

# MICROALGAE

The World's most important plant

## Introduction to Microalgae

*"In blue-green algae we find three and one-half billion years of life on this planet encoded in their nucleic acids (RNA/DNA). At the same time, all microalgae supply that fresh burst of primal essence that manifested when life was in its birthing stages. At a moment in history when the survival of the human species is in jeopardy, many people have begun instinctively to turn to these original life forms for nutritional support."*

Paul Pitchford, **Healing with Whole Foods, 1993**

Eleven areas of research are reviewed, ranging from algae's ability to enhance brain function to issues of safety. A few common components found within microalgae, such as antioxidants, essential fatty acids, and amino acids, are significant across a range of topics.

Perhaps one of the reasons microalgal nutrients appear to work in so many areas is that nature is conservative in its designs. Solutions that work are retained. For example, [chlorophyll](#), an "invention" that allows organisms to capture sunlight and produce sugars, first appeared in blue-green microalgae billions of years ago and is now used as a survival strategy by all higher plants. Animals in turn depend upon chlorophyll-containing plants, directly or indirectly, as a food source.

## Ancient organic molecules

These kinds of threads are repeated countless times throughout nature. Ancient organic molecules, such as [amino acids](#), which were found in blue-green microalgae at the dawn of life, now act as basic building blocks for all of earth's creatures. Potent [antioxidants](#) (e.g., beta-carotene or glutathione) that originated in primitive microalgae are conserved and widely used across nature. Likewise, essential fatty acids (EFAs) are critical structural components of cell membranes and play a foundational role in our brain chemistry. Microalgae are the primary source of EFAs in the food chain! In short, microalgae at the bottom of the food chain provide an ancient biomolecular [pharmacopoeia](#) upon which most of cellular life now depends.

## Remarkable Nutritive Qualities of Microalgae

*"Gram-for-gram microalgae may be the most nutrient dense food on Earth."*

The primitive character of microalgae's cellular organization gives it a number of advantages over higher plants and animals as a food source. For starters, practically the entire organism can be nutritious, with minimal indigestible structures. By contrast, typically less than half of the dry weight of plants and animals has nutritional value. Primitive blue-green algae are composed almost entirely of nutritionally useful and uniform cells. Furthermore, microalgae exhibit superior photosynthetic efficiency, using light approximately three times more efficiently than higher plants. <sup>2</sup>

Microalgae are among the most productive organisms on the planet.

## Aphanizomenon flos-aquae, blue-green algae

"Why does Aph. flos-aquae [Aphanizomenon flos-aquae, a blue-green algae]—small and simple as it seems to be—contain more micronutrients than any other known food?...Aph. flos-aquae cells are about 20 to 30 times smaller than the cells within the food we usually eat. Because of this, Aph. flos-aquae contains 20 to 30 times the membrane surface area." <sup>3</sup>Aph. flos-aquae's smaller cell size means a larger ratio of cell membrane surface compared to the rest of the cell. In the case of blue-green algae, the cell membrane is where some of the most important nutrients are concentrated.

Aph. flos-aquae algae produces more cell membrane material without getting larger by creating a vast system of membrane inpouchings similar to the brain's infoldings. In other words, if the cell membrane were ironed flat, it would be many times the apparent size of the cell.

One of the most remarkable nutritional aspects of microalgae is its high content of usable protein—ranging from 50% to 70%! This is a far higher percentage than the choicest edible parts of any higher plant or animal. Algal protein has shorter and less complex polypeptide chains—making it easier to digest than plant or animal protein. Red meat has a surprisingly low net protein utilization index of 18%, compared to AFA's 75%. The net protein utilization index is a measure of how completely amino acids are assimilated by humans. In fact, some microalgae, such as Aph. flos-aquae, contain all ten essential amino acids that humans require from their diets—in a profile similar to that recommended by the National Academy of Sciences.

Not least, "microalgae are considered to be the primary source of unsaturated fatty acids in the food chain." Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are two relatively rare and valuable fatty acids found in microalgae. The reason that fish oils are so rich in polyunsaturated fatty acids (PUFAs) is that microalgae are abundant in their food chain. Unlike seafood, microalgal oils are cholesterol free. The nutritional value and therapeutic merits of PUFAs have been widely documented.

## Enhanced Brain Function, Behavior, and Learning

*"Blue-green algae and my new diet have helped me focus and concentrate better in school and on my homework. I am more relaxed and I don't have stomachaches anymore. I have more friends now and my mom is happier too."*

--Chelsea, 8 years old

The brain contains and uses one of the highest concentrations of nutrients of any organ in the body. Oxygen consumption is the best indicator of "fuel use" -- almost everyone recognizes how vital oxygen is to the brain. Unlike many organs (e.g., the liver) that have cellular fuel reserves, the brain is almost entirely dependent upon a continuous blood supply for fuel. Children's brains are even hungrier, more metabolically active, and proportionally larger than adults' brains. Per pound of body weight, children eat more food, drink more fluids, and breathe more air than adults, thereby increasing their potential exposure to toxins. Also, younger children's blood-brain barriers and intestinal linings are not as developed and are therefore less protective than those of most adults. This means that more incompletely digested foods and toxins can leak into a child's bloodstream and brain.

Beta-carotenes and antioxidants found abundantly in microalgae may contribute to protecting the central nervous system (CNS) from oxidative stress. Lipids, which comprise most of the brain tissue, are especially sensitive to oxidative damage. Researchers in Israel and Japan have demonstrated the protective effects of antioxidants in experimental animal brain trauma models. <sup>43,44</sup> Oxidative stress has been implicated in the pathogenesis of some disorders of the brain; hence antioxidants have become attractive therapeutic agents. <sup>45</sup> Furthermore, brain trauma and injury tends to increase whole-body oxidative stress. <sup>46</sup>

In 1985, Gabriel Cousens published two case studies on the use of AFA blue-green algae in the improvement of Alzheimer's disease. He reported "some significant return of function" such as decreased hand tremors, better balance, and improved short term memory, attention span, judgment, and reasoning in one patient; in the second patient there was no significant return of previously lost function, but there was a halting of the typical "progressive degeneration associated with Alzheimer's" along with a corresponding improvement in the patient's marital relationship. <sup>50</sup>

Andrew Valencia and colleagues at the Neurolab Clinic associated with the University of New Mexico demonstrated that patients suffering from mild brain injury who ate Aph. flos-aquae showed a

25% improvement in about half the time as patients who did not receive algae. <sup>52</sup> According to Valencia, in his study of more than 150 patients over two years, patients who ate AFA algae alone had improvements similar to those in a two-month hospital-based rehabilitation program. However, the best results were achieved when neuro-rehabilitation was combined with eating *Aph. flos-aquae* algae, better than *Aph. flos-aquae* alone or the hospital program alone. Valencia's research team hypothesized that *Aph. flos-aquae* algae seems to promote reparative neuroplasticity - or, in lay terms, rewiring of the circuitry of the brain.

Valencia also conducted electrophysiological studies of brain waves and found that the ingestion of *Aph. flos-aquae* algae was linked with pronounced improvements in brain function, notably in the ability to focus and discriminate between various auditory signals.

## Benefits:

### **At least six research studies have demonstrated the benefits of *Aph. flos-aquae* on improving children's cognition, mood, behavior, and academic performance:**

Sevilla and Aguirre's study of 1,567 students at the Monseñor Velez School in Nandaime, Nicaragua, demonstrated an 81% increase in the average standardized test scores among malnourished children eating only .5 to 1 gram of *Aph. flos-aquae* a day over a six-month period. Subjects showed significantly increased classroom attendance and participation, as well as marked improvement in overall health. Academically, the Velez school went from having one of the lowest national scholastic test scores to achieving one of the best. <sup>53</sup>

Claudia Jarratt, family therapist at the Center for Family Wellness in Harvard, Massachusetts, studied 105 children given *Aph. flos-aquae* and found a significant improvement in behavior as shown by both parent and teacher ratings. The children, who displayed a variety of behavioral problems, consumed between 0.5 and 1 gram of *Aph. flos-aquae* daily and were observed over a ten-week period. Data from the Achenbach Child Behavior Checklists (parent and teacher versions) and extensive case histories were collected for all participants. Significant improvements were found on all 11 parent rating scales in pre- to post-test behavior. These findings were corroborated by teachers' ratings, which revealed significant improvements in seven of the ten behavioral problem areas measured. The use of an expectancy scale revealed little correlation between parents' initial expectations of treatment benefits and final outcomes. <sup>54</sup> Subsequently, Claudia Jarratt has continued to work with an additional 250 children, using an AFA-based program, with similar positive results. <sup>55</sup>

My own research team studied 26 students with reading difficulties, who participated in a three-month *Aph. flos-aquae* supplement study. All were enrolled in the Stilwell Learning Center, a reading tutorial program in Sierra Vista, Arizona. Participants included 18 boys and 14 girls, ranging from 6 to 17 years old, with a mean age of 11. The children were randomly assigned to one of two groups, (1) the low-*Aph. flos-aquae*, 1.5 grams, treatment group (n = 13) or (2) the high-*Aph. flos-aquae*, 3 grams, treatment group (n = 13). There was also a non *Aph. flos-aquae* comparison group.

Both *Aph. flos-aquae* treatment groups showed significant improvements on the following measures over the three-month trial period: attention and concentration indices, a sequential memory index, standardized academic testing, behavioral parent and teacher reports, health symptoms, tutorial attendance records, and decreased toxic levels of aluminum. Regardless of the assigned treatment group (i.e., high or low), both groups demonstrated significant improvements compared to pre-test baseline measures and a small non-supplemented comparison group. <sup>56</sup>

A team of medical researchers headed by Dr. Krylov of the University of Illinois concluded, after examining hundreds of well-documented case histories, that *Aph. flos-aquae* appears promising for the treatment of depression and AD/HD as well as several other health challenges. <sup>58</sup>

## Improved Immune Function

*"We may be different in gender, color of hair and skin, religion, and job. But we have a common bond — we are survivors. Our parents survived long enough to conceive us. Grandparents had the same claim for your parents. The thing that made this possible is that precious commodity—the immune system."*

--Schmidt, Smith, and Sehnert  
**Beyond Antibiotics**, 1993

School records of children eating AFA blue-green algae showed a dramatic improvement in class attendance in two studies. Both research teams, along with school personnel reports, suggested that the increased attendance of students who ate blue-green algae was related to decreased sick days. [71,72](#)

In a study of 100 children diagnosed with a zinc deficiency and given either zinc sulfate or blue-green algae tablets, those given blue-green algae demonstrated a superior immune response. The zinc found in blue-green algae may be about three times more effective than zinc from mineral sources. [73](#)

## Increased antibody production and enhanced immune function

Researchers have found increased antibody production and enhanced immune function in animals supplemented with blue-green algae. [78, 79](#)

Several studies, animal and human, have demonstrated the ability of microalgae to increase macrophage movement. [80-82](#) The dietary use of blue-green algae is reported to enhance the immune response in laboratory mice, by stimulating macrophage functions, phagocytosis and enhanced interleukin-1 production. [83, 84](#)

Gitte Jensen, Ph.D., an immunologist at McGill University, working with a team of researchers at the Royal Victoria Hospital in Montreal, demonstrated improved trafficking of immune cells to be among the effects of *Aph. flos-aquae* algae on the human immune system. Many immune cells (e.g., natural killer [NK] cells) do their primary work outside of the bloodstream in the tissues. *Aph. flos-aquae* algae increased the number of white blood cells that moved from the bloodstream into the tissues to do their search-and-destroy mission. [86](#)

In a follow-up double-blind study, Jensen's team replicated the initial results and also found that longer-term consumers of *Aph. flos-aquae* demonstrated greater benefits than those taking algae for the first time. Yet even short-term consumers showed some benefits. Dr. Jensen's team found that within two hours of eating *Aph. flos-aquae* there was a significant migration of natural killer cells from the blood into the surrounding tissues. Natural killer cells play a key role in our defense system as they "patrol for invading microbes and infected or transformed precancerous cells." This gentle immune boost was rapid, short-term, and cell-type specific. [87](#)

In a retrospective review of medical cases, researchers found positive evidence that *Aph. flos-aquae* blue-green algae might be useful in the treatment of chronic fatigue, Epstein Barr infection, fibromyalgia, and AIDS. These diseases all involve significant immune system, and sometimes viral, components. Such anecdotal evidence suggests that at least some autoimmune diseases may respond favorably to blue-green algae. [88](#)

## Antiviral, Antibacterial, and Antifungal Effects

*"We have given too much attention to the enemy  
and have to some extent overlooked our defenses."*

—M. Behar, **World Health**,  
February-March, 1974

Microorganisms, bacteria, and fungi have been exploited for almost a century to provide useful drugs, antibiotics, and other pharmacologically active compounds. [95](#)

Antibiotics, active against bacteria, fungi, and even viruses, have been isolated from marine algae, especially macroalgae. [96](#) Microalgae as well as macroalgae are able to produce a wide variety of pharmacologically active compounds.

