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Current knowledge on potential health benefits of *Spirulina*

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Abstract

Spirulina is a microscopic filamentous alga that is rich in proteins, vitamins, essential amino acids, minerals and essential fatty acids like γ-linolenic acid (GLA). It is produced commercially and sold as a food supplement in health food stores around the world. Up to very recently, the interest in *Spirulina* was mainly in its nutritive value. Currently, however, numerous people are looking into the possible therapeutic effects of *Spirulina*. Many pre-clinical studies and a few clinical studies suggest several therapeutic effects ranging from reduction of cholesterol and cancer to enhancing the immune system, increasing intestinal lactobacilli, reducing nephrotoxicity by heavy metals and drugs and radiation protection. This paper presents a critical review of some published and unpublished data on therapeutic effects of *Spirulina*.

Introduction

Spirulina is an unbranched, helicoidal, filamentous blue-green alga or cyanobacterium. The trichome consists of cylindrical cells of 1-12 μm in diameter. It is found as an almost unialgal culture in many alkaline lakes with a very high pH, sometimes reaching 11. Such a pH prohibits the growth of most other algae.

Spirulina has a long history of use as food. There are reports that *Spirulina* was used traditionally by Mexicans during the Aztec civilization for over 1000 years (Ciferri & Tiboni, 1985). Its use as a food by the natives in the Lake Chad area has also been documented by the French phycologist Dangeard (Ciferri & Tiboni, 1985). Its safety for human food has since been established through various toxicological studies sponsored by the United Nations Industrial Development Organization (Chamorro-Cevalos, 1980).

Early interest in *Spirulina* focussed mainly on its potential as a source of protein and vitamins. *Spirulina* is 60–70% protein by weight and contains a rich source of vitamins, especially vitamin B_{12} and pro-vitamin A (β-carotene), minerals, especially iron, and is one of the few sources of dietary γ-linolenic acid (GLA). At present there are several companies producing *Spirulina* and the product is sold as a food supplement in many health food stores around the world. Current annual commercial production of food-grade *Spirulina* totals about 800 000 kg.

Recently, more attention has been given to the study of the therapeutic effects of *Spirulina*. A number of published and unpublished reports suggest significant therapeutic effects of *Spirulina* or *Spirulina* extracts. The objective of this paper is to give an overview of the work done on some therapeutic effects of *Spirulina* (*S. platensis* and *S. maxima*) with emphasis on the recent pub-

lished literature and assess the potential for future pharmaceutical use.

Summary of studies on therapeutic effects of *Spirulina*

The published information on the therapeutic effects of *Spirulina* is summarized in Table 1. More information on published and unpublished studies is also included in the text.

Effects against Hyperlipidemia

The first report on the reduction of serum cholesterol by *Spirulina* was that done on rats by Devi and Venkataraman (1983). Since then several workers have confirmed these findings in animal and human experiments. In *Spirulina* feeding experiments in rats, Kato *et al.* (1984) have reported that the elevation in total cholesterol, LDL + VDL cholesterol and phospholipids in serum caused by cholesterol feeding was reduced when the high cholesterol diet was supplemented with 16%

Table 1. A summary of studies on therapeutic effects of *Spirulina*.

