



DAFE'-E-SART'AN (ANTICANCER) ACTIVITY OF T'AH'LAB (SPIRULINA) - A REVIEW

**MD ANZAR ALAM^{*1}, NAFIS HAIDER², SADIQUE HUSAIN³,
SHAMIM AHMAD⁴ AND TANWIR ALAM⁵**

^{*1}PG Scholar, Dept. of Moalajat (Medicine) National Institute of Unani Medicine (NIUM),
Bangalore-560091 India,

²Assistant Professor, Dept. of Pharmacy ITS Paramedical (Pharmacy) College
Murad Nagar, Ghaziabad, U.P., India

³PG Scholar, Dept. of Ilmul Advia (Pharmacology) National Institute of Unani Medicine (NIUM),
Bangalore-560091 India,

⁴PG Scholar, Dept. of Ilmul Advia (Pharmacology) National Institute of Unani Medicine (NIUM),
Bangalore-560091 India,

⁵Assistant Professor, Dept. of Preventive and Social Medicine Allama Iqbal Unani Medical College
(AIUMC) Muzzafarnagar, U.P., India.

ABSTRACT

T'ah'lab (طحلب) is an Arabic word which means a green substance float on the surface of water, commonly known as algae/spirulina. Spirulina is a photosynthetic, filamentous, spiral-shaped, multicellular and green-blue micro alga. There are many species of spirulina, mainly two: *Spirulina maxima* and *Spirulina platensis*, which are used for medicinal purposes. *Spirulina* is painstaking as an excellent food, lacking toxicity. Spirulina has carotenoids, chlorophyll and the unique blue pigment phycocyanin. Phycocyanin can provide admirable health benefits have been identified to include immuno-modulator, anti-oxidant, anti-cancer, anti-obesity, hypoglycaemic, anti-hyperlipidemic, anti-inflammatory, anti-hypertensive, anti-asthmatic, anti-microbial, anti-parasitic and neuro-protective effects. It acts as natural remedy for many ailments for centuries in ancient systems of medicine, e.g. Ayurveda, Unani and Chinese Medicines. After the assessment of literature about spirulina and its medicinal value, it is found that it can treat all ailments except "death". So, it can also be called as *Maddat-ul-hayat/Aab-e-hayat* (elixir of life).

KEY WORDS: *T'ah'lab*, Spirulina, Cancer, *Sartan*, Unani Medicine, C-Phycocyanin.



MD ANZAR ALAM

PG Scholar, Dept. of Moalajat (Medicine) National Institute of
Unani Medicine (NIUM), Bangalore-560091 India

*Corresponding author

INTRODUCTION

Spirulina is a photosynthetic, filamentous, spiral-shaped and multicellular edible microbe. According to Botanists' directory it is -a micro-algae belonging to *Chyanophyceae* class; but according to bacteriologists it is a bacterium, due to its prokaryotic structure. Before Columbus (1492), there is information that it was worn as food in Mexico during the Aztec civilization some 400 years ago. It is the nature's richest and most complete source of nutrition. Spirulina has an inimitable blend of nutrients that no single spring can proffer. The alga contains a wide spectrum of prophylactic and curative nutrients that include B-complex vitamins, minerals, proteins, gamma-linolenic acid and the super anti-oxidants such as β -carotene, vitamin E, trace elements and a number of uncharted bio-active compounds. Because of its perceptible capability to stimulate entire human physiology, spirulina exhibits therapeutic functions such as antioxidant properties were demonstrated as inhibition of lipidperoxidation by its extract,¹ immuno-enhancing effect,² anticancer,³ blood lipid-lowering effect,⁴ anti-diabetic,⁵ antibacterial,⁶ antiviral,⁷ anti-inflammatory,⁸ anti-allergic,⁹ immuno-modulator activity,¹⁰ and plethora of beneficial functions. Spirulina expenses appear to cheer the growth of intestinal microflora as well. Recent studies have indicated that Spirulina has assets of reducing heavy metals and nephrotoxic substances from the body.¹¹ Spirulina is a good probiotic. Probiotics are good for health as they reinforce the immune system to avert disease and cancer. Spirulina's probiotic outcome helps in maintaining healthy microflora thus helps in better digestion, absorption and protection from infection. Studies confirm that this possession is due to its combination and remarkable concentration of nutrients. The name spirulina comes from a Latin word meaning minute spiral. There are numerous species of spirulina. The ones most commonly used in medicinal/nutritional supplements are *Spirulina platensis* and *Spirulina maxima*. In classical text, *T'ah'lab* classified as three types: *Hazazul Maa* (Coiled and separate), *Ghazalul Maa* (Filamentous