### Beneficial effects of Microalgae

Beneficial effects in leprosy were first observed in the 1940s. "Jorgensen and Convit fed a soup made from concentrated Chlorella to eighty patients at a treatment colony in Venezuela. The improvement in those patients' physical condition was the first documented evidence of the potential of microalgae as a health supplement." [97](#)

Antibacterial, antiviral, and antifungal properties have been found in dozens of micro-algae species. [99-101](#)

Compounds and extracts from blue-green algae, as well as other microalgae, showing HIV inhibitory activity are often active against other retroviruses such as Herpes simplex virus types 1 & 2, simian immunodeficiency virus (SIV), cytomegalovirus, measles virus, mumps virus, and influenza A virus. [113-117](#)

Aph. flos-aquae blue-green algae shows an inhibitory effect on the growth of Salmonella bacterial strains, in amounts greater than 2 mg. [122](#) A hot water extract of the green alga, Chlorella, given to mice infected with Listeria mono-cytogenes, significantly increased the survival rates of mice, as well as demonstrating an increased immune cellular response. [123,124](#) Unicellular green algae have also been shown to increase resistance against E. coli and cytomegalovirus infections. [125-128](#)

Beta-carotene, which is plentiful in microalgae, may also decrease susceptibility to respiratory infections. As beta-carotene is transformed into vitamin A, deficiencies associated with vitamin A—such as increased risk of respiratory disease—might be reduced. [130,131](#)

## Improved Cellular Repair

Paleobiologists, such as J. William Schopf, describe how some blue-green algal species have changed little in the last few billion years. Fossils of blue-green algae from central Australia, dating back more than 3.5 billion years, reveal early forms that are quite similar to living species today.

It appears that blue-green algae achieved a sort of biological perfection—with perhaps little need to evolve—accompanied by strong protective mechanisms that minimized genetic mutations. [137](#)

## Masters of regeneration

Two studies by Devi and his team demonstrated the ability of algal diets to stimulate the regeneration of blood serum and liver proteins in rats. [140,141](#)

Because microalgal protein is composed of shorter and less complex polypeptide chains—with an abundance of all essential amino acids—it can be more readily utilized at the cellular level. One can think of it as supplying the foundational building blocks for cellular repair in easily usable form.

### **Might algal diets be able to confer to other cells some aspect of protection from genetic mutations?**

Researchers at the Institute of Molecular and Subcellular Biology in Slovakia found that freeze-dried *Aph. flos-aquae* blue-green algae demonstrated anti-mutagenic effects on bacterial cells exposed to a mutagen [a substance that disrupts DNA/RNA transcription, causing mutations] using the standard Ames test. When the algae powder was added to the cell culture at the same time as the chemical mutagen, there was no benefit. However, if the algae powder was added to the cell culture medium 2 to 24 hours before exposure to the mutagenic agent, a significant anti-mutagenic effect was evident. [142](#) The most intense suppression of mutagenic activity was achieved when the algae powder was mixed in the cell culture medium 24 hours before the addition of the mutagen. This suggests that the algal phytochemicals were utilized by the cell culture as a protective cellular influence rather than neutralizing the chemical mutagen directly.

Steve Gagne, a macrobiotic counselor and author of *The Energetics of Food* (1990), reports that "Algae are the masters of regeneration—they probably are the most highly regenerative foods on the planet." [145](#)

In support of this empirical observation, it is noteworthy that microalgal extracts added to culture mediums dramatically increase human cell survival rates. In 1984, a U.S. Patent (no. 4,468,460) was granted to S. Kumamoto for A Method of Human Cell Culture. Described as follows: "A method of culture of human cells is disclosed which comprises effecting the cultivation in a culture medium containing an extract of microalgae...said method permitting the normal successive cultivation of human cells to be maintained efficiently without any morphological and genetic mutations over a greater number of successive generations than has hitherto been possible." [146](#)

## Radiation Protective Effects

*"The transfer of energy that is produced by radiation is similar to that caused by other forms of acute injury such as an automobile crash or a bullet wound...The difference between a bullet and an X ray lies principally in the size of the particle. While a bullet destroys tissues and entire organs, a particle of radiation collides with single atoms or molecules deep within the cells."* 153

—H. Needleman and P. Landrigan,  
**Raising Children Toxic Free**, 1994

Beta-carotene derived from the microalga *Dunaliella* demonstrates anti-mutagenic effects on human lymphocytes, as shown in a Chinese study using in vitro micronucleus and chromosomal aberration tests. The inhibitory effect of microalgae-extracted beta-carotene on mutagenesis induced by both gamma-rays and mitomycin, a known mutagenic agent, was demonstrated. 143

New research provides evidence that dietary flavonoids (i.e., pigments) may help repair a range of free radical damage in DNA and offer protection against strand breaks and base alterations in our cells' genetic material. Scientists at the University of Auckland, New Zealand, demonstrated that antioxidant flavonoids can reduce the incidence of single-strand breaks in irradiated solutions of double-stranded DNA, in vitro. Using advanced pulse radiolysis measurements, scientists found that electron transfer from the flavonoids to free radical attack sites on DNA appears to result in a faster chemical repair, lessening the oxidative damage to DNA. 144

## Remarkable Radioprotective Effects

Numerous animal and in vitro studies using microalgae have demonstrated remarkable radioprotective effects. 160-164 When microalgae was administered orally to mice, radio-protective effects of microalgae were shown to occur both before and immediately after exposure to sub-lethal gamma-rays. 165

Beta-carotene and other carotenoids, found abundantly in microalgae, are known to be potent free-radical quenchers and lipid antioxidants. Natural beta-carotene (50 mg/kg diet), obtained from the unicellular alga, *Dunaliella*, was fed to rats exposed to a single high dose of whole-body radiation (4 Gy). Radiated control animals, not fed algal carotenoids, suffered a significant loss of body weight and decreased liver concentrations of beta-carotene and retinol, compared to algal beta-carotene supplemented rats. Normal increase in body weight and the absence of ill effects were noted in the groups of rats whose diet was supplemented by beta-carotene before and after irradiation. 155

Extracts of phycocyanin (the blue pigment) from blue-green algae helped to restore the efficiency of anti-oxidant defenses, dehydrogenase activity, and energy-rich phosphate levels in rats exposed to X-rays (dose of 5 Gy). 159

Several animal and in vitro studies using microalgae have demonstrated remarkable radioprotective effects. 160-164 When microalgae was administered orally to mice, radio-protective effects of microalgae were shown to occur both before and immediately after exposure to sub-lethal gamma-rays. 165 Significant benefits were observed in the number of bone marrow cells and the spleen weight.



## Cancer Protective Effects

*"At present we have overwhelming evidence...(that) none of the risk factors for cancer is...more significant than diet and nutrition."*

— B. Reddy, Committee on Diet, Nutrition and Cancer, 1992

Dozens of large-scale studies have disclosed evidence that eating vegetables rich in beta-carotene reduces the risks of cancer. [173-176](#) It is important to note, however, that isolated beta-carotene (sold as a supplement on its own or in multivitamin formulas) does not provide the same benefits. In fact, the large-scale study referred to as "CARET" (Carotenoid and Retinol Efficacy Trial) found that synthetic beta-carotene supplements were correlated with increased—not decreased—morbidity and mortality from cancer. [15](#)

Because microalgae are the foods richest in natural beta-carotene, several species, notably *Dunaliella* and *Spirulina*, have been extensively tested for anticancer effects and these effects have been well documented. [177-185](#)

Researchers at the Harvard University School of Dental Medicine demonstrated that algal extracts rich in beta-carotene applied to cancerous tumors in the mouths of hamsters reduced the number and size of tumors or caused them to disappear. [186](#) In a further study, when an algal extract was administered to 20 hamsters pre-treated to develop mouth cancer, none of the animals developed the disease. By comparison, two pretreated control groups that did not receive any algal extract (40 animals) all developed mouth cancer. Interestingly, when beta-carotene alone was given (provided by Sigma Chemical Company) fully half the animals developed cancer. [187](#) This research team has continued to replicate these effects, repeatedly demonstrating the ability of blue-green algal extracts to inhibit and prevent tumor growth and cancer. [188-190](#)

## Powerful Anticancer Properties

Beta-carotene is not the only cancer-protective substance to be found in microalgae. Cancer researchers at the University of Hawaii isolated a blue-green algal pigment, called cryptophycin, that demonstrates powerful anticancer properties—especially useful in the chemotherapy of drug-resistant tumors. [192, 193](#) Other new algal protein compounds have also exhibited "multidrug-resistance reversing activities" that may be useful in the treatment of difficult, drug-resistant tumors. [194-196](#)

In some cases the survival rates of algae-treated mice increased nearly 80% over control groups. [214](#) Such findings suggest that presurgical treatment with extracts of microalgae might decrease or prevent metastasis or tumor progression. [215](#)

"In research in Japan, phycocyanin (the blue pigment of blue-green algae) was extracted and...[given] orally...[to] mice with liver cancer. The survival rate of the treatment group was significantly higher than the control group not given phycocyanin. After five weeks, 90% of the phycocyanin group survived, but only 25% of the control group were still alive. After eight weeks, 25% of the phycocyanin group still survived, yet none of the control group was alive. This suggests eating phycocyanin may increase the survival rate of cancer stricken organisms." [218](#)

"Whole body irradiation" animal studies suggest there may be a potential benefit for cancer patients given algal beta-carotene before and after radiation treatments to protect against cellular damage caused by free radicals induced from irradiation. [222](#) Additionally, Japanese researchers using an animal model found that components of unicellular algae may be beneficial in the alleviation of cancer chemotherapy side effects (e.g., immune suppression) while supporting the anti-tumor activity of the chemotherapeutic agents. [223](#)

## Detoxification Support

*"Since 1950, at least 70,000 new chemical compounds have been invented and dispersed into our environment through new consumer commodities, industrial products, and food. We are by default conducting a massive clinical toxicological trial. And our children and their children are the experimental animals."*

—H. Needleman and P. Landrigan,  
**Raising Children Toxic Free**, 1994 [222](#)

*"Methionine was probably one of the first amino acids available in Earth's ancient primordial seas billions of years ago. This amino acid was (and is still) used by primitive bacteria and blue-green algae to biosynthesize glutathione, possibly Earth's first antioxidant (protection) tripeptide molecule. Methionine in this form has been shown to help humans detoxify lead and copper contamination in the blood."* [224](#)

Blue-green algae is one of the richest food sources of detoxifying polypeptides, including methionine and glutathione, along with B-vitamin precursors. Once ingested, these molecules are modified as needed. Such polypeptides are essential in the protection of DNA, the family jewels, and are essential in the chemistry of detoxification. [226](#) Also glutathione, along with ascorbate, may help to protect against polyunsaturated fatty acid (PUFA) oxidation. [227](#)

When microalgal supplementation was given to rats consuming a high fructose (60%) diet, a preventive effect on the liver triglyceride level was observed, along with lowered plasma cholesterol. The researchers reported that the microalgae helped reduce liver fats that were elevated by the excessively fructose-rich diet. [233](#)

## Stimulate Liver Function

Chlorophyll, which microalgae contains in abundance, can help to stimulate liver function, increase bile secretion, and protect cellular functions. [234](#) Also, "chlorophyll appears to promote regeneration of damaged liver cells." [235](#)

Medical researchers have demonstrated that green microalgae increase the detoxification of harmful chemicals like chlordecone, dioxin, and PCBs. [241](#) In a study of chlordecone poisoned rats, ingested algae decreased the half-life of the chemical toxins from 40 to 19 days. [242](#)

Several grams of *Aph. flos-aquae* blue-green algae eliminated excessive aluminum from children in a three-month study. Also, parents reported significant decreases in negative health symptoms, suggestive of improved detoxification pathways. [243](#) Aluminum exposure in humans is unavoidable. Some aluminum absorption occurs with the ingestion of food and medicines. Greater amounts of aluminum are present in antacids. [244](#) Blue-green algae may be helpful for dialysis patients, who have a greater risk for aluminum accumulation and an increased risk of neurotoxicity.

