

Dietary Supplementation with *Chlorella pyrenoidosa* Produces Positive Results in Patients with Cancer or Suffering From Certain Common Chronic Illnesses

Randall E. Merchant is a professor of anatomy and neurosurgery at Virginia Commonwealth University's Medical College of Virginia. Cynthia A. Andre is a clinical research coordinator and social worker at Virginia Commonwealth University's Medical College of Virginia.

Introduction

Laboratory and clinical studies from Japan have reported that broken cell wall preparations and extracts of *Chlorella pyrenoidosa*, a unicellular green alga, as well as other *Chlorella* species when either given orally or injected, promote growth and healing. Furthermore, these preparations stimulate the immune system in such a way that the host is protected from infection and cancer. *Chlorella pyrenoidosa* grows naturally in fresh water and has the highest content of chlorophyll (28.9 g/kg) of any known plant on earth. This species' proteins contain all the amino acids known to be essential for the nutrition of animals and human beings. There are also vitamins found in *Chlorella pyrenoidosa* including: vitamin C, provitamin A (B-carotene), thiamine (B1), riboflavin (B2), pyridoxine (B6), niacin, pantothenic acid, folic acid, vitamin B12, biotin, choline, vitamin K, lipoic acid, and inositol. Minerals in *Chlorella pyrenoidosa* include: phosphorus, calcium, zinc, iodine, magnesium, iron, and copper. *Chlorella* has a strong cell wall that prevents its native form from being adequately broken down and absorbed by the human digestive system and so special processing is required to break its cell wall (Mitsuda et al., 1977). In addition to amino acids, peptides, proteins, vitamins, sugars and nucleic acids, *Chlorella pyrenoidosa* contains a water-soluble substance known as *Chlorella* Growth Factor (CGF) (Steenblock, 1987). Approximately 5% of raw *Chlorella pyrenoidosa* is CGF; composed primarily of amino acids, proteins, and nucleic acids believed to be derived from the nuclei of the algae.

What *Chlorella* is and How *Chlorella* Products Are Grown

Chlorella pyrenoidosa is a species of green algae that grows in fresh water. This life form emerged over 2.5 billion years ago, and was the first form of plant with a well-defined nucleus. There are fossils from the pre-Cambrian period that clearly indicate the presence of *Chlorella*. Because *Chlorella* is a microscopic organism, it was not discovered until the late 19th century, deriving its name from the Greek, "chloros" meaning green and "ella" meaning small.

Each *Chlorella pyrenoidosa* microorganism is composed of a nucleus, starch grains, chloroplasts and mitochondria surrounded by a cell wall composed mainly of cellulose. Under normal conditions, *Chlorella* divides into four daughter cells in less than 24 hours. The length of *Chlorella*'s life cycle depends on the strength of the sunlight, temperature and availability of nutrients.

Although the algae grow naturally in fresh water, *Chlorella pyrenoidosa* destined for human consumption is generally cultivated in large, fresh mineral water pools under direct sunlight. The growing process must be carefully inspected and sanitary conditions are meticulously maintained to ensure there is no contamination of the *Chlorella* with other microorganisms. Once the fresh-water pools have enough *Chlorella* cells in them, the algae are harvested and the tough cell walls of the *Chlorella* must then be broken down to increase the algae's digestibility. This can only be accomplished with the patented process utilizing the DYNO-Mill[™], a unique method developed under the guidance of Mr. Hideo Nakayama of the Sun *Chlorella* Corporation. All of the other methods, which include heating or treatment with enzymes, compromise *Chlorella*'s digestibility, therefore eliminating full health benefits of *Chlorella*. The DYNO-Mill[™] physically disintegrates the cell wall by using only natural, mechanical means and therefore there is no need for chemicals, enzymes or heating that can compromise its nutritional value, while assuring optimum assimilation and digestion (Mitsuda et al., 1977). With the DYNO-Mill[™] technique, *Chlorella* is more than 85% digestible. Once the cell wall has been broken, *Chlorella* is spray-

dried producing powder and molded into tablets using a direct press machine. The final results are solid tablets of pure *Chlorella pyrenoidosa*.

The recommendations as to the number of *Chlorella* tablets and *Chlorella* liquid extract which should be consumed daily may vary. For example, the maintenance dosage of *Chlorella* tablets and *Chlorella* liquid extract for those in good health is 15 tablets (3g) and 30 ml. Those with severe medical conditions may increase the daily dosage as much as three times, depending on their specific needs.