Application	Subject	Summary of results	Reference
Hyperlipidemia	Rat	Total cholesterol level in serum lowered. HDL-cholesterol level increased, while LDL-cholesterol level suppressed.	Kato *et al.*, 1984
	Rat	Rate of increase of triglycerides level in serum and liver suppressed by lipase activity.	Iwata *et al.*, 1987, 1990
	Human	In a study involving 30 patients, total serum cholesterol, LDL-cholesterol, and AI (Athero-genic Index) lowered. HDL-cholesterol increased concurrently.	Nakaya *et al.*, 1988
Adipohepatosis	Rat	Condition suppressed, and recovery stimulated.	Kato *et al.*, 1984
Antitumor	Hamster	Studies showed that β-carotene, a nontoxic carotenoid, had a cytostatic and cytotoxic dose-dependent effect on hamster and human cell lines.	Schwartz & Sklar, 1987
	Hamster	An extract of *Spirulina-Dunaliella* shown to prevent tumor development in hamster buccal pouch.	Schwartz *et al.*, 1988
Immune system	Mouse	Delayed-type hypersensitivity caused by diisocyanate suppressed in mice fed with *Spirulina*.	Nagao *et al.*, 1991
	Mouse	Primary immune response against thymus-dependent and independent antigens enhanced.	Hayashi *et al.*, 1992
Radioprotective effect	Mouse	Ethanol extract of *Spirulina* resulted in significant reduction of micronucleus frequencies induced by γ-radiation.	Oishen *et al.*, 1989
Renal toxicity	Rat	*Spirulina* diet showed protective effect against renal failure induced by inorganic mercury and 3 known pharmaceuticals: para-aminophenol, gentamicin, and cisplatin.	Yamane *et al.*, 1988
	Rat	Phycocyanin showed protective effect against renal failure induced by mercury and cisplatin.	Fukino *et al.*, 1990
Intestinal flora	Rat	Population of *Lactobacillus* and Bifidobacteria in the intestine notably increased.	Tsuchihashi *et al.*, 1987
Diabetes	Rat	*Spirulina* water-soluble fraction effective in lowering serum glucose at fasting. *Spirulina* water-insoluble fraction suppressed glucose level at glucose loading.	Takai *et al.*, 1991
Obesity	Human	Doulbe-blind cross-over study vs. placibo supplemental dietary intake of 2.8 g of *Spirulina* 3 times d^{-1} over 4 wk showed statistically significant reduction of body weight in obese outpatients.	Becker *et al.*, 1986
Hypertension	Rat	Elevation of blood pressure suppressed.	Iwata *et al.*, 1990

Spirulina. Adipohepatosis induced by high fat and high cholesterol diet was also cured rapidly when the diet was supplemented with *Spirulina*. In a study involving rats, Iwata *et al.* (1987) found that feeding *Spirulina* at 5%, 10% and 15% of the diet resulted in a significant inhibition of total and HDL-cholesterol ($p<0.01$), triglyceride ($p<0.05$) and phospholipid ($p<0.01$) in fructose-induced hypolipidemic rats. However, no difference in liver lipids was found between the high fructose diet and *Spirulina* diet groups. In an attempt to elucidate the mechanism of the hypotriglyceridemic effect of *Spirulina*, the activities of two kinds of lipases, lipoprotein lipase (LPL) and hepatic triglyceride lipase (H-TGL) which are released into blood by intravenous injection of heparin were determined (Iwata *et al.*, 1990). The *Spirulina* diet group showed a statistically significant ($p<0.01$) increase in the activity of LPL than the high fructose diet group. There was no significant difference in the activity of H-TGL in the two groups. Since LPL is a key lipolytic enzyme in the metabolism of TG-rich lipoproteins, the hypotriglyceridemic effect of *Spirulina* may be through its effect on metabolism of lipoproteins. The oil-soluble fraction of *Spirulina* (phospholipids and glucolipids) was also found to suppress cholesterol level in the serum and liver of rats (K. Iwata, pers. comm.).

The only human study to date of the hypocholestrolemic effect of *Spirulina* is that by Nakaya *et al.* (1988). In this study 30 male volunteers who had mild hyperlipidemia and mild hypertension were divided into two groups. Group A subjects were given *Spirulina* at 4.2 g d^{-1} and group B subjects the same amount of *Spirulina* for 4 wk and were observed for the next 4 wk without giving *Spirulina*. The results showed a statistically significant reduction of LDL-cholesterol ($p<0.05$) in Group A subjects after 8 wk. The LDL-cholesterol also fell significantly in Group B subjects after 4 wk ($p<0.05$), but thereafter increased to its baseline value after administration of *Spirulina* was discontinued. No significant difference was observed in the level of HDL-cholesterol. On the other hand, the atherogenic index (a measure of fat deposition in arteries) declined significantly in Group A subjects ($p<0.01$) after 4 wk.