Blue-green algae have been shown to reduce lead toxicity, as well. [245](#) The beneficial effects of blue-green algae may be due to the presence of the abundance of antioxidants, including beta-carotene and SOD enzymes. Numerous studies have demonstrated a strong relationship between childhood learning disabilities and body stores of heavy metals, particularly lead. [246, 247](#)

Blue-green algae have multiple liver-protective factors, including amino acids (e.g., methionine, arginine, and isoleucine), chelating trace minerals, and potent antioxidants, such as phycocyanins and superoxide dismutase (SOD).

## Anti-inflammatory and Antioxidant Effects

*"Many of the elderly in the United States—and quite a few of the not-so-elderly— experience terrible pain in their joints. Their fingers may become twisted and swollen, and they may be unable to button a coat without large doses of anti-inflammatory drugs...Many come to feel crippled and useless. By the age of 35, 35% of Americans have diagnosable arthritis in their knees. At least 85% of those over the age of 70 have it, and many have it severely."*

- J. Robbins, **Diet for A New America**, 1987

Prokaryotes, organisms without a nuclear membrane (e.g., blue-green algae), display a more diverse array of antioxidant pigments and a broader selection of carotenoids than terrestrial plants and most green algae. Scientists at the University of Wisconsin, Department of Food Microbiology, report that because of the remarkable health benefits of algal and microbial carotenes, there will likely be a substantial increase in the world-wide demand for a full range of these important antioxidants. <sup>252</sup> Carotenoids represent one of the most widely distributed and structurally diverse classes of natural pigments, with important functions in photosynthesis, nutrition, and protection against photo-oxidative damage.

Rats and chickens fed a natural algal form of beta-carotene showed at least a tenfold higher accumulation of overall beta-carotene in their livers than those control animals fed equivalent amounts of synthetic all-trans beta-carotene supplement. The higher accumulation of the natural algal carotenoids, over the synthetic isolated beta-carotene, likely indicates a greater therapeutic value, according to the researchers. <sup>253</sup>

Researchers have reported that natural algal beta-carotene is superior to a synthetic beta-carotene supplement in terms of raising lipophilic antioxidants (protecting PUFAs) in human serum. <sup>254</sup> Also, natural algal extracts of 9-cis beta-carotene are shown to have a higher antioxidant potency compared to synthetic all-trans beta-carotene with in vitro experiments. <sup>255</sup>

## Boost the human body's Antioxidant Defenses

Pigments, phytochemicals, vitamins, and trace elements from algae and higher plants can help boost the human body's antioxidant defenses. <sup>256, 257</sup> *Aph. flos-aquae* has an unusually wide variety of antioxidants, such as tocopherols, beta-carotene, flavonoids, superoxide dismutase, glutathione, taurine, tryptophan, phenolic acid, and vitamins C, E, B5, and B2. Antioxidants are biomolecules that protect organisms from the damaging effects of reactive oxygen species (free radicals) that are constantly formed in biological systems.

Blue-green algae contain a wide range of antioxidants in the form of specific trace minerals, amino acids, vitamins, and especially pigments – an impressive variety of carotenes along with potent green and blue pigments. Depending on the source of blue-green algae, the amount of phycocyanin can range up to 15% of its dry weight.

Replicated studies with a range of experimental animal models have established the potent antioxidant and anti-inflammatory effects of phycocyanin. In rodents, experimentally-induced colitis as well as edemas of the paw and ear all responded positively to C-phycocyanin. <sup>260-264</sup>

Gitte Jensen, an immunologist from McGill University, and her team at the Royal Victoria Hospital in Montreal report that *Aph. flos-aquae* algae may help to inhibit and to reverse inflammatory conditions. The researchers observed that small dilutions of *Aph. flos-aquae* algae tend to dampen the release of reactive oxygen species from certain phagocytic cells in human blood. <sup>267</sup>

Scientists at the University of Padova, Italy, found that diatoms, golden brown unicellular algae, produce anti-inflammatory chemicals that are the main active ingredients in mud-pack treatments. In European health spas the use of mud-packs for the treatment of rheumatic and osteoarthritic patients has a long and relatively successful history. The maturation of thermal mud is dependent upon the full colonization of the mud by thermophilic microorganisms, with diatoms producing anti-

inflammatory sulfoglycolipids (SGL), similar to those in blue-green algae. A typical cycle of treatments requires 12 packs of thermal mud.

“On this basis we calculated the amount of SGL taken up by each patient in a cycle of treatments, and found a figure not far from the recommended dose of non-steroid anti-inflammatory drugs utilized for the same pathology. However, unlike pharmaceutical preparations, the amount of SGL taken up by the patients after the mud-packs does not exert any adverse gastrointestinal effect on these patients,” reported the scientists. <sup>268</sup> Additionally, the anti-inflammatory action of SGL is consistent with the decrease of serum interleukin-1 observed in arthrosic patients treated with mud-packs. <sup>269</sup>

Overall, evidence suggests that microalgae demonstrates at least four antioxidant properties:

1. Scavenging of reactive oxygen species (free radicals).
2. Regeneration of endogenous antioxidants, such as SOD and glutathione reductase.
3. Chelation of heavy metals.
4. Repair of oxidation-damaged proteins

## Improved Circulation and Heart Function

*"The human heart so far surpasses all known motors in functional capacity that we can hardly hope to improve on it, even with the most ingenious machine produced by man...It beats 100,000 times per day, approximately 40 million times in a year...It pumps two gallons of blood per minute and 100 gallons per hour, through a vascular system of about 60,000 miles in length—2 1/2 times the circumference of the earth."*

—Bircher-Benner, **Nutrition Plan for High Blood Pressure Problems**, 1993

Microalgae's potent range of antioxidants, in addition to its healthy balance of EFAs, offer top-quality cardio-vascular support. Dietary supplementation with algal beta-carotene may normalize the elevated LDL oxidation in patients with diabetes, and thus delay the onset and further development of atherosclerosis in these patients.<sup>275</sup> *Aph. flos-aquae* algae has high concentrations of polyunsaturated fatty acids (PUFAs) which account for almost 10% of its dry weight. Even more important, it has a high percentage of the omega-3 fatty acids, comparing extremely favorably with most plants, seeds, nuts, and other microalgae. Natural algae-rich beta-carotene supplementation appears to normalize the diabetic-enhanced LDL oxidation levels and consequently may be of importance in delaying the accelerated development of atherosclerosis in these patients. "EFAs have lubricating qualities and increase cell membrane flexibility. They are known to reduce blood cholesterol and thus help to prevent cardiovascular disease...EFAs are especially useful because of the efficiency with which they increase the solubility of cholesterol deposits and wash these deposits away from our artery walls...As the consumption of fish oils or essential fatty acids found in *Aph. flos-aquae* increases, the tendency for blood platelets to aggregate decreases and blood pressure goes down." <sup>279</sup>

## Support Heart Function

Algae-derived omega-3 fatty acids may support heart function, reduce blood viscosity, decrease arteriosclerosis (a disease of hardened arterial walls) and lower high blood pressure, according to research of Zvi Cohen at The Laboratory for Micro-algal Biotechnology in Israel and Helen Norman at the United States Department of Agriculture. <sup>280</sup> The flexibility of any cell membrane is directly proportional to the amount and type of polyunsaturated fatty acids (PUFAs) it contains. Research reveals that algae supplementation can significantly reduce high levels of arachidonic acid (AA) in the blood and liver lipids and cause a significant increase in the percentages of the omega-3 polyunsaturated fatty acids (PUFAs). <sup>281</sup>

Dr. Rafail Kushak and colleagues demonstrated that *Aph. flos-aquae* essential fatty acids are more easily assimilated than those of soybean oil and offer superior cardiovascular benefits. While both soybean oil and blue-green algae contain the essential omega-3 fatty acid, alpha-linolenic acid (LNA), the scientists found that rats required triple the amount of soybean oil in their diets to achieve the same level of circulating LNA as rats fed algae. Also, *Aph. flos-aquae* significantly increased both eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) blood plasma levels far more effectively than did soybean oil. <sup>282</sup> Both EPA and DHA are essential for optimal cardiovascular and brain function and can be synthesized in the body from LNA.

Microalgae-derived DHA supplements markedly enhanced the DHA status levels in serum and platelets of healthy vegetarian subjects. Researchers also found a substantial increase of EPA and a lowering of total and LDL-cholesterol: HDL-cholesterol ratios, suggestive of a decreased risk factor for heart disease in the DHA algal supplemented group. <sup>283</sup> Microalgae supplementation may be especially important for vegetarians who have a limited intake of fish and eggs.

Japanese White rabbits fed on a ten-week load of high-cholesterol diet and powdered *Chlorella*, showed a significant suppression of total and beta-lipoprotein cholesterol levels, along with less aortic atheromatous lesions. However, rabbits in the control, with no algae in their diet, showed a dramatic increase in serum total cholesterol and beta-lipoprotein cholesterol levels, with resulting symptoms of atherosclerosis. <sup>291</sup>

Homocysteine blood levels are a significant predictor for risk of heart attack, the number one killer of adults in America. <sup>296</sup> Importantly, homocysteine can be transformed into the amino acid methionine—its beneficial alter form—with the help of B vitamins; especially folic acid in conjunction with B-6 and B-12. Microalgae contain a variety of B-vitamins and methionine.

Hawaiian scientists have developed a way to grow and extract heart-healthy substances from microalgae. Currently a randomized, double-blind trial is underway in association with Michigan State University, to evaluate whether astaxanthin, a natural antioxidant from microalgae, reduces blood serum levels of C-reactive protein (CRP). CRP is an indicator of low-grade arterial inflammation and one of the single strongest predictors of risk of future heart problems in apparently healthy men and women. <sup>298</sup>

## Allergy and Asthma Relief

*"If you are sitting on a tack, it takes a lot of aspirin to make it feel good. If you are sitting on two tacks, removing just one does not result in a 50 percent improvement."*

—Sidney Baker, **Detoxification and Healing**, 1997

A daily dose of beta-carotene, from an algae extract, demonstrated a protective effect against exercise-induced asthma.

Two studies have found that the inclusion of blue-green algae in the diet contributes to a reduction of anaphylactic and immune-type allergic reactions in animal studies. Serum histamine levels are significantly inhibited in rats administered *Spirulina*. These results suggest that blue-green algae may contain compounds that act to inhibit mast cell-mediated, immediate-type allergic reactions. <sup>302, 303</sup>

Researchers at Massachusetts General Hospital, affiliated with Harvard Medical School, found that algal oils significantly reduced blood levels of arachidonic acid in rats. <sup>305</sup> Arachidonic acid produces molecules (leukotrienes) that trigger allergic reactions and contribute to water retention (edema) and puffiness. These molecules may be 1,000 times more problematic than histamine in contributing to asthmatic bronchial constriction. <sup>306</sup>

A daily dose of beta-carotene, from an algae extract, demonstrated a protective effect against exercise-induced asthma. Of thirty-eight patients given 64 mg of algal beta-carotene extract daily for

one week, 53% were protected from exercise-induced asthma. All of the patients in the placebo condition showed a significant post-exercise reduction of breathing in a forced expiratory volume test. <sup>307</sup>

## Fewer Allergies, Skin Problems, and Asthma

A pilot study that used a survey developed by the National Center for Health Statistics (1996) reported fewer allergies, skin problems, and asthma among *Aph. flos-aquae* consumers. The algae eaters scored significantly better than average on numerous measures of health, when scores were compared to normative baseline data. <sup>308</sup>

In Japan blue-green algae is reported "to forestall pancreatic exhaustion and return balance to the flow of enzymatic secretions." <sup>310</sup> Good digestion requires that the body secrete sufficient hydrochloric acid and pancreatic enzymes into the stomach to process foods. Certain food allergies can be traced to poor digestion combined with "leaky gut syndrome" that allows undigested proteins to enter the blood; the immune system reacts to these large molecules as foreign invaders. " *Aph. flos-aquae* blue-green algae contains carotenes and chlorophyll, both of which are able to dramatically stimulate specialized cells around the intestinal walls to secrete lubricating material and thus help to prevent this type of allergic reaction." <sup>311</sup> The omega-3 fatty acids are likely to be helpful as well.

