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Spirulina maxima improves insulin sensitivity, lipid profile, and total antioxidant status in obese patients with well-treated hypertension: a randomized double-blind placebo-controlled study

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Abstract. – OBJECTIVE: *Spirulina maxima* consumption is known to be associated with enhanced cardiovascular and metabolic health. Human studies on this topic have recently been described in a few papers; however, potential protective cardiovascular properties of *Spirulina* in obese patients receiving standard pharmacological antihypertensive treatment remain to be elucidated. Putative beneficial cardiovascular effects of *Spirulina* supplementation in well treated, obesity-related hypertension were studied in a double-blind placebo-controlled trial.

PATIENTS AND METHODS: Total 50 obese subjects with treated hypertension, each randomized to receive 2 g of *Spirulina* or a placebo daily, for three months. At baseline and after treatment anthropometric parameters, plasma lipid levels, inflammation, and oxidative stress biomarkers along with insulin sensitivity estimated by euglycemic clamp were assessed.

RESULTS: After three months of *Spirulina* supplementation significant decrease in body mass ($p < 0.001$), body mass index (BMI; $p < 0.001$) and waist circumference (WC; $p = 0.002$) were observed in *Spirulina* group. Spirulina had also significant, lowering effect on low-density lipoprotein cholesterol (LDL-C; $p < 0.001$) and interleukin-6 (IL-6) concentration ($p = 0.002$) in supplemented patients compared to placebo group. *Spirulina* supplementation considerably improved total antioxidant status (TAS; $p = 0.001$) and insulin sensitivity ratio (M; $p < 0.001$) in *Spirulina* group compared to placebo-treated individuals.

CONCLUSIONS: The favorable influence of *Spirulina* supplementation on insulin sensitivity, plasma lipid levels along with inflammation and oxidative stress biomarkers reported in this study creates the promise for new therapeutic approaches in obese patients with well-treated hypertension.

Key Words:
Spirulina, Obesity, Oxidative stress, Randomized trial.

Introduction

Obesity leads to hypertension, often referred to as obesity-related hypertension, through various mechanisms[1]. Coexisting obesity and hypertension significantly increase the progression of atherosclerosis and global cardiovascular risk[2-4].

Recent evidence has shown that both obesity and hypertension are associated with oxidative stress and chronic low-grade inflammatory responses[5-7]. Oxidative stress and inflammatory processes play major roles in endothelial dysfunction

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in cardiovascular diseases and are involved in the progression of insulin resistance. By generating an excess of superoxide anions and hydrogen peroxide – H_2O_2, insulin resistance has been shown to induce oxidative stress. Altogether, oxidative stress, inflammation, and increasing insulin resistance are involved in the mechanisms that lead to modulation of vascular endothelium, smooth muscle contractility, and organ function[8]. Understanding the mechanism involved in the development of obesity-related hypertension is crucial to identifying new therapeutic options that can decrease cardiovascular and metabolic risk in affected patients.

In recent years, numerous publications have provided evidence of the effect of natural substances-supplements on improving endothelial function, and thus reducing the risk of cardiovascular diseases[9,10]. *Spirulina maxima* (*Arthrospira maxima*) is a species of cyanobacterium, belonging to the Athrospira genus of the Oscillatoriaceae family[11], used as a food additive because of its high levels of protein and essential nutrients, such as carotenoids, vitamins, and minerals[12]. It also contains antioxidants that can help protect cells from damage. Evidence has accumulated to demonstrate that *Spirulina* inhibits viral replication[13], prevents anemia[14] and fatty liver disease[15], and possess hypoglycemic[16] and hypolipemic[17,18] properties. The mechanisms through which *Spirulina* exerts its protective cardiovascular effects are the subject of an intense research effort. *Spirulina* mediates the synthesis and release of nitric oxide (NO) by the endothelium; it is also responsible for the release of cyclooxygenase – a metabolite of arachidonic acid that dilates blood vessels. Isolated from *Spirulina*, convertase enzyme inhibitory peptide is used to study the effect on blood pressure. Phycocyanin (PC), a blue dye with antioxidant properties derived from *Spirulina*, has been reported to improve parameters associated with vascular dysfunction, including blood platelet aggregation, vascular inflammation, and altered lipid profile[19,20].

