An Overview on Benefits of Chlorella vulgaris Products

Yasmin Alaidy Elsaeed Mohammed, Nermien Attia Abd elmoniem Ibrahim, Eman Ahmed Alaa Eldin, Heba Osama Mohammed Helmy, Marwa AbdEl-Moniem Amer Gad

Forensic Medicine and Clinical Toxicology Department, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Yasmin Alaidy Elsaeed Mohammed

Email: yasminelaidy2015@gmail.com

Abstract:

Microalgae are an assorted group of both single-celled and multiple-celled microorganisms which have survived all sorts of harsh environmental conditions to become the oldest surviving organisms on earth. They have been used to provide nutrition to humans and animals for centuries. Chlorella is one such single-celled algae which have huge nutritional value as it is enriched with proteins, minerals, lipids, etc. The focus on Chlorella as a nutritional source has increased just a few decades back as research proved that chlorella has a range of health benefits-ranging from hypertension to fibromyalgia. The market of chlorella is bound to increase in the years to come as more and more people become aware of its health benefits.

Keywords: Chlorella vulgaris,Microalgae, Nutrition.

TobRegul Sci. ™ 2023; 9(1): 8184 - 8192

DOI: doi.org/10.18001 /TRS.9.1.579

Introduction:

Previous studies reported that chlorellin, amixture of fatty acids from Chlorella vulgaris showed inhibitory activity against both Gram-positive and Gram-negative bacteria **(1).** Linolenic acid in ethanolic extracts of Chlorella vulgaris also exhibited antibacterial activity against Staphylococcus aureus (a common cause of skin infections) and Salmonella typhi the causative agent for typhoid or enteric fever in humans. This property enables Chlorella vulgaris to be used as a natural antibiotic as a promising alternative to the conventional synthetic drugs with a broader spectrum of activities against pathogenic infections **(2).** Microalgae secrete certain compounds that inhibit viral attachment and bacterial growth **(3).**

Polysaccharides in Chlorella vulgaris also display other health-promoting effects, such as antitumor, antiviral and potent immunomodulation, indicating the potential for medical uses **(4).** β-1,3-glucan, one of the most important polysaccharides found in Chlorella vulgaris, has been gaining popularity in recent years due to its dietary qualities and therapeutic values in enhancing human health such as free radicals scavenging and reduction of blood lipids **(5).**

Studies showed that chlorophyll has tissue-stimulating properties and was found to accelerate wound healing. As chlorophyll has a similar chemical composition and structure to hemoglobin, involved in oxygen and CO2 interchange, thus aiding the healing process through good oxygenation **(6).** Similarly, the tissue stimulating properties of Chlorella vulgaris also have

immense potential in cosmetic and skin care products, as the extract was found to stimulate the production of skin collagen, reducing wrinkles and slowing down the ageing process **(7).** Extracellular polysaccharides produced by chlorella vulgaris caused significant antitussive effect, anti-inflammatory and bronchodilator in test animals, also seem to be an effective agent to prevent chronic inflammation of the airway, which is the predominant symptom of certain respiratory diseases including bronchial asthma **(8).**

Benefits of Chlorella Products:

Cardiovascular effects:

Elevated total cholesterol and triglycerides and abnormal metabolism of lipoproteins and apolipoproteins are responsible for an increased risk of cardiovascular disease.Chlorella supplementation decreases serum cholesterol levels in model animals **(9, 10).**

Shibata et al. (11) reported that the indigestible fraction of Chlorella possesses hypercholesteromic activity, which improves cholesterol catabolism via the upregulation of hepatic cholesterol 7α-hydroxylase expression**.**

Chlorella administration resulted in marked changes in total cholesterol, triglycerides, lutein, zeaxanthin, and α-carotene levels as well as asignificant decrease in very low-density lipoprotein, cholesterol, apolipoprotein B, and high-density lipoprotein/triglyceride levelsin hyperlipemia and mild hypercholesterolemic patients in a small, open-label trial **(12).**

Studies were investigated the effects of dried Chlorella powder on blood pressure, cerebral stroke lesions, and the life span of a stroke-prone spontaneously hypertensive (SHRSP) rat model. In SHRSP rats fed Chlorella (5%, 10% and 20%) for 13 weeks, elevated blood pressure significantly decreased in the10% and 20% Chlorella groups compared with the untreated controls **(13).**