## Safety Issues

Industrial chemicals and microbial pathogens can contaminate any food. In recent years, the news media have broadcast many stories of illness and death related to bacteria-contaminated poultry, mercury in fish, aflatoxin in moldy peanuts, and viruses in uncooked shellfish. The Food and Drug Administration reports that food-borne infections caused by *Salmonella* alone are responsible for an estimated 6.5 million cases of human illness and 9,000 deaths annually in the United States. <sup>312</sup>

The primary safety concern with wild-grown algae comes from contaminant algal species that, under certain conditions, may grow in the same lake and thus be harvested along with the food algae. Known toxins that could potentially contaminate edible algae are amenable to regulatory assessment, using reliable laboratory analysis for signs of toxins, along with safety guidelines and consumption rates for the food. <sup>313,314</sup> A reputable microalgae company will guarantee that accurate and independent tests are done on each batch of harvested algae to ensure purity and safety.

## Freshness is Important

Another concern is how fresh or nutritionally intact the final product is. One of the best freshness indicators for microalgae is the amount and kind of chlorophyll breakdown products it contains. In one comparison of five companies that harvested wild microalgae the percentage of intact chlorophyll ranged from 0 to 65% (average of 21%). <sup>315</sup> Breakdown products of chlorophyll include pheophytins and, potentially, pheophorbides. <sup>3</sup> The latter are known to be toxic. Careful harvesting and avoidance of heat will minimize these breakdown products. The same is true of any species of microalgae and also of all chlorophyll-rich "green" foods.

## References

1. Passwater R, Soloman N, eds Algae: The next generation of superfoods. *The Experts' Optimal Health Journal*, 1997; 1:2.
2. Pirt S. *Biochemical Society Trans.* 1980; 8:479 cited by Aaronson and Dubinsky. Mass production of microalgae. *Experientia.* 1982; 43(suppl):42.
3. Abrams K. *Algae to the Rescue.* Logan House, 1996: 61.
4. Abrams K. *Algae to the Rescue.* Logan House, 1996: 31.
5. Braverman R. *The Healing Nutrients Within: Facts, Findings and New Research on Amino Acids.* Keats Publishing, 1987.
6. Shimizu Y. Microalgal metabolites: a new perspective. *Annual Review of Microbiology.* 1996; 50:442.
7. Cohen A, Norman H, Heimer Y. Microalgae as a source of omega 3 fatty acids. *World Review of Nutrition and Diet.* 1995; 77:1-31.
8. Simopoulou A. Omega 3 fatty acids in health and disease in growth of development. *American Journal of Clinical Nutrition.* 1991; 54:438-63.
9. Challem J. *Spirulina.* Keats Publishing, 1981: 5.
10. Lee W, Rosenbaum M. In *Chlorella*, Keats Publishing, 1987:19.
11. Oswald W, Goluike C. The algaatron, a novel microbial culture system. *The Sun at Work.* January 1966; 11(1).
12. Oswald W, Goluike C. Man in space: he takes along his wastes problem. *Wastes Engineering.* September 1961; 32(9).
13. Tabibul Islam. Wonder Cure for Malnutrition. *MISAnet/Inter Press Service*, June 2, 1988.
14. Federal Centers for Disease Control and Prevention, Atlanta, 1993.
15. Omenn G et al. Risk factors for lung cancer and for intervention effects in CARET, the Beta-Carotene and Retinol Efficacy Trial. *Journal of the National Cancer Institute.* November 1996; 88(21):1550-9.
16. DeCava J. *The Real Truth About Vitamins & Antioxidants.* Price-Pottenger Foundation, 1997: 121.
17. Hocman G. Prevention of Cancer: Vegetables and Plants. *Comparative Biochemistry and Physiology.* 1989; 93B(2): 201-12.
18. United States Public Health Service. *The Surgeon General's Report on Nutrition and Health.* Warner Books, 1989.
19. Kamath S, reported in *American Medical News*, May 24/31, 1985.
20. Serdula M et al. Fruit and Vegetable Intake Among Adults in 16 States: Results of a Brief Telephone Survey. *American Journal of Public Health*, 1995; 85(2):236-39.
21. DeCava J. *The Real Truth About Vitamins & Antioxidants.* Price-Pottenger Foundation, 1997: 121.
22. Stitt P. *Fighting the Food Giants.* Natural Press, 1980: 144.
23. Select Committee On Nutrition and Human Needs, United States Senate. *Dietary Goals for the United States.* Washington, DC: United States Printing Office, 1977.
24. *Physician's Desk Reference for Herbal Medicine.* Medical Economics Company, 1999.
25. Werback M. *Nutritional Influences on Illness: A Sourcebook of Clinical Research.* Third Line Press, 1993.
26. Arasaki S, Arasaki T. *Low Calorie, High Nutrition Vegetables From the Sea: To Help You Look and Feel Better.* Japan Publishing, 1983: 59.
27. Hoppe H. *Marine Algae in Pharmaceutical Science.* De Gruyter and Co, 1975.

28. Abrams K. *Algae to the Rescue*. Logan House, 1996: 31.
29. Smith R. Where is the wisdom...! *British Medical Journal*. 1991; 303:798-9.
30. May M. Disturbing Behavior. *Environmental Health Perspectives*. June 2000; 108(6):A262-67.
31. Crawford M. The early development and evolution of the human brain. *Upsala Journal of Medical Sciences. Supplement*. 1990; 48:43-78.
32. Crawford M et al. Evidence for the unique function of docosahexaenoic acid during the evolution of the hominid brain. *Lipids*. 1999; 34(suppl):S39-S47.
33. Broahurst C, Cunnane S, Crawford M. Rift Valley lake fish and shellfish provided brain-specific nutrition for early Homo. *British Journal of Nutrition*. January 1998; 79(1):3-21.
34. Laguna M, Villar R, Calleja J, Cadavid I. Effects of *Chlorella stigmatophora* extract on the central nervous system. *Planta Medica*. April 1993; 59(2):125-30.
35. Villar R, Laguna R, Calleja J, Cadavid I. Effects of *Skelettonema costatum* extracts on the central nervous system. *Planta Medica*. October 1992; 58(5):398-404.
36. Villar R, Laguna M, Calleja J, Cadavid I. Effects of *Dunaliella tertiolecta* extracts on the central nervous system. *Planta Medica*. October 1992; 58(5):404-9.
37. Takenaka H et al. Protective effect of *Dunaliella bardawil* on water-immersion-induced stress in rats. *Planta Medica*. October 1993; 59(5):421-4.
38. Tanaka K et al. Oral administration of a unicellular green algae, *Chlorella vulgaris*, prevents stress-induced ulcer. *Planta Medica*. October 1997; 63(5):465-6.
39. Challem J. *Spirulina*. Keats Publishing, 1981:16.
40. Shinpo K et al. Paper presented at the 36th Conference of Japanese Society of Nutrition and Food Science; 1982: 102.
41. Jarratt C, Jewett M, Peters S, Tragash E. *The Children and Algae Report*, The Center for Family Wellness, Harvard, Mass., 1995.
42. Bruno J, Gittelman J, Tuchfeld B. Lowered aluminum, with better detoxification and improved cognitive, behavioral ratings by children eating *Aphanizomenon flos-aquae*. Submitted for publication, 2000.
43. Bitterman N, Melamed Y, Ben-Amotz A. Beta-carotene and CNS oxygen toxicity in rats. *Journal of Applied Physiology*. March 1994; 76(3):1073-6.
44. Komatsu M, Hiramatsu M. The efficacy of an antioxidant cocktail on lipid peroxide level and superoxide dismutase activity in aged rat brain and DNA damage in iron-induced epileptogenic foci. *Toxicology*. August 2000; 148(2-3):143-8.
45. Vatassery G. Vitamin E and other endogenous antioxidants in the central nervous system. *Geriatrics*. September 1998; 53(Suppl 1); S25-S7.
46. Shohami E et al. Closed head injury in the rat induces whole body oxidative stress: overall reducing antioxidant profile. *Journal of Neurotrauma*. May 1999; 16(5):365-76.
47. Annapurna A, et al. Bioavailability of blue-green algae carotenoids in preschool children. *Journal of Clinical Biochemistry and Nutrition*. 1991; 10:145-51.
48. Jama J et al. Dietary antioxidants and cognitive function in a population-based sample of older persons. The Rotterdam Study. *American Journal of Epidemiology*. 1996; 144(3):275-80.
49. Brunett L. New ways to explain the brain. *Wisconsin Alumni Journal*. Summer 2000:36.
50. Cousens G. Report of treatment of Alzheimer's disease with *Alphanax Klamathonmenon flos-aqua* [sic]. *Orthomedicine*. Winter/Spring, 1985; 8(1):2.
51. Cousens G. Microalgae: First and finest superfood. *Body Mind Spirit*. April 1995; 14(3):12-18.



52. Valencia A, Walker J. A multi-axial treatment paradigm for mild traumatic brain injury to achieve reparative functional metaplasticity. Paper presented at the Third World Congress on Brain Injury; June 1999; Quebec City, Canada.
53. Sevilla I, Aguirre N. Study on the Effects of Super Blue-Green Algae on the Nutritional Status and School Performance of First-, Second-, and Third-Grade Children Attending the Monsenor Velez School in Nandaime, Nicaragua [dissertation, in Spanish]. Universidad CentroAmericana, Nicaragua, 1995.
54. Jarratt C, Jewett M, Peters S, Tragash E. *The Children and Algae Report*. The Center for Family Wellness, Harvard Mass., 1995.
55. Jarratt C. Personal communication, December 1998.
56. Bruno J, Gittelman J, Tuchfeld B. Lowered aluminum, with better detoxification, and improved cognitive, behavioral ratings by children eating *Aphanizomenon flos-aquae*. Submitted for publication, 2001.
57. Foldoe, M. A Case Study of The Perceived Effects of Eating *Aphanizomenon Flos-Aquae*, a Blue-Green Algae, On the Attention, Academic, and Social Behavior of Three Elementary School-Aged Children diagnosed with Attention Deficit/Hyperactivity Disorder (AD/HD) [thesis]. Sonoma State University, 1999.
58. Krylov V et al. Retrospective epidemiological study using medical records to determine which diseases are improved by *Aphanizomenon flos-aquae* supplements. Submitted for publication, 2000.
59. Drapeau C. Results of Survey of AFA consumers. Presented at Klamath Falls, Oregon, August 8, 1998.
60. Buletsa B, Ihnatovych I, Lupych P, Pulyk O. The prevalence, structure and clinical problems of multiple sclerosis in the Transcarpathian area based on epidemiological study data. *Lik Sprava*. Oct-Dec 1996; (10-12):163-5.
61. Bourre J et al. Function of dietary polyunsaturated fatty acids in the nervous system. *Prostaglandins Leukotrienes and Essential Fatty Acids*. 1993; 48:5-15.
62. Kushak R et al. Favorable effects of blue-green algae *Aphanizomenon flos-aquae* on rat plasma lipids. *Journal of the American Nutraceutical Association*. 2000; 2(3):59-65.
63. Colquhoun I, Bunday S. A lack of essential fatty acids as a possible cause of hyperactivity in children. *Medical Hypotheses*. May 1981; 7(5):673-9.
64. Duvner T. Gamma-linolenic acid as a treatment in AD/HD. Paper presented at the Sixth European Conference of Neurodevelopmental Delay, Stockholm, reported in *Hyperactive Children Support Group Journal*. 1994:48.
65. Murray C, Lopez A. Alternative projections of mortality and disability by cause 1990 to 2020: Global Burden of Disease Study. *Lancet*. May 1997; 349(9064):1498-504.
66. Christensen L. *Diet-Behavior Relationships*. American Psychological Association Publications, 1996:168.
67. Taylor J. The algae AD/HD connection: Can blue-green algae be of help with attention deficit/hyperactivity disorder? *Network of Hope Newsletter*. February 1998.
68. Cited in: Carroll L, Tober J. *The Indigo Children: The New Kids Have Arrived*. Hay House Inc. 1999:188.
69. Beisel W. History of nutritional immunology: introduction and overview. *Journal of Nutrition*. March 1992; 122(3 Suppl):591-6.
70. Beisel W. Nutrition in pediatric HIV infection: setting the research agenda. Nutrition and immune function: Overview. *Journal of Nutrition*. 1996; 126(10 Suppl):2611-15.
71. Sevilla I, Aguirre N. Study on the Effects of Super Blue-Green Algae on the Nutritional Status and School Performance of First-, Second-, and Third-Grade Children Attending the Monseñor Velez School in Nandaime, Nicaragua [doctoral dissertation, in Spanish].