Promotion of Health and Healing by *Chlorella*

We know that neither disintegrated cell-wall preparations of *Chlorella pyrenoidosa* nor CGF has any direct action against cancer cells or infective agents, and so the exact mechanism by which *Chlorella* enhances immunoreactivity remains unclear. Animal studies have demonstrated that *Chlorella pyrenoidosa* affects the immune system by stimulating an increase in number and activities of macrophages and polymorphonuclear leukocytes (Kojima et al., 1973; Miyazawa et al., 1988; Tanaka et al., 1986; Konishi et al., 1985; Komiyama et al., 1986; Yamaguchi et al., 1985). An acidic polysaccharide prepared from *Chlorella* cell wall has also been shown to induce the production of interferon in vitro and in mice (Umezawa et al., 1982) and therefore, part of *Chlorella pyrenoidosa*'s anticancer effect in part may be mediated through the actions of this cytokine.

Miyazawa et al. (1988) examined the effects of *Chlorella pyrenoidosa* on anti-tumor activities of C3H/He mice. They reported that mice acquired antitumor immunity by inoculation with some derivatives from *Chlorella*. Autoclaved and heat-extracts of *Chlorella* enhanced macrophage activity and cytotoxic activity of lymphocytes. Mice were given subcutaneous transplants of MM-2 tumor cells and then divided into 4 treatment groups. At designated times when tumors reached a certain size or prior to tumor inoculation, mice received multiple injections of 1×10^{10} . *Chlorella pyrenoidosa* cells or 3 mg of its extract by 6 intraperitoneal injections made every other day. Groups receiving autoclaved cells or protein-containing *Chlorella* extracts showed an anti-tumor effect. Administration only following tumor inoculation had no significant impact on survival.

Komiyama et al. (1986) reported that an acidic polysaccharide purified from the hot water extract of *Chlorella pyrenoidosa* possessed anti-tumor activity against five transplantable murine tumors in vivo. The extract showed remarkable life prolongation effects in mice bearing sarcoma 180, and was also active against Lewis lung carcinoma, Meth-A fibrosarcoma, IMC carcinoma, and B16 melanoma growing in the peritoneal cavity. Meth-A cells admixed with the extract and then subcutaneously inoculated, showed remarkable inhibition of tumor growth. The extract enhanced cytotoxicity of murine macrophages for EL-4 tumor cells in vitro, lymphoproliferative effects in vitro, and carbon clearance in vivo.

Treatment of cancer and chronic diseases with drugs may relieve symptoms and slow progression or as in the case of hypertension, reduce the risk of cardiovascular disease. Drug treatment may also, unfortunately, require the life-long use of an agent that may have adverse side effects. For this reason, there is a great deal of interest in non-pharmacological interventions which can reduce or eliminate the need for drugs for various illnesses. Based on the research from Japan, we have hypothesized that adding *Chlorella* to the diet could be one such non-pharmacological approach. The principal focus of the research reviewed here, therefore, was to provide solid evidence from small clinical trials that dietary supplementation with two products derived from *Chlorella pyrenoidosa* tablets and *Chlorella* liquid extract, could relieve symptoms and improve quality of life in people suffering from a primary brain tumor, fibromyalgia syndrome, hypertension, or ulcerative colitis.

Malignant Brain Tumor

The prognosis for patients with the type of brain tumor known as a malignant glioma is extremely poor with expected survival in the range of one to two years. Standard treatment for these tumors usually consists of surgical debulking followed

by radiotherapy and/or chemotherapy. It is also known that patients harboring a malignant glioma have a marked, generalized depression of immune competence affecting both cellular and humoral immune mechanisms (Young and Merchant, 1990; Young et al., 1991). These immune deficiencies are present in the preoperative period, prior to radiotherapy, chemotherapy or steroid administration.

Our clinical study in patients with a history of glioma was designed to test whether dietary supplements derived from *Chlorella pyrenoidosa* would help them maintain their health and resistance to infection, as well as restore their immune functions (Merchant et al., 1990). A total of 21 patients participated in the study; 15 had a glioblastoma multiforme (GBM), four with low-grade astrocytoma, one had an anaplastic astrocytoma (AA), and one with a high-grade oligodendroglioma. They supplemented their daily diet with 20 g *Chlorella* tablets and 150 ml of *Chlorella* liquid extract for up to two years. During this time, each patient's general health was monitored by monthly physical and neurological examinations, as long as they survived or for the two years they participated. Complete blood counts, differentials, cytometric determinations of natural killer (NK) cells and T cell subsets, and in vitro lymphocyte activation assays to assess level of immunosuppression, were performed on the blood samples. Imaging studies of the brain and blood tests were performed at 3-4 months intervals. Time to tumor recurrence (TTR) was defined as the number of months between the start of *Chlorella* supplementation and the MRI/CT scan that indicated the area of the glioma had increased. Survival was defined as the number of months that the patient remained alive after joining the study, irrespective of whether there had been any evidence of tumor growth.