Arterial stiffness is a well-established risk factor of cardiovascular disease **(14).** Previous studies have reported that antioxidants, potassium and n-3 unsaturated fatty acids decrease arterial stiffness **(15).** Nitric oxide (NO), derived from arginine in the vascular endothelium is an important modulator of arterial stiffness **(16).**

Chlorella products contain antioxidants, vitamins, potassium, arginine and n-3 unsaturated fatty acids. TheefficacyofChlorellasupplementationinreducingcardiovascularriskfactorswasassessedin a meta-analysisof19randomizedcontrolledtrialsincluding797subjects. This study concluded that Chlorella supplementation improves total cholesterol levels, low-density lipoprotein, systolic blood pressure, diastolic blood pressure and fasting blood glucose levels **(17).**

Antidiabetic effect:

Chlorella supplementation improves glycemic control in obesity and diabetes via the activation of protein kinase B phosphorylation in skeletal muscle which increase the expression of glucose transporter 4 leading to decrease insulin resistance. Chlorella supplementation combined with aerobic exercise training showed more pronounced effects on the improvement

of glycemic control via increased activation of muscle phosphorylation signaling in type 2-diabetic rats **(18).**

Oral administration of Chlorella 60 min before glucose administration (0.5 g/kg body weight) resulted in a transient hypoglycemic effect at 90 min after glucose administration without an increase in insulin secretion. Chlorella supplementation increased 2-deoxyglucose uptake in the liver and soleus muscles of streptozotocin-treated mice and was likely the cause of the observed hypoglycemic effects **(19).**

Chlorella supplementation is beneficial for preventing diabetes complications such as cataracts by feeding a diet containing 7.3% (w/w) Chlorella powder to11-week old rats with streptozotocin-induced diabetes, possibly due to the activity of its antioxidant compounds **(20).**

Antioxidant effect:

Microalgae have powerful antioxidant properties, which could be due to interactions of several biomolecules with various antioxidant capabilities. Chlorella vulgaris is one of the microalgae with the highest antioxidant activity **(3, 21).**

Bioactive compounds from phenolic origin and carotenoids could be the possible biomolecules that account for antioxidant and radical scavenging activities of microalgae **(21, 22** (GSH) **(23).** Chlorella exhibit a better lipid peroxidation inhibitory activity than glutathione **(24).** Chlorella vulgaris enhances vitamin C and E concentrations in hepato-pancrease as well as muscle tissues **(25).**

Chlorella aqueous extract containing substantial amounts of antioxidants also exhibit anti proliferative activity in human hepatoma cells **(26).** Chlorella vulgaris hot-water extract and acetone extract are reported to have antitumor activity **(27).** Lipophilic pigments, including carotenoids, antherxanthin, zeaxanthin, and lutein, extracted from Chlorella cells were observed to significantly inhibit the growth of human colon cancer cells **(28).** Chlorella supplementation can modulate immunomyelopoietic activity and disengage tumor-induced suppression of various cytokines and related cell activities in tumor-bearing mice **(29).**

Alzheimer's disease is a severe neurodegenerative condition affecting humans, the erythrocytes of Alzheimer's disease patients are known to be in an excessively oxidized state **(30).** Alpha- Tocopherol and carotenoids such as lutein are important lipophilic antioxidants in human erythrocytes **(31).** Erythrocyte lutein levels were found to be significantly lower in Alzheimer's disease patients than in normal subjects **(32).** Chlorella supplementation maintaining the normal function of erythrocytes and has beneficial effects on Alzheimer's disease-related dementia in humans as chlorella products contain substantial amounts of lutein (approximately 200 mg/100 g dry weigh). So, Chlorella improving and maintaining erythrocyte antioxidant status and lutein levels in humans **(33).**

Major depressive disorder is a widespread mental disorder that greatly impairs the quality of life of humans. Approximately 12% of people experience at least one episode of depression during their lifetime **(34).** The therapeutic effect of dried Chlorella vulgaris extract administration (1.8 g/day) for six weeks was evaluated in patients with major depressive disorder, after treatment, the participants exhibited improvements in physical and cognitive symptoms of

depression **(35).** As oxidative stress is an important pathophysiological mechanism underlying major depressive disorder, major depressive disorder has been effectively reversed via antioxidant therapy **(36).** These observations suggest that the therapeutic effectiveness of Chlorella supplementation may result from the action of its antioxidant nutrients and compounds **(37).**