and stellate) and *Kharuz Zafade* (Condensed).^{12,13}

Classification of Spirulina (T'ah'lab)

Phylum- Cyanobacteria
Class- Cyanophyceae
Order- Oscillatoriales
Genus- *Spirulina*, *Arthrospira*
Species- *platensis* and *maxima*

Synonymous for Spirulina

Greek- *Oolisoon*
Arabic- *T'ah'lab*,
Hazazul Maa,
Ghazalul Maa,
Kharuz Zafade,
Persian- *Jughraba*, *Pashme waza*
Siryani- *Tahalba*

Nature has always been a good spring for food, drugs. Many of presently available drugs are imitative directly or indirectly from them. The first predictable report on spirulina, dates back to the 16th century CE, it is whispered to have been a nutritional source for the Aztecs and Mesoamericans.¹⁴ It is assured by NASA that the nutritional value of 1000kg of fruits and vegetables equals to 01kg of spirulina. Therefore in long-term space missions NASA (CELSS) and European space agency (MELISSA) projected that spirulina serves as a chief source of food and nutrition.^{15,16} The penalties of malnutrition represent a global problem, which affects morbidity as well as mortality. Increased tissue production of prostaglandin E2 as a result of high intake of linoleic acid in a polyunsaturated fatty acid deficient diet, causes inhibition of the proliferation and cytokine production of Th1 cells, the mediators of cellular immunity,¹⁷ the beneficial possessions of spirulina as a nutritional and dietary supplement casing all major areas of health benefits. Since dyslipidemia, oxidative and inflammatory stresses are measured to be the causal factors for diabetes; spirulina has great swear as a functional food for management of type-2 diabetes.¹⁸ The aqueous extract of spirulina was found to have a major crash on the immune system by increasing the phagocytic

activity of macrophages, stimulating the NK cells. It also played a responsibility in the activation and mobilization of T and B cells due to its stimulatory possessions in the production of cytokines and antibodies.¹⁹ It has been seen to have an inhibitory effect on the release of histamine from mast cells during an allergic inflammatory response.²⁰ Spirulina has been established to recover weight gain and correct anaemia in both HIV-infected and HIV-negative cases.²¹ Spirulina also was reported to decrease blood pressure by promoting vasodilation and restricting vasoconstriction.²² Spirulina contributes to the functional safeguarding of the intestinal epithelium which acts as a first line of mucosal barrier against infections.²³ Spirulina (Blue green algae/*T'ah'lab*) are also used in *Unani* Medicine for the treatment of wound healing, diabetes mellitus, arthritis, stiffness, *sartan* and in hernia.²⁴⁻³⁰ Numerous studies investigating the effectiveness and the impending clinical applications of Spirulina in treating several ailments have been performed and a few randomized controlled trials and systematic reviews suggest that this alga may improve numerous symptoms and may even have an anticancer activity. *Sartan* (cancer) is an *Arabic* word which means crab (cancer). According to *Unani* Medicine, *sartan* is basically disease of black bile i.e. excessive production and collection of *sauda*. The knowledge of *Sartan* (cancer) in the *Unani* system of medicine can be traced to ancient times (131-200 AD).³¹ Cancer is hyper-proliferative disorder that involves transformation, dys-regulation of apoptosis, proliferation, invasion, angiogenesis and metastasis.³² While remaining faithful to Hippocrates's humoral theory, Galen (129-200) extended Hippocrates' definitions of cancer and classified tumours into three major types, (i) *Onkoi* (lumps or masses) (ii) *Karkinomas* (non-ulcerating) cancers & (iii) *Karkinos* (malignant ulcers).^{33,34} According to *Rhazes* (Razi) in his book *Kitab Al-Mansoori* he describes *Sartan* as *maraz-e-muhlik* (fatal disease).³⁵ According to *Ibne-Sina* *sartan* is a *sil'a* (swelling) arising from "burning" of *sauda* (black bile) humor, by burning it is preordained that the increase of instinctive warmth, her become pathological so, *Sartan* mostly occurs in soft tissues (*Aa'zae Ratab*) like breast,

