

## **Anti-Inflammatory**

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### **Clinical potential of Spirulina as a source of phycocyanobilin.**

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Recent research reveals that free bilirubin functions physiologically as a potent inhibitor of NADPH oxidase activity. The chromophore phycocyanobilin (PCB), found in blue-green algae and cyanobacteria such as Spirulina, also has been found to be a potent inhibitor of this enzyme complex, likely because in mammalian cells it is rapidly reduced to phycocyanorubin, a close homolog of bilirubin. In light of the protean roles of NADPH oxidase activation in pathology, it thus appears likely that PCB supplementation may have versatile potential in prevention and therapy -- particularly in light of rodent studies demonstrating that orally administered Spirulina or phycocyanin (the Spirulina holoprotein that contains PCB) can exert a wide range of anti-inflammatory effects. Until PCB-enriched Spirulina extracts or synthetically produced PCB are commercially available, the most feasible and least expensive way to administer PCB is by ingestion of whole Spirulina. A heaping tablespoon (about 15 g) of Spirulina can be expected to provide about 100 mg of PCB. By extrapolating from rodent studies, it can be concluded that an intake of 2 heaping tablespoons daily would be likely to have important antioxidant activity in humans -- assuming that humans and rodents digest and absorb Spirulina-bound PCB in a comparable manner. An intake of this magnitude can be clinically feasible if Spirulina is incorporated into "smoothies" featuring such ingredients as soy milk, fruit juices, and whole fruits. Such a regimen should be evaluated in clinical syndromes characterized and in part mediated by NADPH oxidase overactivity in affected tissues.

Publication Types:

- Review

PMID: 18158824 [PubMed - indexed for MEDLINE]

**Antiinflammatory and antihyperalgesic activity of C-phycoyanin.**

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**BACKGROUND:** C-phycoyanin (C-PC), a biliprotein found in blue green algae, such as *Spirulina platensis*, is often used as a dietary nutritional supplement due to its various therapeutic values. In addition, the antiinflammatory activity of C-PC partly through inhibition of proinflammatory cytokine formation, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) expression has been demonstrated in many in vitro and in vivo studies. However, whether C-PC also has antihyperalgesic activity in inflammatory nociception has not been investigated. **METHODS:** Using a carrageenan-induced thermal hyperalgesia model, we evaluated the effect of C-PC on nociception by measuring paw withdrawal latency. To clarify the mechanisms involved, the expression of iNOS and COX-2 and the formation of nitrate and tumor necrosis factor-alpha (TNF-alpha) in the rat paw were determined. **RESULTS:** Pre- or posttreatment with C-PC (30 or 50 mg/kg, IP) significantly attenuated carrageenan-induced inflammatory nociception and the induction of iNOS and COX-2 at the late phase, (4 h) accompanied by an inhibition of the formation of TNF-alpha, prostaglandin E(2), nitrate and myeloperoxidase activity. **CONCLUSIONS:** Based on these results, it is suggested that the inhibition of NO and prostaglandin E(2) overproduction through suppressing iNOS and COX-2 induction and attenuation of TNF-alpha formation and neutrophil infiltration into inflammatory sites by C-PC may contribute, at least in part, to its antihyperalgesic activity.

Publication Types:

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

PMID: 19299804 [PubMed - indexed for MEDLINE]

**Selective inhibition of cyclooxygenase-2 by C-phycoyanin, a biliprotein from *Spirulina platensis*.**

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We report data from two related assay systems (isolated enzyme assays and whole blood assays) that C-phycoyanin a biliprotein from *Spirulina platensis* is a selective inhibitor of cyclooxygenase-2 (COX-2) with a very low IC(50) COX-2/IC(50) COX-1 ratio (0.04). The extent of inhibition depends on the period of preincubation of phycoyanin with COX-2, but without any effect on the period of preincubation with COX-1. The IC(50) value obtained for the inhibition of COX-2 by phycoyanin is much lower (180 nM) as compared to those of celecoxib (255 nM) and rofecoxib (401 nM), the well-known selective COX-2 inhibitors. In the human whole blood assay, phycoyanin very efficiently inhibited COX-2 with an IC(50) value of 80 nM. Reduced phycoyanin and phycoyanobilin, the chromophore of phycoyanin are poor inhibitors of COX-2 without COX-2 selectivity. This suggests that apoprotein in phycoyanin plays a key role in the selective inhibition of COX-2. The present study points out that the hepatoprotective, anti-inflammatory, and anti-arthritic properties of phycoyanin reported in the literature may be due, in part, to its selective COX-2 inhibitory property, although its ability to efficiently scavenge free radicals and effectively inhibit lipid peroxidation may also be involved. Copyright 2000 Academic Press.