Hepatoprotective effect:

Studies indicate that Chlorella extract has a protective effect on carbon tetrachloride-induced acute hepatic injury in mice, presumably due to the inhibition of carbon tetrachloride-induced cytochrome P450 activation and the activation of antioxidant enzymes and free radical scavengers **(38).**

Non-alcoholic fatty liver disease (NAFLD) is a group of metabolic disorders that involving abnormal fat accumulation of more than 5–10% in hepatocytes, it affects 10–35% of the world population **(39).** It includes steatosis, non-alcoholic steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma **(40).** Chlorella supplementation have beneficial effects on reducing weight and serum glucose levels and improving inflammatory biomarkers as well as liver function in NAFLD patients **(41).**

Detoxification effect:

Chlorella has long been associated with detoxification of toxic heavy metals. It binds and eliminates different radioisotopes of strontium, technetium, uranium, cobalt and thalium. Chlorella vulgaris can remove toxic metals from the body due to its adsorption properties **(42).**

Dioxins are a group of polychlorinated dibenzo-p-dioxin and dibenzofuran-related compounds that are industrial contaminants and ubiquitous environmental pollutants **(43).** These compounds are easily absorbed in the mammalian gastrointestinal tract and then stored in the liver, adipose tissue, and breast milk due to their lipophilic properties **(44).**Chlorella supplementation significantly inhibited the gastrointestinal absorption of dioxins (approximately 2–53% decrease), indicating that Chlorella supplementation might be useful in promoting dioxin excretion **(45).**

Heterocyclic amines have been established as carcinogenic chemicals that form when amino acids, sugars, and creatine in muscle meats (beef, pork, fish, and poultry) react with one another during cooking at high temperatures **(46).** Chlorella supplementation decreased urinary excretion of the predominant metabolite of carcinogenic heterocyclic amines, suggesting that Chlorella either inhibits the intestinal absorption of heterocyclic amines or inactivates carcinogenic compounds **(47).**

Methyl mercury is a neurotoxic metal compound that is converted from inorganic mercury by microorganisms in aquatic environments and is then accumulated in fish and shellfish through marine food chains. So, the major route of human exposure to methyl mercury is the consumption of sea food. Chlorella consumption is reported to increase the excretion of methyl mercury and lower tissue mercury levels in methyl mercury-treated mice **(48, 49).** As well as lowering of hair and blood mercury levels in Chlorella-treated participants may result from the

promotion of fecal methyl mercury excretion via accelerated bile secretion, the binding of methyl mercury to dietary fiber in the intestinal tract and increased feces production **(50).**

Immunomodulatory effect:

Allergic disease is a prevalent aberrant immune responsive against innocuous environmental proteins (antigens) **(51).** Chlorella hot-water extract supplementation useful for suppressing allergic responses with a predominant type 2 helper T-cell response **(52).**

Chlorella supplementation increases salivary immunoglobulin-A secretion and improves mucosal immune function in humans **(53).** Chlorella supplementation increases natural killer cell activity, produces interferon-γ, interleukin-12, and interleukin-1β, in a randomized, double-blinded, placebo-controlled trial conducted in healthy adults ingested with Chlorella vulgaris (5 g/day) or placebo **(54).**

Stress is well known to disturb homeostasis and impaired immunological functions. Chlorella supplementation reportedly stimulates the pool of hematopoietic stem cells and activates leukocytes. Also Chlorella supplementation is an effective tool for the prophylaxis of myelo suppression caused by single or repeated stressors **(55).**

Chlorella supplementation produced a significant reduction in stress-related hypothalamic–pituitary–adrenal axis activation due to decreased corticotrophin releasing factor gene expression in the hypothalamic paraventricular nucleus and a lower adrenocorticotropic hormone response. The hyperglycemia induced by the stressor was similarly reduced **(56).**

Safety:

Foods derived from microalgae are included in the definition of novel foods in the novel food regulation (NFR) **(57).**

Several microalgae including Chlorella vulgaris are commercialized and used mainly as nutritional supplements for both terrestrial and aquatic animals **(2).**

