

Immunity

Zh Mikrobiol Epidemiol Immunobiol. 2001 Mar-Apr;(2):114-8.

[Biological activity of Spirulina]

[Article in Russian]

[Blinkova LP, Gorobets OB, Baturu AP.](#)

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In this review information of *Spirulina platensis* (SP), a blue-green alga (photosynthesizing cyanobacterium) having diverse biological activity is presented. Due to high content of highly valuable proteins, indispensable amino acids, vitamins, beta-carotene and other pigments, mineral substances, indispensable fatty acids and polysaccharides, SP has been found suitable for use as bioactive additive. SP produces an immunostimulating effect by enhancing the resistance of humans, mammals, chickens and fish to infections, the capacity of influencing hemopoiesis, stimulating the production of antibodies and cytokines. Under the influence of SP macrophages, T and B cells are activated. SP sulfolipids have proved to be effective against HIV. Preparations obtained from SP biomass have also been found active against herpesvirus, cytomegalovirus, influenza virus, etc. SP extracts are capable in inhibiting cancerogenesis. SP preparations are regarded as functional products contributing to the preservation of the resident intestinal microflora, especially lactic acid bacilli and bifidobacteria, and to a decrease in the level of *Candida albicans*. The biological activity of SP with respect to microorganisms holds good promise for using these microalgae as components of culture media.

Publication Types:

- English Abstract
- Review

PMID: 11548244 [PubMed - indexed for MEDLINE]

Activation of the human innate immune system by Spirulina: augmentation of interferon production and NK cytotoxicity by oral administration of hot water extract of Spirulina platensis.

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Spirulina platensis is a cyanobacterial species that is surmised to potentiate the immune system leading to suppression of cancer development and viral infection. Here, we identified the molecular mechanism of the human immune potentiating capacity of Spirulina by analyzing blood cells of volunteers with pre and post oral administration of hot water extract of Spirulina. NK functions represented by IFN gamma production and cytotoxicity were enhanced after administration of Spirulina in >50% subjects. IFN gamma was produced in an IL-12/IL-18-dependent fashion. In vitro stimulation of blood cells with BCG cell wall skeleton (CWS) allowed more potent IL-12 p40 production in cells from volunteers given Spirulina than in cells without pre-exposure to Spirulina. As BCG-CWS serves as a ligand for Toll-like receptor (TLR) 2 and 4 to raise the maturation stage of monocytes/macrophages, Spirulina may be involved in the signaling responses through Toll in blood cells even when orally administered. These observations indicated that in humans Spirulina acts directly on myeloid lineages and either directly or indirectly on NK cells. The presence of co-operative IL-12 and IL-18 is critically important for NK-mediated IFN gamma production.

Publication Types:

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

PMID: 11962722 [PubMed - indexed for MEDLINE]

Enhancement of human adaptive immune responses by administration of a high-molecular-weight polysaccharide extract from the cyanobacterium *Arthrospira platensis*.

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The effect of consumption of Immulina, a high-molecular-weight polysaccharide extract from the cyanobacterium *Arthrospira platensis*, on adaptive immune responses was investigated by evaluation of changes in leukocyte responsiveness to two foreign recall antigens, *Candida albicans* (CA) and tetanus toxoid (TT), in vitro. Consumption of Immulina by 11 healthy male volunteers caused an immediate, but temporary, increase of CA-induced CD4+ T-helper (Th) cell proliferation ($P < .02$). TT-induced Th cell proliferation was increased in individuals over 50 years of age ($P < .05$) and correlated with age ($P < .02$). Consumption for 8 days enhanced the CA-induced B cell proliferation ($P < .02$), but after 56 days a diminution was seen ($P < .03$). The CA-elicited production of the Th1 cytokines tumor necrosis factor (TNF)-alpha, interleukin (IL)-2, and interferon (IFN)-gamma was increased after Immulina administration for 3 days ($P < .001$, $< .03$, and $< .007$, respectively), and increased IL-2 production persisted after 56 days ($P < .004$). The TNF-alpha, IFN-gamma, and IL-6 responses to TT were enhanced after 8 and 14 days ($P < .002$ -.05), while IL-5 responses increased significantly within 3 days ($P < .04$) and fell below baseline levels after 14 days ($P < .008$). Conversely, consumption for 3 days inhibited the IL-4 responses to both CA and TT ($P < .008$ and $P < .03$, respectively). No effects on IL-10 responses were observed. Upon addition to normal mononuclear cells in vitro, Immulina elicited strong TNF-alpha, IL-1beta, and IL-6 responses, indicating that it acts by inducing a pro-inflammatory state. Taken together, the data suggest that Immulina causes an age-dependent, temporary enhancement of adaptive immune responses.

