

# Cardioprotective

J Med Food. 2002 Summer;5(2):91-6.

## **Hypocholesterolemic effect of spirulina in patients with hyperlipidemic nephrotic syndrome.**

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In nephrotic syndrome, large amounts of plasma proteins are lost in urine, causing a decrease in the plasma oncotic pressure. This leads to enhanced hepatic synthesis of albumin and other proteins, including lipoproteins, causing a secondary hyperlipidemia. Essential fatty acids such as gamma-linolenic acid (GLA) can prevent accumulation of cholesterol in the body, and spirulina has an appreciable amount of GLA. In this study 23 patients (age 2 to 13 years) with nephrotic syndrome received either medication (group I) or medication plus 1 g/day Spirulina (group II). Height, weight, and serum levels of fasting blood sugar, triglycerides, total cholesterol (TC), and low- and high-density cholesterol fractions (LDL-C and HDL-C, respectively) were measured before and after the 2-month study period. Mean height and weight were normal compared with healthy, age-matched Indian children. Lipoprotein cholesterol levels were significantly increased at baseline. TC significantly decreased by 116.33 mg/dl, LDL-C by 94.14 mg/dl, and triglycerides by 67.72 mg/dl in group II; in control group I, these values fell by 69.87, 61.13, and 22.62 mg/dl, respectively. The LDL-C:HDL-C ratio also decreased significantly, by 1.66 in group II and 1.13 in group I. TC:HDL-C decreased by 1.96 in group II and 1.19 in group I. HDL-C:LDL-C also improved significantly in both the groups. It can be concluded that spray-dried Spirulina capsules, rich in antioxidants, GLA, amino acids, and fatty acids, helped reduce the increased levels of lipids in patients with hyperlipidemic nephrotic syndrome.

Publication Types:

- Clinical Trial
- Randomized Controlled Trial
- Research Support, Non-U.S. Gov't

PMID: 12487756 [PubMed - indexed for MEDLINE]

Cardioprotective

**A randomized double-blind, placebo-controlled study to establish the effects of spirulina in elderly Koreans.**

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**AIMS:** This study was conducted to determine the antioxidant capacity, immunomodulatory and lipid-lowering effects of spirulina in healthy elderly subjects and to document the effectiveness of spirulina as a functional food for the elderly. **METHODS:** A randomized double-blind, placebo-controlled study was performed. The subjects were 78 individuals aged 60-87 years and were randomly assigned in a blinded fashion to receive either spirulina or placebo. The elderly were instructed to consume the spirulina or placebo at home, 8 g/day, for 16 consecutive weeks. **RESULTS:** In male subjects, a significant plasma cholesterol-lowering effect was observed after the spirulina intervention ( $p < 0.05$ ). Spirulina supplementation resulted in a significant rise in plasma interleukin (IL)-2 concentration, and a significant reduction in IL-6 concentration. A significant time-by-treatment interaction for total antioxidant status was observed between spirulina and placebo groups ( $p < 0.05$ ). In female subjects, significant increases in IL-2 level and superoxide dismutase activity were observed ( $p < 0.05$ ) after spirulina supplementation. There were significant reductions in total cholesterol in female subjects. **CONCLUSIONS:** The results demonstrate that spirulina has favorable effects on lipid profiles, immune variables, and antioxidant capacity in healthy, elderly male and female subjects and is suitable as a functional food. 2008 S. Karger AG, Basel.

Publication Types:

- Randomized Controlled Trial
- Research Support, Non-U.S. Gov't

PMID: 18714150 [PubMed - indexed for MEDLINE]

Yakugaku Zasshi. 2008 May;128(5):717-23.

**[Biological activities of exogenous polysaccharides via controlling endogenous proteoglycan metabolism in vascular endothelial cells]**

[Article in Japanese]

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Proteoglycan contains glycosaminoglycans, which are endogenous sulfated polysaccharides, in the molecule. The metabolism of proteoglycans regulates cell behavior and cellular events. It is possible that exogenous polysaccharide-related molecules exhibit their biological activities by two mechanisms. One is the interaction with cells and the other is the interaction with growth factors/cytokines that regulate proteoglycans. In this review, we describe sodium spirulan, a sulfated polysaccharide obtained from a hot-water extract of the blue-green alga *Spirulina platensis*, as an exogenous polysaccharide that stimulates the release of proteoglycans from vascular endothelial cells. Factors that regulate endothelial proteoglycan metabolism are also being described as possible target molecules of exogenous polysaccharides. Further research is required to obtain exogenous polysaccharide-related molecules that exhibit useful biological activities through controlling endothelial proteoglycan metabolism for protection against vascular lesions such as atherosclerosis.