Many researchers found that the levels of heavy metals in Chlorella vulgaris does not exceed the maximum levels as established in their jurisprudence.There are no indications of significant adverse effects related to Chlorella vulgaris consumption, therefore Chlorella vulgaris is generally recognized as safe **(58).**

The safety of consuming the microalga and its products is generally considered safe if cultivated in a proper way and non-contaminated environment **(59).**

References:

1. Mostafa, S. M. S. (2012): Microalgal biotechnology: Prospects and applications. In D. Nabin Kumar (Ed.), Plant Science (pp. 275–314). London, UK: IntechOpen Ltd.
2. Ahmad, M. T., Shariff, M., Yusoff, F. M., Goh, Y. M., and Banerjee, S. (2020): Applications of microalga Chlorella vulgaris in aquaculture. Reviews in Aquaculture, 1, 1 –19.

3. Guedes, A.C., Sousa-Pinto, I.and Malcata, F.X. (2015): Application of microalgae protein to aquafeed. In: Kim S (ed), Handbook of Marine Microalgae Biotechnology Advances, 2015th edn, pp. 93–125. Elsevier Academic Press, Oxford, UK.
4. Tabarsa, M., Shin, I. S., Lee, J. H., Surayot, U., Park, W., and You, S. (2015): An immune-enhancing water-soluble αglucanfrom Chlorella vulgaris and structural characteristics. Food Science and Biotechnology, 24, 1933–1941.
5. Safi, C., Zebib, B., Merah, O. and Pontalier, P. (2014); Morphology, composition, production, processing and applications of Chlorella vulgaris: A review. Renewable and Sustainable Energy Reviews, 35, 265–278.
6. Ferruzzi, M. G., and Blakeslee, J. (2007): Digestion, absorption, and cancer preventive activity of dietary chlorophyll derivatives. Nutrition Research, 27, 1 –12.
7. Ru, I. T. K., Sung, Y. Y., Jusoh, M., Abdul Wahid, M. E. and Nagappan, T. (2020): Chlorella vulgaris: a perspective on its potential for combining high biomass with high value bioproducts, Applied Phycology, 1:1, 2-11.
8. El-Naggar, N. E., Hussein, M. H., Dessuuki, S. A. S. and Dalal, S. R. (2020): Production, extraction and characterization of chlorella vulgaris soluble polysaccharides and their applications in AgNPs biosynthesis and biostimulation of plant growth. Sci. Rep; 10:3011.
9. Cherng, J.Y., Shih, M.F. (2005): Preventing dyslipidemia by Chlorella pyrenoidosa in rats and hamsters after chronic high fat diet treatment. Life Sci. 76, 3001–3013.
10. Mora, S., Otvos, J.D., Rifai, N., Rosenson, R.S., Buring, J.E. and Ridker, P.M. (2009): Lipoprotein particle profiles by nuclear magnetic resonance compared with standard lipids and apolipoproteins in predicting incident cardiovascular disease in women. Circulation, 119, 931–939.
11. Shibata, S., Hayakawa, K., Egashira, Y. and Sanada, H. (2007): Hypocholesteromic mechanism of Chlorella: Chlorella and its indigestible fraction enhance hepatic cholesterol catabolism through up-regulation of cholesterol 7α-hydroxylase in rats. Biosci. Biotechnol. Biochem. 71, 916–925.
12. Ryu, N.H., Lim, Y., Park, J.E., Kim, J., Kim, J.Y., Kwon, S.W. and Kwon, O. (2014): Impact of daily Chlorella consumption on serum lipid and carotenoid profiles in mild hypercholesterolemic adults: A double-blinded, randomized, placebo-controlled study. Nutr. J. 13, 57.
13. McFarlane, S.I., Jean-Lours, G., Zizi, F., Whaley-Connel, A.T., Ogedegbe, O., Nakaryus, A.N. and Maraj, I. (2012): Hypertension in the high-cardiovascular-risk populations. Int. J. Hypertens. 746369.
14. Vlachopoulos, C., Aznaouridis, K., Terentes-Printzios, D., Ioakeimidis, N. and Stefanadis, C. (2012): Prediction of cardiovascular events and all-cause mortality with brachial-ankle elasticity index: A systematic review and meta-analysis. Hypertension, 60, 556–562.
15. He, F.J., Marciniak, M., Carney, C., Markandu, N.D.;,Anand, V., Fraser, W.D., Dalton, R.N., Kaski, J.C. and MacGregor, G.A.(2010): Effects of potassium chloride and potassium bicarbonate on endothelial function, cardiovascular risk factors, and bone turnover in mild hypertensives. Hypertension, 55, 681–688.
16. Plantinga, Y., Ghiadoni, L., Magagna, A., Giannarelli, C., Franzoni, F. and Salvetti, A. (2007): Supplementation with vitamins C and E improves arterial stiffness and endothelial function in essential hypertensive patients. Am. J. Hypertens, 20, 392–397.