Publication Types:

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

PMID: 18598175 [PubMed - indexed for MEDLINE]

Phycocyanin enhances secretory IgA antibody response and suppresses allergic IgE antibody response in mice immunized with antigen-entrapped biodegradable microparticles.

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In the present study, we have investigated the effects of phycocyanin, a biliprotein of *Spirulina platensis*, on mucosal and systemic immune responses and allergic inflammation in C3H/HeN and BALB/cA mice. To induce the antigen-specific antibodies in the peripheral lymphoid tissues such as Peyer's patches and mesenteric lymph nodes, biodegradable ovalbumin-entrapped poly (DL-lactide-co-glycolide) particles were used as an antigen. Two weeks after the onset of phycocyanin ingestion, mice were immunized with an aqueous ovalbumin (OVA) solution. Starting at one week after the primary immunization, the mice were subjected to oral immunization with the biodegradable OVA microparticles twice a week. IgA, IgE and IgG1 antibodies were determined by ELISA. The OVA microparticles of 4-microm diameter successfully induced antigen-specific antibodies. In the mice that received phycocyanin treatment for 6 wk, a marked increase in the antigen-specific, as well as the total, IgA antibody level was observed in the Peyer's patches, mesenteric lymph nodes and intestinal mucosa as well as in the spleen cells. Both antigen-specific IgG1 and IgE antibody levels in the serum were suppressed by ingestion of phycocyanin for 8 wk. However, inflammation of the small intestine, monitored as vascular permeability by the Evans blue-leaking method was reduced by phycocyanin at 6 wk, which preceded the suppression of antigen-specific IgG1 and IgE antibody production by 2 wk. These results suggest that phycocyanin enhances biological defense activity against infectious diseases through sustaining functions of the mucosal immune system and reduces allergic inflammation by the suppression of antigen-specific IgE antibody.

PMID: 15242017 [PubMed - indexed for MEDLINE]

C-Phycocyanin inhibits 2-acetylaminofluorene-induced expression of MDR1 in mouse macrophage cells: ROS mediated pathway determined via combination of experimental and In silico analysis.

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We studied the effects of C-Phycocyanin (C-PC), a biliprotein from *Spirulina platensis* on the 2-acetylaminofluorene (2-AAF)-induced expression of MDR1, encoded by the multidrug resistance (MDR1) gene, in mouse macrophage cell line (RAW 264.7). Our experimental and In silico studies revealed a significant inhibition of 2-AAF-induced expression of MDR1 protein in C-PC treated mouse macrophage cell line. MDR1 induction by 2-AAF was dependent on ROS (reactive oxygen species)-Akt (protein kinase B)-NF-kappaB (Nuclear factor kappa B) signaling pathway. Generation of ROS, phosphorylation of Akt and corresponding nuclear translocation of NF-kappaB, the events that play a major role in the induction of MDR1 expression, were decreased significantly in C-PC treated cells. NADPH oxidase inhibitor, DPI (Diphenyl iodide), and pharmacological inhibitor of Akt, Akt inhibitor IV, also showed a reduction in MDR1 expression, although not to the same extent as C-PC mediated inhibition of MDR1 expression. To further understand the mechanism, we created a computational model of the detailed ROS-Akt-NF-kappaB pathway. C-PC was modeled purely as a ROS scavenger and this representation matched the experimental trends accurately. Also the ROS levels determined through In silico investigation showed that C-PC was more effective in reduction of MDR1 expression than inhibitors of NADPH oxidase and Akt. Our experimental and In silico studies collectively suggest that 2-AAF induces MDR1 by ROS dependent pathway and C-PC is a potential negative regulator of MDR1 expression. This down regulation of MDR1 expression, induced by xenobiotics such as 2-AAF, suggests C-PC's usefulness in overcoming the drug resistance in cellular systems.