So long as the active ingredients in *Spirulina* are not known, attention is being paid to seeking its possible therapeutic actions. Various studies point to a possible beneficial effect of *Spirulina* on the concentration of blood serum lipids[16,21], and fasting glucose[22]. Its effects on body weight or blood pressure result in small but significant reductions of these parameters in animals[23,24]. Human studies on this topic have recently been described in a few papers[25,26]; however, the results pertained to the effects of *Spirulina* in individuals who, at the time of trial, were not taking medications. Recently, we have found that supplementation of *Spirulina maxima* improves endothelial function by lowering arterial stiffness index (SI), blood pressure and weight in overweight patients with hypertension without evidence of cardiovascular disease[27]. Our results performed in overweight hypertensive individuals led us to investigate the hypothesis of the positive effect of *Spirulina maxima* supplementation on further endothelium-related, cardiovascular risk factors in the selected group of patients with obesity and hypertension.

The aim of the study was to examine the influence of oral *Spirulina maxima* supplementation after 3 months of treatment on the insulin sensitivity, lipid profile along with immune and oxidative stress parameters in obese individuals with stable treated hypertension.

Patients and Methods

Study Population

The study procedure obtained an approval of the Research Ethics Committee of Poznan University of Medical Sciences, case no. 599/12. Informed consent was obtained from all patients. The study was conducted in accordance with Helsinki Declaration.

Among the 142 registered individuals with hypertension and obesity from our outpatient clinic, a total of 50 (25 men, 25 women) were enrolled.

The inclusion criteria encompassed: body mass index (BMI) $\geq$ 30 kg/m^2, age 25-60 years, stable body weight (< 3 kg self-reported change during the previous three months), well-controlled hypertension (systolic blood pressure (SBP) < 160 mmHg and/or diastolic blood pressure (DBP) < 100 mmHg) with stable, one drug treatment for at least 6 months (Table I).

The exclusion criteria involved: secondary hypertension or secondary obesity; diabetes mellitus; coronary artery disease, stroke, congestive heart failure, or malignancy; use of any dietary supplements during the three months prior to the study; a current modification of antihypertensive therapy; abnormal kidney or liver function; a history of infection in the month prior to the study; nicotine or alcohol abuse; or other condition that, according to the investigators, would make contribution to the study not suitable for the patient or could prevent, limit, or confound the protocol-specified efficacy assessments.

Table I. Baseline characteristics of Spirulina group and placebo group.

Analyzed parameters	Spirulina group	Placebo group	p^1
GenderM/F	12/13	13/12	NS
Age	49.3 ± 8.7	50.2 ± 7.2	NS
BMI (kg/m^2)	33.5 ± 6.7	33.3 ± 6.2	NS
WC (cm)	105.2 ± 15.3	102.4 ± 14.0	NS
SBP (mmHg)	148 ± 15	151 ± 15	NS
DBP (mmHg)	84 ± 9	85 ± 9	NS
TC (mmol/l)	5.5 ± 1.1	5.2 ± 0.9	NS
LDL-C (mmol/l)	3.5±0.9	3.6 ± 0.9	NS
HDL-C (mmol/l)	1.4 ± 0.3	1.3 ± 0.4	NS
TG (mmol/l)	1.9 ± 1.0	2.0 ± 1.2	NS
TAS (mmol/l)	1.8 ± 0.3	1.8 ± 0.2	NS
IL – 6 (mmol/l)	4.3 ± 0.6	4.4 ± 0.7	NS
GLU (mmol/l)	5.5 ± 0.8	5.5 ± 0.7	NS
INS (µIU/ml)	32.1 ± 4.2	31.8 ± 3.7	NS
M (mg/kg/min)	3.2 ± 1.8	3.4 ± 1.7	NS
Time since diagnosis of hypertension	5.7 ± 2.1	5.6 ± 2.5	NS
Hypertensive theraphy			
ACEI	12	11	NS
ARB	2	4	NS
CCB	9	8	NS
BB	4	3	NS
Diuretic	7	6	NS

Data are arithmetic mean ± SD; NS, not significant; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; TAS, total antioxidant state; Il-6, interleukin-6; INS, insulin; M, insulin sensitivity ratio, ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker: sartan; CCB: calcium channel blocker; BB: beta-blocker.1Differences were tested using Mann-Whitney U test.