Universidad CentroAmericana, Nicaragua 1995.

72. Bruno J, Gittelman J, Tuchfeld B. Lowered aluminum, with better detoxification and improved cognitive, behavioral ratings by children eating *Aphanizomenon flos-aquae*. Submitted for publication, 2001.

73. Younghaung W et al. The study on curative effect of zinc-containing blue-green algae for zinc deficient children. Paper presented at the Fifth International Phycological Congress; Qingdao, China; June 1994.

74. Alexander M, Newmark H, Miller R. Oral betacarotene can increase the number of OKT4+ cells in human blood. *Immunology Letter*. 1985; 9(4):221-4.

75. Abrams, K. *Algae to the Rescue*. Logan House, 1996:71.

76. Bendich, A. Carotenoids and the immune response. *Journal of Nutrition*. 1989; 119:112-5.

77. Okai Y, Higashi-Okai K. Possible immunomodulating activities of carotenoids *in vitro* cell culture experiments. *International Journal of Immunopharmacology*. December 1996; 18(12):753-8.

78. Qureshi M, Ali R. *Spirulina platensis* exposure enhances macrophage phagocytic function in cats. *Immunopharmacology and Immunotoxicology*. 1996; 18(3):457-63.

79. Qureshi M et al. Immune enhancement potential of *Spirulina platensis* in chickens. *Poultry Science*. 1994; 73:46.

80. Qureshi M, Garlich J, Kidd M. Dietary *Spirulina platensis* enhances humoral and cell-mediated immune functions in chickens. *Immunopharmacology and Immunotoxicology*. 1996; 18(3):465-76.

81. Jensen G, Ginsberg D, Huerta P, Drapeau C. Consumption of *Aphanizomenon flos-aquae* has rapid effects on the circulation and function of immune cells in humans. A novel approach to nutritional mobilization of the immune system. *Journal of the American Nutraceutical Association*. January, 2000; 2(3)50-8.

82. Drapeau C. Increased macrophage activity observed in college basketball players eating AFA using live blood analysis. Presentation at Klamath Falls, Oregon; August 8, 1998.

83. Hayashi O, Katoh T, Okuwaki Y. Enhancement of antibody production in mice by dietary *Spirulina platensis*. *Journal of Nutritional Science and Vitaminology* (Tokyo). October 1994; 40(5):431-41.

84. Hayashi O, Hirahashi T, Katoh T, Miyajima H, Hirano T, Okuwaki Y. Class-specific influence of dietary *Spirulina platensis* on antibody production in mice. *Journal of Nutritional Science and Vitaminology* (Tokyo). 1998; 44(6):841-51.

85. Terziev V, Planski B, Encheva I. Use of nonspecific agents and vaccination in bronchopneumonia prevention in cattle. *Vet Med Nauki* [Bulgarin]. 1983; 20(1):36-9.

86. Manoukian R et al. Effects of the blue-green algae *Aphanizomenon flos-aquae* (L.) Ralphs on human natural killer cells. In *Phytoceuticals: Examining the health benefits and pharmaceutical properties of natural antioxidants and phytochemicals*. IBC Library Series 1911, ch. 3.1. Boston, March 1998; 233-41.

87. Jensen G, Ginsberg D, Huerta P, Drapeau C. Consumption of *Aphanizomenon flos-aquae* has rapid effects on the circulation and function of immune cells in humans. A novel approach to nutritional mobilization of the immune system. *Journal of the American Nutraceutical Association*. January 2000; 2(3):50-8.

88. Krylov V et al. Retrospective epidemiological study using medical records to determine which diseases are improved by *Aphanizomenon flos-aquae* supplements. Submitted for publication, 2000.

89. Horrobin E et al. The nutritional regulation of T-lymphocyte function. *Medical Hypotheses* 1979; 5:969.
90. Tornabene T et al. Lipid and lipopolysaccharide constituents of cyanobacterium *Spirulina platensis*. *Ecol Prog Serv*. March 1985; 22:121.
91. Cheng-Wu Z, Chao-Tsi T, Zhen Z. The effects of polysaccharide and phycocyanin from *Spirulina platensis* on peripheral blood and hematopoietic system of bone marrow in mice. *Proceedings of the Second Asia-Pacific Conference on Algal Biotechnology*. National University of Singapore; 1994:58.
92. Kovats E. Potentiation of HIV envelope glycoprotein and other immunogens by endotoxin and its molecular fragments. *International Journal of Immunopharmacology*. March 1996; 43(3):248-56.
93. Besednova N, Smolina T, Mikheiskaia L, Ovodova R. Immunostimulating activity of the lipopolysaccharides of blue-green algae. *Zhurnal Mikrobiologii, Epidemiologii I Immunobiologii*(Russian). December 1979; (12):75-9.
94. Abrams K. *Algae to the Rescue*. Logan House, 1996:75.
95. Woodruff H. Natural products from microorganisms. *Science*. June 1980; 208(449):1225-9.
96. Witvrouw M, De Clercq E. Sulfated polysaccharides extracted from sea algae as potential antiviral drugs. *General Pharmacology*. October 1997; 29(4):497-511.
97. Bewick P et al. *Chlorella: The Emerald Food*. Ronin Publishing, 1984.
98. Schmidt R. Treatment for Leprosy. *Price-Pottenger Nutrition Foundation Health Journal*. 1997;21(3).
99. Martinez-Nadal F. Antimicrobial activity of *Spirulina maxima*. Paper presented at the Tenth International Congress of Microbiology, Mexico City; August 1970.
100. Jorjani G, Amirani P. Antibacterial activities of *Spirulina platensis*. *Maj Limy Puz Danisk Jundi Shap* (Danish). 1978; 1:14-18.
101. Ostensvik O, Skulberg O, Underdal B, Hormazabal V. Antibacterial properties of extracts from selected planktonic freshwater cyanobacteria — a comparative study of bacterial bioassays. *Journal of Applied Microbiology*. 1998; 84(6):1117-24.
102. Kreitlow S, Mundt S, Lindequist U. Cyanobacteria – a potential source of new biologically active substances. *Journal of Biotechnology*. April 1999; 70(1-3):61-3.
103. Frankmolle W et al. Antifungal cyclic peptides from the terrestrial blue-green alga *Anabaena laxa*. I. Isolation and biological properties. *Journal of Antibiotics* (Tokyo). September 1992; 45(9):1451-7.
104. Aaronson A, Dubinsky Z. Mass production of microalgae. *Experientia*. 1982; 43(Suppl.):44.
105. Gustafson K et al. AIDS antiviral sulfolipids from cyanobacteria. *Journal of the National Cancer Institute*. 1989; 81:1254-8.
106. Cardellina J et al. A chemical screening strategy for the dereplication and prioritization of HIV-inhibitory aqueous natural products extracts. *Journal of Natural Products*. July 1993; 56(7):1123-9.
107. Lau A et al. Inhibition of reverse transcriptase activity by extracts of cultured blue-green algae (cyanophyta). *Planta Medica*. April 1993; 59(2):148-51.
108. Ayehunie S, Belay A, Baba T, Ruprecht R. Inhibition of HIV-1 replication by an aqueous extract of *Spirulina platensis* (*Arthrospira platensis*). *Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology*. May 1998;18(1):7-12.
109. Hayashi et al. Calcium spirulan, an inhibitor of enveloped virus replication, from a blue-green algae *Spirulina platensis*. *Journal of Natural Products*. 1996; 59:83-7.

110. Ayeahunie S, Belay A, Baba T, Ruprecht R. Inhibition of HIV-1 replication by an aqueous extract of *Spirulina platensis* (*Arthrospira platensis*). *Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology*. May 1998; 18(1):7-12.
111. Loya S, Reshef V, Mizrachi E et al. The inhibition of the reverse transcriptase of HIV-1 by the natural sulfoglycolipids from cyanobacteria: contribution of different modalities to their high potency. *Journal of Natural Products*. 1998; 61(7):891-5.
112. Schaeffer D, Krylov V. Anti-AIDS activity of extracts and compounds from algae and cyanobacteria. *Ecotoxicology and Environmental Safety*. 2000; 45(3):208-27.
113. Gandhi M, Boyd M et al. Properties of cyanovirin-N (CV-N): inactivation of HIV-1 by sessile cyanovirin-N. *Developments in Biological Standardization*. 2000; 102:141-8.
114. Hayashi T, Hayashi K, Maeda M, Kojima I. Calcium spirulan, an inhibitor of enveloped virus replication, from a blue-green alga *Spirulina platensis*. *Journal of Natural Products*. January 1996; 59(1):83-7.
115. Hayashi K, Hayashi T, Kojima I. A natural sulfated polysaccharide, calcium spirulan, isolated from *Spirulina platensis*: in vitro and ex vivo evaluation of anti-herpes simplex virus and anti-human immunodeficiency virus activities. *AIDS Research and Human Retroviruses*. 1996; 12(15):1463-71.
116. Larsen L, Moore R, Patterson G. Beta-carotenes from the blue-green alga *Dichothrix baueriana*. *Journal of Natural Products*. March 1994; 57(3):419-21.
117. Hayashi K et al. An extract from *Spirulina platensis* is a selective inhibitor of *Herpes simplex* virus type 1 penetration into HeLa cells. *Phytotherapy Research*. 1993; 7:76-80.
118. Guzman-Murillo M, Ascencio F. Anti-adhesive activity of sulphated exopolysaccharides of microalgae on attachment of red sore disease-associated bacteria and *Helicobacter pylori* to tissue culture cells. *Letters of Applied Microbiology*. June 2000; 30(6):473-8.
119. Fabregas J et al. In vitro inhibition of the replication of *Haemorrhagic septicaemia* virus and African swine fever virus by extracts from marine microalgae. *Antiviral Research*. November 1999; 44(1):67-73.
120. Krylov V et al. Retrospective epidemiological study using medical records to determine which diseases are improved by *Aphanizomenon flos-aquae* supplements. Submitted for publication 2000.
121. Drapeau C. Results of Survey of AFA Consumers. Presentation at Klamath Falls, Oregon, August 8, 1998.
122. Lahitova N, Doupovcova M, Zvonar J, Chandoga J, Hocman G. Antimutagenic properties of fresh-water blue-green algae. *Folia Microbiologica*. 1994; 39(4):301-3.
123. Hasegawa T et al. Augmentation of the resistance against *Listeria monocytogenes* by oral administration of a hot water extract of *Chlorella vulgaris* in mice. *Immunopharmacology and Immunotoxicology*. 1994; 16(2):191-202.
124. Haegawa T et al. Hot water extracts of *Chlorella vulgaris* reduce opportunistic infection with *Listeria monocytogenes* in C57BL/6 mice infected with LP-BM5 murine leukemia viruses. *International Journal of Immunopharmacology*. 1995; 17(6):505-12.
125. Tanaka K et al. Augmentation of host-defense by a unicellular green algae, *Chlorella vulgaris*, to *Escherichia coli* infection. *Infection and Immunity*. 1986; 53:267.
126. Ibusuki K, Minamishima Y. Effect of *Chlorella vulgaris* extracts on murine cytomegalovirus infections. *Natural Immunity and Cell Growth Regulation*. 1990; 9:121.
127. Konishi F et al. Enhanced resistance against *Escherichia coli* infection by subcutaneous administration of the hot-water extract of *Chlorella vulgaris* in cyclophosphamide-treated mice. *Cancer Immunology and Immunotherapy*. 1990; 32(1):1.