Over the course of the investigation, we noted that our patients as a whole, experienced fewer than expected respiratory infections and influenza-like illnesses. From a purely subjective standpoint, most patients also commented that they felt that the *Chlorella* supplement had helped them maintain their strength and decreased their usual number of colds and other common illnesses. These findings appear to support the theory of Tanaka et al. (1986) that some *Chlorella* species protect a host from causative agents of opportunistic infections in immunocompromised states related to malignancy, chronic disease, and organ transplantation. We also found it a positive factor for the patient that the nutritional supplementation with *Chlorella* allowed them to participate more actively in their own treatment and care. The discipline and positive attitude of our patients along with their strong will to survive their tumor certainly contributed to the maintenance of their better than expected clinical status.

Blood tests provided more objective data on the status of each patient's hematologic and immune functions. Quantitative analyses of erythrocyte components indicated that 90% of our patients' values remained within normal limits (WNL) of variation or returned to the normal range within four months of adding *Chlorella* to the diet. Baseline total leukocyte counts and differentials were within the normal range for 60% of the patients, but by eight months in the study, all but one of the patients' counts were within the normal range. The maintenance of standard peripheral blood cell values or their return to normal limits indicated that circulating leukocytes and myeloid progenitors in patients consuming *Chlorella* were less affected by tumor, chemotherapeutic drugs, and/or the immunosuppressive medication, dexamethasone.

We also examined the relative proportions of lymphocytes bearing specific T cell and NK markers in blood samples. Baseline concentrations of CD3+ T cells were abnormally low in eleven patients, but these values returned to normal percentages in six. The proportion of CD3+ lymphocytes in three patients with normal baselines, however, moved below the normal range. The percentage of CD4+ helper T cells in eleven patients was in the normal range at baseline, while seven were below and two above. Both of the high and three of the low eventually had normal percentages of cells expressing the CD4+ phenotype. The proportion of CD4+ eventually fell in only three patients whose baseline proportion of CD4+ cells was normal. Baseline percentages of lymphocytes expressing the suppressor/cytotoxic T cell phenotype (CD8+) were normal in twelve patients and low in five and high in three. All three of the high and two of the low had their proportion of CD8+ cells become normal after joining the study. These results suggested that dietary *Chlorella* supplementation helped glioma patients maintain normal quantities and proportions of peripheral blood T lymphocytes. When cell numbers which were normal fell below the normal range, this generally correlated with tumor recurrence.

Although, the number of peripheral blood NK cells do not appear to be affected in patients harboring a glioma (Young et al., 1991), we determined the percentages of [CD56.sup.+] NK cells in the blood of most of our patients. Nine of the sixteen patients tested had normal numbers of [CD56.sup.+] lymphocytes and in the others, the values were below the normal range. For most of our patients, the percentages of NK cells, however, proved to be quite variable, moving between normal and low over the time they were supplementing their diets with Chlorella. From our results, we could not determine whether Chlorella had any modulatory or protective effect on the number and functions of circulating NK cells in our patients.

The response of peripheral blood lymphocytes to mitogens is suppressed in malnourished cancer patients as well as those with a glioma (Young et al., 1991). In our study, in vitro mitogenic assays using phytohemagglutinin, indicated that most (13 out of 19) patients' baseline samples showed a normal lymphocytic response, while in the other patients this reaction was suppressed. Within two months of adding Chlorella pyrenoidosa to their diet, however, lymphocytes from four of the latter group showed normal mitogenic reactivity. Only one patient whose baseline lymphocyte mitogenic response was WNL was suppressed later. Collectively, these results suggested that the nutritional benefits of dietary Chlorella may have helped our patients' lymphocytes maintain a normal reactivity to pathogens, and thus contributed to the decreased incidence of infections that was observed in our pool.

While patients were in our study, we monitored their functional condition by monthly interviews and physical examinations. We also observed the status of their glioma by MRI/CT scan. These latter studies revealed a tumor recurrence or death (without evidence of tumor progression) in nine of the evaluable patients during the first year of the study. Three of the eleven patients who completed one year of the study without evidence of tumor recurrence, had renewed growth of their tumor in the second year. At the end of two years, nine patients, six with GBM and all three with low-grade astrocytoma, were alive and of these, only two of the GBM patients had shown MRI/CT evidence of tumor recurrence.