uterus, stomach, intestine, pancreas, prostate, oral cavity & lungs etc.³⁶ On account of the high morbidity and mortality of cancer diseases, problems encountered in their healing and the toxic effects of cancer chemotherapy, an attempt has been made to review the published narratives on the anticancer effects of the moderately safe edible spirulina (*T'ah'lab*). Scientific organizations such as the National Cancer Institute have published guidelines for lowering the risks of all kinds of cancers. Poor diet is associated with 35% of cancer deaths. High-fat, low-fiber diets greatly increase risks of prostate, colon, gland and breast cancer.³⁷ One of the most famous reports was published by The National Research Council in 1982. *Diet, Nutrition and Cancer* concluded that foods rich in β -carotene and Vitamin A reduce cancer risks.³⁸

METHODS

Exploration of published articles associated to spirulina and its active components on cancer was conducted and abstracts or full articles in English were incorporated for the preparation of this review from online basis. For the convenience of the readers, various studies have been categorized as follows: anticancer effects of spirulina, its extracts; anticancer activity of its active principles; studies elucidating the mechanism of action. We have measured for our review in the progression obtained from scientific publications with substantiation based methods and information scrutiny. The databases utilized for obtaining information are scientific research publications from journals indexed/available through PubMed, Scopus, and Google Scholar, Science Direct. Relevant facts were also obtained from general databases such as Google and Classical text from a library source (National Institute of Unani Medicine, Kottigepalya, Magadi Main Road, Bangalore-560091 Karnataka, India).

Active Component

Spirulina contains large amounts of natural β -carotene, phycocyanin, C-phycocyanin (C-PC), Calcium spir-ulan (Ca-SP), Selenium-containing phycocyanin (Se-PC), superoxide

dismutase, catalase, glutathione reductase, glutathione peroxidase.

Mechanisms of Anticancer Effects

C-phycoerythrin (C-PC), a water-soluble, non-toxic fluorescent protein pigment with potent anti-oxidant, immuno-modulator, antiviral, anti-inflammatory and anti-cancer properties isolated from *Spirulina platensis*. It is of great importance because of its various medical and pharmacological properties, which restrained the growth of human leukaemia K562 cells. This type effect of phycoerythrin was at first deliberate following the growth of the K562 cells in semi-solid agar culture at concentrations of 20, 40, 80, and 160 mg-1. The results showed that phycoerythrin inhibited the growth of the K562 leukaemia cells in a dose-dependent approach with statistically significant inhibition pragmatic at 80 and 160 mg-1. The effect of phycoerythrin was further studied using cell viability measurement using XTT dye reduction assay. Phycoerythrin was again found to inhibit cell viability in a dose-and time-dependent manner. The IC50 value of C-PC was found to be 72.5 mg-1. Furthermore, flow cytometric assay based on DNA content analysis revealed that accumulation of K562 cells occurred in the G-1 phase when cells were incubated in C-PC for 6 days. There were higher percentages of cells in the G-1 phase at phycoerythrin concentrations of 40 and 80 mg-1. DNA fragment analysis did not show the ladder formation typically observed in apoptosis, indicating that a different mechanism may be at play in the inhibition process.³⁹ Calcium spirulan (Ca-SP), a novel polysaccharide isolated from *Spirulina platensis* which inhibits the tumour invasion and metastasis. Seven intermittent iv injections of 100 µg of Ca-SP in mice caused a marked decrease of lung tumor colonization of B-16-BL6 cells in a spontaneous lung metastasis model.⁴⁰ It is reported that polysaccharides of *Spirulina platensis* enhance the endonuclease activity and repair DNA. This result indicates that the presence of the extract significantly enhanced both the repair activity of radiation-damaged DNA excision and the unscheduled DNA synthesis.⁴¹ *Spirulina platensis* extract significantly reduces the micronucleus frequencies induced by gamma-radiation in mouse bone marrow cells.⁴² First time study