128. Hasegawa T et al. Accelerated restoration of the leukocyte number and augmented resistance against *Escherichia coli* in cyclophosphamide-treated rats orally administered with a hot water extract of *Chlorella vulgaris*. *International Journal of Immunopharmacology*. 1990; 12:883.
129. Bock K, Sabin N. *The Road to Immunity*. Pocket Books, 1997:177.
130. Sommer A et al. Increased risks of respiratory disease and diarrhea in children with pre-existing mild vitamin A deficiency. *American Journal of Clinical Nutrition*. 1984; 40:1090-95.
131. Pinnock C et al. Vitamin A status in children who are prone to respiratory tract infections. *Australian Pediatric Journal*. 1986; 22(2):95-9.
132. Nikitin A, Simvolokov S. The efficacy of the natural antibacterial preparation chlorophyll in the combined treatment of acute lung abscesses. *Ter Arkh* (Russian). 1989; 61(8):113-6.
133. Bowers W. Chlorophyll in wound healing and suppurative disease. *American Journal of Surgery*. 1947; 73:37.
134. Aposhyan S. *Natural Intelligence: Mind-Body Integration and Human Development*. William and Wilkins, 1999:150.
135. Rothschild L, Cockell C. Radiation: microbial evolution, ecology, and relevance to Mars missions. *Mutation Research*. 1990; 430:281.
136. Tomitani A et al. Chlorophyll b and phycobilins in the common ancestor of cyanobacteria and chloroplasts. *Nature*. July 1999; 400(6740):159-62.
137. Pennisi E. *Science News*. March 12, 1994.
138. Greife H, Molnar S. Studies of nucleic acid metabolism in rats by use of carbon-14-labeled purine and pyrimidine bases and nucleic acids: Anabolic pathways of nucleic acid derivatives. *Tierphysiologie* (German). 1978; 40(5):248-56.
139. Berthold H et al. Evidence for incorporation of intact dietary pyrimidine (but not purine) nucleosides into hepatic RNA. *Proceedings of the National Academy of Science USA*. October 1995; 92(22):10123-7.
140. Devi M. The effect of algal protein diets on the regeneration of serum and liver proteins in protein depleted rats. *Plant Foods for Human Nutrition*. 1983; 33:287.
141. Devi M et al. Serum protein regeneration studies on rats on algal diets. *Nutrition Research International*. 1979; 19:785.
142. Lahitova, N, Doupovcova M, Zvonar J, Chandoga J, Hocman G. Antimutagenic properties of fresh-water blue-green algae. *Folia Microbiologica*. 1994; 39(4):301-3.
143. Ma G, Xue K, Wu J, Yuan S, Qin H. Antimutagenic effects of beta-carotene from *Dunaliella salina* (Chinese). *Chung Kuo Yao Li Hsueh Pao*. May 1998; 19(3):282-4.
144. Anderson R et al. Reduction in free-radical-induced DNA strand breaks and base damage through fast chemical repair by flavonoids. *Free Radical Research*. July 2000; 33(1):91-103.
145. Gagne S. *Energetics of Food*. Spiral Sciences Inc., 1990: 273.
146. Kumamoto S. (1984, August 28) U.S. Patent # 4,468,460 for Method of Human Cell Culture.
147. Apsley J. *The Regeneration Effect*. Genesis Communications, 1996.
148. Krasnikova N. Proliferation of the epithelium surrounding a skin wound in hairless mice exposed to sodium chlorophyllin. *Biull Eksp Biol Med* (Russian). October 1973; 75(10):99-102.
149. Krasnikova N. Experimental use of an aqueous solution of sodium chlorophyllin to speed the healing of skin wounds. *Eksp Khir Anesteziol* (Russian). Sep-Oct 1972; 17(5):19-

22.

150. Hughes J, Latner L. Chlorophyll and hemoglobin regeneration after hemorrhage. *Journal of Physiology*. 1936; 86:388.
151. Patek A. Chlorophyll and regeneration of blood. *Archives of Internal Medicine*. 1936; 57:76.
152. Arasaki S, Arasaki T. *Low Calorie, High Nutrition Vegetables From the Sea: To Help You Look and Feel Better*. Japan Publications, 1983: 60.
153. Needleman H, Landrigan P. *Raising Children Toxin Free*, Avon Books, 1994: 138.
154. Weiss J, Landauer M. Radioprotection by antioxidants. *Annals of the New York Academy of Science*. 2000; 899:44-60.
155. Ben-Amotz A et al. Natural beta-carotene and whole body irradiation in rats. *Radiation and Environmental Biophysics*. November 1996; 35(4):285-8.
156. Umegaki K, Takeuchi N, Ikegami S, Ichikawa T. Effect of beta-carotene on spontaneous and X-ray-induced chromosomal damage in bone marrow cells of mice. *Nutrition and Cancer*. 1994; 22(3):277-84.
157. Bewick E et al. *Chlorella: The Emerald Food*. Ronin Publishing, 1984: 20.
158. Kumar S et al. Inhibition of radiation-induced DNA damage in plasmid pBR322 by chlorophyllin and possible mechanism(s) of action. *Mutation Research*. March 1999; 425(1):71-9.
159. Karpov L et al. The postradiation use of vitamin-containing complexes and a phycocyanin extract in a radiation lesion in rats. *Radiats Biol Radioecol* (Russian). May-Jun 2000; 40(3):310-4.
160. Sarma L, Tiku A, Kesavan P, Ogaki M. Evaluation of radioprotective action of a mutant (E25) form of *Chlorella vulgaris* in mice. *Journal of Radiation Research* (Tokyo). December 1993; 34(4):277-84.
161. Vacek A, Rotkovska D, Bartonickova A. Radioprotection of hemopoiesis conferred by aqueous extract from chlorococcal algae (*Ivastimul*) administered to mice before irradiation. *Experimental Hematology*. 1990; 18:234-37.
162. Rotkovska D, Vacek A, Bartonickova A. The radioprotective effects of aqueous extract from chlorococcal freshwater algae (*Chlorella kessleri*) in mice and rats. *Strahlenther Onkologie*. November 1989; 165(11):813-6.
163. Rotkovska D, Vatsek A, Bartonichikova A. Increase in the radiation resistance of mice using *Ivastimul*. *Radiobiologija* (Russian). Sep-Oct 1989; 29(5):652-4.
164. Qishen P, Guo B, Kolman A. Radioprotective effect of extract from *Spirulina platensis* in mouse bone marrow cells studied by using the micronucleus test. *Toxicology Letters*. August 1989; 48(2):165-9.
165. Singh S, Tiku A, Kesavan P. Post-exposure radioprotection by *Chlorella vulgaris* (E-25) in mice. *Indian Journal of Experimental Biology*. August 1995; 33(8):612-5.
166. Apsley J. *The Regeneration Effect*. Genesis Communications. 1996:75.
167. Abrams K. *Algae to the Rescue*. Logan House. 1996:32.
168. Ben-Amotz A et al. Effect of natural beta-carotene supplementation in children exposed to radiation from the Chernobyl accident. *Radiation Environmental Biophysics*. October 1988; 37(3):187-93.
169. Christian Drapeau (former Cell Tech research director). Personal communication, August 1998.
170. Cited by Linet M. Evolution of cancer epidemiology. *Epidemiology Review*. 2000; 22(1):35.
171. Murakami A, Ohigashi H, Koshimizu K. Anti-tumor promotion with food

- phytochemicals: a strategy for cancer chemoprevention. *Bioscience, Biotechnology, and Biochemistry*. January 1996; 60(1):1-8.
172. Hocman G. Prevention of Cancer: vegetables and plants. *CBP: Comparative Biochemistry and Physiology B*. 1989; 93(2):201-12.
173. Sarkar A et al. Beta-carotene prevents lipid peroxidation and red blood cell damage in experimental hepatocarcinogenesis. *Cancer Biochemistry and Biophysics*. 1995; 15(2):111-25.
174. Tinkler J et al. Dietary carotenoids protect human cells from damage. *Journal of Photochemistry and Photobiology*. 1994; 26(3):282-5.
175. Garewal H et al. Emerging role of beta-carotene and antioxidant nutrients in prevention of oral cancer. *Archives of Otolaryngology*. 1995; 121(2):141-4.
176. Le Marchand L et al. Intake of specific carotenoids and lung cancer risk. *Cancer Epidemiology*. 1993; 2:183-7.
177. Johnson E, Schroeder W. Microbial carotenoids. *Advanced Biochemistry Engineering and Biotechnology*. 1996; 53:119-178.
178. Mittal A et al. Modulatory potential of *Spirulina fusiformis* on carcinogen metabolizing enzymes in Swiss albino mice. *Phytotherapy Research*. March 1999; 13(2):111-4.
179. Kozlenko R, Henson, R. The study of *Spirulina*, effects on the AIDS virus, cancer and the immune system. *Healthy & Natural*. 1996; 3(5):66-7.
180. Fujii Y, Sakamoto S, Ben-Amotz A, Nagasawa H. Effects of beta-carotene-rich algae *Dunaliella bardawil* on the dynamic changes of normal and neoplastic mammary cells and general metabolism in mice. *Anticancer Research*. Mar-Apr 1999; 13(2):389-93.
181. Xue L. Experimental study on extract of *Dunaliella salina* in preventing NSAR-induced cancer of proventriculus in mice. *Chung Hua Yu Fang I Hsueh Tsa Chih* (Chinese). November 1993; 27(6):350-3.
182. Nagasawa H et al. Suppression by beta-carotene-rich algae *Dunaliella bardawil* of the progression, but not the development, of spontaneous mammary tumours in SHN virgin mice. *Anticancer Research*. Mar-Apr 1991; 11(2):713-7.
183. Nagasawa H et al. Inhibition by beta-carotene-rich algae *Dunaliella* of spontaneous mammary tumourigenesis in mice. *Anticancer Research*. Jan-Feb 1989; 9(1):71-5.
184. Combs W et al. In vivo and in vitro effects of B-carotene and algae extracts in murine tumor models. *Nutrition and Cancer*. 1989; 12(4):371-9.
185. Nagasawa H et al. Inhibition by beta carotene rich algae *Dunaliella* of spontaneous mammary tumourigenesis in mice. *Anticancer Research*. 1989; 9:71.
186. Schwartz J, Shklar G, Suda D. Inhibition of experimental oral carcinogenesis by topical beta carotene. *Carcinogenesis*. 1986; 7(5):711-5.
187. Schwartz J, Shklar G, Reid S, Trickler D. Prevention of experimental oral cancer by extracts of *Spirulina-Dunaliella* algae. *Nutrition and Cancer*. 1988; 11(2):127-34.
188. Schwartz J, Sloane D, Shklar G. Prevention and inhibition of oral cancer in the hamster buccal pouch model associated with carotenoid immune enhancement. *Tumor Biology*. 1989; 10:297-309.
189. Shklar G, Schwartz J. Tumor necrosis factor in experimental cancer regression with alpha-tocopherol, beta-carotene, canthaxanthin and algae extract. *European Journal of Cancer and Clinical Oncology*. May 1988; 24(5):839-50.
190. Schwartz J, Shklar G. Regression of experimental hamster cancer by beta-carotene and algae extracts. *Journal of Oral and Maxillofacial Surgery*. June 1987; 45(6):510-5.
191. Mathew B et al. Evaluation of chemoprevention of oral cancer with *Spirulina fusiformis*. *Nutrition and Cancer*. 1995; 24(2):197-202.
192. Smith C, Zhang X. Mechanism of action of cryptophycin. *Journal of Biological*

*Chemistry*. 1996; 271(11):6192-8.

193. Smith C, Zhang X, et al. Cryptophycin: a new antimicrotubule agent active against drug-resistant cells. *Cancer Research*. July 1994; 54(14):3779-84.

194. Ogino J et al. Dendroamides, new cyclic hexapeptides from a blue-green alga. Multidrug-resistance reversing activity of dendroamide A. *Journal of Natural Products*. June 1996; 59(6):581-6.

195. Smith C et al. Reversal of multiple drug resistance by tolyporphin, a novel cyanobacterial natural product. *Oncology Research*. 1994; 6(4-5):211-8.

196. Smith C, Carmeli S, Moore R, Patterson G. Scytophycins, novel microfilament-depolymerizing agents which circumvent P-glycoprotein-mediated multidrug resistance. *Cancer Research*. March 1993; 53(6):1343-7.

197. Vermeil C, Morin O. Experimental role of the unicellular algae *Prototheca* and *Chlorella* (chlorellaceae) in anti-cancer immunogenesis. *Comptes Rendus Des Seances De La Societe De Biologie Et De Ses Filiales*. October 1976; 170(3):646-9.