Of 142 obese patients screened at our outpatient clinic, 31 did not meet the inclusion criteria (22 showed unstable body weight and 9 had insufficient blood pressure control), whereas 61 met the exclusion criteria (3 with secondary hypertension and/or obesity; 13 with diabetes mellitus; 3 with a history of coronary artery disease; 3 with congestive heart failure; 7 with a history of use of dietary supplements; 8 with a current need for modification of antihypertensive therapy; 12 with abnormal liver, kidney, or thyroid gland function; 8 with clinically significant inflammatory processes; 2 with a history of infection within the month before the study; 10 showing nicotine or alcohol abuse). After screening, 50 patients fulfilled all inclusion criteria and none of the exclusion criteria, so they were allocated equally into the *Spirulina* group and the placebo group. All subjects completed the study, and no significant changes in diets, physical activity, or medication were recorded.

Design of the Study

The study was planned as a randomized double-blind placebo-controlled trial composed of two parallel groups. Randomization process was conducted by an independent statistician. Individuals participated the study were randomly divided with a ratio 1:1 to receive four capsules of Hawaiian *Spirulina* (Cyanotech Corporation, Kailua-Kona, Hawaii, USA) or a placebo consisted of pure microcrystalline cellulose, every morning for 3 months. Each Hawaiian *Spirulina* capsule contained 0.5 g of *Spirulina maxima* composed of 60%–70% protein, gamma-linolenic acid (GLA), beta-carotene, iron, PC. Both applied supplements were packed in indistinguishable bottles. Participants of the study were advised to continue their habitual diet and exercise activity throughout the study. At the baseline and following 3 months of treatment, the anthropometric parameters, biochemical parameters, and blood pressure were measured, and laboratory tests were performed for both groups. The intention-to-treat (ITT) population consisted of 50 patients.

Anthropometric and Blood Pressure Parameters

Anthropometric measurements were performed in patients that wore light-weight clothing and no shoes. Weight was calculated to the nearest 0.1 kg and height was measured to the nearest

0.1 cm. Obesity was defined as a BMI over 30 kg/m^2. Waist circumference (WC) was measured to the nearest 0.5 cm at the level of the iliac crest at the end of normal expiration. The blood pressure measurement was performed seated, in line with the guidelines of the European Society of Hypertension[28] by the use of digital electronic tensiometer (model 705IT, Omron Corporation, Kyoto, Japan). The definition of hypertension was based on the measurement of arterial blood pressure (the average of three measurements obtained after 10 minutes of physical resting by the patients, twice at two different visits in 1 month).

Biochemical Parameters

Blood samples were taken from each individual following an overnight fast and after lying in a supine position for 30 minutes.

Total antioxidant status (TAS) was measured using a TAS Randox kit (Randox Laboratories, Ltd., Crumlin, UK) and via spectrophotometry (SPECORD M40; Carl Zeiss, Jena, Germany)[29]. In our analysis, the intra-assay coefficient of variation was 2.8%, and the interassay coefficient of variation was 6.1%. The sensitivity of the assay, as reported by the manufacturer, was a mean minimal detectable value of 0.21 mmol/L.

The concentration of interleukin 6 (Il-6) was measured using an enzyme-linked immunosorbent assay (R&D System Europe: Quantikine® Human Il-6 immunoassay, Minneapolis, MN, USA). In our analysis, the intra-assay coefficient of variation was 7.4%, and the interassay coefficient of variation was 5.2%[30].

Insulin sensitivity was evaluated by the euglycemic hyperinsulinemic clamp technique, described elsewhere[31]. On the morning of the study, two venous catheters were inserted into the antecubital veins: the first for infusing insulin and glucose, and the second in the contralateral arm for sampling blood; that arm was heated to approximately 60 °C. Insulin (Actrapid HM, Novo Nordisk, Copenhagen, Denmark) was given as a primed-continuous intravenous infusion for 3 h. Arterialized blood glucose was obtained every 5 min. The glucose infusion rate approached stable values during the final 40 min of the study, and the rate of whole-body glucose uptake (the M value) was calculated as the mean glucose infusion rate from 80 to 120 min. Plasma insulin was determined by immunoassay (DIAsource immunoassays S.A., Nivelles, Belgium).

Plasma total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL), triglycerides (TG), and fasting glucose were all estimated by a Dimension EXL with LM Integrated Chemistry System Analyzer (Siemens Healthcare GmbH, Erlangen, Germany)[32]. The values for LDL cholesterol were evaluated according to the described formula[33]. The intra-assay and interassay coefficients of variation were, respectively, 1.3% and 0.8% for TC, 0.5% and 1% for TG, 2.3% and 2.4% for HDL cholesterol, and 1.6% and 1% for glucose.

