

Effects of *spirulina* consumption on body weight, blood pressure, and endothelial function in overweight hypertensive Caucasians: a double-blind, placebo-controlled, randomized trial

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Abstract. – OBJECTIVE: Some studies have demonstrated the beneficial effects of *Spirulina maxima* (*Arthrospira maxima*) consumption on glycemic, lipid, and blood pressure parameters. The aim of this study was to investigate the effect of *Spirulina maxima* on body weight, blood pressure, and endothelial function.

PATIENTS AND METHODS: In this randomized double-blind placebo-controlled trial, 40 patients with hypertension but lacking evidence of cardiovascular disease were enrolled to receive daily either 2.0 g Hawaiian *spirulina* or placebo for three months. Anthropometric parameters, systolic blood pressure (SBP), diastolic blood pressure (DBP), and stiffness index (SI) using digital plethysmography were measured before and after the intervention.

RESULTS: After three months, there was no change in body mass index (BMI) or weight in either the *spirulina* or the placebo group. However, a significant reduction in SBP and SI was observed. The patients in the *spirulina* group showed significant reductions in BMI (26.9 ± 3.1 vs. 25.0 ± 2.7 kg/m², $p = 0.0032$), weight (75.5 ± 11.8 vs. 70.5 ± 10.3 kg, $p < 0.001$), SBP (149 ± 7 vs. 143 ± 9 mmHg, $p = 0.0023$), and SI (7.2 ± 0.6 vs. 6.9 ± 0.7 m/s, $p < 0.001$). The tested parameters did not change in the placebo group.

CONCLUSIONS: This study demonstrates that three months of regular consumption of *Spirulina maxima* not only improves BMI and weight but also results in improvements in blood pressure and endothelial function *spirulina* in overweight patients with hypertension but lacking evidence of cardiovascular disease.

Key Words:

Spirulina, Hypertension, Body mass index, Endothelial function.

Introduction

Hypertension is one of the most common diseases in the world. According to recent data, nearly one billion people or 26% of the adult population of the world suffers from hypertension¹. Elevated blood pressure is seen in both developed (333 million people) and undeveloped (639 million) countries¹. Data from 2013 shows that about 30%-40% of the European population show signs of hypertension². Hypertension is considered a major risk factor for cardiovascular events. Elevated blood pressure is correlated with an increased risk of ischemic heart disease³, stroke⁴, and heart failure⁵. Endothelial dysfunction in hypertension appears long before cardiovascular events occur. There is as of now no simple, reliable test that could detect endothelial dysfunction. Increased carotid intima-media thickness has been proposed as a signal of subclinical endothelial dysfunction⁶. Arterial stiffness has also been described as a marker of early endothelial changes⁷. The presence of subclinical endothelial damage in hypertension points to increased cardiovascular risk and allows for early intervention.

In recent years, some publications have shown evidence of the positive effects of certain supplements on endothelial function and on reducing global cardiovascular risk⁸. *Spirulina maxima* (*Arthrospira maxima*) is a cyanobacterium (blue-green alga) that has a very long history of use as food for humans. *Spirulina* is a rich source of protein, vitamins, minerals, carotenoids, and phycocyanins⁹. Its safety as a food has been established through toxicological studies¹⁰. *Spirulina* has been reported to have beneficial effects against oxidative stress^{11,12}, hyperglycemia¹³, and hypercholesterolemia¹⁴. There is increasing evidence of its role in controlling chronic diseases such as diabetes¹⁵, bronchial asthma¹⁶, and cancer¹⁷.

The aim of the present work is thus to determine the hypotensive activity of *spirulina* in patients with hypertension. This study also investigated the effects of *spirulina* on endothelial function as measured by digital plethysmography in patients with hypertension but lacking evidence of cardiovascular disease.

Patients and Methods

Study Patients

The study protocol was approved by the Research Ethics Committee of Poznan University of Medical Sciences, case no. 599/12. Informed consent was obtained from all patients. The study was performed in accordance with the Declaration of Helsinki.

Among the 52 registered patients with hypertension screened in our outpatient clinic, a total of 40 (21 men, 19 women) were enrolled.

The inclusion criteria were body mass index (BMI) equal to or lower than 29.99 kg/m², age 40 to 60 years, stable body weight (< 3 kg self-reported change during the previous three months), and well-controlled hypertension (meaning systolic blood pressure (SBP) less than 160 mmHg or diastolic blood pressure (DBP) less than 100 mmHg) with stable treatment for at least six months (the patients receiving only one medication).