on human for the effect of Spirulina on oral leukoplakia (a pre cancerous lesion) in pan-tobacco chewers in Kerala, India. For this study 44 subjects are involving, in the intrusion group and 43 in the placebo group, they found that supplementation with Spirulina at 1 g/day for 1 year resulted in entire regression of lesions in 45% of the intrusion group and 7% in the control group.⁴³ Algae-derived phycoerythrin had a cytostatic and cytotoxic activity against squamous cell carcinoma (human or ham-ster).²² Polysaccharide extract of Spirulina inhibited the proliferation of ascitic hepatoma cells of mice and also decrease the tumour progression when injected at a dose of 200 mg/kg.⁴⁴ Selenium-containing phycoerythrin (Se-PC) of *Spirulina platensis* have been reported to show potent cancer chemo-preventive activities.⁴⁵ C-phycoerythrin induce the activation of pro-apoptotic gene and down regulation of anti-apoptotic gene expression and then facilitate the transduction of tumoural apoptosis signals that resulted in the apoptosis of HeLa cells in vitro.⁴⁶ β-carotene of spirulina may converted into vitamin-A. According to the findings of the National Cancer Institute, United States of America, an intake of 6.0 mg β-carotene daily may be effective in minimizing the risk of cancer. The regulatory effect of phycoerythrin (PC) from *Spirulina platensis* was investigated on cluster of differentiation 59 (CD59) gene expressions of HeLa cells and anti-tumoural mechanism.⁴⁷ It is found to be significantly decrease in multiplication of human chronic myeloid leukaemia cell line (K562) after the use of C-phycoerythrin.⁴⁸ Inhibition activity of *spirulina platensis* proteins photo-immobilization biomaterial on proliferation of cancer cells.⁴⁹ β-carotene reduces the oral Submucous fibrosis.⁵⁰ Spirulina in the Management of Erosive Oral Lichen Planus.⁵¹ protection against radiation induced damage,⁵² phycoerythrin significant decrease dehydrogenase activity in rats after post radiation,⁵³ C-phycoerythrin induces apoptosis in the doxorubicin resistant human hepatocellular-carcinoma cell line HepG2,⁵⁴ Spirulina fusiformis was observed on the hepatic and extra hepatic carcinogen metabolizing enzymes in Swiss albino mice at a dose of 800 mg/kg b.w. given orally.⁵⁵

Polysaccharide of spirulina has chemo-protective and radio-protective capability, and may be a potential adjunct to cancer therapy.⁵⁶ Chemo-modulation of carcinogen metabolising enzymes, antioxidant profiles, skin and forestomach papilloma genesis by *Spirulina platensis*,⁵⁷ spirulina extract significant reduction of the micronucleus frequencies induced by gamma-radiation.⁵⁸ Oral administration of hot-water extract of *Spirulina*, cyanobacterium *Spirulina platensis*, leads to augmentation of NK cytotoxicity in humans.⁵⁹ *S. platensis* extract has a beneficial role in regression of cancer progression,⁶⁰ anti-mutagenic effects of *Spirulina* is reported on male and female mice,⁶¹ polysaccharide of spirulina enhances hematopoietic cell proliferation and inhibits its apoptosis in mice bearing tumour treated with chemotherapy,⁶² spirulina have capable to inhibit carcinogenesis due to anti-oxidant properties that protect tissues and also reduce toxicity of liver, kidney and testes,⁶³ *S. platensis* is an adjunctive means to inhibit the dysplastic changes occurring in the hamster cheek pouch mucosa.⁶⁴