198. Mishima T et al. Inhibition of tumor invasion and metastasis by calcium spirulan (Ca-SP), a novel sulfated polysaccharide derived from blue-green algae, *Spirulina platensis*. *Clinical and Experimental Metastasis*. 1998; 16(6):541-50.

199. Tanaka K et al. A novel glycoprotein obtained from *Chlorella vulgaris* strain CK22 shows antimetastatic immuno-potential. *Cancer Immunology and Immunotherapy*. February 1998; 45(6):313-20.

200. Hayakawa Y, Hayashi T et al. Calcium spirulan as an inducer of tissue-type plasminogen activator in human fetal lung fibroblasts. *Biochimica Et Biophysica Acta*. March 1997; 1355(3):241-7.

201. Noda K et al. A water-soluble antitumor glycoprotein from *Chlorella vulgaris*. *Planta Medica*. October 1996; 62(5):423-6.

202. Tokuda H et al. Inhibition of 12-O-TPA promoted mouse skin papilloma by digalactosyl diacylglycerols from the freshwater cyanobacterium *Phormidium tenue*. *Cancer Letters*. 1996; 104(1):91-5.

203. Vermeil C, Morin O, Le Bodic L. The stimulation of tumoricidal peritoneal macrophages can be directly induced by peritoneal implantation of unicellular algae in humans. *Archives De L Institut Pasteur De Tunis* (French). Mar-Jun 1985; 62(1-2):91-4.

204. Higashi-Okai K, Okai Y. Potent suppressive activity of chlorophyll a and b from green tea (*Camellia sinensis*) against tumor promotion in mouse skin. *Journal of UOEH* (Japanese). September 1998; 20(3):181-8.

205. Okai Y et al. Suppressing effects of chlorophyllin on mutagen-induced umu C gene expression in *Salmonella typhimurium* (TA 1535/pSK 1002) and tumor promoter dependent ornithine decarboxylase induction in BALB/c 3T3 fibroblast cells. *Mutation Research*. August 1996; 370(1):11-7.

206. Breinholt V et al. Dietary chlorophyllin is a potent inhibitor of aflatoxin B1 hepatocarcinogenesis in rainbow trout. *Cancer Research*. 1995; 55(1):57-62.

207. Singh et al. Inhibitory potential of *Chlorella vulgaris* (E-2S) on mouse skin papillomagenesis and xenobiotic detoxification system. *Anticancer Research*. 1999; 19:1887-92.

208. Tanaka K et al. Oral administration of *Chlorella vulgaris* augments concomitant antitumor immunity. *Immunopharmacology and Immunotoxicology*. 1990; 12(2):277-91.

209. Konishi F et al. Antitumor effect induced by a hot water extract of *Chlorella vulgaris*: resistance to meth-A tumor growth mediated by CE-induced polymorphonuclear leukocytes. *Cancer Immunology and Immunotherapy*. 1985; 19(2):73-8.



210. Tanaka K et al. Augmentation of antitumor resistance by a strain of unicellular green algae, *Chlorella vulgaris*. *Cancer Immunology and Immunotherapy*. 1984; 17(2):90-4.
211. Nomoto K, Yokokura T, Satoh H, Mutai M. Antitumor activity of *Chlorella* extract, PCM-4, by oral administration. *Gan To Kagaku Ryoho* (Japanese). March 1983; 10(3):781-5.
212. Morin O, Guilard R, Guihard D, Vermeil C. New approach to the study of the experimental inhibitory effect of the unicellular alga *Chlorella pyrenoidosa* against the murine sarcomas BP8 and L1210. *Comptes Rendus Des Seances De La Societe De Biologie Et De Ses Filiales* (French). 1980; 174(1):74-81.
213. Neveu P et al. Modulation of antibody synthesis by an antitumor algae. *Experientia*. December 1978; 34(12):1644-5.
214. Miyazawa Y et al. Immunomodulation by a unicellular green algae (*Chlorella pyrenoidosa*) in tumor-bearing mice. *Journal of Ethnopharmacology*. December 1988; 24(2):135-46.
215. Tanaka K et al. A novel glycoprotein obtained from *Chlorella vulgaris* strain CK22 shows antimetastatic immunopotentiality. *Cancer Immunology and Immunotherapy*. February 1998; 45(6):313-20.
216. Carbonnelle D et al. Antitumor and antiproliferative effects of an aqueous extract from the marine diatom *Haslea ostrearia* (simonsen) against solid tumors: lung carcinoma (NSCLC-N6), kidney carcinoma (E39) and melanoma (M96) cell lines. *Anticancer Research*. 1999; 19:621-4.
217. Berge J et al. Antiproliferative effects of an organic extract from the marine diatom *Skeletonema costatum* (grev.) against a non-small-cell bronchopulmonary carcinoma line (NSCLC-N6). *Anticancer Research*. 1997; 17:2115-20.
218. Henrikson R. *Earth Food Spirulina*. Ronore Enterprises. 1989: 69.
219. Lijjima N et al. Anti-tumor agent and method of treatment therewith. US patent pending, ref. P1150-726-A82679, Application filed 15 Sep. 1982.
220. Patent claim filed by Dainippon Ink and Chemicals and Tokyo Kenkyukai for "Anti-tumor agents containing phycobilin — also used to treat ulcers and hemorrhoid bleeding" (1983, JP58065216-A830418).
221. Cited in: Challem J. *Spirulina*. Keats Publishing, 1981: 17.
222. Ben-Amotz A et al. Natural beta-carotene and whole body irradiation in rats. *Radiation and Environmental Biophysics*. November 1996; 35(4):285-8.
223. Konishi F et al. Protective effect of an acidic glycoprotein obtained from culture of *Chlorella vulgaris* against myelosuppression by 5-fluorouracil. *Cancer Immunology and Immunotherapy*. June 1996; 42(5):268-74.
224. Abrams K. *Algae to the Rescue*. Logan House, 1996:26.
225. Arenesen E. Serum total homocysteine and coronary heart disease. *International Journal of Epidemiology*. August 1995; 24(4):704-9.
226. Baker S. *Detoxification and Healing: The Key to Optimal Health*. Keats Publishing, 1997.
227. Tel-Or E, Huflejt M, Packer L. The role of glutathione and ascorbate in hydroperoxide removal in cyanobacteria. *Biochemical and Biophysical Research Communications*. October 1985; 132(2):533-9.
228. Cui J, Wakabayashi S, et al. Isolation and sequence studies of cysteinyl peptides from *Spirulina* glutathione reductase: comparison of active site cysteine peptides with those of other flavoprotein disulfide oxidoreductases. *Journal of Biochemistry* (Tokyo). March 1989; 105(3):390-4.
229. Sundquist A, Fahey R. Evolution of antioxidant mechanisms: thiol-dependent peroxidases and thioltransferase among prokaryotes. *Journal of Molecular Evolution*.

November 1989; 29(5):429-35.

230. Torres-Duran P, et al. Studies on the preventive effect of *Spirulina maxima* on fatty liver development induced by carbon tetrachloride, in the rat. *Journal of Ethnopharmacology*. February 1999; 64(2):141-7.

231. Torres-Duran P, et al. *Spirulina maxima* prevents induction of fatty liver by carbon tetrachloride in the rat. *Biochemistry and Molecular Biology International*. April 1998; 44(4):787-93.

232. Vadiraja B, Gaikwad N, Madyastha K. Hepatoprotective effect of C-phycoerythrin: Protection for carbon tetrachloride and R(+)-pulegone-mediated hepatotoxicity in rats. *Biochemical and Biophysical Research Communications*. 1998; 249(2):428-31.

233. Gonzalez de Rivera C, et al. Preventative effect of *Spirulina maxima* on the fatty liver induced by a fructose-rich diet in the rat, a preliminary report. *Life Science*. 1993; 53(1):57-61.

234. Dashwood R, Guo D. Protective properties of chlorophylls against the covalent binding of heterocyclic amines to DNA in vitro and in vivo. Paper presented at the Princess Takamatsu Symposium. 1995; 23:181-9.

235. Challem J. *Spirulina*. Keats Publishing. 1981: 14.

236. Sukenik A, Takahashi H, and Modady S. Dietary lipids from marine unicellular algae enhance the amount of liver and blood omega-3 fatty acids in rats. *Annals of Nutrition and Metabolism*. 1994; 38(2):85-96.

237. Levin, G, Yeshurun M, Mokady S. In vivo antiperoxidative effect of 9-cis beta-carotene compared with that of the all-trans isomer. *Nutrition and Cancer*. 1997; 27(3):293-7.

238. Gagne S. *Energetics of Food*. Spiral Science Inc. 1990: 274.

239. Challem J. *Spirulina*. Keats Publishing. 1981: 18.

240. Yamane Y. The effect of *Spirulina* on nephrotoxicity in rats. Paper presented at Annual Symposium of the Pharmaceutical Society of Japan, April 15, 1988.

241. Lee W, Rosenbaum M. *Chlorella*. Keats Publishing. 1987: 17.

242. Pore R. Detoxification of chlordecone poisoned rats with *Chlorella* and *Chlorella*-derived sporopollenin. *Drug and Chemical Toxicology*. 1984; 7(1):57-7.

243. Bruno J, Gittelman, J, Tuchfeld B. Lowered aluminum, with better detoxification, and improved cognitive, behavioral ratings by children eating *Aphanizomenon flos-aquae*. Submitted for publication 2001.

244. Burnatowska-Hledin M, Kaiser L, Mayor G. Aluminum, parathyroid hormone, and osteomalacia. *Special Topics in Endocrinology and Metabolism*. 1983; 5:201-26.

245. Shastri D, Kumar M, Kumar A. Modulation of lead toxicity by *Spirulina fusiformis*. *Phytotherapy Research*. May 1999; 13(3):258-60.

246. Rimland B and Larson G. Hair mineral analysis and behavior: an analysis of 51 studies. *Journal of Learning Disabilities*. 1983; 16:279-85.

247. Phil R, and Parkes M. Hair element content in learning disabled children. *Science*. 1977; 198:204-6.

248. Valencia A, Walker J. A multi-axial treatment paradigm for mild traumatic brain injury to achieve reparative functional metaplasticity. Paper presented at the Third World Congress on Brain Injury, Quebec City, Canada. June 1999.

249. Golubkina N et al. The selenium haemostasis during experimental anaphylaxis reaction in rats treated with reduced glutathione and selenium enriched *Spirulina*. *Voprosy Meditsinskoi Khimii* (Russian). Jan-Feb 2000; 46(1):22-7.

250. Young R, Bergei J. Use of chlorophyllin in the care of geriatric patients. *Journal of the American Geriatric Society*. January 1980; 28(1):46-7.