Publication Types:

- English Abstract
- Review

PMID: 18451618 [PubMed - indexed for MEDLINE]

**Antihyperlipemic and antihypertensive effects of *Spirulina maxima* in an open sample of Mexican population: a preliminary report.**

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**BACKGROUND:** *Spirulina maxima* is a filamentous cyanobacterium used as food supplement because of its high nutrient contents. It has been experimentally proven, in vivo and in vitro that posses several pharmacological properties. The purpose of this study was to evaluate the effects of *Spirulina maxima* orally supplied (4.5 g/day, for 6 weeks) to a sample of 36 subjects (16 men and 20 women, with ages between 18-65 years) on serum lipids, glucose, aminotransferases and on blood pressure. The volunteers did not modify their dietary habits or lifestyle during the whole experimental period. From each subject, a sample of blood was drawn in fasting state of 12 hours to determi the plasma concentrations of glucose, triacylglycerols (TAG), total cholesterol (TC), cholesterol associated to high density lipoprotein (HDL-C) and aspartate aminotransferase (AST). Anthropometric measurements including systolic (SYST-P) and diastolic (DIAST-P) blood pressure, height, weight and Body Mass Index (BMI) were also recorded. **RESULTS:** Comparing initial and final data, the results showed that there were no significant changes in the values of glucose and AST, but significant differences in TAG, TC, and HDL-C, were observed: TAG 233.7 +/- 177.8 vs. 167.7 +/- 100.7 mg/dL ( $p < 0.001$ ), TC 181.7 +/- 37.5 vs. 163.5 +/- 34.4 mg/dL ( $p < 0.001$ ), C-HDL 43.5 +/- 14.4 vs. 50 +/- 18.8 mg/dL ( $p < 0.01$ ). The univariate analysis showed that the changes in the HDL-C and TC concentrations were dependent on TAG concentration ( $p = 0.247$  and  $p = 0.108$ , respectively); nevertheless the calculated values for cholesterol associated to low density lipoprotein (LDL-C) were significantly reduced by the *Spirulina maxima* treatment but independently of the TAG changes. In addition, significant differences were found comparing initial and final SYST-P and DIAST-P blood pressure in both male and female: SYST-P male 121 +/- 9 vs. 111 +/- 8 mm Hg ( $p < 0.01$ ), DIAST-P male 85 +/- 6.5 vs. 77 +/- 9 mm Hg ( $p < 0.01$ ); SYST-P female 120 +/- 9.5 vs. 109 +/- 11 mm Hg ( $p < 0.002$ ), DIAST-P female 85 +/- 11 vs. 79 +/- 7.5 mm Hg ( $p < 0.03$ ). **CONCLUSION:** The *Spirulina maxima* showed a hypolipemic effect, especially on the TAG and the LDL-C concentrations but indirectly on TC and HDL-C values. It also reduces systolic and diastolic blood pressure.

Publication Types:

- Clinical Trial
- Research Support, Non-U.S. Gov't

PMID: 18039384 [PubMed - indexed for MEDLINE]

Cardioprotective

## **Protective effect of Spirulina against doxorubicin-induced cardiotoxicity.**

[Khan M, Shobha JC, Mohan IK, Naidu MU, Sundaram C, Singh S, Kuppusamy P, Kutala VK.](#)