Anti-cancer and immune system effects

According to a Japanese patent, (Dainippon Ink & Chemicals, 1983), phycocyanin, the blue pigment common in cyanobacteria and constituting about 15% of *Spirulina* was extracted and given orally to laboratory mice that had been injected with liver tumor cells. The survival rate of the treatment group was increased significantly over that of the controls. It was found that lymphocyte activity of the treatment group was significantly higher than that of the corresponding activity of the control group suggesting some sort of stimulation of the immune system. Daily ingestion of a small dosage of phycocyanin maintained or accelerated normal cell functions to prevent malignancy such as cancer or to inhibit its growth or recurrence (Dainippon Ink & Chemicals, 1983).

β-carotene and *Spirulina-Dunaliella* extracts were shown to inhibit carcinogenesis in hamster buccal pouch (Schwartz & Sklar, 1987). In subsequent studies, Schwartz *et al.* (1988) were able to demonstrate that an extract of *Spirulina* and *Dunaliella* prevented tumor development in hamster buccal pouch at much lower doses than in their previous study. The algal extract which was rich in β-carotene and administered by mouth, prevented tumor formation. Carcinomas that were beginning to develop were observed to be destroyed probably by an immune response. This was surmised from the dense lymphocytic-monocytic infiltrate (Schwartz *et al.*, 1988). The lymphocytes, according to these authors, were T-cells supporting the concept that the algal extract can prevent cancer development by stimulating an immune response to destroy selectively small initial foci of developing malignant cells. This effect of *Spirulina* in the prevention of tumors is not at all surprising as there is a strong epidemiological evidence linking Vitamin A intake and decreased cancer risks (Peto, 1981). It is also known that β-carotene or pro-vitamin A, and not preformed Vitamin A from animal sources, correlated with lower cancer rates (Shekelle, 1981).

Spirulina is rich in β-carotene having 10 times the concentration in carrots on a dry-weight basis. Since the algal extract used also contained phycocyanin and other constituents, the immune response observed could also have been the result of the effect of these other components.

Recently, Nagao *et al.* (1991) have also reported that the delayed-type hypersensitivity caused by toluen-2, 4-diisocyanate was suppressed in mice fed with a *Spirulina*-added feed for 5 wk. In a more recent study, Hayashi *et al.* (1992) measured the immune response of mice to a thymus-dependent antigen of sheep red blood cells and a thymus-independent antigen of polyvinylpyrrolidon. The immune response of mice fed with *Spirulina*-added feeds for 40 to 50 d was found to be significantly enhanced, especially at an earlier stage of the primary immune response. In a further study (T. Kato, pers. comm.), the effect of *Spirulina* upon the cellular immune response, like the contact-type hypersensitivity response caused by a hapten antigen of picryl chloride (PC), was followed. The contact-type hypersensitivity of mice fed with *Spirulina*-added feeds for 30–40 d was significantly suppressed compared to the control group fed with the basal diet.

Radiation protective effects

The radioprotective effect of a crude ethanol precipitate (CEP) of *Spirulina platensis* was studied using the micronucleus test in polychromatic erythrocytes (PCE) of bone marrow of mice. In this system the extract caused a significant reduction of micronucleus frequencies induced by γ-radiation (Qishen *et al.*, 1989). Gamma-radiation followed by treatment with CEP led to about the same radioprotective effect as CEP treatment followed by γ-radiation. From this the authors concluded that the protective compound probably acts as a DNA-stabilizing factor, and they ruled out the possibility of a radical scavenging mechanism. The ability of CEP to reduce the incidence of micronucleated bone marrow cells is believed to reflect its antimutagenic and repair-stimulating capacities much as has been postulated by Schwartz *et al.* (1988).