CONCLUSION

Nowadays Tahlab is being used as a healing agent due to its immuno-modulator, anti-oxidant, anti-cancer properties and its capability to reinforce the immune system.

REFERENCES

1. Benedetti S, Benvenuti F, Pagliarani S, Francogli S, Scoglio S, Canestrari F. Antioxidant properties of a novel phycocyanin extract from the blue-green alga *Aphanizomenon flos-aquae*. *Life Sci* 75:2353-2362, (2004).
2. Hayashi O, Katoh T, Okuwaki Y. Enhancement of antibody production in mice by dietary *Spirulina platensis*. *J Nutr Sci Vitaminol* 40:431-441, (1994).
3. Babu ML. Evaluation of chemoprevention of oral cancer with *Spirulina fusiformis*. *Nutr Cancer* 24:197-202, (1995).
4. Raziq Anwer, Anzar Alam, Saima Khursheed, Shaikh Mohd. Kashif, Hifzul Kabir, Tasneem Fatma. *Spirulina*: possible pharmacological evaluation for *insulin*-like protein. *J Apl Phycol* 25(3):883-889, (2013).
5. Anzar M.A Shamim A, Nafis H, Tanwir M.A. Drugs Indicated for The Management of Ziaabetes Shakri (Diabetes Mellitus) in Unani Medicine – An Overview. *International Journal of Pharmamedix India* 1(3):460-74, (2013).
6. Isobe K, Hayashi O, Hirahashi T, Katoh T, Okuwaki Y. Bactericidal activity of mouse macrophages stimulated with *Spirulina* extracts. *J Kagawa Nutr* 26:61-66, (1995).
7. Gustafson KR, Cardellina JH II, Fuller RW, Weslow OS, Kiser RF, Snader KM.

Tahlab is known to recover hunger and Vitamin A status in children and in pregnant women correspondingly. It has ability to decrease blood sugar levels in diabetes patients, have advantageous possessions on patients anguish from hepatitis, pancreatitis, and cirrhosis of liver, can supportive in cataracts and glaucoma, gastric ulcers, circulation disorders and in controlling anaemia and night blindness. It has high contents of essential poly unsaturated fatty acids and is helpful in lowering cholesterol level in serum and liver, thus making it an effective ingredient in formulations for those patients who are suffering from heart problem. It is hoped that this reassess critique would be a spring of support and guidance for the fascinated investigators to demeanour further preclinical and clinical studies on the use of spirulina for the healing of cancer. In cancer research, the use of complementary and alternative medicine has increased over the past decade.

ACKNOWLEDGMENT

The authors wish to express sincere thanks to all the contributors. Special thanks go to Dr. Abdul Azeez, Lecturer, Department of Regimenal Therapy and for their supervision and suggestion throughout the course of shaping this article. There is no conflict of interest.