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The generation of reactive oxygen species and mitochondrial dysfunction has been implicated in doxorubicin (DOX)-induced cardiotoxicity. The aim of the present study was to determine whether Spirulina, a blue-green algae, could serve as a cardioprotective agent during DOX treatment in a mouse model. Mice were treated with DOX (4 mg/kg bw, intraperitoneally), weekly, for 4 weeks. Spirulina was administered orally for 3 days twice daily, then for 7 weeks along with the four equal injections of DOX. Cardiotoxicity was assessed, at 3 weeks after the end of the DOX-treatment period, by mortality, volume of ascites, liver congestion, oxidative stress and ultrastructural changes of heart tissue. The DOX-treated animals showed higher mortality (53%) and more ascites. Myocardial damage, as assessed by ultrastructural changes, showed loss of myofibrils, cytoplasmic vacuolization and mitochondrial swelling. Myocardial superoxide dismutase and glutathione peroxidase activities were decreased and lipid peroxidation was increased. Pretreatment with Spirulina significantly protected the mice from DOX-induced cardiotoxic effects as evidenced from lower mortality (26%), less ascites, lower levels of lipid peroxidation, normalization of antioxidant enzymes and ultrastructural studies showing minimal damage to the heart. In vitro cytotoxic studies using ovarian cancer cells demonstrated that Spirulina did not compromise the anti-tumor activity of doxorubicin. These results suggest that Spirulina has a protective effect against cardiotoxicity induced by DOX and it may, therefore, improve the therapeutic index of DOX. Copyright 2005 John Wiley & Sons, Ltd.

Publication Types:

- Research Support, N.I.H., Extramural

PMID: 16372368 [PubMed - indexed for MEDLINE]

Cardioprotective

**C-phycoyanin protects against ischemia-reperfusion injury of heart through involvement of p38 MAPK and ERK signaling.**

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We previously showed that C-phycoyanin (PC), an antioxidant biliprotein pigment of *Spirulina platensis* (a blue-green alga), effectively inhibited doxorubicin-induced oxidative stress and apoptosis in cardiomyocytes. Here we investigated the cardioprotective effect of PC against ischemia-reperfusion (I/R)-induced myocardial injury in an isolated perfused Langendorff heart model. Rat hearts were subjected to 30 min of global ischemia at 37 degrees C followed by 45 min of reperfusion. Hearts were perfused with PC (10 microM) or *Spirulina* preparation (SP, 50 mg/l) for 15 min before the onset of ischemia and throughout reperfusion. After 45 min of reperfusion, untreated (control) hearts showed a significant decrease in recovery of coronary flow (44%), left ventricular developed pressure (21%), and rate-pressure product (24%), an increase in release of lactate dehydrogenase and creatine kinase in coronary effluent, significant myocardial infarction (44% of risk area), and TdT-mediated dUTP nick end label-positive apoptotic cells compared with the preischemic state. PC or SP significantly enhanced recovery of heart function and decreased infarct size, attenuated lactate dehydrogenase and creatine kinase release, and suppressed I/R-induced free radical generation. PC reversed I/R-induced activation of p38 MAPK, Bax, and caspase-3, suppression of Bcl-2, and increase in TdT-mediated dUTP nick end label-positive apoptotic cells. However, I/R also induced activation of ERK1/2, which was enhanced by PC treatment. Overall, these results for the first time showed that PC attenuated I/R-induced cardiac dysfunction through its antioxidant and antiapoptotic actions and modulation of p38 MAPK and ERK1/2.

PMID: 16373583 [PubMed - indexed for MEDLINE]

**A novel protein C-phycoyanin plays a crucial role in the hypocholesterolemic action of Spirulina platensis concentrate in rats.**

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This study was designed to clarify the mechanisms of the hypocholesterolemic action of Spirulina platensis concentrate (SPC) and identify the novel hypocholesterolemic protein derived from SPC. We investigated the effects of casein or SPC on the solubility of cholesterol, taurocholate binding capacity in vitro, cholesterol absorption in Caco-2 cells, and cholesterol metabolism in rats for 10 d. We also evaluated the effects of SPC, C-phycoyanin (PHY), and PHY residue on cholesterol metabolism in rats fed a high-cholesterol diet for 5 d, and SPC or SPC-acetone extract for 10 d. SPC had a significantly greater bile acid-binding capacity than casein in vitro. Micellar cholesterol solubility and cholesterol uptake by Caco-2 cells was significantly lower in the presence of SPC compared with casein. Fecal excretion of cholesterol and bile acids was significantly greater in rats fed the SPC-supplemented diet than in those fed the casein control diet. Serum and liver cholesterol concentrations were significantly lower in rats fed SPC than in those fed casein. Thus, the hypocholesterolemic action of SPC may involve the inhibition of both jejunal cholesterol absorption and ileal bile acid reabsorption. Although no studies to date have found a hypocholesterolemic protein among the algal proteins, we report here the discovery of a hypocholesterolemic effect in the novel protein C-phycoyanin. This study provides the first direct evidence that PHY, a novel hypocholesterolemic protein derived from Spirulina platensis, can powerfully influence serum cholesterol concentrations and impart a stronger hypocholesterolemic activity than SPC in animals.