There are also unpublished reports from scientists and doctors about the radioprotective effect of *Spirulina* in experiments conducted on child victims of the Chernobyl radiation. In a study involving 49 children, 3–7 yr old, in Beryozovka, administration of *Spirulina* for 45 d resulted in an increase in T-cell suppressors and beneficial hormones. In addition the radioactivity of the urine decreased in 83% of the children (Report by T. Belookaya, Chairman, Byelorussian Committee of 'Children of Chernobyl').

Effects against nephrotoxicity

According to Yamane *et al.* (1988), rats with high mercury dosage showed rising blood urea nitrogen (BUN) and serum creatinine which are both indicators of acute nephritis. The addition of 30% *Spirulina* in the diet resulted in a significant decrease in BUN and serum creatinine levels. Rats given 3 pharmaceuticals, para-aminophenol (anodyne), gentamicin (anti-biotic), and cis-dichlorodiamino-platinum (anti-cancer), showed similar kidney improvement on a *Spirulina* diet. In a follow-up study, Fukino *et al.* (1990) found similar effects of *Spirulina* on renal toxicity induced by inorganic mercury and cisplatin. In addition to BUN and serum creatinine, urinary excretion of alkaline phosphatase (ALP) and glutamic oxaloacetate transaminase (GOT) were measured as further indicators of renal function. The activities of both enzymes were significantly reduced in the group that were fed 30% *Spirulina*. The effective component was found in the water-soluble fraction of the *Spirulina* extract. Within the water-soluble fraction, the substances with a molecular weight of more than 100000 were believed to be responsible. From this observation it was suggested that phycocyanin may be responsible in the suppression of renal toxicity.

Effects on intestinal flora

Tsuchihashi *et al.* (1987) have shown that an intake of *Spirulina* at 5% of the diet increased the

population of *Lactobacillus* in the caecum of rats by 3 times over the control group of rats not fed *Spirulina*. In humans, *Lactobacillus* is believed to have three functions: improving digestion and absorption of foods, protection from infection and stimulation of the immune system. In patients with an Acquired Immune Deficiency Syndrome (AIDS), nutrient malabsorption associated with 'opportunistic infections' can speed up the expression of the symptoms of the disease. One recommended strategy for halting the progression of AIDS is based on nutrient supplementation as well as supplemental *Lactobacillus* (Archer & Glinsmann, 1985).

Effects against diabetes, obesity and hypertension

According to Takai *et al.* (1991), a water-soluble fraction of *Spirulina* was found to be effective in lowering the serum glucose level at fasting while the water-insoluble fraction suppressed glucose level at glucose loading. In a double-blind-cross-over study versus placebo, Becker *et al.* (1986) have found that a supplementary diet of 2.8 g of *Spirulina* 3 times d^{-1} over 4 wk resulted in a statistically significant reduction of body weight in obese outpatients. *Spirulina* has also been found to suppress high blood pressure in rats (Iwata *et al.*, 1990).

Other effects

A number of other possible therapeutic effects can also be inferred from the chemical composition of *Spirulina*.

Gamma-linolenic acid effects and Spirulina

Gamma linolenic acid (GLA) is an essential fatty acid and a precursor for the body's prostaglandins. The postaglandin PGE1 is involved in many essential body functions including regulation of blood pressure and cholesterol synthesis. PGE1 is formed usually from linolenic acid after the latter is converted to GLA with the help of the enzyme delta-6-desaturase. It is reported that delta-6-desaturase is easily inhibited by substances common to modern living, including saturated fats and alcohol, thus resulting in GLA deficiency and suppressed PGE1 formation (Tudge, 1981). Clinical studies show dietary intake of GLA can help arthritis (Kunkel, 1982), heart disease (Kernoff, 1977), obesity (Vadaddi & Horrobin, 1979) and zinc deficiency (Huang, 1982). Alcoholism, manic depression, aging symptoms and schizophrenia have also been partially ascribed to GLA deficiency (Horrobin, 1981a & b; Horrobin & Huang, 1983).

Spirulina has a high content of GLA, 1–1.5% of the dry weight, and is the only source of GLA apart from mother's milk and the oil of evening primrose. Some of the effects described in the preceding sections on therapeutic effects of *Spirulina* could be due to the role of GLA just discussed.