Publication Types:

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

PMID: 11062000 [PubMed - indexed for MEDLINE]

**Effects of phycocyanin extract on prostaglandin E2 levels in mouse ear inflammation test.**

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Recently it was demonstrated that phycocyanin, a biliprotein isolated from microalgae *Spirulina*, exerts anti-inflammatory activity in several animal models of inflammation. In this report, the effects of phycocyanin on prostaglandin E2 (PGE2) concentrations and phospholipase A2 (PLA2) activity were determined in arachidonic acid (AA) and 12-O-tetradecanoyl phorbol 13-acetate (TPA)-induced mouse ear oedema, respectively. Phycocyanin (50-200 mg/kg p.o.) inhibited in a dose-dependent manner PGE2 levels in mouse ear treated with AA. Also, phycocyanin (100-400 mg/kg p.o.) moderately reduced PLA2 activity in TPA-induced mouse ear inflammation test. In this model triamcinolone (10 mg/kg p.o.) used as reference drug exerted a remarkable inhibitory effect on PLA2 activity. These results provide the first evidence that the anti-inflammatory effects of phycocyanin may result, at least partially, from inhibition of PGE2 production and a moderate inhibition of PLA2 activity.

PMID: 11190776 [PubMed - indexed for MEDLINE]

**Role of histamine in the inhibitory effects of phycocyanin in experimental models of allergic inflammatory response.**

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It has recently been reported that phycocyanin, a biliprotein found in the blue-green microalgae *Spirulina*, exerts anti-inflammatory effects in some animal models of inflammation. Taking into account these findings, we decided to elucidate whether phycocyanin might exert also inhibitory effects in the induced allergic inflammatory response and on histamine release from isolated rat mast cells. In in vivo experiments, phycocyanin (100, 200 and 300mg/kg post-orally (p.o.)) was administered 1 h before the challenge with 1 microg of ovalbumin (OA) in the ear of mice previously sensitized with OA. One hour later, myeloperoxidase activity and ear edema were assessed. Phycocyanin significantly reduced both parameters. In separate experiments, phycocyanin (100 and 200 mg/kg p.o.) also reduced the blue spot area induced by intradermal injections of histamine, and the histamine releaser compound 48/80 in rat skin. In concordance with the former results, phycocyanin also significantly reduced histamine release induced by compound 48/80 from isolated peritoneal rat mast cells. The inhibitory effects of phycocyanin were dose dependent. Taken together, our results suggest that inhibition of allergic inflammatory response by phycocyanin is mediated, at least in part, by inhibition of histamine release from mast cells.

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**Inhibitory effects of Spirulina in zymosan-induced arthritis in mice.**

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The anti-inflammatory effect of microalgae Spirulina was studied in zymosan-induced arthritis in mice. Four days after the intra-articular injection of zymosan (15 mg/ml), Spirulina (100 and 400 mg/kg perorally) was administered to animals for 8 days. The mice were then killed and beta-glucuronidase was measured in the synovial fluid. Each knee joint was totally removed for histopathological studies. Spirulina significantly reduced the levels of beta-glucuronidase that had been increased by zymosan. Histopathological and ultrastructural studies showed inhibition of the inflammatory reaction, whereas no destruction of cartilage, well-preserved chondrocytes, and normal rough endoplasmic reticulum and mitochondria were seen. The anti-arthritic effect exerted by Spirulina as shown in this model may be at least partly due to the previously reported antiinflammatory and antioxidative properties of its constituent, phycocyanin. To our knowledge, this is the first report on the anti-inflammatory effect of Spirulina in an experimental model of arthritis.

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**Anti-inflammatory effect of *Spirulina fusiformis* on adjuvant-induced arthritis in mice.**

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The present study was carried out to evaluate the anti-inflammatory effect of *Spirulina fusiformis* on adjuvant-induced arthritis in mice. Arthritis was induced by intra dermal injection of complete Freund's adjuvant (0.1 ml) into the right hind paw of Swiss albino mice. *Spirulina fusiformis* (800 mg/kg/b.wt) was orally administered for 8 d (from 11th to 18th day) to arthritic animals after adjuvant injection. The anti-inflammatory activity of *Spirulina fusiformis* was assessed by measuring paw volume, body weight, levels of lysosomal enzymes, tissue marker enzymes and glycoproteins in control and experimental animals. In adjuvant-induced arthritic animals, the levels of lysosomal enzymes, tissue marker enzymes, glycoproteins and the paw volume were increased significantly. However the body weight was found to be reduced when compared to control animals. Oral administration of *Spirulina fusiformis* (800 mg/kg/b.wt) significantly altered these above physical and biochemical changes observed in arthritic animals to near normal conditions. Hence results of this study clearly indicate that *Spirulina fusiformis* has promising anti-inflammatory activity against adjuvant-induced arthritic animals.

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