Collectively, these results suggest that dietary supplementation with Chlorella pyrenoidosa alone or in combination with surgery, radiation and/or chemotherapy did not alter the prognostic parameters significantly for survival in patients with high-grade gliomas. Older patients and those with massive tumors, still survived fewer months in a predictable fashion. However, we believe that survival and TTR in younger patients and/or with smaller burdens on MRI/CT scan were better than expected. The median total survival for the eleven patients who died over the course of the trial was 17 months; 17 months for the five who had large tumor when they began the study and 19 months for those with a lower baseline tumor burden.

The results of our small clinical trial suggested that adding Chlorella pyrenoidosa to the diets of brain tumor patients may offer some protection from the deleterious effects of tumor, chemotherapy, and radiation. In our patients, immune responses and leukocyte counts remained in the normal range or improved regardless of tumor burden and other types of treatment they received. The supplement, however, appeared to have little influence on the natural progression of disease in patients who were very ill or incapacitated from their disease when they began taking Chlorella pyrenoidosa. Most of the patients who had a low tumor burden and were in good physical condition when they began the study clearly had longer than expected TTRs and survival. Overall, they also remained relatively free of unrelated maladies and opportunistic infections, which commonly afflict those on myelosuppressive therapies and/or corticosteroids.

Fibromyalgia Syndrome

It has been estimated that 2-4% of the American population suffers from fibromyalgia syndrome (FMS); a condition where the major complaint is a generalized aching accompanied by fatigue, sleep problems, morning stiffness, and/or headaches. The definitive diagnosis of FMS is based on standards established by The American College of Rheumatology (ACR); these criteria relate to the severity of a patient's tenderness at a minimum of 11 tender points in 18 characteristic locations measured by palpation (Russell et al., 1986; Wolfe et al., 1990). From this, a tender point index (TPI) is then calculated by taking into account the level of pain a patient demonstrates at each site.

Some patients with FMS can get relief of their symptoms with non-pharmacologic methods such as gentle aerobic exercise or by increasing the amount of sleep while at the same time maintaining a regular sleep schedule. Tricyclic antidepressants are also commonly used in the treatment of FMS and randomized, controlled trials of these anti-depressants have shown them to improve sleep and provide modest relief of stiffness and tenderness (Russell et al. 1986). Up to the present, however, no food, dietary supplement, or herbal preparation has been proven effective for FMS in controlled studies.

Over the past four years, we conducted two consecutive clinical trials of Chlorella in subjects with FMS. The first investigation was an open-label pilot study which involved 18 highly symptomatic people who had 2+ palpable tenderness at 11 or more of the 18 ACR-defined tender points, and a TPI of at least 22 (Merchant et al., 2000). Each day for two months, they added to their diets 10 g of Chlorella tablets and 100 ml of Chlorella liquid extract. Amelioration of FMS symptoms was validated and quantified using semi-objective and subjective outcome measures administered at the two monthly clinic visits.

We found that the addition of the two Chlorella products to the diet led to a mean net decrease of two tender points; from 17 at baseline to 15 by the end of the study. Moreover, the average TPI which was 32 at baseline fell to 25. This 22% decrease in the intensity of pain was statistically significant ($p=0.01$). Compilations of the results from patient interviews, self-assessment questionnaires, and visual analog scales also revealed improvements in pain (by 21%), sleep (by 8%) and anxiety (by 15%).

Although the results of our first, pilot study suggested that adding Chlorella to the diet improved symptoms of FMS, we recognized that some of these data were based on subjective responses given by our participants who knew they were consuming Chlorella. Therefore, there was a chance that these results could be biased and the patients could have experienced some placebo-effect. Nevertheless, the possibility that subjects with EMS could have their level of pain (as measured by the TPI) significantly decreased by simply adding the two Chlorella supplements to the diet suggested that a placebo-controlled and blinded clinical trial was warranted. Therefore, a larger, more comprehensive clinical trial in subjects with EMS was next undertaken to expand on these results, and determine if similar findings would occur following a double-blinded, placebo-controlled crossover design (Merchant and Andre, 2001).

For this second trial, a total of 43 people were enrolled and randomized such that approximately half consumed 50 tablets (10 g) of Chlorella and 100 ml of Chlorella liquid extract each day for three months, and the other half consumed 50 placebo tablets (10 g) and 100 ml of placebo liquid extract each day for a comparable period. Neither the patients nor the physician conducting the assessments knew which of the dietary supplements the subjects were consuming at any given time. Following a one month washout period, subjects crossed-over from Chlorella to placebo or visa versa. Thirty-four subjects completed the entire trial.