Publication Types:

- In Vitro

PMID: 16177207 [PubMed - indexed for MEDLINE]

**Phycobiliprotein C-phycoyanin from *Spirulina platensis* is powerfully responsible for reducing oxidative stress and NADPH oxidase expression induced by an atherogenic diet in hamsters.**

[Riss J](#), [Décordé K](#), [Sutra T](#), [Delage M](#), [Baccou JC](#), [Jouv N](#), [Brune JP](#), [Oréal H](#), [Cristol JP](#), [Rouanet JM](#).

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The effects of spirulina and its chromophore phycocyanin, both without bound Se or selenium-enriched, were studied on plasma cholesterol, early atherosclerosis, cardiac production of superoxide anions, and NAD(P)H oxidase expression in hamsters. Forty hamsters were divided into 5 groups of 8 and fed an atherogenic diet for 12 weeks. They received by gavage either 7.14 mL/(kg day) phycocyanin (PC), Se-rich phycocyanin (SePC), spirulina (SP) or Se-rich spirulina (SeSP) in water, or water as control. SeSP and SePC supplied 0.4 microg of Se per 100 g body weight. Plasma cholesterol and non-HDL cholesterol concentrations were lower in group consuming SePC. HDL-cholesterol was never affected. SePC significantly increased plasma antioxidant capacity by 42% compared with controls. A sparing effect in liver glutathione peroxidase (87% on average) and superoxide dismutase (56% on average) activity was observed for all the groups compared to controls. Aortic fatty streak area was significantly reduced in the experimental groups, especially by PC (82%) and SePC (85%). Cardiac production of superoxide anion significantly decreased by approximately 46-76% in the four experimental groups and especially in SePC group (76%). The expression of p22phox subunit of NAD(P)H oxidase decreased by 34% after consumption of SePC. The results indicate that chronic consumption of Se-rich spirulina phycocyanin powerfully prevents the development of atherosclerosis. The underlying mechanism is related mainly to inhibiting pro-oxidant factors and at a lesser extent improving the serum lipid profile.

PMID: 17696484 [PubMed - indexed for MEDLINE]



J Cardiovasc Pharmacol. 2006 Jan;47(1):9-20.

## **C-phycoyanin ameliorates doxorubicin-induced oxidative stress and apoptosis in adult rat cardiomyocytes.**

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Doxorubicin (DOX), a potent antineoplastic agent, poses limitations for its therapeutic use due to the associated risk of developing cardiomyopathy and congestive heart failure. The cardiotoxicity of doxorubicin is associated with oxidative stress and apoptosis. We have recently shown that Spirulina, a blue-green alga with potent antioxidant properties, offered significant protection against doxorubicin-induced cardiotoxicity in mice. The aim of the present study was to establish the possible protective role of C-phycoyanin, one of the active ingredients of Spirulina, against doxorubicin-induced oxidative stress and apoptosis. The study was carried out using cardiomyocytes isolated from adult rat hearts. Doxorubicin significantly enhanced the formation of reactive oxygen species (ROS) in cells as measured by the 2',7'-dichlorodihydrofluorescein diacetate and dihydroethidium fluorescence. The doxorubicin-induced reactive oxygen species formation was significantly attenuated in cells pretreated with C-phycoyanin. It was further observed that the doxorubicin-induced DNA fragmentation and apoptosis, as assayed by TUNEL assay and flow cytometry coupled with BrdU-FITC/propidium iodide staining, were markedly attenuated by C-phycoyanin. C-phycoyanin also significantly attenuated the doxorubicin-induced increase in the expression of Bax protein, release of cytochrome c, and increase in the activity of caspase-3 in cells. In summary, C-phycoyanin ameliorated doxorubicin-induced oxidative stress and apoptosis in cardiomyocytes. This study further supports the crucial role of the antioxidant nature of C-phycoyanin in its cardioprotection against doxorubicin-induced oxidative stress and apoptosis.

