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Nutraceutical Supplementation in Obese Patients and Effects on Anthropometric, Metabolic, and Inflammatory Parameters

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Abstract The aim of this study was to evaluate if Metabolic® Ultra, a nutraceutical containing Chitosan and α-Lipoic acid (Nutraceutical), can decrease anthropometric measures and ameliorate metabolic values, inflammatory status, and cytokine parameters in patients with obesity. We enrolled 60 Caucasian obese (BMI ≥ 30 kg/m^2) nondiabetic patients, aged ≥ 18 of either sex. Patients were randomized to take placebo or Nutraceutical for 6 months, in a randomized, double-blind, placebo-controlled design. Nutraceutical and placebo were self-administered twice a day, 3 tablets fifteen minutes before lunch and dinner. A significant decrease of weight, BMI, and Abd. Cir. were observed after 6 months of Nutraceutical treatment ($p< 0.05$ vs Baseline) compared to placebo. No Waist Cir. and Hip Cir. variations were observed in both groups. No variation of FPG, FPI, and Homa index were recorded in both groups compared to Baseline. A significant TC, LDL-C, and Tg decrease was recorded at 6 months in the Nutraceutical group compared to the placebo group ($p< 0.05$ vs Baseline, respectively), and a significant TC, and LDL-C decrease was found at 6 months compared to placebo group ($p< 0.05$, respectively). No significant HDL-C variation was observed in the Nutraceutical group, although there was an increasing trend. High-sensitivity C-reactive protein was significantly reduced at 6 months in the Nutraceutical group ($p< 0.05$ vs Baseline, and $p< 0.05$ vs placebo), while the ADN was raised to 6 months in the Nutraceutical group ($p< 0.05$ vs Baseline, and $p< 0.05$ vs placebo). No significant change was seen for IL-6 and TNF-α at the end of the study in both treatments. All the patients who finished the study and underwent OGTT at Baseline and after 6 months were euglycemic at the end of the second hour in both groups. We can conclude that a nutraceutical containing Chitosan and α-Lipoic acid can be helpful in reducing weight and BMI, in improving lipid profile, and in reducing inflammatory parameters, without affecting the glycemic status of obese patients.

Keywords: *α-Lipoic acid, inflammation, obesity, chitosan*

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1. Introduction

Obesity is an increasingly widespread problem, due to poor nutrition and reduced physical activity, and is associated with alterations affecting both fat cells and endothelial cells [1].

The adipocytes, in fact, in addition to having a storage function, are able to produce various factors and cytokines that play a role in paracrine regulation by influencing the remodeling of adipose tissue, regulating insulin resistance and inflammation indices [2].

Obesity causes insulin resistance through several mechanisms that include an altered insulin signal and an interference with glucose transport within the muscle and adipose tissue, resulting in an increased hepatic glucose production [3].

Our group already conducted several studies on obese and diabetic patients to evaluate whether weight loss improves insulin resistance and inflammatory indices; in particular, we used drugs such as sibutramine [4,5,6,7,8] and orlistat [9,10,11,12], both as monotherapy or combined with L-carnitine, a cofactor implicated in the β-oxidation of fatty acids.

These studies have shown the effectiveness of these drugs in reducing body weight and improving inflammatory and insulin resistance parameters in diabetic and obese subjects. However, in recent years, several concerns have emerged regarding the safety profile of these drugs, which

led, after the results publication of the SCOUT study (Sibutramine Cardiovascular Outcomes Trial) [13], to the withdrawal of sibutramine in August 2010, and to the publication of an FDA note concerning rare, but severe cases of liver injury in patients receiving orlistat [14], which showed the need to find alternative solutions to promote weight loss in the obese and diabetic patients.

Of course, the first advice must be the diet, with the right contribution in terms of quality and quantity, when diet is not enough, the nutraceutical approach can be an alternative to traditional drug therapy.

Nutraceuticals as dietary support often disappoint in results; several products have been marketed in the latest years, without being supported by scientific data. Among nutraceuticals, chitosan can play a role in obese patients. Chitosans are a family of deacetylated chitins. Although not naturally present in human tissue, chitosan is nontoxic, nonimmunogenic, biodegradable and biocompatible [15].