The exclusion criteria were obesity, secondary hypertension, diabetes, a history of coronary artery disease, stroke, congestive heart failure or malignancy, a history of use of any dietary supplement within the three months prior to the study, a current need for modification of antihypertensive therapy, abnormal liver or kidney

function, any clinically significant process, a history of infection in the month prior to the study, nicotine or alcohol abuse, or other condition that, in the opinion of the investigators, would make participation not in the best interest of the patient or could prevent, limit, or confound the protocol-specified efficacy assessments.

Study Design

The study was designed as a randomized double-blind placebo-controlled trial with two parallel groups. Randomization was performed by an independent statistician. The participants were randomly assigned (in a 1:1 ratio) to receive either four capsules of Hawaiian *spirulina* (Cyanotech Corporation, Hawaii, USA) or a placebo with their morning meal for three months. All supplements were packed in unlabeled bottles. Each Hawaiian *spirulina* capsule contained 0.5 g of *Spirulina maxima* (60%-70% protein, gamma-linolenic acid (GLA), beta carotene, iron, phycocyanin (PC). The placebo consisted of pure microcrystalline cellulose. All patients were advised to continue their habitual diet and exercise patterns throughout the study. At the baseline, and following three months of treatment, anthropometric parameters and blood pressure were measured and digital plethysmography was performed for both groups. The intention-to-treat (ITT) population consisted of 40 patients.

Anthropometric and Blood Pressure Measurements

During the anthropometric measurements, patients wore lightweight clothing and no shoes. Weight was measured to the nearest 0.1 kg and height was measured to the nearest 0.1 cm¹⁸. Blood pressure was measured seated, according to the guidelines of the European Society of Hypertension¹⁹, using a digital electronic tensiometer (model 705IT, Omron Corporation, Kyoto, Japan).

Arterial Stiffness Measurement

A photoplethysmograph (Pulse Trace Micro Medical, Rochester, UK) transmitting infrared light at 940 nm was placed on the index finger of the right hand. All recommendations for standardizing of subjects' conditions were heeded. Measurements were taken after at least 10 min rest in recumbent position, at similar times of the day. All subjects were allowed to acclimatize to the temperature of 22 ± 1 degrees Celsius for at least 30 min before recording commenced. All

subjects had to refrain for at least 3 h from smoking and eating and for at least 10 h from drinking alcohol before measurements. The digital output from the photoplethysmograph was recorded in the form of a wave called the “digital volume pulse” (DVP). The DVP exhibited a characteristic “notch” or point of inflection in its downslope (Figure 1). The time between the first and second peak is called the peak to peak time (PPT). The SI is the proportional constant relating the patient’s height to the PPT.

$$SI = \text{Patient's height (m)} / \text{Peak to peak time (s)}$$

Dietary and Supplement Intake

Every fourteen days, and also three days before the laboratory tests, dietary intake was assessed on the basis of interviews (24-hour recall). The amount of nutrients in the daily diet was evaluated using a dietetics computer program (Dieta 5.0, 2011; IŻŻ, Warszawa, Poland). The intake of nutrients during the study was constant and was comparable between the groups. Physical activity was constant and unchanged in all subjects at the beginning and after treatment.

In this study, a single daily dosage of the supplement was used in order to facilitate the patients taking it. During the interview with each patient on the first day of the study, the physician described the daily *spirulina* supplement and its benefits. Every 14 days, the patient visited the dietician to record the number of pills consumed over the previous two-week period. During the first visit to the dietician, each patient received a diary in which to enter the time the supplement was taken each day. On subsequent visits, the di-

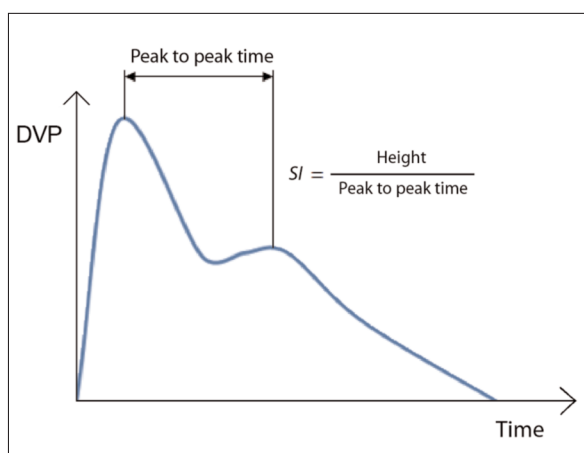


Figure 1. Digital volume pulse (DVP).

ary was checked by either a dietician or a physician. The investigators maintained a log of all drugs dispensed and returned. The supply of the drug for each subject was accounted for throughout the study, with the required compliance being 90%.