Publication Types:

- Research Support, N.I.H., Extramural

PMID: 16424780 [PubMed - indexed for MEDLINE]

Cardioprotective

Vopr Pitan. 2003;72(6):28-31.

**[Use of blue-green micro-seaweed *Spirulina platensis* for the correction of lipid and hemostatic disturbances in patients with ischemic heart disease]**

[Article in Russian]

[Ionov VA, Basova MM.](#)

Changing in lipid spectrum, immunological state and coagulation in the 68 patients with IHD and atherogenic dyslipidemia who were taking biomass microalga *Spirulina platensis* was investigated. Modification of traditional plan of therapy of IHD when adding microalga *Spirulina p.* influences correcting effect to cascade procoagulation and immunopathological reactions, characteristic of atherosclerosis process.

Publication Types:

- Clinical Trial
- English Abstract

PMID: 14870586 [PubMed - indexed for MEDLINE]

Space Med Med Eng (Beijing). 2003 Jun;16(3):184-6.

**[Effects of spirulina on serum lipids, erythrocyte membrane fluidity and vascular endothelial cells in tail-suspended rats]**

[Article in Chinese]

[Huang JM](#), [Bai SM](#), [Hu ZX](#), [Yang CL](#), [Zhu DB](#), [Shi JP](#).

Objective: To study the changes of erythrocyte membrane fluidity, serum lipid and vascular endothelial cell caused by simulated weightlessness in rats and the beneficial effect of spirulina. Method: Thirty male SD rats were divided into 3 groups: free control group (group A) and two simulated weightlessness groups (groups B, C). Rats in group A and B were fed with normal forage, and the rats in group C were fed with normal forage supplemented with 5% (W/W) spirulina. Water was taken ad libitum. Result: Levels of serum CHO, HDL, TG, HDL-C/CHO and erythrocyte membrane fluidity decreased significantly, and number of vascular endothelial cells in plasma increased markedly in group B as compared with those in group A; The ratio of LDL-C/HDL-C, and atherosclerosis index (AI) decreased, number of vascular endothelial cells significantly lowered; level of CHO, HDL-C and value of the IDmax of plasma as well as erythrocyte membrane fluidity remarkably increased in group C compared with those in group B. Conclusion: Spirulina can improve the physiological conditions of erythrocyte membrane fluidity, serum lipid and vascular endothelial cell caused by simulated weightlessness in rats.

Publication Types:

- English Abstract

PMID: 12934612 [PubMed - indexed for MEDLINE]

**Fatty acid composition of Chlorella and Spirulina microalgae species.**

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Two New Age foods which contain high concentrations of whole food nutrients are the single-celled microalgae Chlorella and Spirulina. They are accepted as functional foods, which are defined as products derived from natural sources, whose consumption is likely to benefit human health and enhance performance. These foods are used as a supplement/ingredient or as a complete food to enhance the performance and state of the human body, or improve a specific bodily function. Functional foods are used mainly as products to nourish the human body after physical exertion or as a preventive measure against ailments. We determined the fatty acid compositions, particularly polyunsaturated fatty acid compositions, of Chlorella and Spirulina by capillary column-gas chromatography. The data obtained show that Spirulina contains unusually high levels of gamma-linolenic acid, an essential polyunsaturated fatty acid.

Publication Types:

- Comparative Study

PMID: 11767135 [PubMed - indexed for MEDLINE]

Nutr Sci Vitaminol (Tokyo). 1990 Apr;36(2):165-71.

**Effects of *Spirulina platensis* on plasma lipoprotein lipase activity in fructose-induced hyperlipidemic rats.**

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The effects of *Spirulina platensis* on lipoprotein lipase activity and hepatic triglyceride lipase activity in post-heparin plasma were studied in fructose-induced hyperlipidemic rats. Male Wistar rats aged 3 weeks old (body weight, 54 g) were fed on the high-fructose diet (68%) or the high-fructose diets containing *Spirulina* at the level of 5, 10, and 15%, respectively, for 4 weeks. The dietary hyperlipidemia caused by the high-fructose diet was improved by *Spirulina* feeding, accompanied by a significant increase in the lipoprotein lipase activity in post-heparin plasma.

PMID: 2117648 [PubMed - indexed for MEDLINE]

J Ethnopharmacol. 2001 Apr;75(1):37-44.