Chitosan acts by binding cholesterol, fatty acids, and bile acids in the stomach and intestine, followed by increased fecal excretion of fatty acids and cholesterol metabolites. Chitosans may exert a weight loss effect [16].

The primary objective of this study will be to evaluate weight loss compared to placebo, after 6 months of treatment with Metabolic® Ultra (Nutraceutical) in obese patients. The secondary objectives, instead, will be to evaluate the variations of some metabolic and inflammatory parameters and of some adipocytokines.

2. Materials and Methods

2.1. Study Design

This 6-months, double-blind, randomized, placebo-controlled, clinical trial was conducted at the Department of Internal Medicine and Therapeutics, University of Pavia (Pavia, Italy), among patients attending the Center for Prevention, Surveillance, Diagnosis and Treatment of Rare Diseases.

The study protocol was approved by the local institutional ethical committee and was conducted in accordance with the 1994 Declaration of Helsinki, and its amendments and the Code of Good Clinical Practice. All patients provided written informed consent to participate in this study after a full explanation of the study was given.

Material and methods

We enrolled 60 Caucasian obese (BMI ≥ 30 kg/m^2) nondiabetic patients aged ≥ 18 of either sex.

Suitable patients, identified from review of case notes and/or computerized clinic registers, were contacted by the investigators in person or by telephone.

Patients were excluded, if they have impaired renal function (defined as serum creatinine level higher than the ULN for age and sex); endocrine disorders or gastrointestinal disorders; current or previous evidence of ischemic heart disease, heart failure, or stroke; weight change of > 3 Kg during the preceding 3 months; malignancy; and significant neurological or psychiatric disturbances, including alcohol or drug abuse. Excluded medications (within the previous 3 months) were anorectic agents, laxatives, β-agonists (other than inhalers), diuretics, cyproheptadine, anti-depressants, anti-serotoninergics, phenothiazines, barbiturates, oral corticosteroids, and anti-psychotics. Women who were pregnant or breastfeeding or of childbearing potential and not taking adequate contraceptive precautions were also excluded.

2.2. Treatment

Patients were randomized to take placebo or Nutraceutical for 6 months, in a randomized, double-blind, placebo-controlled design. Nutraceutical (Table 1a) and placebo (Table 1b) were self-administered twice a day, 3 tablets fifteen minutes before lunch and dinner. Both Nutraceutical and placebo were supplied as identical, opaque, tablets in coded bottles to ensure the blind status of the study. Randomisation was done using a drawing of envelopes containing randomisation codes prepared by a statistician. Medication compliance was assessed by counting the number of tablets returned at the time of specified clinic visits. Throughout the study, we instructed patients to take their first dose of new medication on the day after they were given the study medication. At the same time, all unused medication was retrieved for inventory. All medications were provided free of charge.

Table 1a. Quali-quantitative composition of Nutraceutical

Ingredient	Mg/tablet
Chitosan (Liposan Ultra)	500
α-Lipoic Acid	10
Microcrystalline cellulose	285
Corn starch; Polyvinylpyrrolidone; Glyceryl behenate; Hydroxypropylcellulose; Silicon dioxide; Flavour; Magnesium stearate.	325

Table 1b. Quali-quantitative composition of Placebo

Ingredient	Mg/tablet
Microcrystalline cellulose	795
Corn starch; Polyvinylpyrrolidone; Glyceryl behenate; Hydroxypropylcellulose; Silicon dioxide; Flavour; Magnesium stearate.	325

2.3. Diet and Physical Activity

At Baseline, all patients were already following an adequate diet. The controlled-energy diet (~600 kcal daily deficit) was based on NCEP-ATP III recommendations [17], that contained 50% of calories from carbohydrates, 30% from fat (< 7% saturated, up to 10% polyunsaturated, and up to 20% monounsaturated), and 20% from proteins, with a maximum cholesterol content of 300 mg/d, and 35 g/d of fiber. Standard diet advice was given by a dietitian and/or specialist physician. Individuals were also encouraged to maintain their usual physical activity.