17. Fallah, A.A., Sarmast, E.D., Dehkordi, S.H., Engardeh, J., Mahmoodnia, L., Khaledifar, A. and Jafari, T. (2018): Effect of Chlorella supplementation on cardiovascular risk factors: A meta-analysis of randomized controlled trials. Clin. Nutr, 37, 1892–1901.
18. Horii, N., Hasegawa, N., Fujii, S., Uchida, M., Iemitsu, K., Inoue, K. and Iemitsu, M. (2019): Effect of combination of chlorella intake and aerobic exercise training on glycemic control in type 2 diabetic rats. Nutrition, 63–64, 45–50.
19. Vecina, J.F., Oliveira, A.G., Araujo, T.G., Baggio, S.R., Torello, C.O., Saad, M.J.A. and Queiroz, M.L.S. (2014): Chlorella modulates insulin signaling pathway and prevents high-fat diet-induced insulin resistance in mice. Life Sci. 95, 45–52.
20. Bito, T., Okumura, E., Fujishima, M. and Watanabe, F. (2020): Potential of Chlorella as a Dietary Supplement to Promote Human Health. Nutrients, 12, 2524.
21. Goiris, K., Muylaert, K., Fraeye, I., Foubert, I., De Brabanter, J. and De Cooman, L. (2012): Antioxidant potential of microalgae in relation to their phenolic and carotenoid content. Journal of Applied Phycology 24: 1477–1486.
22. Safafar, H., Uldall Nørregaard, P., Ljubic, A., Møller, P., Løvstad Holdt, S and Jacobsen, C. (2016): Enhancement of protein and pigment content in two Chlorella spp. cultivated on industrial process water. Journal of Marine Science and Engineering 4: 84.
23. Zahran, E. and Risha, E. (2014): Modulatory role of dietary Chlorella vulgaris powder against arsenic-induced immunotoxicity and oxidative stress in nile tilapia (Oreochromis niloticus). Fish and Shellfish Immunology 41: 654–662.
24. Bengwayan, P.T., Laygo, J.C., Pacio, A.E., Poyaoan, J.L.Z., Rebugio, J.F. and Yuson, A.L.L. (2010): A comparative study on the antioxidant property of Chlorella (Chlorella sp.) tablet and glutathione tablet. E-International Scientific Research Journal 2: 25 –35.
25. Radhakrishnan, S., Saravana Bhavan, P., Seenivasan, C., Shanthi, R.and Muralisankar, T. (2014): Replacement of fishmeal with Spirulina platensis, Chlorella vulgaris and Azolla pinnata on nonenzymatic and enzymatic antioxidant activities of Macrobrachium rosenbergii. The Journal of Basic & Applied Zoology 67: 25 –33.
26. Wu, L.C., Ho, J.A., Shieh, M.C. and Lu, I.W. (2005): Antioxidant and anti proliferatives of Spirulina and Chlorella water extracts. J. Agric. Food Chem. 53, 4207–4212.
27. Tanaka, K., Tomita, Y., Tsuruta, M., Konishi, F., Okuda, M. and Himeno, K. (1990): Oral administration of Chlorella vulgaris augments concomitant antitumor immunity. Immunopharmacol. Immunotoxicol. 12, 277–291.
28. Cha, K.H., Koo, S.Y. and Lee, D.U. (2008): Antiproliferative effects of carotenoids extracted from Chlorella ellipsoidea and Chlorella vulgaris on human colon cancer cells. J. Agric. Food Chem. 56, 10521–10526.
29. Romos, A.L., Torello, C.O. and Queiroz, M.L.S. (2010): Chlorella vulgaris modulates immunomyelopoietic activity and enhances the resistance of tumor-bearing mice. Nutr. Cancer, 62, 1170–1180.
30. Selkoe, D.J. (2001): Alzheimer's disease: Genes, proteins, and therapy. Physiol. Rev. 81, 741–766.
31. Nakagawa, K., Kiko, T., Hatade, K., Asai, A., Kumra, F., Sookwong, P., Tsuduki, T.; Arai, H. and Miyazawa, T. (2008): Development of ahigh-performance liquid chromatography-based assay for carotenoids in human red blood cells: Application to clinical studies. Anal. Biochem. 381, 129–134.