Like the first clinical trial, the overall objective of the second study was to determine if adding Chlorella to the diet of the FMS patients produced improvements in their clinical and functional status. A baseline examination preceded each patient's commencing the diet and each subject was reexamined monthly during the seven-month period of the study. Physician assessments included a physical exam with blood studies, articular examination, and determination of the number of tender points and TPI were done at the beginning and end of each arm of the crossover. Patient-rated outcome measures included the Fibromyalgia Impact Questionnaire (FIQ) (Burckhardt et al. 1991), a patient questionnaire, and the Hassles Scale.

The tender point exams showed that after three months of dietary supplementation with the two Chlorella products, there was a statistically significant ($p=0.009$) decrease of 1.1 tender points on average and a statistically significant ($p=0.024$) difference in the number of tender points between the two diet supplements. The average TPI after three months on the Chlorella supplements fell by 1.8 points (7.6%) which approached statistical significance ($p=0.068$). After three months on the placebo, the average TPI decreased by only 0.5 points. While the differences in the average percentage improvement in TPI after three months on either of the two groups of dietary supplements was not significant, it was noted that 62% of the subjects showed a better TPI (i.e. less pain) after consuming Chlorella compared to that after they took the placebo.

Assessment of functional abilities or limitations by the FIQ showed that when they were consuming Chlorella, there was a steady, statistically significant, improvement. When they were taking placebo, levels of improvement varied and were not statistically significant. When the subjects were consuming Chlorella, there was a steady decrease in the FIQ score, from an average of 58.4 at baseline to 47.0 at the end of the three-month supplement period. This mean drop of 11.4 (19.5%) in the score indicated the improvement in function was highly statistically significant ($p < 0.001$). It was also noteworthy that improvements in the FIQ after one month and two months with Chlorella were also statistically significant, ($p=0.03$) and ($p=0.01$), respectively. When subjects were consuming placebo, there was a statistically significant improvement at one month comparable to that seen when they were taking Chlorella. But, unlike with the Chlorella, the improvement appeared to plateau although the slight improvement in FIQ at two months remained statistically significant ($p=0.04$). By the end of the three-month period, however, improvement in the FIQ from baseline was only 7.4% and was not statistically significant. Comparisons of the FIQ for Chlorella and placebo indicated that there was a very strong trend ($p=0.058$) for better response of participants when they were consuming Chlorella. The collective results of the FIQ also indicated that after consuming Chlorella, 32 subjects' fibromyalgia symptoms were improved, while nine said they were worse and for four their symptoms were unchanged. This is contrast to the results after consuming placebo, which indicated that only 14 subjects' FMS symptoms were better while for 16 they were worse and for four unchanged.

The ten questions of the patient questionnaire dealt with issues of pain, anxiety, sleep disturbances, and gastrointestinal difficulties. When participants were consuming the two Chlorella supplements, there were steady, statistically significant improvements in scores compared to baseline such that by the end, there was a mean total decrease of 12.6 points ($p < 0.001$). Compared to how they were on placebo, there was a statistically significant ($p=0.004$) improvement in FMS symptoms while the subjects were taking Chlorella but not while they consumed placebo. With regards to anxiety as assessed by the Hassles Scale, after the subjects had consumed Chlorella for three months, there was a statistically significant ($p=0.01$) mean drop of 13.0 (25.9%) in the score. When the subjects were consuming placebo, there was also an improvement of 14.7% in the level of anxiety but which was not statistically significant. Collectively, the results of our two clinical trials, the pilot study as well as the double-blind, placebo-controlled study, led us to conclude that for the majority of people with FMS, dietary Chlorella supplementation helped relieve pain and other symptoms.

Hypertension

Hypertension is a serious public health problem that affects an estimated 50 million in the United States. High blood pressure is defined as a mean sitting systolic blood pressure (SiSBP) that exceeds 140 mm Hg, or a mean sitting diastolic blood pressure (SiDBP) of 90 mm Hg or higher. Pharmacological treatment of hypertension has been shown to decrease the risk of these diseases and their complications. A variety of non-pharmacological treatments can be effective in lowering blood pressure and have been emphasized increasingly as useful ways for both prevention and treatment of hypertension. The four principal non-pharmacological methods for lowering blood pressure are weight control (or loss), diet modification, exercise, and reduced alcohol consumption. Dietary modifications are designed to reduce the intake of sodium and dietary fat while at the same time increasing the consumption of calcium, magnesium, potassium, and dietary fiber. Diet studies have led to the hypothesis that cations and fiber which occur together in such "whole foods" as fruits, nuts, vegetables, and cereals, act in synergy to produce a hypotensive effect. More clinical trials of specific foods, food groups and dietary patterns, however, are clearly warranted. Therefore, the objective of our clinical trial was to determine if daily dietary supplementation with Chlorella lowered the blood pressure of individuals with a history of mild to moderate hypertension and who otherwise ingested a normal, nonvegetarian diet (Merchant and Andre, 2001).