Publication Types:

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

PMID: 17303067 [PubMed - indexed for MEDLINE]

[Immunostimulating activity of the lipopolysaccharides of blue-green algae]

[Article in Russian]

[Besednova NN](#), [Smolina TP](#), [Mikheïskaia LV](#), [Ovodova RG](#).

The whole cells of blue-green algae and lipopolysaccharides isolated from these cells were shown to stimulate the production of macro-(mainly) and microglobulin antibodies in rabbits. The macro- and microphage indices in rabbits increased significantly after the injection of LPS isolated from blue-green algae 24--48 hours before infecting the animals with a virulent *Y. pseudotuberculosis* strain. Besides, the inhibiting action of this strain on the migration of phagocytes to the site of infection was abolished immediately after the injection. The use of the indirect hemagglutination test allowed to prove the absence of close antigenic interrelations between blue-green algae and the following organisms: *Spirulina platensis*, *Microcystis aeruginosa*, *Phormidium africanum* and *P. uncinatum*.

Publication Types:

- English Abstract

PMID: 117655 [PubMed - indexed for MEDLINE]

Vopr Pitan. 2006;75(2):19-21.

[Studies of immunomodulation caused by selenium-enriched phycocyanin]

[Article in Russian]

[Egorova EA](#), [Gmoshinskii IV](#), [Zorin SN](#), [Mazo VK](#).

An influence was studied in rats of selenium enriched phycocyanin (Se-PC) from food microalgae Spirulina on anaphylactic reaction severity and circulating antibody response against model allergen--hen's egg white ovalbumin. Se-PC was introduced into diet in form of protein isolate precipitated with ammonia sulphate. Se-PC dosage made up to 450 mcg per rat daily that corresponded to 5 mcg of selenium. There were no differences revealed between experimental and control group that received standard diet in severity of anaphylactic reaction. Nevertheless rats receiving Se-PC demonstrated significantly increased specific IgG response. The probable immunomodulating properties of Se-PC included into food are discussed.

Publication Types:

- English Abstract

PMID: 16729754 [PubMed - indexed for MEDLINE]

Immunopharmacol Immunotoxicol. 2001 May;23(2):281-9.

Enhancement of chicken macrophage phagocytic function and nitrite production by dietary *Spirulina platensis*.

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The effects of dietary *Spirulina platensis* on chicken macrophage phagocytic function and nitrite production were examined. Day old broiler (meat-type) chicks were randomly assigned to various pens of electrically heated wire batteries. Dietary treatment groups included a basal diet with no dietary *Spirulina* added, and three additional groups with 0.5, 1.0 and 2.0% dietary *Spirulina*. Feed and water were provided for ad libitum consumption from one day of age. Sephadex-elicited macrophages were harvested at 14, 35 and 42 days of age. Phagocytosis assay was performed by co-incubating sheep red blood cells (SRBC) with the adherent macrophage monolayers. For nitrite quantification, macrophage cultures from various dietary treatment groups were stimulated in the presence or absence of 1 microg/mL of *Escherichia coli* lipopolysaccharide. These culture supernatant fractions were then tested for nitrite levels using the Greiss reagent technique. All *Spirulina* dietary group macrophages exhibited an enhanced phagocytic activity in terms of overall phagocytic percentage (range = 28 to 39% versus 24 to 25% in the basal group) and the average number of SRBC per phagocytic macrophage (range = 2.2 to 3.6 versus 1.8 to 2.5 in the basal group). This increase was linear with each incremental increase of dietary *Spirulina*. While LPS-induced nitrite levels in macrophages from basal diet group ranged from 60 to 278 microM over the three developmental ages, these levels in all *Spirulina* dietary groups were significantly higher (0.5% group range = 198 to 457 microM; 1.0% group range = 161 to 359 microM and 2.0% group range = 204 to 420 microM). These data clearly show that *Spirulina platensis* feeding upregulates macrophage phagocytic as well as metabolic pathways leading to increased nitric oxide synthase activity. These findings therefore imply that *Spirulina platensis* may enhance the functions of mononuclear phagocytic system thereby increasing the disease resistance potential in chickens.

Publication Types:

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

PMID: 11417854 [PubMed - indexed for MEDLINE]

Effect of spirulina on the secretion of cytokines from peripheral blood mononuclear cells.

[Mao TK](#), [VAN DE Water J](#), [Gershwin ME](#).