32. Kiko, T., Nakagawa, K., Tsuduki, T., Suzuki, T., Arai, H. and Miyazawa, T. (2012): Significance of lutein in red blood cells of Alzheimer's disease patients. J. Alzheimers Dis. 28, 593–600.
33. Miyazawa, T., Nakagawa, K., Takekoshi, H., Higuchi, O., Koto, S., Kondo, M., Kimura, F. and Miyazawa, T. (2013): Ingestion of Chlorella reduced the oxidation of erythrocyte membrance lipids in senior Japanese subjects. J. Oleo Sci. 62, 873–881.
34. Andrade, L., Caraveo-Anduaga, J.J., Berglung, P., Bijl, R.V., de Graaf, R., Vollebergh, W., Dragomirecka, E., Kohn, R., Keller, M. and Kessler, R. (2003): The epidemiology of major depressive episodes: Results from the international consortium of psychiatric epidemiology (ICPE) surveys. Int. J.MethodsPsychiatryRes. 12, 3–21.
35. Panahi, Y. Badeli, R., Karami,G. R.,Badeli,Z. and Sahebkar, A. (2015): Arandomized controlled trial of 6-week Chlorella vulgaris supplementation in patients with major depressive disorder. Comp. Ther. Med. 23, 598–602.
36. Valko,M.,Leibfritz,D.,Moncol,J.,Cronin,M.T.,Mazur,M. and Telser,J. (2007): Free radicals and antioxidants in normal physiological functions and human disease. Int. J. Biochem. Cell Biol. 39, 44–84.
37. Vijayavel, K., Anbuselvam, C. and Balasubramanian, M.P. (2007): Antioxidant effect of the marine algae Chlorella vulgaris against naphthalene-induced oxidative stress in the albino rats. Mol. Cell Biochem. 303, 39–44.
38. Li, L., Kim, Y. and Lee, Y.W.(2013): Chlorella vulgaris extract ameliorates carbon tetrachloride-induced acute hepatic injury in mice. Exp. Toxicol. Pathol, 65, 73–80.
39. Paradis, V., Bedossa, P. (2008): Definition and natural history of metabolic steatosis: Histology and cellular aspects. Diabetes Metab. 2008, 34, 638–642.
40. Ben, M.D., Polimeni, L., Baratta, F., Pastori, D., Loffredo, L. and Angelico, F. (2014): Modern approach to the clinical management of non-alcoholic fatty liver disease. World J. Gastroentrol, 20, 8341–8350.
41. Ebrahimi-Mameghani, M., Sadeghi, Z., Farhangi, M.A., Vaghef-Mehrabany, E. and Aliashrafi, S. (2017): Glucose homeostasis, insulin resistance and inflammatory biomarkers in patients with non-alcoholic fatty liver disease: Beneficial effects of supplementation with microalgae Chlorella vulgaris: A double-blind placebo-controlled randomized clinical trial. Clin. Nutr, 36, 1001–1006.
42. Yadav, M., Kumar, V., Sandal, N. and Chauhan, M., K. (2022): Qualitative evaluation of Chlorella vulgaris for removal of toxic metals from body.Journal of applied Phycology.34 (6):1-12.
43. Schecter, A., Startin, J., Wright, C., Kelly, M., Papke, O., Lis, A., Ball, M. and Olson, J.R. (1994): Dioxins in, U.S. food and estimated daily intake. Chemosphere, 29, 2261–2265.
44. Schecter, A., Papke, O., Lis, A., Ball, M., Ryan, J.J., Olson, J.R., Li, L. and Kessler, H. (1996): Decrease in milk and blood dioxin levels over two years in a mother nursing twins: Estimates of decreased maternal and increased infant dioxin body burden from nursing. Chemosphere, 32, 543–549.
45. Morita, K.; Matsueda, T.; Iida, T.; Hasegawa, T. Chlorella accelerates dioxin excretion in rats. J. Nutr. 1999, 129, 1731–1736.