Statistical Analysis

It was calculated that a sample size of at least 20 patients in each group would yield at least an 80 % chance of detecting a treatment effect as statistically significant at the 0.05 alpha level. The data are shown as means \pm SDs. Statistical calculations were carried out using Statistica (Statistica data analysis software system, version 10, StatSoft, Inc., 2011; Aliso Viejo, CA, USA). The normal distribution of each group was checked using the Shapiro-Wilk test. To examine the differences between the control group and the placebo group, the Mann-Whitney or unpaired *t*-test was used. A *p*-value of less than 0.05 was regarded as significant.

Results

Table I shows the *spirulina* and placebo groups. There were no significant differences across gender, age, weight, BMI, SBP and DBP. The time since hypertension was also diagnosed, and the quantity and type of drug were compared.

After three months of treatment with *spirulina*, significant decreases in SBP, DBP, and SI were observed in the spirulina group (Table II).

Spirulina showed significant activity in decreasing BMI and weight. Spirulina also had a hypotensive effect. There was a significant decrease in SBP in the spirulina group, and the trend towards diminishing DBP was also observed, though was not significant.

No endothelial dysfunction was measured by digital plethysmography. SI was in the normal range in both the spirulina group and the placebo group. The intervention with spirulina diminished the SI value, and this was significant change.

Discussion

There is increasing interest in the study of the potential cardioprotective effects of dietary supplements. Patients with subclinical markers of

Table 1. Baseline characteristics of *Spirulina* group and Placebo group.

Analyzed parameters	Spirulina group	Placebo group	p ¹
Gender M/F	21/19	20/20	NS
Age	53.0 ± 5.8	53.6 ± 5.5	NS (0.63)
High (m)	1.68 ± 0.06	1.67 ± 0.07	NS (0.32)
BMI (kg/m ²)	26.9 ± 3.1	25.7 ± 3.2	NS (0.29)
Weight (kg)	75.5 ± 11.8	70.4 ± 15.9	NS (0.15)
SBP (mmHg)	149 ± 7	150 ± 7	NS (0.36)
DBP (mmHg)	91 ± 5	93 ± 6	NS (0.81)
SI (m/s)	7.2 ± 0.6	7.3 ± 0.5	NS (0.81)
Time since diagnosis of hypertension	3.1 ± 2.3	3.0 ± 1.8	NS
Medication	15	14	NS
ARB	8	9	NS
CCB	10	9	NS
BB	4	5	NS
Diuretic	3	3	NS

Data are arithmetic mean ± SD; NS: not significant; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; SI: index of arterial stiffness; ACEI: angiotensin-converting enzyme inhibitor; CCB: calcium channel blocker; BB: beta-blocker. ¹Differences were tested using Mann-Whitney U test.

early endothelial dysfunction have also been extensively investigated. There are a number of dietary supplements whose beneficial influence on the endothelium has been assessed in many trials. There are many published papers that seem to suggest an improvement in arterial stiffness related to flavonoid consumption²⁰. Some authors²¹ have demonstrated that dark chocolate and cocoa consumption is associated with significant reductions in arterial stiffness in women. Some studies have demonstrated that regular consumption of pistachio nuts²² or of garlic extract²³ results in improvements in endothelial function. To the best of our knowledge, the beneficial effect of spirulina on arterial stiffness has not been explored much. Our trial studies a group of patients with well-controlled hypertension of relatively short duration, undergoing monotherapy and without any visible marks of cardiovascular complications. This population did not reveal endothelial dysfunction in the arterial stiffness measurements. Nevertheless, three months of spirulina treatment resulted in a significant diminution of arterial stiffness, as measured by digital plethysmography.

To date, there have been various models of the pathogenesis of arterial stiffness. There are likely to be several complementary mechanisms that contribute to the induction of arterial stiffness, including inflammation, a decrease in bioavailable nitric oxide, and extracellular matrix remodeling²⁴. There is a great need for studies of the detailed mechanism of spirulina action on arterial

stiffness in humans. Increased aortic endothelial nitric oxide synthase expression in rats on spirulina could be one such mechanism²⁵. The positive effect of spirulina administration on oxidative stress status and inflammatory processes, as reported in some trials²⁶, could be the next attempt to elucidate the influence of spirulina on arterial stiffness.