2.4. Assessments

Before starting the study, all patients underwent an initial screening assessment that include a medical history, physical examination, vital signs (blood pressure and heart rate), a 12-lead electrocardiogram, measurements of height and body weight, calculation of BMI, abdominal circumference (Abd. Cir.), waist circumference (Waist Cir.), and hip circumference (Hip Cir.), fasting plasma glucose (FPG), fasting plasma insulin (FPI), homeostatic model assessment of insulin resistance (Homa index),

total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglycerides (Tg), adiponectin (ADN), interleukin-6 (IL-6), high-sensitivity C-reactive protein (Hs-CRP), and tumor necrosis factor-α (TNF-α). All parameters were assessed at baseline and after 3, and 6 months since the study start. Moreover, at baseline, and after 6 months, patients underwent an oral glucose tolerance test (OGTT).

All parameters were determined in fasting state, after a 12-h overnight fast, in the plasma. Venous blood samples were taken for all patients between 8 and 9 a.m. and were drawn from an antecubital vein with a 19-gauge needle without venous stasis.

We used plasma obtained by addition of Na_2-EDTA, 1 mg/ml, and centrifuged at 3000 g for 15 minutes at 4°C. Immediately after centrifugation, the plasma samples were frozen and stored at -80°C for no more than 3 months. All measurements were performed in a central laboratory.

BMI was calculated by the investigators as weight in kilograms divided by the square of height in meters.

Plasma glucose was assayed using a glucose-oxidase method (GOD/PAP, Roche Diagnostics, Mannheim, Germany) with intra- and interassay coefficients of variation (CsV) <2% [18].

Plasma insulin was assayed with Phadiaseph insulin radio immuno assay (RIA) (Pharmacia, Uppsala, Sweden) by using a second antibody to separate the free and antibody-bound 125 I-insulin (intra- and interassay CsV 4.6 and 7.3%, respectively) [19].

The Homa index was calculated as the product of basal glucose (mmol/l) and insulin levels (μU/ml) divided by 22.5 [20].

Total cholesterol and Tg levels were determined using fully enzymatic techniques [21,22] on a clinical chemistry analyzer (HITACHI 737; Hitachi, Tokyo, Japan); intra- and interassay CsV were 1.0 and 2.1 for TC measurement, and 0.9 and 2.4 for Tg measurement, respectively. High density lipoprotein-cholesterol level was measured after precipitation of plasma apo B-containing lipoproteins with phosphotungstic acid [23] intra- and interassay CsV were 1.0 and 1.9, respectively; LDL-C level was calculated by the Friedewald formula [24].

Adiponectin level was determined using ELISA kits (B-bridge International, Sunnyvale, CA). Intraassay CsV were 3.6% for low- and 3.3% for high-control samples, whereas interassay CsV were 3.2% for low- and 7.3% for high-control samples, respectively [25].

Interleukin-6 was determined using commercially available Enzyme-Linked Immuno Sorbent Assay (ELISA) kits according to manufacturer instructions (R & D Systems, Minneapolis, MN, USA). The intra- and interassay CsV were 4.9% and 7.1% respectively [26].

TNF-α level was assessed using commercially available ELISA kits according to manufacturer's instructions (Titer-Zyme EIA kit; Assay Designs, Ann Arbor, MI). Intraassay CsV were 4.5% for low- and 3.6% for high-concentration samples whereas the interassay CsV were 6.0% for low and 11.8% for high-concentration samples, respectively [27].

High sensitivity C-reactive protein was measured with use of latex-enhanced immunonephelometric assays on a BN II analyser (Dade Behring, Newark, Delaware, USA). The intra- and interassay CsV were 5.7% and 1.3%, respectively [28].

2.4.1. Oral glucose Tolerance Test

All patients drank a glass of water (200 ml), in which 75g of glucose had been dissolved over a period of 5 min in the morning, between 8 and 9 a.m. after a 12-h fast, and after dietary assessment to ensure a carbohydrate intake > 150 g/ day over the previous 3 days [29]. Normal physical activity was allowed over the previous 3 days. No smoking was allowed during the test. Blood samples were collected in EDTA-containing tubes (Becton Dickinson, Meylan Cedex, France) through a venous catheter from an antecubital vein immediately before and at 120 min after the glucose load for the measurement of the considered parameters of the study.

2.4.2. Safety Measurements

Treatment tolerability was assessed at each study visit using an accurate interview of patients by the investigators, and comparisons of clinical and laboratory values with baseline levels. Safety monitoring included physical examination, vital sign assessment, weight, adverse events, and laboratory tests.