Our study was open to people of either sex, 21 years of age or older with mild (mean SiDBP 90-104 mm Hg) to moderate (mean SiDBP 105-115 mm Hg) hypertension and who were willing to discontinue all medication given specifically for their hypertension. A total of 33 subjects were enrolled and they ranged in age from 22 to 73 years (mean of 50). Subjects had been diagnosed with hypertension for 11 years on average (range 0-47 years), and all but six were taking a drug daily for their hypertension. The mean heart rate of the group was 73.7 [+ or -] 10.2, and their SiSBP was 136.8 [+ or -] 11.5 and mean SiDBP was 90.8 [+ or -] 6.2.

Following a one-month washout of drug and the daily consumption of placebo, 24 subjects remained in the trial. Seven were dropped because they no longer met eligibility criteria for mild to moderate hypertension, and two withdrew because of side effects of having stopped taking their antihypertensive drug treatment. After a month off their hypertension medicine and dietary supplementation with placebo, their mean heart rate rose slightly to 76.5 [+ or -] 9.9 and their SiSBP rose to an average of 141.6 [+ or -] 14.4, and mean SiDBP rose by 4.3 mm Hg to 96.5 [+ or -] 6.6. While the increase in mean SiSBP was not statistically significant, the rise in mean SiDBP was ($p=0.004$).

Using these levels, blood pressure changes in the subjects were assessed. After one or two months of dietary Chlorella supplementation with 10 g of Chlorella tablets and 100 ml of Chlorella liquid extract, their heart rates, SiSBP, and SiDBP changed only slightly from the end of the placebo/washout period. Coming off the antihypertensive medications for a month, alone may have been responsible for the increase in SiDBP and during dietary Chlorella supplementation there was essentially no increase (i.e. worsening) on average of the SiDBP.

Since only working with "average" changes in SiDBP might mask individual responses (i.e. decreases in SiDBP) among the subjects, each subject's response was also characterized by three different criteria. Using criteria of the pharmaceutical industry, six of the subjects enrolled had an excellent response to the dietary supplement; that is that after two months of taking Chlorella, their SiDBP was below 90 mm Hg. Furthermore, another three subjects although having a SiDBP above 90 mm Hg, still showed between a 4 and 9 mm Hg drop in their SiDBP. The remaining 15 subjects, however, were considered inadequately treated by stopping their anti-hypertensive medication and adding Chlorella to their diet; i.e. SiDBP either rose during this period or fell by less than 4 mm Hg. Thus, following the conventional pharmacological criteria for assessing response, it can be stated that 38% of our subjects showed some improvement in their hypertension by adding Chlorella to their diet.

This improvement with Chlorella supplementation, however was amplified when only a 4mm Hg change in SiDBP was used to evaluate the response. When the first SiDBP of subjects (when most were taking an anti-hypertensive medication) was compared to their last visit (after three months off medication and two months of taking Chlorella), five subjects showed improvement, six had an essentially unchanged SiDBP, and 13 had a worsening of their hypertension. Therefore, according to these criteria, the SiDBP of eleven subjects had as good or better control of their blood pressure with the dietary supplement as they had by taking an anti-hypertensive drug. This effect was even more dramatic when these same criteria were applied to compare the SiDBP after one month off medication and placebo and after two months of dietary Chlorella. Here nine subjects showed improved SiDBP, seven were stable, and one-third showed a worsening of their hypertension. This finding that two-thirds of the subjects' SiDBP either improved or was stable without their anti-hypertensive medications suggested that for these subjects dietary supplementation with Chlorella either improved or kept their hypertension under control.

Physical exams and electrocardiograms did not change between the beginning and end of the study period. Blood cell counts, routine serum chemistries and urinalysis of the study population were within normal limits and no single variable significantly changed over the three-month course of the investigation. However, when serum total cholesterol, high- and low-density cholesterol were measured, the averages and standard deviations were WNL, but there were numerous statistically significant changes over the course of the investigation. First, there was a significant drop in serum cholesterol from the beginning until the end of the study; $p=0.003$. High-density cholesterol dropped after two months of dietary Chlorella ($p=0.03$) as did low-density cholesterol ($p=0.003$).