Sulfolipid effects and Spirulina

A recent study by the National Cancer Institute in the USA (NCI) has revealed a number of extracts from cyanobacteria (particularly *Lyngbya lagerheimii*, strain DN-7-1, and *Phormidium tenue*, strain CN-2-1) to be remarkably effective against the human immunodeficiency virus (HIV-1) (Gustafson *et al.*, 1989). The active components were found to be the sulfonic acid containing components of glycolipids. Indeed, because of the urgency for the identification and comparative clinical evaluation of new anti-AIDS drugs, the NCI has selected the sulfolipid class as a high priority for further preclinical and subsequent clinical testing (Gustafson *et al.*, 1989).

Spirulina is known to contain glycolipids and sulfolipids (Kataoaka & Misaki, 1983). *Spirulina* contains about 5–8% lipids and of that 40% are glycolipids and 2.5% sulfolipids (Venkataraman & Becker, 1985). A recent analysis of sulfolipids in *Spirulina* in our laboratory has shown that *Spirulina* contains about 1% sulfolipids on a dry-weight basis. Some of the immune enhancement effects of *Spirulina* discussed above may result from sulfolipids.

Iron bioavailability effects and Spirulina

Iron is the most common mineral deficiency in the world. *Spirulina* contains high iron concentrations. Its bioavailability has been tested in comparison to ferrous sulfate which is the typical iron supplement. *Spirulina* fed rats absorbed 60% more iron than rats fed the iron supplement (Johnson & Shubert, 1986).

Discussion

Several therapeutic effects of *Spirulina* have been demonstrated in many animal and a few human studies. Some of the earlier studies are based on very few data sets and thus lack statistical validity. Most of the recent studies on therapeutic effects done on animals must also be demonstrated in humans. They also need more elaboration and confirmation. However, the potential for diverse and significant therapeutic applications is clear and deserves more attention. This is particularly so in the case of therapeutic effects against hyperlipidemia and general enhancement of the immune response. Published as well as unpublished studies have shown significant therapeutic effects of *Spirulina* at very low concentrations in the diet suggesting that the effect may be due to factors other than a mere nutritional one. It remains to be seen whether an active component or a group of active substances could be ascribed to these therapeutic effects.

Systematic screening of algae for bioactive compounds has largely been limited to the examination of marine macrophytes usually for antimicrobial or anti-cancer activities (Hoppe *et al.*, 1979; Noda *et al.*, 1989a, b). Microalgae, particularly cyanobacteria, have received much less attention, largely because of difficulties in collection, mass cultivation and harvesting. Recent developments in large-scale culturing of algae have resulted in greater attention on the search for pharmaceuticals from a diverse group of algae including cyanobacteria (Flores & Wolk, 1986; Cannell *et al.*, 1988; Gustafson *et al.*, 1989; Patterson *et al.*, 1991).

When a substance of significant pharmaceutical properties is found in a plant extract, the active principle is often synthesized for use. Such is, for example, the case with β-carotene which is produced from *Dunaliella* and is also chemically synthesized. Under some circumstances, the active compound may be difficult to synthesize economically. It may thus be necessary to exploit the substance from plant extracts. An example is the extraction of phycocyanin from *Spirulina* for food coloring and for use in immuno-fluorescence studies. In this case the alga from which the extract has to be obtained must pass rigorous screening for toxicity before approval is granted for use. Should useful pharmaceuticals prove to be present, algae such as *Spirulina* have the following advantages over other algae: (a) the technology for mass cultivation and harvest of *Spirulina* is readily available; (b) *Spirulina* has undergone two decades of toxicity testing in addition to its known human use for centuries (Chamorro-Cevalos, 1980; Boudene, 1976); (c) *Spirulina* is sold in many parts of the world as a health food; (d) microbiological and heavy metal standards have been established for *Spirulina* products. Another attractive feature of *Spirulina* is that its rich source of protein may still be exploited after the extraction of the desired pharmaceuticals (Jassby, 1988). These and other considerations may attract more investigation into the therapeutic effects of *Spirulina* in the future. Certainly, its effect on immune response and cancer are worth investigating.