ABSTRACT The purpose of this study was to evaluate the immunomodulatory activity of Spirulina, a bluegreen alga used as a food supplement. The effects of Spirulina on the secretion of three cytokines from unstimulated and stimulated human peripheral blood mononuclear cells (PBMC) were examined. In resting PBMC, Spirulina stimulated secretion of interleukin (IL)-1beta, IL-4, and interferon (IFN)-gamma to nearly 2.0, 3.3, and 13.6 times basal levels, respectively. Spirulina induced levels of IFN-gamma (229 +/- 104 pg/ml) that were comparable to those seen after phytohemagglutinin (PHA) stimulation (476 +/- 121 pg/ml). However, it was much less mitogenic than PHA (13.1 +/- 6.9 pg/ml) with respect to the induction of IL-4 secretion (0.34 +/- 0.1 pg/ml). In PHA-stimulated cells, Spirulina enhanced secretion of IL-1beta, IL-4, and IFN-gamma by 2.9, 4.0, and 1.6 times, respectively. Although Spirulina stimulates several cytokines, it is clearly more effective in the generation of a Th1-type response. This in vitro study offers additional data for consideration of the potential therapeutic benefits of Spirulina.

PMID: 19281334 [PubMed - in process]

Lik Sprava. 2003 Jul-Aug;(5-6):102-5.

[Evaluation of the efficacy of a plant adaptogen (spirulina) in the pathogenic therapy of primary tuberculosis in children]

[Article in Ukrainian]

[Kostromina VP](#), [Derkach OV](#), [Symonenkova NV](#), [Riechkina OO](#), [Otroshchenko AO](#).

The use of spirulina and its efficiency have been studied in a comparative aspect as a systemic biocorrector, in a combined treatment of tuberculosis in 26 children. It has been ascertained that application of spirulina as a pathogenetic means of remediation permits shortening the intoxication syndrome regression time, reducing the frequency of adverse reactions in administering antituberculous preparations.

Publication Types:

- Clinical Trial
- Comparative Study
- English Abstract

PMID: 14618819 [PubMed - indexed for MEDLINE]

Isolation of three high molecular weight polysaccharide preparations with potent immunostimulatory activity from *Spirulina platensis*, *Aphanizomenon flos-aquae* and *Chlorella pyrenoidosa*.

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This research describes the identification of three new high molecular weight polysaccharide preparations isolated from food-grade microalgae that are potent activators of human monocytes/macrophages: "Immulina" from *Spirulina platensis*, "Immunon" from *Aphanizomenon flos-aquae*, and "Immurella" from *Chlorella pyrenoidosa*. These polysaccharides are structurally complex and have estimated molecular weights above ten million daltons. All three polysaccharides are highly water soluble and comprise between 0.5 % and 2.0 % of microalgal dry weight. Immunostimulatory activity was measured using a transcription factor-based bioassay for nuclear factor kappa B (NF-kappa B) activation in THP-1 human monocytes/macrophages. Using this system the EC(50) values for these microalgal polysaccharides are between 20 and 110 ng/ml (about 10pM). THP-1 activation was confirmed by measuring immune cytokine mRNA induction using reverse transcriptase-polymerase chain reaction (RT-PCR). Each polysaccharide substantially increased mRNA levels of interleukin-1beta (IL-1beta) and tumor necrosis factor-alpha (TNF-alpha). These polysaccharides are between one hundred and one thousand times more active for in vitro monocyte activation than polysaccharide preparations that are currently used clinically for cancer immunotherapy.

Publication Types:

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

PMID: 11731916 [PubMed - indexed for MEDLINE]

Calcium spirulan as an inducer of tissue-type plasminogen activator in human fetal lung fibroblasts.