251. Tomitani A et al. Chlorophyll b and phycobilins in the common ancestor of cyanobacteria and chloroplasts. *Nature*. July 1999; 400(6740):159-62.
252. Johnson E, Schroeder W. Microbial carotenoids. *Advances in Biochemical Engineering and Biotechnology*. 1996; 53:119-78.
253. Ben-Amotz A, Mokady S, Edelstein S, Avron M. Bioavailability of a natural isomer mixture as compared with synthetic all-trans-beta-carotene in rats and chicks. *Journal of Nutrition*. July 1989; 119(7):1013-9.
254. Ben-Amotz A, Levy Y. Bioavailability of a natural isomer mixture compared with synthetic all-trans beta-carotene in human serum. *American Journal of Clinical Nutrition*. May 1996; 63(5):729-34.
255. Levin G, Mokady S. Antioxidant activity of 9-cis compared to all-trans beta-carotene in vitro. *Free Radical Biological Medicine*. July 1994; 17(1):77-82.
256. Kelly F. Use of antioxidants in the prevention and treatment of disease. *Journal of The International Federation of Clinical Chemistry*. March 1998; 10(1):21-3.
257. Frei B. Reactive oxygen species and antioxidant vitamins: mechanism of action. *American Journal of Medicine*. September 1994; 97(3A):5S-13S:22S-28S.
258. Apsley J. *The Regeneration Effect*. Genesis Communications. 1996: 85.
259. Balz Frei cited in: *The Wall Street Journal* - Interactive Edition, Green and slimy and two billion years old? Eat it. January 9, 2000.
260. Romay C, Gonzalez R. Phycocyanin is an antioxidant protector of human erythrocytes against lysis by peroxy radicals. *Journal of Pharmacy and Pharmacology*. April 2000; 52(4):367-8.
261. Gonzalez R et al. Anti-inflammatory activity of phycocyanin extract in acetic acid-induced colitis in rats. *Pharmacology Research*. 1999; 39(1):55-9.
262. Romay C, Ledon N, Gonzalez R. Phycocyanin extract reduces leukotriene B4 levels in arachidonic acid-induced mouse-ear inflammation test. *Journal of Pharmacy and Pharmacology*. May 1999; 51(5):641-2.
263. Romay C, Ledon N, Gonzalez R. Further studies on anti-inflammatory activity of phycocyanin in some animal models of inflammation. *Inflammation Research*. August 1998; 47(8):334-8.
264. Romay C et al. Antioxidant and anti-inflammatory properties of C-phycocyanin from blue-green algae. *Inflammation Research*. 1998; 47(1):36-41.
265. Baker J. In: *Natural Products and Drug Development*. Krogsgaard-Larsen, Brogger Christensen, Kofod, eds. Muksgaard, Copenhagen. 145-63.
266. Okai Y, Higashi-Okai K. Potent anti-inflammatory activity of pheophytin A derived from edible green algae, *Enteromorpha profilera* (Sujiao-nori). *International Journal of Immunopharmacology*. June 1997; 19(6):355-8.
267. Jensen, G. Written communication, February 2000.
268. Tolomio C et al. Colonization by diatoms and antirheumatic activity of thermal mud. *Cell Biochemistry and Function*. 1999; 17:29-33.
269. Ceccettin, M, Bellometti S, et al. Serum interleukin-1 changes in arthrosic patients after mud-pack treatment. *Phys Rehab Kur Med*. 1995; 5:92-3.
270. Sukenik A, Takahashi H, Mokady S. Dietary lipids from marine unicellular algae enhance the amount of liver and blood omega-3 fatty acids in rats. *Annals of Nutrition and Metabolism*. 1994; 38(2):85-96.
271. Kremer J, Lawrence D, Jubiz W. Different doses of fish-oil fatty acid ingestion in active rheumatoid arthritis: a prospective study of clinical and immunological parameters. In: *Dietary -3 and -6 Fatty Acids: Biological Effects and Nutritional Essentiality*. Galli C, Simopoulos, AP eds. Plenum Publishing, 1989:343-50.

272. Krylov V, Drapeau C, et al. Retrospective epidemiological study using medical records to determine which diseases are improved by *Aphanizomenon flos-aquae* supplements. Submitted for publication 2001.
273. Sanchez A. Cited in: *HeartInfo*, March 13, 2000.
274. Kelly F. Use of antioxidants in the prevention and treatment of disease. *Journal of The International Federation of Clinical Chemistry*. March 1998; 10(1):21-3.
275. Levy Y et al. Dietary supplementation of a natural isomer mixture of beta-carotene inhibits oxidation of LDL derived from patients with Diabetes mellitus. *Annals of Nutrition and Metabolism*. March 2000; 44(2):54-60.
276. Mietus-Snyder, M and Malloy, M. Endothelial dysfunction occurs in children with two genetic hyperlipidemias: Improvement with antioxidant vitamin therapy. *Journal of Pediatrics*. 1998; 133(1):35-40.
277. Paredes-Carbajal M et al. Effects of dietary *Spirulina maxima* on endothelium dependent vasomotor response of rat aortic rings. *Life Science*. 1997; 61(15):PL 211-9.
278. Smith D et al. Eskimo plasma constituents, dihomo-linolenic acid, eicosapentaenoic acid and docosahexaenoic acid inhibit the release of atherogenic mitogens. *Lipids*. 1989; 24:70-5.
279. Abrams K. *Algae to the Rescue*. Logan House. 1996:39-40.
280. Cohen Z, Norman H, Heimer Y. Microalgae as a source of omega three fatty acids. *Plants in Human Nutrition*. 1995; 77:1-31.
281. Sukenik A, Takahashi H, Mokady S. Dietary lipids from marine unicellular algae enhance the amount of liver and blood omega-3 fatty acids in rats. *Annals of Nutrition and Metabolism*. 1994; 38(2):85-96.
282. Kushak R et al. Favorable effects of blue-green algae *Aphanizomenon flos-aquae* on rat plasma lipids. *Journal of the American Nutraceutical Association*. January 2000; 2(3):59-65.
- 283 Conquer J, Holub B. Supplementation with an algae source of docosahexaenoic acid increases (n-3) fatty acid status and alters selected risk factors for heart disease in vegetarian subjects. *Journal of Nutrition*. 1996; 126:3032-9.
284. Reddy S, Sanders, T Obeid O. The influence of maternal vegetarian diet on essential fatty acid status of the newborn. *European Journal of Clinical Nutrition*. 1994; 48:358-68.
285. Neuringer M et al. The essentiality of n-3 fatty acids for the development and function of the retina and brain. *Annual Review of Nutrition*. 1988; 8:517-41.
286. Pan W et al. Hemostatic factors and blood lipids in young Buddhist vegetarians and omnivores. *American Journal of Clinical Nutrition*. 1993; 58:354-9.
287. Kushak R, Drapeau C, van Cott E, Winter H. Blue-green alga *Aphanizomenon flos-aquae* as a source of dietary polyunsaturated fatty acids and a hypo-cholesterolemic agent. Paper presented at the Annual Meeting of the American Chemical Society. Anaheim, California. March 21-25, 1999.
288. Rolle I, Pabst W. The cholesterol-lowering effect of the unicellular green alga - *Scenedesmus acutus*. *Nutrition and Metabolism*. 1980; 24(5):291-301.
289. Hori K, Ishibashi G, Okita T. Hypo-cholesterolemic effect of blue-green alga, ishikurage (*Nostoc commune*) in rats fed atherogenic diet. *Plant Foods Human Nutrition*. 1994; 45(1):63-70.
290. de Caire G, de Cano M, de Mule C, Steyerthal N, Piantanida M. Effect of *Spirulina platensis* on glucose, uric acid and cholesterol levels in the blood of rodents. *International Journal Experimental Botany*. 1995; 57:93-6.
291. Sano T, Tankaka Y. Effect of dried, powdered *Chlorella vulgaris* on experimental atherosclerosis and alimentary hypercholesterolemia in cholesterol-fed rabbits. *Artery*.

1987; 14(2):76-84.

292. Santo T et al. Effect of lipophilic extract of *Chlorella vulgaris* on alimentary hyperlipidemia in cholesterol-fed rats. *Artery*. 1988; 15(4):217-24.
293. Rolle I, Pabst W. Uber die cholesterinsenkende Wirkung der einzelligen Grunalge *Scenedesmus acutus*. *Nutritional Metabolism* (English abstract). 1980; 24:291-301.
294. Conquer J, Holub B. Effects of supplementation with an algae source of docosahexaenoic acid on risk factors for heart disease in vegetarians. Abstract of the 64th Congress of the European Arteriosclerosis Society. Utrecht, Netherlands. June, 1995: 10-13.
295. Morris D et al. Serum carotenoids and coronary heart disease. The Lipid Research Clinics Coronary Primary Prevention Trial and Follow-up Study. *Journal of the American Medical Association*. 1994; 272:1439-41.
296. Arenesen E. Serum total homocysteine and coronary heart disease. *International Journal of Epidemiology*. August 1995; 24(4):704-9.
297. Iwata K, Inayama T, Kato T. Effects of *Spirulina platensis* on plasma lipoprotein lipase activity in fructose-induced hyperlipidemic rats. *Journal of Nutritional Science and Vitaminology*(Tokyo). April 1990; 36(2):165-71.
298. Delio M. Blue Goo and the Healthy Heart. *Wired News*, Aug. 30, 2000
299. Krylov V et al. Retrospective epidemiological study using medical records to determine which diseases are improved by *Aphanizomenon flos-aquae* supplements. Submitted for publication 2000.
300. Schmidt M, Smith L, Sehnert K. *Beyond Antibiotics: Healthier Options for Families*. North Atlantic Books, 1993: 74.
301. Cited in: Challem J. *Spirulina*. Keats Publishing. 1981: 17-8.
302. Kim H, Lee E, Cho H, Moon Y. Inhibitory effect of mast cell-mediated immediate-type allergic reactions in rats by *Spirulina*. *Biochemistry and Pharmacology*. 1998; 55(7):1071-6.
303. Yang H, Lee E, Kim H. *Spirulina platensis* inhibits anaphylactic reaction. *Life Sciences*. 1997; 61(13):1237-44.
304. Hayashi O et al. Class specific influence of dietary *Spirulina platensis* on antibody production in mice. *Journal of Nutritional Science and Vitaminology* (Tokyo). December 1998; 44(6):841-51.
305. Kushak R et al. Favorable effects of blue-green algae *Aphanizomenon flos-aquae* on rat plasma lipids. *Journal of the American Nutraceutical Association*. January 2000; 2(3):59-65.
306. Bisgaard H. Leukotrienes and prostaglandins in asthma. *Allergy*. 1984; 69:413-20.
307. Neuman I, Nahum H, Ben-Amotz A. Prevention of exercise-induced asthma by a natural isomer mixture of beta-carotene. *Annals of Allergy and Asthma Immunology*. June 1999; 82(6):549-53.
308. Drapeau C. *Results of Survey of AFA Consumers*. Presentation at Klamath Falls, Oregon, August 8, 1998.
309. Bruno J, Gittelman J, Tuchfeld B. Lowered aluminum, with better detoxification and improved cognitive, behavioral ratings by children eating *Aphanizomenon flos-aquae*. Submitted for publication, 2001.
310. Cited in: Challem J. *Spirulina*. Keats Publishing. 1981: 17.
311. Abrams K. *Attention Deficit Hyperactivity Disorder: A Nutritional Approach*. Book Crafter. 1998: 48-9.
312. Center for Food Safety and Applied Nutrition. *MMWR. Morbidity and Mortality Weekly Report*. 1993; 42(41).

313. Carmichael W, An J. Using an enzyme linked immunosorbent assay (ELISA) and a protein phosphatase inhibition assay (PPIA) for the detection of microcystins and nodularins. *Natural Toxins*. November 1999; 7(6):377-385.
314. Iverson F, Truelove J. Toxicology and seafood toxins: domoic acid. *Natural Toxins*. 1994; 2(5):334-9.
315. Drapeau C. *Aphanizomenon flos-aquae*: blue green-algae. Cell Tech, 1999: 8.
316. Henrickson R. *Earth Food: Spirulina*. Ronore Enterprises, 1989:90.
317. Nakashima M et al. Extraction of light filth from *Spirulina* powders and tablets: collaborative study. *Journal - Association of Official Analytical Chemists*. May-Jun 1989; 72(3):451-3.
318. Gilroy D et al., Assessing potential health risks from microcystin toxins in blue-green algae dietary supplements. *Environmental Health Perspectives*. 2000; 108(5):437.
319. Hitzfeld et al. Cyanobacterial toxins in drinking water treatment. *Environmental Health Perspectives*. March 2000; 108(1):119.
320. Schaeffer D, Malpas P, Barton L. Risk assessment of microcystin in dietary *Aphanizomenon flos-aquae*. *Ecotoxicology and Environmental Safety*. September 1999; 44(1):73-80.
321. Barton et al. Determination of a safe level of microcystins as a contaminant of *Aphanizomenon flos-aquae*: a new algal dietary supplement for humans. Cited by Bergwall R. The whole truth about some wonderful foods. *New Life Options*. June 1997.
322. Repavich W, Sonzogni W, et al. Cyanobacteria (blue-green algae) in Wisconsin waters: Acute and chronic toxicity. *Water Research*. 1990; 24:222-31.
323. Falconer I, et al. Toxicity of *Microcystis aeruginosa* in drinking water to growing pigs, as an animal model for human injury and risk assessment. *Environmental Toxicology and Water Quality*. 1994; 9:131.
324. Jensen G. Personal communication. 1999.
325. Jensen G. Personal communication. 1999.
326. Tiberg E et al. Allergy to green algae (*Chlorella* among children). *Journal of Allergy and Clinical Immunology*. 1995; 96:257-9.
327. Tiberg E. Microalgae as aeroplankton and allergens. *Advances in Aerobiology*. 1987; 51:171-3.
328. Jitsukawa K, Suizu R, Hidana A. *Chlorella* photosensitization. New phytophotodermatitis. *International Journal of Dermatology*. May 1984; 23(4):263-8.