46. Kinze, M.G., Dolbere, F.A., Carroll, K.L., Moore, D.H., II and Felton, J.S. (1994): Effect of cooking time and temperature on the heterocyclic amine content of fried beef patties. Food Chem. Toxicol, 32, 595–603. 129.
47. Lee,I., Tran,M., Evans-Nguyen,T., Stickle,D., Kim,S., Han,J, Park,J.Y. and Yang,,M. (2015):.Detoxification of chlorella supplement on heterocyclic amines in Korean young adults. Environ. Toxicol. Pharm. 2015, 39, 441–446.
48. Uchikawa, T., Yasutake, A., Kumamoto, Y., Maruyama, I., Kumamoto, S. and Ando, Y. (2010): The influence of Parachlorella beijerinckii CK-5 on the absorption and excretion of methylmercury (MeHg) in mice. J. Toxicol. Sci. 35, 101–105.
49. Harding, G., Dalziel, J. and Vass, P. (2018): Bioaccumulation of methylmercury within the marine food web of the outer bay of Fundy, gulf of maine. PLoS ONE, 13, e0197220.
50. Maruyama, I., Uchikawa, T., Kanno, T., Ando, Y., Kitsuki, H. and Yasutake, A. (2018): Chlorella supplementation decreases methylmercury concentrations of hair and blood in healthy volunteers. Fundam. Toxicol. Sci. 5, 117–122.
51. Nauta, A., Engels, F., Knippples, L.M., Garssen, J., Nijkamp, F. and Redegeld, F.A. (2008): Mechanisms of allergy and asthma. Eur. J. Pharmcol, 585, 354–360.
52. Hsu, H.Y., Jeyashoke, N., Yeh, C.H., Song, Y.J., Hua, K.F. and Chao, L.K. (2010):Immunostimulatory bioactivity of algal polysaccharides from Chlorella pyrenoidosa activates macrophages via Toll-like receptor 4. J. Agric. Food Chem. 58, 927–936.
53. Otsuki, T., Shimizu, K., Iemitsu, M.and Kono, I. (2011): Salivary secretory immunoglobulin a secretion increases after 4-weeks ingestion of chlorella-derived multicomponent supplement in humans: A randomized cross over study. Nutr. J. 10, 91.
54. Abel, A.M., Yang, C., Thakar, M.S. and Malarkannan, S. (2018): Natural killer cells: Development, maturation, and clinical utilization. Front. Immunol. 9, 1869.
55. De Souza Queiroz, J., Barbosa, C.M.V., da Rocha, M., Bincoletto, C., Paredes-Gamero, E.J., de Souza Queiroz, M. L. and Neto,J.P. (2013): Chlorella vulgaris treatment ameliorates the suppressive effects of single and repeated stressors on hematopoiesis. Brain Behav. Immun. 2013, 29, 39–50.
56. Queiroz, J.S., Blasco, I.M., Gagliano, H., Daviu, N., Román, A.G., Belda, X., Carrasco, J., Rocha, M.C., Neto, J.P. and Armario, A. (2016): Chlorella vulgaris reduces the impact of stress on hypothalamic-pituitary-adrenal axis and brain c-fos expression. Psychoneuroendocrinology 2016, 65, 1–8.
57. Van der Spiegel, M., Noordam, M.Y. and van der Fels-Klerx, H.J. (2013): Safety of novel protein sources (insects, microalgae, seaweed, duckweed, and rapeseed) and legislative aspects for their application in food and feed production. Comprehensive Reviews in Food Science and Food Safety 12: 662–678.
58. Cho, S. (2011): GRAS Exemption Claim for Chlorella Vulgaris as an Ingredient in Foods. Original submission to U.S Food and Drug Administration. GRAS notice 000396. pp 1–57. NutraSource, Clarksville, MD.
59. Tang, G. and Suter, P.M. (2011): Vitamin A, nutrition, and health values of Algae: Spirulina, Chlorella, and Dunaliella. Journal of Pharmacy and Nutrition Sciences 1: 111–118.