### **Hepatoprotective**

Med Hypotheses. 2009 Mar;72(3):330-2. Epub 2008 Sep 11.

#### Genistein and phycocyanobilin may prevent hepatic fibrosis by suppressing proliferation and activation of hepatic stellate cells.

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Hepatic fibrosis reflects hepatotoxin-mediated activation of hepatic stellate cells, resulting in their proliferation and transformation to myofibroblasts that secrete collagen. This activation is suppressed by estrogen, an effect which explains the decreased risk for hepatic fibrosis enjoyed by premenopausal women and by postmenopausal women receiving hormone replacement therapy. Since stellate cells have been found to express the beta but not the alpha isoform of the estrogen receptor, it can be predicted that nutritional intakes of the soy isoflavone genistein - a selective agonist for ERbeta in the low nanomolar plasma concentrations achievable with these intakes - have potential for suppressing hepatic fibrosis, in both men and women. The antiproliferative impact of estrogen on stellate cells is mediated at least in part by suppression of NADPH oxidase activity; oxidant production by this enzyme complex plays a crucial role in stellate cell activation. Alternatively, it may be feasible to inhibit NADPH oxidase with phycocyanobilin (PCB), a biliverdin homolog found in spirulina that has recently been shown to inhibit the NADPH oxidase activity of human cell cultures in low micromolar concentrations. Joint administration of soy isoflavones and PCB in appropriate doses might have considerable potential for prevention of hepatic fibrosis in atrisk subjects.

PMID: 18789597 [PubMed - indexed for MEDLINE]

Lik Sprava. 2000 Sep;(6):89-93.

## [Clinical and experimental study of spirulina efficacy in chronic diffuse liver diseases]

[Article in Ukrainian]

#### <u>Gorban' EM, Orynchak MA, Virstiuk NG, Kuprash LP, Panteleĭmonova</u> <u>TM, Sharabura LB</u>.

The results of examination of 60 patients presenting with chronic diffuse disorders of the liver and seventy experimental animals with toxic affection of the liver, having been administered spirulina treatments, suggest clinical-andlaboratory effectiveness of this drug. The hepatoprotective properties of spirulina are referrable to its antiinflammatory, antioxidant, membrane-stabilizing, and immunocorrecting actions. In this way the employment of spirulina is believed to be pathogenetically validated in chronic diffuse liver conditions, permitting stabilizing the process and preventing the transformation of chronic hepatitis into hepatocirrhosis.

Publication Types:

• English Abstract

PMID: 11455931 [PubMed - indexed for MEDLINE]

Biochem Biophys Res Commun. 1998 Aug 19;249(2):428-31.

# Hepatoprotective effect of C-phycocyanin: protection for carbon tetrachloride and R-(+)-pulegone-mediated hepatotoxicty in rats.

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Effect of C-phycocyanin (from Spirulina platensis) pretreatment on carbontetrachloride and R-(+)-pulegone-induced hepatotoxicity in rats was studied. Intraperitoneal (i.p.) administration (200 mg/kg) of a single dose of phycocyanin to rats, one or three hours prior to R-(+)-pulegone (250 mg/kg) or carbontetrachloride (0.6 ml/kg) challenge, significantly reduced the hepatotoxicity caused by these chemicals. For instance, serum glutamate pyruvate transaminase (SGPT) activity was almost equal to control values. The losses of microsomal cytochrome P450, glucose-6-phosphatase and aminopyrine-N-demethylase were significantly reduced, suggesting that phycocyanin provides protection to liver enzymes. It was noticed that the level of menthofuran, the proximate toxin of R-(+)-pulegone was nearly 70% more in the urine samples collected from rats treated with R-(+)-pulegone. The possible mechanism involved in the hepatoprotection is discussed. Copyright 1998 Academic Press.

Publication Types:

• Research Support, Non-U.S. Gov't

PMID: 9712713 [PubMed - indexed for MEDLINE]

Hepatol Res. 2008 May;38(5):511-20. Epub 2007 Nov 21.

#### C-Phycocyanin ameliorates 2-acetylaminofluorene induced oxidative stress and MDR1 expression in the liver of albino mice.