2.4.3. Statistical Analysis

An intention-to-treat (ITT) analysis was conducted in patients who had received ≥1 dose of study medication were included in the tolerability analysis if they had received ≥1 dose of trial medication after randomization and had undergone a subsequent tolerability observation. Continuous variables were tested using a two-way repeated measures analysis of variance (ANOVA). Intervention effects were adjusted for additional potential confounders using analysis of covariance. Analysis of variance was also used to assess the significance within and between groups. The null hypothesis that the expected mean weight change from the end of the study did not differ significantly between placebo, and Nutraceutical was tested using a two-way repeated measures analysis of variance (ANOVA) model. Similar analyses were applied to the other variables. The statistical significance of the independent effects of treatments on the other variables was determined using ANCOVA. A 1-sample t test was used to compare values obtained before and after treatment administration; 2-sample t tests were used for between-group comparisons. Statistical analysis of data was performed using the Statistical Package for Social Sciences software version 25.0 (SPSS Inc., Chicago, Illinois, USA). Data were presented as mean (SD). For all statistical analyses, $p < 0.05$ were considered statistically significant [30].

3. Results

3.1. Study Sample

A total of 60 patients were enrolled in the study. Of these, 30 were randomized to Nutraceutical supplementation and 30 to placebo. Fifty-nine patients completed the study:

there is 1 patient who did not complete the study at 3 months in the placebo group and the reason for premature withdrawal was the lost to follow-up.

Anthropometric parameters

A significant decrease of weight was observed after 6 months of Nutraceutical treatment ($p< 0.05$ vs Baseline) compared to placebo. The same trend was obtained for BMI and Abd. Cir. at 6 months in the Nutraceutical group compared to the placebo group ($p< 0.05$ vs Baseline, respectively). No Waist Cir. and Hip Cir. variations were observed in both groups for the whole treatment time (Table 2 and Table 3).

3.1.1. Glycemic Parameters

No variation of FPG and FPI was recorded in both groups compared to Baseline. Regarding insulin resistance, there was not a significant change of Homa index in both groups (Table 2 and Table 3).

3.1.2. Lipid Profile

A significant TC, and LDL-C decrease was recorded at 6 months in the Nutraceutical group compared to the placebo group ($p< 0.05$ vs Baseline, respectively), and a significant TC, and LDL-C decrease was found at 6 months compared to placebo group ($p< 0.05$, respectively). No significant HDL-C variation was observed in the Nutraceutical group, although there was an increasing trend. Triglycerides decreased at 6 months in the Nutraceutical group compared to the placebo group after 6 months of treatment (Table 2 and Table 3).

3.1.3. Cytokines and Inflammation Parameters

High-sensitivity C-reactive protein was significantly reduced at 6 months in the Nutraceutical group ($p< 0.05$ vs Baseline, and $p< 0.05$ vs placebo), while the ADN was raised to 6 months in the Nutraceutical group ($p< 0.05$ vs Baseline, and $p< 0.05$ vs placebo). No significant change was seen for IL-6 and TNF-α at the end of the study in both treatments (Table 2 and Table 3).

3.1.4. OGTT Results

All 30 patients who underwent OGTT at Baseline were euglycemic at the end of the second hour in the Nutraceutical group and in the placebo group. At the end of the study, 30 patients in the Nutraceutical group and 29 patients in the placebo group underwent OGTT: all patients were euglycemic at the end of the second hour (Table 4a and Table 4b).

3.1.5. Safety Parameters

No adverse events were recorded in all the phases of the study.

Table 2. Anthropometric and biochemical parameters at Baseline, 3 and 6 months in placebo group