- AIDS-antiviral sulfolipids from cyanobacteria (blue green algae). *J Natl Cancer Inst* 81:1254-1258, (1989).
8. Romay C, Ledon N, Gonzalez R, Further studies on anti-inflammatory activity of phycocyanin in some animal models of inflammation. *Inflamm Res* 334-338, (1998).
 9. Kim H, Lee E, Cho H, Moon Y. Inhibitory effect of mast cell mediated immediate-type allergic reactions in rats by *Spirulina*. *Biochem Pharmacol* 55:1071-1076, (1998).
 10. Rasool M, Sabina EP, Appraisal of immuno modulatory potential of *Spirulina fusiformis*: an in vivo and in vitro study. *Nat Med (Tokyo)* 63(2):169-75, (2009).
 11. Yamane Y, Fukino H, Icho T, Kato T, Shimamatsu H, Effect of *Spirulina (Spirulina platensis)* on the renal toxicity induced by inorganic mercury and para-aminophenol. *Summary of Abstracts. 108th Conference of the Pharmaceutical Society of Japan*, 58, (1998).
 12. Momin HM. Tohfatul Momineen. (Persian). Dar Matba Hasni; 170, (1272).
 13. Ghani HN, Khazainul Advia. (Urdu). New Delhi: Published by Idara Kitab-Us-Shifa; 1014-1015, (2010).
 14. Diaz DCB. *The Discovery and Conquest of Mexico* London: Routledge; 1517-1521, (1928).
 15. Characterization of *Spirulina* biomass for CELSS diet potential. Normal, Al.: Alabama A&M University. (1988).
 16. Cornet JF, Dubertret G, The cyanobacterium *Spirulina* in the photosynthetic compartment of the MELISSA artificial ecosystem. Workshop on artificial ecological systems. France: Marseille, DARA-CNES. (1990).
 17. Sammon AM, Dietary Linoleic acid, immune inhibition and disease. *Postgrad Med J* 75(881):129-132, (1999).
 18. Eun HL, Ji-Eun P, Young-Ju C, Kap-Bum H, Wha-Young K. A randomized study to establish the effects of spirulina in type 2 diabetes mellitus patients. *Nut Res Practice* 2(4):295-300, (2008).
 19. Schwartz J, Shklar G, Regression of experimental hamster cancer by beta carotene and algae extracts. *J Oral Maxillofac Surg* 45(6):510-515, (1987).
 20. Subhashini J, Mahipal SV, Reddy MC, Mallikarjuna R M, Rachamalla A, Reddanna P. Molecular mechanisms in C-Phycocyanin induced apoptosis in human chronic myeloid leukaemia cell line-K562. *Biochem Pharmacol*, 68(3):453-462,(2004).
 21. Chen T, Wong YS. In vitro antioxidant and antiproliferative activities of selenium-containing phycocyanin from selenium-enriched *Spirulina platensis*. *J Agric Food Chem* 25;56(12):4352-4358, (2008).
 22. Schwartz J, Shklar G, Reid S, Trickler D. Prevention of experimental oral cancer by extracts of *Spirulina-Dunaliella* algae. *Nutr Cancer* 11(2):127-134, (1988).
 23. Shklar G, Schwartz J, Tumor necrosis factor in experimental cancer regression with alphasatocopherol, beta-carotene, canthaxanthin and algae extract. *Eur J Cancer Clin Oncol* (1988).
 24. Ibn-Sina. *Al-Qanoon Fit tib*, Urdu translated by Hkm. Ghulam Hussain Kantoori. Published by New Delhi: Idara Kitab-Us-Shifa; 2:354.(5):839-850, (2012).
 25. Ibn-Baitar. *Al-Jame' le Mufradat Al-Advia wa Al-Aghzia* (Urdu). New Delhi: Central Council for Research in Unani Medicine. Ministry of Health & Family Welfare. Govt. of India; 3:215-216, (1999).
 26. Baghdadi IH, *Al-Mukhtarat Fit tib* (Urdu). New Delhi: Central Council for Research in Unani Medicine. Ministry of Health & Family Welfare. Govt. of India; 2:161, (2005).
 27. Razi ABMZ, *Kitab Al-Havi fit Tib* (Urdu). New Delhi: Central Council for Research in Unani Medicine. Ministry of Health & Family Welfare. Govt. of India; 21:95, (2007).
 28. Khan MA, *Al-Ikseer* (Urdu). New Delhi: Aijaz Publishing House; 2:1197,(2003).
 29. Ibn Rushd, *Kitab Al-Kulliyat* (Urdu). New Delhi: Central Council for Research in Unani Medicine. Ministry of Health & Family Welfare. Govt. of India; 307,(1987).
 30. Maghrabi ASI, *Kitab Al-Fath Fi Al-Tadawi* (Urdu Translation by Hkm. Abdul Bari). Delhi: Published by NCPD Printers; 122-123, (2007).