Diet and Supplement Intake

The assessment of diet was performed every 14 days including 3 days before the laboratory tests by dietary intake interviews (24-hour recall). Dietetics computer program (Dieta 5.0, 2011, IŻŻ, Warsaw, Poland) was used to evaluate the level of nutrients present in the daily diet. The caffeine consumption, intake of nutrients and physical activity during the study were constant and comparable between the groups at the beginning and after the intervention.

On the beginning of the study, during the interview, each patient was informed by a physician on the taking of single daily dosage of *Spirulina* supplement and its benefits. Patients were inspected on the visit every 14 days to confirm the number of capsules of *Spirulina* consumed over the two-week period. At the first nutrition visit, each patient had received a diary from a dietician to record the time the supplement was taken each day. The diary was checked by either a dietician or a physician on preceding visits. A log of all drug dispensed and returned was maintained by investigators. Supplements for each individual was accounted for throughout the study. Compliance demanded was 90%.

Statistical Analysis

The data are shown as mean ±SD. Statistics were performed with the Statistica version 10.0 (Statistica data analysis software system, version 10, StatSoft, Inc. 2011, Aliso Viejo, CA, USA). Shapiro-Wilk test was used to check the normal distribution in each group. The differences between the control group and the placebo group were evaluated by Mann-Whitney test or unpaired *t*-test. To show the differences between the effect of treatment a one-way repeated-measure ANOVA was used. ITT analysis was performed. *p*-value of less than 0.05 was regarded as significant.

Results

The baseline characteristics of both groups are shown in Table I. There were no statistically significant differences between the two groups with respect to the anthropometric, biochemical parameters and hypertension diagnosis time or therapy before the study. All participants completed the study, and no significant changes in diets, physical activity, or antihypertensive therapy were recorded in the studied population. After three months of *Spirulina* supplementation, a significant decrease in particular anthropometric parameters such as body mass, BMI and WC and TC concentration were observed in *Spirulina* group. *Spirulina* had also significant, lowering effect on LDL-C and IL-6 concentration in supplemented individuals compared to placebo group. *Spirulina* supplementation significantly improved TAS and M in supplemented group compared to placebo-treated individuals. Detailed characteristic is summarized in Table II. ANOVA analysis revealed that statistically significant interaction between treatment and time factors (with both factors being statistically significant) was observed for TAS, insulin sensitivity, LDL cholesterol level. M and TAS levels were found to be significantly higher in the *Spirulina* group than in the placebo group. LDL was significantly lower in the *Spirulina* group than in the placebo group. A decrease in glucose and insulin serum concentration and WC was noted in both the *Spirulina* and the placebo group during the course of the study with the time factor being statistically significant; however, no significant interaction between treatment and time factors was found. Increased levels of HDL were observed in both groups, but the differences were not significant. The data in Table III present comparing tests results and the *p*-values for ''treatment'' and ''time'' factors and their interactions, as obtained from the ANOVA analysis.

Discussion

The positive effect of *Spirulina* supplementation on cardiovascular risk factors including lipid profile and insulin sensitivity along with inflammation and oxidative stress level in obese patients with pharmacologically-treated hypertension was a novel finding demonstrated in our study. In this work, we also report the plausible influence of *Spirulina* supplementation on WC parameter in obese patients on antihypertensive therapy and extend our previously obtained results regarding the beneficial action of *Spirulina* treatment into the weight and BMI parameters in overweight, hypertensive patients, to obese individuals with treated hypertension[27].

Here we provide evidence that three months of treatment with *Spirulina* increases insulin sensitivity in obese patients with well-treated hypertension. Results from both experimental[34] and clinical studies[26,35] confirm the hypoglycemic effect of *Spirulina* in diabetic animal models and patients with type-2 diabetes. *Spirulina* has a beneficial effect on fasting plasma insulin and glucose levels[22]. The antidiabetic effect of PC in mice is most likely due to its ability to enhance insulin sensitivity, to ameliorate insulin resistance of peripheral target tissues, and to regulate glucose and lipid metabolism. PC may thus have a potential clinical utility in combating type-2 diabetes[36]. The improvement of insulin sensitivity by *Spirulina* administration for two months has been recently demonstrated by the short insulin tolerance test in a group of 33 insulin-resistant HIV-infected patients[37]. Similar results regarding insulin sensitivity were found in individuals with nonalcoholic fatty liver disease (NAFLD), using the homeostasis model assessment of insulin resistance, after six months of *Spirulina* treatment. However, unlike in our trial, patients treated with several drugs including calcium channel blockers were excluded from the study[38]. We have demonstrated for the first time that treatment with *Spirulina* increases insulin sensitivity in obese patients with treated hypertension. We used the hyperinsulinemic–euglycemic clamp technique, which is the gold standard for assessing insulin resistance in humans. The exact mechanism involved in the influence of *Spirulina* on insulin sensitivity in the investigated group requires further research.