	Placebo		
	Baseline	**3 months**	**6 months**
N	30	29	29
sex (M/F)	15/13	15/12	15/12
Age (years)	52.8 ± 5.9	-	-
Smoking status (M/F)	6/7	6/6	6/6
Height (m)	1.67 ± 0.04	-	-
Weight (Kg)	87.0 ± 6.2	86.5 ± 5.9	86.2 ± 5.8
BMI (Kg/m^2)	31.2 ± 1.1	31.0 ± 1.1	30.9 ± 1.0
Abd. Cir. (cm)	103.6 ± 7.1	103.4 ± 7.0	103.1 ± 6.9
Waist Cir. (cm)	96.9 ± 5.4	96.7 ± 5.3	96.2 ± 5.1
Hip Cir. (cm)	106.6 ± 9.8	106.4 ± 9.6	106.1 ± 9.2
FPG (mg/dl)	84.6 ± 12.1	83.1 ± 11.6	81.4 ± 11.3
FPI (μU/ml)	18.3 ± 7.5	18.1 ± 7.2	18.0 ± 7.1
Homa index	3.9 ± 1.8	3.7 ± 1.6	3.6 ± 1.5
TC (mg/dl)	196.3 ± 17.8	192.1 ± 17.1	190.4 ± 16.8
LDL-C (mg/dl)	133.1 ± 12.4	128.9 ± 11.7	128.2 ± 11.3
HDL-C (mg/dl)	42.5 ± 7.3	43.2 ± 7.9	43.4 ± 8.2
Tg (mg/dl)	103.7 ± 42.4	99.8 ± 40.3	94.1 ± 38.9
Hs-CRP (mg/l)	1.4 ± 0.3	1.4 ± 0.3	1.3 ± 0.2
ADN (μg/ml)	6.1 ± 1.2	6.3 ± 1.3	6.5 ± 1.4
IL-6 (pg/ml)	1.9 ± 0.4	1.8 ± 0.3	1.8 ± 0.3
TNF-α (pg/ml)	2.5 ± 0.8	2.5 ± 0.8	2.3 ± 0.7

Data are expressed as number or mean ± standard deviations (SD)

Abd. Cir.: abdominal circumference; Waist Cir.: waist circumference; Hip Cir.: hip circumference; BMI: body mass index; FPG: fasting plasma glucose; FPI: fasting plasma insulin; Homa index: homeostasis model assessment index; TC: total cholesterol; LDL-C: low density lipoprotein-cholesterol; HDL-C: high density lipoprotein-cholesterol; Tg: triglycerides; Hs-CRP: high-sensitivity C-reactive protein; ADN: adiponectin; IL-6: interleukin-6; TNF-α: tumor necrosis factor-α.

Table 3. Anthropometric and biochemical parameters at Baseline, 3 and 6 months in Nutraceutical group

	Nutraceutical		
	Baseline	**3 months**	**6 months**
N	30	30	30
sex (M/F)	13/16	13/16	13/16
Age (years)	51.4 ± 5.6	-	-
Smoking status (M/F)	8/6	8/6	8/6
Height (m)	1.68 ± 0.05	-	-
Weight (Kg)	89.8 ± 7.8	88.1 ± 7.4	86.4 ± 6.9*
BMI (Kg/m^2)	31.8 ± 1.9	31.2 ± 1.8	30.6 ± 1.5*
Abd. Cir. (cm)	104.3 ± 8.2	103.1 ± 7.8	102.3 ± 7.1*
Waist Cir. (cm)	97.3 ± 5.9	97.0 ± 5.7	96.3 ± 5.4
Hip Cir. (cm)	107.1 ± 9.9	106.5 ± 9.5	106.0 ± 9.1
FPG (mg/dl)	85.8 ± 13.2	82.4 ± 11.9	80.5 ± 10.7
FPI (μU/ml)	17.9 ± 7.2	17.4 ± 6.8	17.1 ± 6.6
Homa index	3.8 ± 1.6	3.6 ± 1.5	3.4 ± 1.3
TC (mg/dl)	198.5 ± 18.6	190.6 ± 16.3	186.2 ± 15.4*°
LDL-C (mg/dl)	134.3 ± 12.9	127.4 ± 10.8	123.3 ± 9.6*°
HDL-C (mg/dl)	43.9 ± 8.5	44.5 ± 8.7	45.2 ± 9.0
Tg (mg/dl)	101.5 ± 40.2	93.7 ± 37.9	88.6 ± 34.1*
Hs-CRP (mg/l)	1.4 ± 0.3	1.2 ± 0.2	1.0 ± 0.1*°
ADN (μg/ml)	6.2 ± 1.4	6.5 ± 1.8	7.1 ± 1.9*°
IL-6 (pg/ml)	1.8 ± 0.4	1.7 ± 0.3	1.6 ± 0.2
TNF-α (pg/ml)	2.3 ± 0.6	2.2 ± 0.5	2.0 ± 0.4

Data are expressed as number or mean ± standard deviations (SD)
*p< 0.05 vs Baseline; °p< 0.05 vs placebo
Abd. Cir.: abdominal circumference; Waist Cir.: waist circumference; Hip Cir.: hip circumference; BMI: body mass index; FPG: fasting plasma glucose; FPI: fasting plasma insulin; Homa index: homeostasis model assessment index; TC: total cholesterol; LDL-C: low density lipoprotein-cholesterol; HDL-C: high density lipoprotein-cholesterol; Tg: triglycerides; Hs-CRP: high-sensitivity C-reactive protein; ADN: adiponectin; IL-6: interleukin-6; TNF-α: tumor necrosis factor-α.