References

Archer DL, Glinsmann WH (1985) Intestinal infection and malnutrition initiate AIDS. Nutrition Research 5: 19.

Becker EW, Jakover B, Luft D, Schmuelling RM (1986) Clinical and biochemical evaluations of the alga *Spirulina* with regard to its application in the treatment of obesity: a double-blind cross-over study. Nutr. Rep. Int. 33: 565–574.

Boudene C (1976) Evaluation of long term toxicity on rats with *Spirulina*. Ann. Nutr. Aliment. 30: 577–588.

Cannell R, Owsianka AM, Walker JM (1988) Results of a large-scale screening programme to detect antibacterial activity from freshwater algae. Br. phycol. J. 23: 41–44.

Chamorro-Cevalos G (1980) Toxicological research on the alga *Spirulina*. UNIDO, UF/MEX/78/048.

Ciferri O, Tiboni O (1985) The biochemistry and industrial potential of *Spirulina*. Ann. Rev. Microbiol. 39: 503–526.

Dainippon Ink & Chemicals (DIC) (1983) Antitumoral agents containing phycobillin. Japanese Patent #58–65216, inventors: N. Iijima, N. Fujii & H. Shimamatsu; assignees: Dainippon Ink & Chemicals & Tokyo Stress Foundation, Apr. 18, 6 pp.

Devi MA, Venkataraman LV (1983) Hypocholestemic effect of bluegreen algae *Spirulina platensis* in albino rats. Nutr. Rep. Int. 28: 519–530.

Flores E, Wolk CP (1986) Production, by filamentous, nitrogen-fixing cyanobacteria, of a bacteriocin and of other antibiotics that kill related strains. Arch. Microbiol. 145: 215–219.

Fukino H, Takagi Y, Yamane Y (1990) Effect of *Spirulina* (*S. platensis*) on the renal toxicity induced by inorganic mercury and cisplatin. Eisei Kagaku 36: 5.

Gustafson KR, Cardellina JH II, Fuller RW, Weislow OS, Kiser RF, Snader KM, Patterson GM, Boyd MR (1989) AIDS-antiviral sulfolipids from cyanobacteria (blue-green algae). J. Natl. Cancer Inst. 81: 1254–1258.

Hayashi O, Inaba Y, Matsunami K, Okuwaki Y, Kato T (1992) Paper presented at the 46th Annual Meeting of The Japanese Society of Nutrition and Food Science, Kurashiki, Japan.

Hoppe HA, Levring T, Tanaka Y, (1979) Marine algae in pharmaceutical science. Walter de Gruyter, Berlin, 807 pp.

Horrobin DF (1981a) The possible roles of prostaglandin E1 and of essential fatty acids in mannia, depression and alcoholism. Progr. Lipids 20: 539–541.

Horrobin DF (1981b) Loss of delta-6-desaturase activity as a key factor in aging. Med. Hypotheses 7: 1211–1220.

Horrobin DF, Huang YS (1983) Schizophrenia: the role of abnormal essential fatty acid and prostaglandin metabolism. Med. Hypotheses 10: 329–336.

Huang YS (1982) Most biological effects of zinc deficiency corrected by GLA. Atherosclerosis 41: 193–208.

Iwata K, Inayama T, Kato T (1987) Effects of *Spirulina platensis* on fructose-induced hyperlipidemia in rats. J. Jap. Soc. Nutr.Food Sci. 40: 463–467.

Iwata K, Inayama T, Kato T (1990) Effects of *Spirulina platensis* on plasma lipoprotein lipase activity in fructose-induced hyperlipidemic rats. J. Nutr. Sci. Vitaminol. 36: 165–171.

Jassby A (1988) *Spirulina*: a model for microalgae as human food. In Lembi C, Waaland JR (eds), Algae and Human Affairs. Cambridge University Press, 149–179.