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Aim: To study the effect of C-Phycocyanin (C-PC), a biliprotein isolated from Spirulina platensis, on 2-acetylaminofluorene (2-AAF) induced oxidative stress and MDR1 expression in the liver of albino mice. Methods: In the present study, albino mice aged 40-60 days were used. The mice were randomly assigned to four groups of six animals each. The first group was treated with the vehicle (absolute alcohol), the second group was treated with C-PC (50 mg/kg body weight), the third group was treated with 2-AAF (25 mg/kg body weight) and the fourth group was treated with C-PC (50 mg/kg body weight) and 2-AAF, daily for 3 days. The mice were sacrificed and the tissues were collected and stored for histology and biochemical studies. Results: 2-AAF induced liver tissue damage in albino mice. 2-AAF treatment resulted in upregulation of MDR1 expression and enhanced the generation of reactive oxygen species (ROS). It also induced phosphorylation of Akt and nuclear translocation of NF-kappaB. Co-administration of C-PC and 2-AAF inhibited the expression of MDR1 by preventing ROS generation, Akt phosphorylation and NF-kappaB nuclear translocation. Conclusion: 2-AAFinduced oxidative stress is reduced by C-PC treatment. C-PC inhibited the 2-AAF induced expression of MDR1 by interfering at the level of ROS generation, Akt phosphorylation and NF-kappaB translocation. This study reveals the usefulness of C-PC in preventing oxidative stress and downregulation of MDR1 induced by xenobiotics like 2-AAF.

PMID: 18034828 [PubMed - in process]

J Ethnopharmacol. 1999 Feb;64(2):141-7.

#### Studies on the preventive effect of Spirulina maxima on fatty liver development induced by carbon tetrachloride, in the rat.

### <u>Torres-Durán PV</u>, <u>Miranda-Zamora R</u>, <u>Paredes-Carbajal MC</u>, <u>Mascher D</u>, <u>Blé-Castillo J</u>, <u>Díaz-Zagoya JC</u>, <u>Juárez-Oropeza MA</u>.

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The aim of the present work was to assess if the feeding of either the oil extract of Spirulina maxima or of its defatted fraction would prevent fatty liver development, induced in rats by a single intraperitoneal dose of carbon tetrachloride (CCl4). Liver and serum lipids were evaluated 4 days after treatment with this agent. Concentration of liver lipids did not differ in rats fed on a purified diet either without or with one of the fractions of Spirulina, except for total cholesterol, which showed a slight increase in the group receiving the oil extract of Spirulina. However, after CCl4 treatment, liver total lipids and triacylglycerols were significantly lower in rats fed on a diet containing any fraction of Spirulina (defatted or the oil fraction) than in rats without Spirulina in their diet. Furthermore, the increased liver cholesterol values, induced by CCl4 treatment, were not observed in rats receiving Spirulina. In addition, rats receiving whole Spirulina in their diet and treated only with the vehicle showed an increase in the percentage of HDL values. The changes in VLDL and LDL induced by CCl4 treatment were not observed in the whole Spirulina group. Furthermore, after CCl4 treatment the values of the liver microsomal thiobarbituric acid-reactive substances were lower in the whole Spirulina group than in the control group. These results support the potential hepatoprotective role of Spirulina.

**Publication Types:** 

• Research Support, Non-U.S. Gov't

PMID: 10197749 [PubMed - indexed for MEDLINE]

Biochem Mol Biol Int. 1998 Apr;44(4):787-93.

### Spirulina maxima prevents induction of fatty liver by carbon tetrachloride in the rat.

<u>Torres-Durán PV, Miranda-Zamora R, Paredes-Carbajal MC, Mascher D, Díaz-Zagova JC, Juárez-Oropeza MA</u>.

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The aim of the present work was to assess the capacity of Spirulina maxima to prevent fatty liver development induced in rats by an intraperitoneal single dose (1 ml/kg) of carbon tetrachloride. Liver and serum lipids were quantified two or four days after treatment with this agent. Liver lipid concentration did not differ in rats fed on a purified diet with or without Spirulina. However, after carbon tetrachloride treatment, liver triacylglycerols were significantly lower in rats fed on a diet with Spirulina 5% than in rats without Spirulina in their diet (P < 0.05). Furthermore, the increased liver cholesterol values, induced by carbon tetrachloride treatment, were not observed in rats that received Spirulina. These results support the potential hepatoprotective role of Spirulina.