Table 4a. Oral glucose tolerance test (OGTT) at Baseline in placebo and Nutraceutical group.

	Placebo	Nutraceutical
Time (minutes)	**Glycemia (mg/dl)**	**Glycemia (mg/dl)**
0	84.6 ± 12.1	85.8 ± 13.2
120	119.7 ± 18.4	117.3 ± 16.1

Data are means ± SD.

Table 4b. Oral glucose tolerance test (OGTT) at 6 months in placebo and Nutraceutical group

	Placebo	Nutraceutical
Time (minutes)	**Glycemia (mg/dl)**	**Glycemia (mg/dl)**
0	81.4 ± 11.3	80.5 ± 10.7
120	118.5 ± 17.9	115.8 ± 17.1

Data are means ± SD.

4. Discussion

Our study demonstrated that Chitosan and α-Lipoic acid decreased some anthropometric parameters as body Weight, BMI, and Abd. Cir., lipid profile (TC, LDL-C, and Tg), and improved inflammatory state in terms of Hs-CRP reduction and ADN increase. After 6 months of therapy, we observed a significant body weight reduction of 3.4 Kg (-3.8 %) in Nutraceutical group compared to placebo group (-0.8 Kg; -0.9 %), a significant BMI reduction of 1.2 Kg/m^2 (-3.8 %) in Nutraceutical group compared to placebo group (-0.3 Kg/m^2; -1.0 %), and a significant Abd. Cir. reduction of 2 cm (-1.9 %) in Nutraceutical group compared to placebo group (-0.5 cm; -0.5 %). These data are quite in line with those of Hernandez-Gonzalez SO [31], Trivedi VR [32], and Lütjohann D [33]. Although both authors have studied Chitosan without adding α-Lipoic acid and for only 3 months, the anthropometrical data has changed in a similar way to ours. In fact, they observed a reduction in the body Weight of 6.0 Kg (-6.6 %), 3.1 Kg (-3.9 %), and 3.5 Kg (-3.7 %), and in BMI of 2.7 Kg/m^2 (-7.9 %), 0.69 Kg/m^2 (-2.2 %), and 0.95 Kg/m^2 (-3.0 %), respectively.

Both authors used different dosages of Chitosan (2250-2500 mg/day in different posology) and this may have also influenced the differences between the 3 studies and our study. The observation period was also different. Our study is similar over time to that of Ni Mhurchu C [34]. He took 250 patients with a BMI higher than our study and gave 3000 mg of Chitosan (our same dosage). He noted that the group treated with Chitosan lost only 0.39 Kg (-0.4 %) compared to placebo group, even if this result was significant (p= 0.03), while the result concerning BMI (-0.17 Kg/m^2, -0.5 %) was modest and nonsignificant (p= 0.07). The Waist Cir. (-0.57 cm, -0.6 %) was also considered in this study, which was not significantly reduced (p= 0.13) and in line with the result obtained in our study. The glucose-lowering effect is still under study. It goes from the hypothesis of the Chitosan ability to prevent the loss of beta-cells and to stimulate beta-cells proliferation in pancreatic islets [35] to that of the inhibition of carbohydrate-hydrolyzing enzymes, resulting in decreased glucose absorption in the small intestine [36]. Our glyco-metabolic assessment focused on FPG, FPI, and Homa index. All the aforementioned parameters were not significantly altered (-5.3 mg/dl,

-6.2 %; -0.8 mU/ml, -4.5 %; -0.4, -10.5 %) with a downward trend, respectively. Even the OGTT performed after 6 months showed no changes compared to the Baseline. In the previously mentioned studies, the Authors also considered FPG. In the Hernandez-Gonzalez SO study [31], FPG was not significantly decreased (+4 mg/dl, +4.3 %), but insulin sensitivity was significantly increased and performed by euglycemic-hyperinsulinemic clamp technique. Fasting plasma glucose significantly decreased (-2.5 mg/dl, -2.6 %; p< 0.01) in Chitosan group compared to placebo group while in the Ni Mhurchu C study [34].