Johnson P, Shubert LE (1986) Availability of iron to rats from *Spirulina*, a blue-green alga. Nutr. Res. 6: 85-94.

Kataoka N, Misaki A (1983) Glycolipids isolated from *Spirulina maxima*: structure and fatty acid composition. Agric. Biol. Chem. 47: 2349–2355.

Kato T, Takemoto K, Katayama H, Kuwabara Y (1984) Effects of *Spirulina* (*Spirulina platensis*) on dietary hypercholesterolemia in rats. J. Jap. Soc. Nutr. Food Sci. 37: 323–332.

Kernoff PBA (1977) Antithrombotic potential of DGLA in man. Br. Med. J. 2: 1441–1444.

Kunkel SL (1982) Suppression of chronic inflamation by evening primrose oil. Progr. Lipids 20: 885–888.

Nagao K, Takai Y, Ono M (1991) Exercises of growing mice, and the effect of the intake of *Spirulina platensis* upon the hapten-specific immune response. Sci. Phys. Power 40: 187–194.

Nakaya N, Honma Y, Goto Y (1988) Cholesterol lowering effect of *Spirulina* Nutr. Rep. Int. 37: 1329–1337.

Noda H, Amano H, Arashima K, Hashimoto S, Nishizawa K (1989a) Studies on the antitumor activity of marine algae. Nippon Suisan Gakkaishi 55: 1259–1268.

Noda H, Amano H, Arashima K, Hashimoto S, Nishizawa K (1989b) Antitumor activity of polysaccharides and lipids from marine algae. Nippon Suisan Gakkaishi 55: 1265–1271.

Patterson GM, Baldwin CL, Bolis CM, Caplan FR, Karuso H, Larsen LK, Levine IA, Moore RE, Nelson CS, Tschappat KD, Tuang GD, Furusawa E, Furusawa S, Norton TR, Raybourne RB (1991) Antineoplastic activity of cultured blue-green algae (Cyanophyta). J. Phycol. 27: 530–536.

Peto R (1981) Can dietary beta carotene materially reduce human cancer rates? Nature 290: 201–208.

Qishen P, Coleman A, Baojiang G (1989) Radioprotective effect of extract from *Spirulina platensis* in mouse bone marrow cells studied by using the micronucleus test. Toxicology Lett. 48: 165–169.

Schwartz JL, Sklar G (1987) Regression of experimental hamster cancer by beta carotene and algae extracts. J; Oral Maxillorfac. Surg. 45: 510–515.

Schwartz JL, Sklar G, Reid S, Trickler D (1988) Prevention of experimental oral cancer by extracts of *Spirulina-Dunaliella* algae. Nutr. Cancer 11: 127–134.

Shekelle RB (1981) Dietary vitamin A and risk of cancer in the Western Electric Study. Lancet 8257: 1185–1189.

Takai Y, Hosoyamada Y, Kato T (1991) Effect of water-soluble and water insoluble fractions of *Spirulina* over serum lipids and glucose resistance of rats. J. Jap. Soc. Nutr Food Sci. 44: 273–277.

Tsuchihashi N, Watanabe T, Takai Y (1987) Effect of *Spirulina platensis* on caecum content in rats. Bull. Chiba Hygiene College, Chiba, Japa,. 5: 27–30.

Tudge C (1981) Why we could all need the evening primrose. New Scientist 506: 23.

Vadaddi KS, Horrobin DF (1979) Weight loss produced by evening primrose oil administration. IRSC Med. Sci. 7: 52.

Venkataraman LV, Becker EW (1985) Biotechnology and utilization of algae-The Indian experience. Sharada Press, Mangalore, India, 114–115.

Yamane Y, Fukino H, Icho T, Kato T, Shimamatsu H (1988) Effect of *Spirulina* (*Spirulina platensis*) on the renal toxicity induced by inorganic mercury and para-aminophenol. Summary of Abstracts: 108th Annual Conference of the Pharmaceutical Society of Japan, p. 58.