In recent decades, great emphasis has been placed on the methods of arterial stiffness measurement. Various arterial parameters can be measured and calculated to evaluate arterial stiffness in noninvasive way, but clinicians still report great difficulties in selecting the most adequate method. Methods include mechanotransduction, tonometry, echo tracking, Doppler ultrasound systems, magnetic resonance, and finger photoplethysmography²⁷. All of these have their own advantages and disadvantages. Any method that is to be commonly used in practice to classify patients to an appropriate group of cardiovascular risk ought to be simple to use, fast, and cheap. Despite the restriction that the SI in digital plethysmography is affected by changes in the stiffness of all conduit vessels, rather than by changes in aortic stiffness alone²⁸, digital plethysmography seems to be such a simple, fast, cheap method.

Our study also revealed that spirulina has anti-hypertensive potential. This effect was visible in the SBP in particular, but to a smaller (non-significant) extent also in DBP, though with a tendency to decrease. Phycocyanin (PC), a blue dye

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 = 40)	Placebo group (n = 40)	Spirulina group (n = 40) [#]	Placebo group (n = 40) [#]	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 = 50								
Gender M/F	21/19	20/20	-	-	-	-	-	-
Age	53.0 ± 5.8	53.6 ± 5.5	-	-	-	-	-	-
BMI (kg/m ²)	26.9 ± 3.1*	25.7 ± 3.2*	25.0 ± 2.7*	25.9 ± 3.0*	0.14	0.35	0.0032	0.46
Weight (kg)	75.5 ± 11.8*	70.4 ± 15.9*	70.5 ± 10.3	72.5 ± 11.8*	0.15	0.41	< 0.0001	0.36
SBP (mmHg)	149 ± 7*	150 ± 7*	143 ± 9*	151 ± 9	0.36	< 0.001	0.0023	0.38
DBP (mmHg)	84 ± 9*	85 ± 9	79 ± 9*	86 ± 7	0.81	< 0.001	0.057	0.19
SI (m/s)	7.2 ± 0.6*	7.3 ± 0.5	6.9 ± 0.7*	7.2 ± 0.4	0.81	< 0.001	< 0.001	0.09

Bold values indicate the differences, significant differences at $p < 0.05$. Data are arithmetic mean ± SD; NS: not significant; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; SI: index of arterial stiffness. [#]Last day of study period; *With normal distribution.

with antioxidant properties derived from spirulina, has been reported to ameliorate systemic blood pressure by enhancing endothelial nitric oxide synthase (eNOS) expression in the aorta when stimulated by adiponectin²⁵. Ischimura et al²⁵ showed a positive correlation between the presence of PC and the production of nitric oxide by the endothelium. They also observed that spirulina supplementation can lower both SBP and DBP in the rat model of metabolic syndrome. A beneficial effect of spirulina on blood pressure has also been observed in human studies. Lee et al²⁶ examined the effect of spirulina intervention in Korean patients with type-2 diabetes. After 12 weeks of supplementation, there was a reduction in blood pressure. Further studies with larger sample sizes and longer durations are required to ascertain the hypotensive effect of spirulina.

In this study, the body mass reduction effect of spirulina was observed in overweight patients. There are various human studies regarding the effect of spirulina on anthropometric parameters in different groups of patients. In patients with ischemic heart disease, a significant loss in body weight was observed after intervention with spirulina²⁹. On the other hand, some studies have demonstrated no influence of spirulina on anthropometric parameters^{26,30}. The discrepancy in these results may be due to the different doses of spirulina used in the studies and the different duration of the studies. According to Fujimoto et al³¹, spirulina reduces the infiltration of macrophages into visceral fat and prevents liver lipid accumulation and oxidative stress, thus resulting in body weight reduction. Further studies are necessary to understand the mechanism by which spirulina affects human body weight.

Conclusions

Our results suggest a hypotensive and body mass reduction effect of spirulina in overweight patients with hypertension but lacking evidence of cardiovascular disease. It seems that spirulina can be used as an adjunctive therapy for hypertension in overweight people. The therapeutic role of spirulina administration needs further investigation.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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