**Effects of the ethanolic extract of *Spirulina maxima* on endothelium dependent vasomotor responses of rat aortic rings.**

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Dietary *Spirulina* decreases, endothelium-dependently, the responses to vasoconstrictor agonists and increases the endothelium-dependent, agonist-induced, vasodilator responses of rat aorta rings. The aim of this study was to analyze, in vitro, the effects of a raw ethanolic extract of *Spirulina maxima* on the vasomotor responses of rat aortic rings to phenylephrine and to carbachol. On rings with endothelium, the extract produced the following effects: (a) a concentration-dependent (60-1000 microg/ml) decrease of the contractile response to phenylephrine; (b) a rightward shift and a decrease in maximal developed tension, of the concentration--response curve to phenylephrine; (c) a concentration dependent relaxation of phenylephrine-precontracted rings. These effects were blocked by L-NAME, and not modified by indomethacin. The extract had no effect on the concentration-response curve to carbachol of rings with endothelium. On endothelium-denuded rings the extract caused a significant rightward shift of the concentration response curve to phenylephrine without any effect on maximal tension development. In the presence of the extract, indomethacin induced a marked decrease in the maximal phenylephrine-induced tension of endothelium-denuded rings. These results suggest that the extract increases the basal synthesis/release of NO by the endothelium and, also, the synthesis/release of a cyclooxygenase-dependent vasoconstricting prostanoid by vascular smooth muscle cells.

Publication Types:

- In Vitro
- Research Support, Non-U.S. Gov't

PMID: 11282441 [PubMed - indexed for MEDLINE]

Cardioprotective

**Effects of dietary *Spirulina maxima* on endothelium dependent vasomotor responses of rat aortic rings.**

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The aim of this study was to evaluate the effects of *Spirulina maxima* on vasomotor responses of aorta rings from male Wistar rats fed on a purified diet. For this purpose, the animals (weighing 200-240 g) were allocated randomly in two groups. One receiving purified control diet (A) and the other receiving purified diet containing 5% *Spirulina* (B). Purified diets were according to American Institute of Nutrition guidelines and adjusted to *Spirulina* protein content. All animals were fed (20 g/day/rat) during two weeks, receiving water ad libitum and 12 h. light-dark cycles. *Spirulina maxima* effects were evaluated by concentration-response (CR) curves of aorta rings with or without endothelium to phenylephrine (PE), both in presence and absence of indomethacin (Indom) or indomethacin plus L-NAME (Indom. + L-NAME), and to carbachol (CCh). Aorta rings with endothelium from group B showed, relative to corresponding rings from group A: 1) a significant decrease in the maximal tension developed in response to PE. 2) this decrease was reverted by Indom. 3) Indom. + L-NAME induced an additional increase in the contractile responses to PE. 4) a significant shift to the left of the CR curve to CCh. No significant differences were observed in the tension developed in response to PE in rings without endothelium from either group. These results suggest that *Spirulina maxima* may decrease vascular tone by increasing the synthesis and release of both a vasodilating cyclooxygenase-dependent product of arachidonic acid and nitric oxide, as well as by decreasing the synthesis and release of a vasoconstricting eicosanoid from the endothelial cells.

Publication Types:

- Research Support, Non-U.S. Gov't

PMID: 9328235 [PubMed - indexed for MEDLINE]

**Ethanollic extract of *Spirulina maxima* alters the vasomotor reactivity of aortic rings from obese rats.**

[Mascher D](#), [Paredes-Carbajal MC](#), [Torres-Durán PV](#), [Zamora-González J](#), [Díaz-Zagova JC](#), [Juárez-Oropeza MA](#).

