24	28.45 ± 4.75	27.88 ± 4.69***

Table 2. Changes in anthropometric measurements in the course of the study. Intra-group statistical analysis at endpoint compared to the baseline. * p < 0.05; ** p < 0.01; *** p < 0.001 (Mean ± Sd).

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	MetabolAid® (L2; N=26)			**Placebo** (L1; N=20)		
Biochemical parameters	BASELINE	MONTH 1	MONTH 2	BASELINE	MONTH 1	MONTH 2
Glycosylated haemoglobin mmoles/mol	34.60 ± 4.27			33.25 ± 2.83		
Glucose mg/dl	93.33 ± 16.10	90.44 ± 14.11	90.06 ± 13.31	93.95 ± 12.96	94.05 ± 11.14	92.63 ± 14.95
Triglycerides mg/dl	84.83 ± 52.61	76.28 ± 35.22	83.17 ± 39.39	85.63 ± 42.37	78.53 ± 27.95	88.74 ± 39.23
Total Cholesterol mg/dl	237.78 ± 26.51	215.22 ± 26.90	207.94 ± 25.11 ***	229.11 ± 26.13	205.53 ± 24.84	207.53 ± 28.62 **
HDL mg/dl	60.59 ± 7.24	59.23 ± 7.15	58.95 ± 8.52	59.00 ± 7.54	56.95 ± 9.02	57.11 ± 8.58 *
LDL mg/dl	158.52 ± 25.17	140.90 ± 23.39	127.43 ± 20.83 ***	153.68 ± 24.88	132.89 ± 23.18	132.95 ± 25.39 ***
Creatinine mg/dl	0.75 ± 0.11	0.85 ± 0.14	0.81 ± 0.12	0.80 ± 0.14	0.91 ± 0.18	0.82 ± 0.12
Urea mg/dl	33.36 ± 7.96	32.09 ± 8.52	32.32 ± 9.15	32.21 ± 10.54	32.37 ± 7.77	31.58 ± 7.44
Uric acid mg/dl	4.66 ± 1.01	4.29 ± 1.09	4.55 ± 1.18	4.97 ± 1.53	4.29 ± 1.03	4.48 ± 0.96
GPT U/l	22.59 ± 7.39	21.59 ± 9.53	21 ± 8.83	21.21 ± 6.82	21.61 ± 9.62	20.05 ± 8.44
GOT U/l	21.00 ± 5.07	21.59 ± 5.66	21.27 ± 6.85	21.11 ± 4.53	21.11 ± 5.51	20.21 ± 5.02

Table 3. Changes in biochemical measurements in the course of the study. Intra-group statistical analysis at endpoint compared to the baseline. * p < 0.05; ** p < 0.01; *** p < 0.001 (Mean ± Sd).

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	Changes in two months	
Anthropometric parameters	**MetabolAid® (L2)**	**Placebo (L1)**
Body weight	-4.04 ± 0.33	-2.04 ± 0.56**
Body mass index (BMI)	-1.60 ± 0.15	-0.81 ± 0.21**
Hear rate (BPM)	-8.43 ± 0.98	-0.25 ± 1.96***
Pabd 1 (cm)	-6.48 ± 0.71	-2.44 ± 0.77***
Pabd 2 (cm)	-5.81 ± 0.90	-5.27 ± 0.99
% Body fat (BF)	-2.04 ± 0.17	-1.15 ± 0.21**
Systolic BP mm Hg	-18.74 ± 2.31	-8.60 ± 3.25**
Diastolic BP mm Hg	-10.57 ± 1.43	-7.20 ± 3.16
Triceps skinfold thickness	-3.69 ± 0.63	-2.25 ± 0.57*
Biochemical parameters		
Glucose mg/dl	-3.28 ± 2.16	-1.32 ± 1.88
Triglycerides mg/dl	-1.67 ± 11.87	3.11 ± 8.06
Total Cholesterol mg/dl	-29.83 ± 4.61	-21.58 ± 5.57
HDL mg/dl	-1.64 ± 0.81	-1.90 ± 0.89
LDL mg/dl	-31.10 ± 3.90	-20.74 ± 4.90

Table 4. Changes in body weight, body mass index, hear rate, waist, fat, systolic and diastolic pressure, triceps skinfold, glucose, triglycerides, total cholesterol and LDL and HDL cholesterol measurements in the course of the study. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ compared with Placebo. Data represent change after two months (Mean ± Std. Error).

	Changes in the first month	
Anthropometric parameters	**MetabolAid® (L2)**	**Placebo (L1)**
Body weight	-2.37 ± 0.29	-1.80 ± 0.37
Body mass index (BMI)	-0.93 ± 0.12	-0.72 ± 0.14
Hear rate (BPM)	-5.07 ± 1.00	-0.60 ± 2.10
Pabd 1 (cm)	-4.28 ± 0.78	-1.72 ± 0.37*
Pabd 2 (cm)	-3.43 ± 0.80	-2.45 ± 0.64
% Body fat (BF)	-1.32 ± 0.18	-0.72 ± 0.13**
Systolic BP mm Hg	-10.26 ± 1.77	-5.95 ± 4.14
Diastolic BP mm Hg	-4.86 ± 1.99	-2.20 ± 2.78
Triceps skinfold thickness	-2.28 ± 0.56	-1.68 ± 0.46
Biochemical parameters		
Glucose mg/dl	-2.89 ± 2.40	0.11 ± 1.53
Triglycerides mg/dl	-8.56 ± 12.23	- 7.11 ± 7.83
Total Cholesterol mg/dl	-22.56 ± 3.45	-23.58 ± 5.64
HDL mg/dl	-1.36 ± 0.46	-2.05 ± 0.92
LDL mg/dl	-17.62 ± 2.69	-20.79 ± 5.21

Table 5. Changes in body weight, body mass index, hear rate, waist, fat, systolic and diastolic pressure, triceps skinfold, glucose, triglycerides, total cholesterol and LDL and HDL cholesterol measurements in the first month. * $p < 0.05$; ** $p < 0.01$ compared with Placebo. Data represent change after two months (Mean ± Std. Error).