31. Vohra SB. Sattan (cancer) and its treatment in Unani Medicine. The American Journal of Chinese Medicine (1981).
32. Singh N, Verma P, Pandey BR, Gilca M. Role of *Withania somnifera* in Prevention and Treatment of Cancer: An Overview. International Journal of Pharmaceutical Sciences and Drug Research 3(4): 274-279,(2011).
33. Margaret MO. Concepts of Cancer from Antiquity to the Nineteenth Century. UTMJ 87(30), (2010).
34. Weiss L. Early concepts of cancer. Cancer Metast Rev 19(3-4):215-217, (2000).
35. Razi ABMZ. *Kitab Al-Mansoori* (Urdu Translation by CCRUM). New Delhi: Central Council for Research in Unani Medicine, Ministry of Health & Family Welfare. Govt. of India; 266-267,(1991).
36. Ibn-Sina. *Al-Qanoon Fit Tib* (Urdu translation, by Hkm. Ghulam Hussain Kantoori). New Delhi: Idara Kitab-Us-Shifa; 4:1278-1280, (2010).
37. Mckenna, Jeffrey, Shea, John. Americans are beginning to get NCI's cancer prevention message. FDA Consumer 22, (1988).
38. National Research Council. Diet, Nutrition and Cancer. National Academy Press, Washington DC; (1982).
39. Liu Y, Xu L, Cheng N, Lin L, Zhang C. Inhibitory effect of phycocyanin from *Spirulina platensis* on the growth of human leukaemia K562 cells. J Appl Phycol 12:125-130,(2000).
40. Mishima T. Inhibition of tumour invasion and metastasis by calcium spirulan (Ca-SP), a novel sulphated poly saccharide derived from a blue-green alga, *Spirulina platensis*. Clin Exp Metastasis 16:541-550,(1998).
41. Qishen P, Baojiang G, Rhong R. Enhancement of endonuclease activity and repair of DNA synthesis by polysaccharide of *Spirulina platensis*. Chinese Genetics Journal (Acta Genetica Sinica) 15:33374-33381, (1988).
42. Qishen P, Baojiang G, Kolman A. Radioprotective effect of extract from *Spirulina platensis* in mouse bone marrow cells studied by using the micronucleus test. Toxicol Letters 48:165-169, (1989).
43. Mathew B. Evaluation of chemoprevention of oral cancer with *Spirulina fusiformis*. Nutr Cancer 24:197-202,(1995).
44. Lisheng L. Inhibitive effect and mechanism of polysaccharide of *Spirulina platensis* on transplanted tumour in mice. Marine Sciences 5:33-38,(1991).
45. Chen T, Wong YS. In vitro antioxidant and antiproliferative activities of seleniumcontaining phycocyanin from selenium-enriched *Spirulina platensis*. J Agric Food Chem 25;56(12):4352-8,(2008).
46. Li B, Gao MH, Zhang XC, Chu XM. Molecular immune mechanism of C-phycocyanin from *Spirulina platensis* induces apoptosis in HeLa cells in vitro. Biotechnol Appl Biochem 43(3):155-64,(2006).
47. Li B, Zhang X, Gao M, Chu X. Effects of CD59 on antitumoral activities of phycocyanin from *Spirulina platensis*. Biomed Pharmacother 59(10):551-60,(2005).
48. Subhashini J. Molecular mechanisms in C-Phycocyanin induced apoptosis in human chronic myeloid leukaemia cell line-K562. Biochem Pharmacol 68(3):453-62,(2004).
49. Guan Y, Guo B. Inhibition activity of spirulina platensis proteins photoimmobilization biomaterial on proliferation of cancer cells. Sheng Wu Yi Xue Gong Cheng Xue Za Zhi 19(1):1-3, (2002).
50. IPE Varghese, Hari S. Role of Beta-carotene in the management of Oral Submucous Fibrosis. 27th Kerala State Dental Conference. (1994).
51. IPE Varghese, Hari S, Joseph PA, Jayashree K. Effect of Spirulina in the Management of Erosive Oral Lichen Planus – A Preliminary Study. Indian Journal of Clinical Practice 8(8), (1998).
52. Chen B, Zhou XC. Protective effect of natural dietary antioxidants on space radiation induced damages. Space Med Med Eng (Beijing) 514-8, (2003).