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**BACKGROUND:** Aortic rings with endothelium excised from fructose-fed obese rats develop more tension in response to phenylephrine and relax less in response to carbachol than corresponding rings from lean rats. This altered vascular reactivity is prevented when *Spirulina maxima* is added to the fructose-rich diet. In the present study the effects of a raw ethanollic extract of *Spirulina maxima* on the vasomotor responses of aorta rings from sucrose-fed obese hypertensive rats were analyzed. **METHODS:** The experiments were performed on aorta rings from sucrose-fed obese male rats. For each experiment, a pair of rings from the same aorta (one with intact endothelium, the other without a functional endothelium) was used. In this study we analyzed, in vitro, the effects of the ethanollic extract of *Spirulina maxima* on the reactivity of the aortic rings to phenylephrine and to carbachol. **RESULTS:** On rings with endothelium, the extract produced the following effects: a) a concentration-dependent (0.06-1.0 mg/mL) decrease of the contractile response to phenylephrine; b) a rightward shift and a decrease in maximal developed tension, of the concentration-response curve to phenylephrine; c) a concentration-dependent relaxation of phenylephrine-precontracted rings. These effects persisted in the presence of indomethacin but were prevented by L-NAME. The extract had no effect on the concentration-response curve of phenylephrine-precontracted rings to carbachol. On endothelium-denuded rings the extract caused a significant rightward shift of the concentration response curve to phenylephrine without any effect on maximal tension development. **CONCLUSIONS:** These results suggest that, in rings from obese rats, the extract, in addition to increasing the synthesis/release of NO, also inhibits the synthesis/release of a cyclooxygenase-dependent vasoconstrictor metabolite of arachidonic acid, which is increased in obesity.

Publication Types:

- In Vitro
- Research Support, Non-U.S. Gov't

PMID: 16314186 [PubMed - indexed for MEDLINE]



**Inhibition of cultured bovine aortic endothelial cell proliferation by sodium spirulan, a new sulfated polysaccharide isolated from *Spirulina platensis*.**

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Sodium spirulan (Na-SP) is a sulfated polysaccharide isolated from the blue-green alga *Spirulina platensis*, which consists of two types of disaccharide repeating units, O-hexuronosyl-rhamnose (aldobiuronic acid) and O-rhamnosyl-3-O-methylrhamnose (acofriose) with sulfate groups, other minor saccharides and sodium ion. Vascular endothelial cells are present on the inner surface of blood vessels in a monolayer and have anticoagulant properties. To address the question whether Na-SP influences the maintenance of endothelial cell monolayers, we investigated the proliferation of cultured bovine aortic endothelial cells treated with Na-SP. It was found that Na-SP has an inhibitory activity on endothelial cell proliferation accompanied with suppression of whole protein synthesis but without non-specific cell damage. The inhibitory activity of Na-SP was the strongest when compared to that of heparan sulfate, heparin, dextran sulfate, dermatan sulfate, chondroitin sulfate A/C and hyaluronan. Furthermore, it was shown that the inhibitory activity of Na-SP disappeared by either desulfation or depolymerization. The present data suggest that Na-SP is a unique sulfated polysaccharide that strongly inhibits vascular endothelial cell proliferation, and the inhibitory activity requires polymerization of sulfated O-rhamnosyl-acofriose repeating units.

Publication Types:

- Comparative Study
- Research Support, Non-U.S. Gov't

PMID: 12094292 [PubMed - indexed for MEDLINE]

**Sodium spirulan as a potent inhibitor of arterial smooth muscle cell proliferation in vitro.**

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Sodium spirulan (Na-SP) is a sulfated polysaccharide with M(r) approximately 220,000 isolated from the blue-green alga *Spirulina platensis*. The polysaccharide consists of two types of disaccharide repeating units, O-hexuronosyl-rhamnose (aldobiuronic acid) and O-rhamnosyl-3-O-methylrhamnose (acofriose) with sulfate groups, other minor saccharides and sodium ion. Since vascular smooth muscle cell proliferation is a crucial event in the progression of atherosclerosis, we investigated the effect of Na-SP on the proliferation of bovine arterial smooth muscle cells in culture. It was found that Na-SP markedly inhibits the proliferation without nonspecific cell damage. Either replacement of sodium ion with calcium ion or depolymerization of the Na-SP molecule to M(r) approximately 14,700 maintained the inhibitory activity, however, removal of sodium ion or desulfation markedly reduced the activity. Heparin and heparan sulfate also inhibited vascular smooth muscle cell growth but their effect was weaker than that of Na-SP; dextran sulfate, chondroitin sulfate, dermatan sulfate and hyaluronan failed to inhibit the cell growth. The present data suggest that Na-SP is a potent inhibitor of arterial smooth muscle cell proliferation, and the inhibitory effect requires a certain minimum sequence of polysaccharide structure whose molecular conformation is maintained by sodium ion bound to sulfate group.