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Calcium spirulan (Ca-SP), a novel sulfated polysaccharide isolated from the blue-green alga *Spirulina platensis*, has been found to have antiviral and heparin cofactor II-dependent antithrombin activities. We have obtained evidence that Ca-SP is a potent inducer of tissue-type plasminogen activator (t-PA) production. The addition of Ca-SP to a culture of IMR-90 human fetal lung fibroblasts increased t-PA concentrations in the conditioned medium, in a dose- and time-dependent manner, but in the cell lysate, t-PA concentrations were unchanged, suggesting that t-PA induced by Ca-SP is easily secreted into the conditioned medium. The amount of newly synthesized t-PA in IMR-90 cells, as measured by labeling with [35S]methionine and subsequent immunoprecipitation of t-PA from conditioned medium, was significantly increased by Ca-SP-stimulation. However, Ca-SP did not increase the t-PA mRNA levels. As previously reported, thrombin stimulated t-PA gene transcription in IMR-90 cells, and the simultaneous treatment with Ca-SP and thrombin caused further enhancement of t-PA production, in a synergistic manner. It would thus appear that Ca-SP increases t-PA production through post-transcriptional processes. IMR-90 cells also produce plasminogen activator inhibitor type-1 (PAI-1), but Ca-SP showed little effect on the PAI-1 production. H-SP, which was obtained by removing the calcium from Ca-SP, had no effect on the t-PA production. Na-SP, which was prepared by replacement of the calcium with sodium, stimulated the t-PA production similarly to Ca-SP. Thus, Ca-SP specifically induces t-PA production, and the molecular conformation of Ca-SP maintained by Ca or Na may be essential for the stimulation of t-PA synthesis.

PMID: 9060995 [PubMed - indexed for MEDLINE]

Dietary *Spirulina platensis* enhances humoral and cell-mediated immune functions in chickens.

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Cornell K-strain White Leghorns and broiler chicks were raised to 7 wks and 3 wks of age respectively, with diets containing various levels (0, 10, 100, 1,000 and 10,000 ppm) of *Spirulina platensis* from day of hatch. Chicks in all treatment groups had comparable body weights. While bursal and splenic weights did not change, the K-strain chicks had larger thymuses ($P < \text{or} = .05$) over the controls (0 ppm group). No differences were observed in anti-sheep red blood cells antibodies during primary response. However, during secondary response, K-strain chicks in all *Spirulina*-dietary groups had higher total anti-SRBC titers with 10,000 ppm group being the highest (6.8 Log₂) versus the 0 ppm (5.5 Log₂) group. In broiler chicks, a one Log increase in IgG ($P < \text{or} = .05$) was observed in 10,000 ppm group over the controls. Similarly, chicks in 10,000 ppm *Spirulina* group had a higher PHA-P-mediated lymphoproliferative response over the 0 ppm controls. Macrophages isolated from both K-strain (10,000 ppm group) and broilers from all *Spirulina* groups had higher phagocytic potential than the 0 ppm groups. *Spirulina* supplementation at 10,000 ppm level also increased NK-cell activity by two fold over the controls. These studies show that *Spirulina* supplementation increases several immunological functions implying that a dietary inclusion of *Spirulina* at a level of 10,000 ppm may enhance disease resistance potential in chickens.

PMID: 8872497 [PubMed - indexed for MEDLINE]

Immunopharmacol Immunotoxicol. 1996 Aug;18(3):457-63.

Spirulina platensis exposure enhances macrophage phagocytic function in cats.

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Bronchoalveolar lavage macrophages isolated from cats were cultured on glass coverslips. Macrophages were exposed to a water-soluble extract of *Spirulina platensis* in concentration range of 0 to 60 micrograms per mL for two hours. *Spirulina*-extract exposure did not cause significant macrophage cytotoxicity over untreated control cultures. Macrophage monolayers from treated and control cultures were incubated with sheep red blood cells (SRBC) as well as viable *Escherichia coli*. The percentages of phagocytic macrophages for both of these particulate antigens were higher (a two-fold increase in SRBC phagocytosis and over 10% increase in *Escherichia coli* uptake) in cultures treated with various concentrations of *Spirulina*-extract. However, the numbers of either types of particles internalized by phagocytic macrophage were not different between the control and treated cultures. These data which showed that *Spirulina platensis* extract enhances macrophage phagocytic function imply that dietary *Spirulina* supplementation may improve the disease resistance potential in cats.

PMID: 8872496 [PubMed - indexed for MEDLINE]

Enhancement of antibody production in mice by dietary *Spirulina platensis*.