53. Karpov LM, Brown II, Poltavtseva NV, Ershova ON, Karakis SG, Vasil'eva TV, *et al.* The postradiation use of vitamin-containing complexes and a phycocyanin extract in a radiation lesion in rats. *Radiats Biol Radioecol* 40(3):310-4, (2000).
54. Roy KR, Arunasree KM, Reddy NP, Dheeraj B, Reddy GV, Reddanna P. Alteration of mitochondrial membrane potential by *Spirulina platensis* C-phycocyanin induces apoptosis in the doxorubicinresistant human hepatocellular-carcinoma cell line HepG2. *Biotechnol Appl Biochem* 47(3):159-67, (2007).
55. Mittal A, Kumar PV, Banerjee S, Rao AR, Kumar A. Modulatory potential of *Spirulina fusiformis* on carcinogen metabolizing enzymes in Swiss albino mice. *Phytother Res* 13(2):111-4, (1999).
56. Zhang HQ, Lin AP, Sun Y, Deng YM. Chemo- and radio-protective effects of polysaccharide of *Spirulina platensis* on hemopoietic system of mice and dogs. *Acta Pharmacol Sin* 22(12):1121-4, (2001).
57. Dasgupta T, Banejee S, Yadav PK, Rao AR. Chemomodulation of carcinogen metabolising enzymes, antioxidant profiles and skin and forestomach papillomagenesis by *Spirulina platensis*. *Mol Cell Biochem* 226(1-2):27-38, (2001).
58. Qishen P, Guo BJ, Kolman A. Radioprotective effect of extract from *Spirulina platensis* in mouse bone marrow cells studied by using the micronucleus test. *Toxicol Lett* 48(2):165-9, (1989).
59. Akao Y, Ebihara T, Masuda H, Saeki Y, Akazawa T, Hazeki K, *et al.* Enhancement of antitumor natural killer cell activation by orally administered *Spirulina* extract in mice. *Cancer Sci* (2009).
60. Grawish ME, Zaher AR, Gaafar AI, Nasif WA. Long-term effect of *Spirulina platensis* extract on DMBA-induced hamster buccal pouch carcinogenesis (immunohistochemical study). *Med Oncol* (2009).
61. Chamorro-Cevallos G, Garduño-Siciliano L, Barrón BL, Madrigal-Bujaidar E, Cruz-Vega DE, Pages N. Chemoprotective effect of *Spirulina* (*Arthrospira*) against cyclophosphamide-induced mutagenicity in mice. *Food Chem Toxicol* 46(2):567-74,(2008).
62. Liu XM, Zhang HQ. Effect of polysaccharide from *Spirulina platensis* on hematopoietic cells proliferation, apoptosis and Bcl-2 expression in mice bearingtumor treated with chemotherapy. *Yao Xue Xue Bao* 37(8):616-20, (2002).
63. Khan Z, Bhadouria P, Bisen PS. Nutritional and therapeutic potential of *Spirulina*. *Curr Pharm Biotechnol* 6(5):373-9, (2005).
64. Grawish ME. Effects of *Spirulina platensis* extract on Syrian hamster cheek pouch mucosa painted with 7,12-dimethylbenz[a]anthracene. *Oral Oncol* 44(10):956-62, (2008).