The influence on lipid parameters seems so far to be the best-proven effect of supplementation with *Spirulina* extract available in the literature. Previous studies[17,39] have demonstrated the hypolipemic activity of *Spirulina* in animals. *Spirulina* in the diet has been found to decrease serum aspartate aminotransferase, TG, and TC in rats. These results suggest that *Spirulina* has hepatoprotective properties through decreasing the liver lipid profile. In this way, *Spirulina* prevents the development of fatty liver induced by hypercholesterolemic diet in mice[18]. The main component of *Spirulina* that acts to decrease the serum con-

Table II. Changes in anthropometrics, blood pressure and biochemical markers during the supplementation in the Spirulina and placebo groups.

Analyzed parameters	Baseline		After 3 months		Compare (*p* value)			
	Spirulina group (n = 25)	Placebo group (n = 25)	Spirulina group (n = 25)#	Placebo group (n = 25)#	Baseline (Spirulina group and Placebo group)	After 3 months (Spirulina group and Placebo group)	Spirulina group (Baseline and after 3 months)	Placebo group (Baseline and after 3 months)
Intention to treat population, n = 0								
Gender M/F	12/13	13/12	–	–	–	–	–	–
Age	49.3 ± 8.7	50.2 ± 7.2	–	–	–	–	–	–
Body mass (kg)	92.96 ± 18.58	95.30 ± 18.31	88.97 ± 17.13	94.94 ± 16.77	0.521	0.089	< 0.001	0.374
BMI (kg/m^2)	33.5 ± 6.7*	33.3 ± 6.2*	31.7 ± 5.8*	33.3 ± 5.8*	0.893	0.171	< 0.001	0.673
WC (cm)	105.2 ± 15.3*	102.4 ± 14.0*	103.4 ± 14.1	101.7 ± 11.2*	0.108	0.394	0.002	0.657
TC (mmol/l)	5.5 ± 1.1	5.2± 0.9*	5.2 ± 0.9	5.4 ± 0.8*	0.191	0.150	< 0.001	0.306
LDL-C (mmol/l)	3.5 ± 0.9*	3.6 ±0.9*	3.0 ± 0.6	3.6 ± 0.9*	0.412	< 0.001	< 0.001	0.223
HDL-C (mmol/l)	1.4 ± 0.3*	1.3±0.4*	1.4 ± 0.3*	1.2 ± 0.4*	0.357	0.002	0.227	0.204
TG (mmol/l)	1.9 ± 1.0	2.0 ± 1.2	1.8±0.9	2.1 ± 1.1	0.334	0.224	0.633	0.981
TAS (mmol/l)	1.8 ± 0.3	1.8 ± 0.2	2.2 ± 1.0	1.8 ± 0.6	0.356	0.001	0.001	0.956
IL – 6 (mmol/l)	4.3 ± 0.6	4.4 ± 0.7	3.9± 0.4	4.1 ± 0.6	0.474	0.002	< 0.001	0.866
GLU (mmol/l)	5.5 ± 0.8	5.5 ± 0.7	5.3 ± 0.9	5.5 ± 0.6*	0.148	0.457	< 0.001	0.048
INS (μIU/ml)	32.1 ± 4.2	31.8 ± 3.7*	29.4 ± 3.4	30.3 ± 7.1	0.344	0.089	0.006	0.354
M (mg/kg/min)	3.2 ± 1.8	3.4 ± 1.7	4.3 ± 2.1	3.0 ± 1.6	0.643	< 0.001	0.001	0.542

Bold values indicate the differences, significant differences at $p < .05$. Data are arithmetic mean ± SD; NS, not significant; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; TAS, total antioxidant state; Il-6, interleukin-6; INS, insulin; M, insulin sensitivity ratio. #Last day of study period. *With normal distribution.

Table III. Changes in anthropometrics, blood pressure and biochemical markers during the supplementation in the Spirulina and placebo groups.