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Mice fed a *Spirulina platensis* diet showed increased numbers of splenic antibody-producing cells in the primary immune response to sheep red blood cells (SRBC). However, immunoglobulin G (IgG)-antibody production in the secondary immune response was hardly affected. The percentage of phagocytic cells in peritoneal macrophages from the mice fed *S. platensis* diet, as well as the proliferation of spleen cells by either concanavalin A (Con A) or phytohemagglutinin (PHA) was significantly increased. Addition of a hot-water extract of *S. platensis* (SHW) to an in vitro culture of spleen cells markedly increased proliferation of these cells, whereas culture of thymus cells was scarcely affected. The *Spirulina* extract also significantly enhanced interleukin-1 (IL-1) production from peritoneal macrophages. Addition to the in vitro spleen cell culture of SHW as well as the supernatant of macrophages stimulated with SHW resulted in enhancement of antibody production, that is, an increase of the number of PFC. These results suggest that *Spirulina* enhances the immune response, particularly the primary response, by stimulating macrophage functions, phagocytosis, and IL-1 production.

PMID: 7891204 [PubMed - indexed for MEDLINE]

Antibacterial activity of volatile component and various extracts of *Spirulina platensis*.

[Ozdemir G](#), [Karabay NU](#), [Dalay MC](#), [Pazarbasi B](#).

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The methanol, dichloromethane, petroleum ether, ethyl acetate extracts and volatile components of *Spirulina platensis* were tested in vitro for their antimicrobial activity (four Gram-positive, six Gram-negative bacteria and *Candida albicans* ATCC 10239). GC-MS analysis of the volatile components of *S. platensis* resulted in the identification of 15 compounds which constituted 96.45% of the total compounds. The volatile components of *S. platensis* consisted of heptadecane (39.70%) and tetradecane (34.61%) as major components. The methanol extract showed more potent antimicrobial activity than dichloromethane, petroleum ether, ethyl acetate extracts and volatile components. Copyright (c) 2004 John Wiley & Sons, Ltd.

Publication Types:

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

PMID: 15478198 [PubMed - indexed for MEDLINE]

Vopr Pitan. 2007;76(2):21-5.

[The influence of Spirulina and Selen-Spirulina on some indexes of rat's immune status]

[Article in Russian]

[Trushina EN](#), [Gladkikh O](#), [Gadzhieva ZM](#), [Mustafina OK](#), [Pozdniakov AL](#).

This paper reviews evidence for the immune-enhancing effect of Spirulina (Sp) and Selen-Spirulina (Se-Sp) in male Wistar rats. The rats of control group fed half-synthetic diet. Rats of experimental groups consumed the half-synthetic diets with Sp (10 g/kg diet) or Se-Sp (350 microg Se/kg diet) for 2 weeks. Using rats lymphocytes in vitro after phytohemagglutinin stimulation was demonstrated that lymphocytes from Sp and Se-Sp groups secreted of interleukin-2 and interferon-gamma more control group. Induction of interleukin-4 was comparable with once of control group. We believed that Sp and Se-Sp are more effective in stimulating a Th-1--type response and hence potentiates cell-mediated immunity. The immunostimulatory effect of Sp and Se-Sp was confirmed by morphologic and morphometric investigation of rats spleen, also with by NBT-test of peritoneal macrophages.

Publication Types:

- Comparative Study
- English Abstract

PMID: 17561650 [PubMed - indexed for MEDLINE]

Toll-like receptor 2-dependent activation of monocytes by Spirulina polysaccharide and its immune enhancing action in mice.

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We reported previously that a high molecular weight polysaccharide fraction (Immulina) from Spirulina was a potent activator of NF-kappa B and induced both IL-1 beta and TNF-alpha mRNAs in THP-1 human monocytes. In the present study, we show that NF-kappa B activation by Immulina is suppressed by antibodies to CD14 and TLR2 but not by antibodies to TLR4. Similarly, NF-kappa B directed luciferase expression was enhanced by Immulina treatment when cells were co-transfected with vectors expressing proteins supporting TLR2- (CD14 and TLR2) but not TLR4-(CD14, TLR4, and MD-2) dependent activation. Mice that consumed a chemically defined chow mixed with an extract containing Immulina exhibited changes in several immune parameters. The ex vivo production of IgA and IL-6 from Peyer's patch cells was enhanced 2-fold and interferon-gamma production from spleen cells was increased 4-fold in Immulina-treated mice. The enhanced production of these factors was most notable with mice that had consumed this extract for 4 or 5 days. These studies shed light on how Immulina activates cells of the innate immune system and suggests that oral consumption of this polysaccharide can enhance components within both the mucosal and systemic immune systems.