Our study also sought to determine if dietary supplementation with Chlorella improved the quality of life of these hypertensive subjects. The Psychological General Well-Being Index was used for this assessment (Dupuy, 1984) with responses summed to create six subscales which measured anxiety, depressed mood, positive well-being, self-control, general health, and vitality. The subjects' perceived level of anxiety was significantly decreased ($p=0.02$) while depressed mood was significantly improved ($p=0.02$) over the course of the study. The subjects' sense of well-being was significantly better ($p=0.007$) and there was a trend for improvement of the subjects' perceived changes in self-control, general health and vitality

by the end of the study. The sum of the scores for the General Well-Being Index showed statistically significant ($p=0.01$) improvements. These results indicated that subjects were feeling better overall and particularly their anxiety and depression improved significantly, because of the combined effects of no longer having to take their regimen of anti-hypertensive drug(s) and supplementing their diets with Chlorella.

Ulcerative Colitis

Ulcerative colitis is a common, chronic form of inflammatory bowel disease that is characterized histologically as inflammation involving the mucosa and submucosa of the rectum and colon. Its most common symptoms are abdominal pain and bloody diarrhea although those afflicted may also suffer from anemia, fatigue, weight loss, rectal bleeding, dehydration and malnutrition. The cause of ulcerative colitis is unknown and there is currently no cure. While available drug therapy for ulcerative colitis is often disappointing, most patients get some relief with a combination of sulfasalazine and corticosteroids. Up to now, no special diet or dietary supplement has been proven effective in the treatment of ulcerative colitis and, therefore, the purpose of our study was to determine if patients strongly symptomatic for ulcerative colitis would benefit from the inclusion of Chlorella in their diet (Merchant and Andre, 2001)

Ulcerative colitis is defined as having documented symptoms of hematochezia and diarrhea, negative stool cultures, and typical sigmoidoscopic findings such as superficial ulcerations, distorted mucosal vascular patterns, granularity, and exudate. From these data, a Disease Activity Index (DAI) can be computed from four subscales, consisting of: stool frequency, rectal bleeding, mucosal appearance, and physician's overall assessment (Kam et al., 1996). To be eligible for our study, subjects had to have suffered from mild to moderate disease for at least year and have a total DAI between 4 and 10, inclusive. The nine subjects enrolled ranged in age from 25 to 56 years and had at baseline, an average DAI of 7.2 [+ or -] 2.4. They supplemented their diets with 10 g of Chlorella tablets and 100 ml of Chlorella liquid extract daily for the two months of the study. Each participant returned to clinic every four weeks when blood samples were taken in order to assess any alterations in serum chemistries, cell counts, and sedimentation rate. A flexible sigmoidoscopic examination was conducted at the end of two months.

Eight subjects completed the entire two-month study and changes in each subclass of their DAI improved such that the total DAI declined from an average 7.2 [+ or -] 2.4 to 2.8 [+ or -] 2.5 (i.e., symptoms improved). The mean decrease in DAI from the beginning to end of study was 61% and was highly statistically significant ($P=0.008$). The decrease in stool frequency was statistically significant ($p=0.016$). The physician's sigmoidoscopic examination of rectal mucosa showed significantly less inflammation ($p=0.02$) and his overall assessment was that the patients' ulcerative colitis was significantly better ($p=0.008$). While the occasions of rectal bleeding were less for most subjects, the change was not significant ($p=0.18$). All blood analyses indicated these values remained within the normal limits of variation.

The effects of dietary Chlorella supplementation on their quality of life were quantified with the Inflammatory Bowel Disease Questionnaire (Guyatt et al., 1989) which contained 32 questions which examined four aspects of the patients' lives: 1) symptoms related to the primary bowel disturbance, 2) systemic symptoms, 3) emotional, and 4) social functions. Their responses on this questionnaire indicated statistically significant and strong trends for improvements in all four categories. Furthermore, they indicated that they believed the severity of their ulcerative colitis had decreased soon after the addition of Chlorella to their diet, and continued to lessen or remain stable over the study's course. Taken together, the DAI results which indicated that every participant's objective symptoms of ulcerative colitis improved, combined with the positive assessment each patient gave in their questionnaires, strongly suggested that all the subjects benefited from supplementing their diet with Chlorella.