Publication Types:

- Research Support, Non-U.S. Gov't

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**[Isolation of pancreatic lipase activity-inhibitory component of spirulina platensis and it reduce postprandial triacylglycerolemia]**

[Article in Japanese]

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In the process of investigating the hypolipidemic effects of *Spirulina platensis*, we found that the aqueous extract of *S. platensis* may inhibit the intestinal absorption of dietary fat by inhibiting pancreatic lipase activity. The aqueous extract of *S. platensis* (500 m/kg) reduced the elevation of rat plasma triacylglycerol levels after oral administration of the lipid emulsion 2 h after administration. To clarify the hypolipidemic effects of *S. platensis*, the active component was isolated and designated 1'-O-(palmitonyl)-2'-O-(caprylonyl) glyceryl-beta-alpha-D-galactopyranoside (glycolipid H-b2). Glycolipid H-b2 was found to inhibit pancreatic lipase activity in a dose-dependent manner. The fractions containing glycolipid H-b2 (250 mg/kg) reduced the elevation of rat plasma triacylglycerol levels after oral administration of the lipid emulsion 2 h after administration. Furthermore, we examined the effects of phycocyanin isolated from *S. platensis* on pancreatic lipase activity. Phycocyanin inhibited the pancreatic lipase activity in a dose-dependent manner. These results suggest that the inhibitory effects of *S. platensis* on postprandial triacylglycerolemia may be due in part to the inhibition of pancreatic lipase activity by glycolipid H-b2 and phycocyanin.

Publication Types:

- English Abstract

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**Effects of dietary Spirulina on vascular reactivity.**

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There are several reports suggesting that Spirulina (Arthrospira) may have a beneficial effect in the prevention of cardiovascular diseases. Here we review the results of studies on the effects of dietary Spirulina on the vasomotor reactivity of aortic rings excised from either lean or obese Wistar rats. We also review preliminary results on the effects of Spirulina intake on plasma lipids and blood pressure in humans. The results of the former studies strongly suggest that Spirulina induces a tone-related increase in the synthesis/release of nitric oxide by the endothelium as well as an increase in the synthesis/release of a vasodilating cyclooxygenase-dependent metabolite of arachidonic acid and/or a decrease in the synthesis/release of a vasoconstricting eicosanoid by the endothelium. In humans, Spirulina maxima intake decreases blood pressure and plasma lipid concentrations, especially triacylglycerols and low-density lipoprotein-cholesterol, and indirectly modifies the total cholesterol and high-density lipoprotein-cholesterol values.

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## **Medicinal agents in the metabolic syndrome.**

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The metabolic syndrome (MS) has become a worldwide health problem. It is difficult for patients to follow a diet/exercise regime that would improve their symptoms, therefore the investigation of agents that may deal with its more serious aspects is an important medical field for research. The cardiovascular consequences associated with the syndrome and some of the therapeutic approaches are discussed. The different agents can be divided into several groups: Inorganic/ organic: Zinc complexes with garlic components as insulin-mimetics; Selenium as antioxidant; Copper, Zinc and Manganese as microcomponents of antioxidant enzymes. Organic: Natural or Synthetic: Glycine is effective in lowering blood pressure, TBARS, intra-abdominal fat tissue and triglycerides in sucrose-fed rats. Pharmaceutical products: Fibrates, Lipid-lowering drugs. Antidiabetics. Anti-gout agents. On the other hand there are natural products such as those of animal origin: Sex hormones (also synthetic) used in the problems of menopause and hypoandrogenism frequently found in the MS, antioxidant Omega-3-oils (fish oils) or Vegetal: for example *Digitalis purpurea*, century-old cardiovascular medication as well as *Magnolia officinalis*; *Spirulina maxima* with beneficial effects as antioxidant and lipid-lowering agent, among others. Prickly Pear Cacti. (*Opuntia Ficus- Indica Cochlospermum vitifolium* (Willd.) Spreng) whose many properties against diabetes and hypercholesterolemia have been empirically known for many years. Perezona (from *Perezia* plants, a.k.a. *Peonia*) described as an antiplatelet aggregating agent. The mixed elements in the Mediterranean diet: Fish, salads (peppers, tomatoes), olive oil, garlic, red wine which combines fish oils, garlic and avocado as well as antioxidants from the rest of its components.

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- Review

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