Chitosan is effective not only in reducing weight, but also in reducing lipid profile via mechanisms involving the promotion of fecal fat excretion and the reduction of caloric intake [37]. Our study has demonstrated a TC, LDL-C, and Tg reduction of 12.3 mg/dl (-6.2 %), 11 mg/dl (-8.2 %), and 12.9 mg/dl (-12.7 %) versus Baseline, respectively, and a significant difference of TC (-4.2 mg/dl, -2.2 %) and LDL-C (-4.9 mg/dl, -3.8 %) versus placebo treatment, respectively. Our lipid profile data obtained with Chitosan at 6 months are not as comparable with the previously cited studies, as they differ in terms of period and daily dosage. In fact, the data of Hernandez-Gonzalez SO [31] report a nonsignificant TC and LDL-C modification of +4 mg/dl (+2.5 %), and of -7 mg/dl (-6.7 %), respectively, but a significant Tg reduction of -70 mg/dl (-33.0 %) (p= 0.028). Trivedi VR [32] also found that TC and LDL-C were not significantly increased at the end of the study (+10 mg/dl, +5.7 %, and +3.0 mg/dl, +2.8 %, respectively), while Tg had decreased (-6.4 mg/dl, -4.4 %), but not significantly. Lütjohann D [33] instead noted that the TC and LDL-C were significantly reduced (-12.5 mg/dl, -6.0 %, and -8.7 mg/dl, -6.7 %, respectively). He did not evaluate Tg levels.

The 6-month study of Ni Mhurchu C [34] has data similar to ours as regards the significant reduction (p <0.01) of TC (-5.0 mg/dl, -2.3 %) and LDL-C (-4.6 mg/dl, -3.3 %), while the reduction of the Tg was not significant.

A final aspect on the lipid profile is given by the HDL-C value. This data is also contrasting in that Hernandez-Gonzalez SO [31], and Trivedi VR [32] have seen a slight, but not significant increase in HDL-C (+4 mg/dl, +11,4 %, and +1.7 mg/dl, +4.1 %, respectively), quite in line with our data (+1.3 mg/dl, +3.0 %), while Lütjohann D [33] has noted a nonsignificant decrease (-1.2 mg/dl, -2.1 %). Finally, Ni Mhurchu C [34] did not see a significant change in HDL-C. Currently, this discrepancy does not seem to have an explanation.

Chitosan has been demonstrated to inhibit the inflammatory responses in macrophages, including the expression and release of proinflammatory mediators as TNF-α and IL-6 [38]. There are few studies in vivo and in the obese patients have shown an action of Chitosan on inflammatory parameters and cytokines. The inflammatory parameters and the cytokines we have analyzed have improved already at 3 months, although not significantly. At 6 months we noticed a significant reduction of Hs-CRP (-0.4 mg/l, -28.6 % vs Baseline, and -0.3 mg/l, -23.1 % vs placebo) and a significant increase in ADN (+0.9 µg/ml, +14.5 % vs Baseline, and +0.6 µg/ml, +8.5 % vs placebo). Although a decreasing trend in IL-6 and TNF-α was noted, they were not significant at 6 months. Kim HM [39] evaluated the action of Chitosan at 5100 mg/day in elderly patients on the levels of some cytokines and since TNF-α was reduced after 2 months of this treatment (-22.8 pg/ml, -28.6 %) also if not significantly compared to Baseline.

5. Conclusions

A nutraceutical containing Chitosan and α-Lipoic acid can be helpful in reducing weight and BMI, in improving lipid profile, and in reducing inflammatory parameters, without affecting the glycemic status of obese patients. Although the study was 6 months long, a period we consider sufficient to evaluate the modification of anthropometric parameters, this period may have been insufficient to verify a significant drop in FPG or a significant increase in the value of HDL-C or a further significant improvement of the other inflammatory parameters evaluated. A final consideration, no less important, was that of adverse events: this Nutraceutical was also found to be safe and well tolerated by all study participants.

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