Publication Types:

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

PMID: 17052671 [PubMed - indexed for MEDLINE]

Immolina, a high-molecular-weight polysaccharide fraction of Spirulina, enhances chemokine expression in human monocytic THP-1 cells.

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INTRODUCTION: Spirulina (*Spirulina platensis*) is a dietary supplement valued for its immune-enhancing properties. We previously reported that the immunostimulatory effect of spirulina can be traced to a high-molecular-weight polysaccharide fraction. This fraction, labeled Immolina, activates nuclear factor kappa-B in human monocytic THP-1 cells and increases expression of proinflammatory cytokines. **OBJECTIVE:** To characterize further the immunostimulatory effects of Immolina on THP-1 cells, we evaluated its effect on genes encoding the chemokines interleukin (IL)-8, MCP-1, MIP-1alpha, MIP-1beta, IP-10, the cytokines tumor necrosis factor (TNF)-alpha, IL-1beta, and the enzyme cyclo-oxygenase-2 (COX-2). **METHODS:** THP-1 cells were exposed to concentrations of Immolina ranging from 1 ng/mL to 100 microg/mL and changes in gene expression were assessed by reverse transcriptase-polymerase chain reaction (RT-PCR). For comparison, THP-1 cells were activated with 1 ng/mL of TNF-alpha, 10 ng/mL of IL-1beta, or 10 ng/mL of lipopolysaccharide using the same assay conditions. To assess the response of THP-1 cells to Immolina at the protein level, we probed culture supernatants using a cytokine array immunoblot assay. **RESULTS:** RT-PCR analysis revealed that Immolina dose-dependently increased the expression of all 5 chemokines tested as well as the expression of TNF-alpha, IL-1beta, and COX-2. The cytokine array immunoblot assay revealed an increase in the chemokines IL-8 and MIP-1beta. Thymidine uptake experiments verified that Immolina did not affect the viability and growth rate of THP-1 cells. **CONCLUSIONS:** The results of the experiments demonstrate that Immolina activates THP-1 cells in a manner that is consistent with the recruitment of diverse populations of leukocytes in response to inflammatory and infectious signals.

Publication Types:

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

PMID: 16813506 [PubMed - indexed for MEDLINE]

Appraisal of immunomodulatory potential of *Spirulina fusiformis*: an in vivo and in vitro study.

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In recent years, *Spirulina* has gained more and more attention from medical scientists as a nutraceutical and a source of potential pharmaceuticals. The present study was conducted to elucidate the immunomodulatory effect of *Spirulina fusiformis* (a cyanobacterium of the family Oscillatoriaceae) in vivo and in vitro. The in vivo effect of *S. fusiformis* (400 or 800 mg/kg body wt.) on humoral immune response, cell-mediated immune response and tumour necrosis factor alpha was investigated in mice. We also evaluated the effect of *S. fusiformis* (50 or 100 microg/ml) in vitro on mitogen (phytohaemagglutinin)-induced T lymphocyte proliferation in heparinized human peripheral blood. For comparison, dexamethasone was used as a standard. In mice, *S. fusiformis* (400 or 800 mg/kg body wt.) administration significantly inhibited the humoral immune response, cell-mediated immune response (delayed-type hypersensitivity reaction (DTH)) and tumour necrosis factor alpha in a dose-dependent manner. In vitro, *S. fusiformis* (50 or 100 microg/ml) decreased the mitogen (phytohaemagglutinin)-induced T lymphocyte proliferation in a concentration-dependent manner when compared with control cells. These observations clearly suggest that *S. fusiformis* has a remarkable immunosuppressive effect, which provides a scientific validation for the popular use of this drug, and helped us in further work on investigating its complete mechanism of action.

Publication Types:

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

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Spirulina in Clinical Practice: Evidence-Based Human Applications.

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Spirulina or Arthrospira is a blue-green alga that became famous after it was successfully used by NASA as a dietary supplement for astronauts on space missions. It has the ability to modulate immune functions and exhibits anti-inflammatory properties by inhibiting the release of histamine by mast cells. Multiple studies investigating the efficacy and the potential clinical applications of Spirulina in treating several diseases have been performed and a few randomized controlled trials and systematic reviews suggest that this alga may improve several symptoms and may even have an anticancer, antiviral and antiallergic effects. Current and potential clinical applications, issues of safety, indications, side-effects and levels of evidence are addressed in this review. Areas of ongoing and future research are also discussed.

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