Analyzed parameters	Treatment *p*-value	Time	Interaction
Gender M/F	–	–	–
Age	–	–	–
BMI (kg/m^2)	0.576	**0.001**	**0.001**
WC (cm)	0.210	**0.026**	0.129
TC (mmol/l)	0.814	0.234	**0.004**
LDL-C (mmol/l)	**0.002**	**0.001**	**0.024**
HDL-C (mmol/l)	0.120	0.620	0.087
TG (mmol/l)	0.147	0.755	0.688
TAS (mmol/l)	**0.031**	0.029	**0.001**
IL – 6 (mmol/l)	0.117	0.741	0.168
GLU (mmol/l)	0.115	**0.002**	0.602
INS (μIU/ml)	0.283	**0.042**	0.949
M (mg/kg/min)	**0.043**	**0.008**	**0.001**

Bold values indicate one-way repeated-measure ANOVA, significant differences at $p < 0.05$. Data are arithmetic mean ± SD; NS, not significant; WC, waist circumference; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; TAS, total antioxidant state; Il-6, interleukin-6; INS, insulin; M, insulin sensitivity ratio. *Last day of study period.

centration of LDL is the lipid-lowering PC, which inhibits the intestinal absorption of cholesterol and increases the concentration of lipoprotein lipase, initiating the process disintegrating lipoproteins, which implies reduced LDL[39]. The presence of polyunsaturated fatty acids – such as palmitic acid, stearic acid, oleic acid, linoleic acid, GLA, and phytochemical constituents such as polyunsaturated fatty acids, fixed oils, amino acids, and flavonoids – is responsible for the antilipemic activity of spirulina[40,41]. In humans, supplementation with 4.5 g of *Spirulina* for three months has been found to diminish levels of TG, TC, LDL, and TC in three individuals with NAFLD[42]. Also, *Spirulina* supplementation at 2 g per day for two months on the lipid profile in 25 subjects with type-2 diabetes has been shown to result in a reduction of TG, TC, and LDL in the studied group[16]. Similar effects in patients with hyperlipidemic nephrotic syndrome were observed following supplementation with 1 g of *Spirulina* per day for the same period[21]. These findings have been confirmed in our study, where three months of *Spirulina* supplementation significantly decreased the level of LDL-C and TC in obese hypertensive patients receiving standard hypotensive therapy. In contrast, the TG level remained stable during the trial in this population, which may be linked with the antihypertensive drug treatment, during which TG levels often remain elevated[43].

Regarding the influence of *Spirulina* on oxidative stress, we observed that its supplementation increased the serum concentration of TAS in examined group. This is probably associated with a positive correlation between the presence of PC and the production of NO by the endothelium. Recently, it has been demonstrated that recombinant apo-c-PC could serve as a potent antioxidant supplement and could be useful in the treatment of oxidatively induced hemolytic anemia[44]. The beneficial effect of *Spirulina* supplementation on tissue lipid peroxidation and oxidative DNA damage has been proven previously in a hypercholesterolemic New Zealand White rabbit model[45]. The positive influence of *Spirulina* administration on oxidative stress status was demonstrated in female patients with preclinical HIV-infections[46], and patients with type-2 diabetes mellitus[25]. Increased level of TAS has been also documented in a population of elderly male Koreans after *Spirulina* supplementation for four months. Reduced levels of inflammation biomarker IL-6 have also been reported by the same authors[47] and are in line with our results. Interestingly, individuals receiving drugs for hypertension were excluded from Koreans study[47] that suggests the putative advantage of *Spirulina* inclusion into the standard antihypertensive treatment and deserves more research.

The present study had some limitations that need to be acknowledged. The group should be larger, in order to allow division by gender; this would permit observation of the changes that might occur in women and men following *Spirulina* treatment. Also, the study was only three months in duration; consequently, we were evaluating the short-term effects of *Spirulina*.

The clinical importance of our results could be also extended by introducing different doses of supplement to the studied population.

Conclusions

The present findings demonstrate clear evidence for a beneficial and clinically important influence of *Spirulina* supplementation on insulin sensitivity, lipid profile, inflammation, and oxidative stress status in patients with obesity-related, well-controlled hypertension. Present results together with our previous findings in overweight subjects with well-controlled hypertension[27] allow us to suggest that *Spirulina* may serve as a valuable addition to routine antihypertensive therapy in obese patients with diagnosed hypertension, by exerting its multiple beneficial actions on cardiovascular risk factors in this population. Nevertheless, further studies on a larger scale, and with a longer duration of observation, are needed to support our data and to explore the exact mechanism of *Spirulina* action in the course of obesity-related hypertension.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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