Publication Types:

• Research Support, Non-U.S. Gov't

PMID: 9584992 [PubMed - indexed for MEDLINE]

Life Sci. 2002 Apr 19;70(22):2665-73.

Arthrospira maxima prevents the acute fatty liver induced by the administration of simvastatin, ethanol and a hypercholesterolemic diet to mice.

<u>Blé-Castillo JL</u>, <u>Rodríguez-Hernández A</u>, <u>Miranda-Zamora R</u>, <u>Juárez-Oropeza MA</u>, <u>Díaz-Zagoya JC</u>.

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An evident fatty liver, corroborated morphologically and chemically, was produced in CD-1 mice after five daily doses of simvastatin 75 mg/Kg body weight, a hypercholesterolemic diet and 20 percent ethanol in the drinking water. After treating the animals, they presented serum triacylglycerols levels five times higher than the control mice, total lipids, cholesterol and triacylglycerols in the liver were 2, 2 and 1.5 times higher, respectively, than in control animals. When Arthrospira maxima was given with diet two weeks prior the onset of fatty liver induction, there was a decrement of liver total lipids (40%), liver triacylglycerols (50%) and serum triacylglycerols (50%) compared to the animals with the same treatment but without Arthrospira maxima. In addition to the mentioned protective effect, the administration of this algae, produced a significant increase (45%) in serum high density lipoproteins. The mechanism for this protective effect was not established in these experiments.

Publication Types:

• Research Support, Non-U.S. Gov't

PMID: 12269393 [PubMed - indexed for MEDLINE]

Life Sci. 1993;53(1):57-61.

## Preventive effect of Spirulina maxima on the fatty liver induced by a fructose-rich diet in the rat, a preliminary report.

<u>González de Rivera C</u>, <u>Miranda-Zamora R</u>, <u>Díaz-Zagoya JC</u>, <u>Juárez-</u> <u>Oropeza MA</u>.

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Cyanobacteria Spirulina maxima from Texcoco Lake in Mexico was administered as a 5% component of a purified diet, to Wistar rats together with a high percentage of fructose (60%) and its effect on several lipid fractions of plasma and liver was studied and compared to those of rats fed purified diets containing 60% of glucose or 60% of fructose. A preventive effect of Spirulina maxima on the fructose-induced increase of the liver triglycerides level was observed together with an elevation of the phospholipid concentration in this tissue. On the other hand Spirulina maxima produced a plasma cholesterol level even lower than that observed in the control group.

Publication Types:

• Research Support, Non-U.S. Gov't

PMID: 8515682 [PubMed - indexed for MEDLINE]

Wei Sheng Yan Jiu. 2007 Jan;36(1):34-6.

### [Antagonistic effects of Se-rich Spirulina platensis on rat liver fibrosis]

[Article in Chinese]

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**OBJECTIVE:** Antagonistic effects of supplement of Se-rich Spirulina platensis (Se-SP) on hepatocirrhosis were investigated with the rat model of liver fibrosis induced by intraperitoneal injection 3% thioacetamide (TAA). METHODS: Parameters of routine liver function, content of malondialdehyde (MDA) and activities of glutathione peroxidase (GPx) and superoxide dismutase (SOD) in rat serum were determined by colorimetry. Content of selenium (Se) was measured by DAN fluorometry method and hyaluronic acid (HA) was detected by radioimmunoassay. Liver fibrosis was diagnosed by HE staining and relative contents of collagen (RCC) were estimated by Masson's trichrome staining. RESULTS: Parameters of liver function in Se-SP group were most recovered in all protective groups. Compared with the model groups, contents of MDA and HA were lower, whereas activities of GPx and SOD were higher (P < 0.05) in rats serum of Se-SP group. The RCC in rats liver of Se-SP group were lower than those of the model groups, where the liver fibrosis were identified dominantly to degree I according to pathological diagnosis. Moreover, Se content in rats serum had positive correlation (r = 0.645) with activity of GPx while a negative correlation (r =0.675) with MDA level. CONCLUSION: The results indicated that Se-SP have detectable antagonistic effects to liver fibrosis, and suggested that enhancement of antioxidation level and liver reserve function might be associated with these effects.

Publication Types:

• English Abstract

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