Conclusion

It has been suggested that consumption of natural "whole foods" rich in macronutrients have many healthful benefits in individuals who otherwise ingest a normal, nonvegetarian diet. Our research has focused on the testing of dietary

supplements derived from *Chlorella pyrenoidosa*, in clinical trials. To date, we have conducted trials in subjects suffering from either brain cancer, fibromyalgia, hypertension, or ulcerative colitis. They consumed 10-20 g of *Chlorella* tablets and 100-150 ml of *Chlorella* liquid extract each day for two or three months. For validity, these studies were designed and carried out according to current conventional methodologies used in the pharmaceutical industry for drug development and testing. The results of these clinical trials suggested that daily dietary supplementation with *Chlorella* may reduce high blood pressure, lower serum cholesterol, accelerate wound healing, and enhance immune functions. Its potential to relieve symptoms, improve quality of life, and normalize body functions in patients suffering from the illnesses studied here suggest that larger, more comprehensive clinical trials of *Chlorella* are warranted for these, as well as other chronic illnesses.

Acknowledgements

The authors wish to express their gratitude to Mr. Tetsuaki Nakayama and the Sun *Chlorella* Corporation of Kyoto, Japan for their support of our clinical research projects. The authors wish to thank Harold F. Young, MD, Christopher M. Wise, MD, Domenic A. Sica, MD, Cynthia B. Bettinger, MD, and Donald F. Kirby, M.D. for their collaboration on these clinical trials.

Reprint requests: Randall E. Merchant, PhD - Virginia Commonwealth University, Medical College of Virginia, Richmond, Virginia 23298-0709 USA Email: rmerchan@hsc.vcu.edu COPYRIGHT 2001 The Townsend Letter Group
COPYRIGHT 2001 Gale Group

Bibliography

- Burckhardt CS, et al. The fibromyalgia impact questionnaire: development and validation. *J Rheumatol.* 1991;18:728-733.
- Dupuy HJ. The psychological general well-being (PGWE) index. In: *Assessment of Quality of Life in Clinical Trials of Cardiovascular Therapies.* NK Wenger, et al. (eds.), LeJacq Publ, New York, NY, pp.170-183, 1984.
- Guyatt G, et al. A new measure of health status for clinical trials in inflammatory bowel disease. *Gastroenterology.* 1989;06:804-810.
- Kam L, et al. A comparison of mesalamine suspension enema and oral sulfasalazine for treatment of active distal ulcerative colitis in adults. *Am J Gastroenterol.* 1996;91:1338-1342.
- Kojima M, et al. A new *Chlorella* polysaccharide and its accelerating effect on the phagocytic activity of the reticuloendothelial system. *Recent Adv. RES Res.* 1973;13:11.
- Komiyama K, et al. An acidic polysaccharide chlon A, from *Chlorella pyrenoidosa*. 2. Anti-tumor activity and immunological response. *Chemotherapy* 1986;34:302-307.
- Konishi F, et al. Anti-tumor effect induced by a hot water extract of *Chlorella vulgaris* (CE): resistance to Meth-A tumor growth mediated by CE-induced polymorphonuclear leucocytes. *Cancer Immunol Immunother.* 1985;19:73-78.
- Merchant RE, et al. Dietary *Chlorella pyrenoidosa* for patients with malignant brain tumor: Effects on immunocompetence, quality of life, and survival. *Phytotherapy Res.* 1990;4:220-231.
- Merchant RE, et al. Nutritional supplementation with *Chlorella pyrenoidosa* for patients with fibromyalgia syndrome: A pilot study. *Phytotherapy Res.* 2000;14:187-173.
- Merchant RE and Andre CA. A review of recent clinical trails of the nutritional supplement, *Chlorella pyrenoidosa*, for fibromyalgia, hypertension, and ulcerative colitis. *J Alternative Therapies Health Medicine.* 2001; In Press.
- Mitsuda H, et al. Effect of the breaking of *Chlorella* cells on the digestibility of *Chlorella* protein. *J Jpn Soc Food Nutr.* 1977;30:93-98.
- Miyazama Y, et al. Immunomodulation by unicellular green algae (*Chlorella pyrenoidosa*) in tumor-bearing mice. *J Ethnopharmacol.* 1988;24:135-146.
- Russell IJ, et al. Is there a metabolic basis for the fibrositis syndrome? *Am J Med.* 1986;81:50-56.
- Steenblock D. *Chlorella, Natural Medicinal Algae.* Aging Research Institute, El Toro, CA, 1087.
- Tanaka K, et al. Augmentation of host defense by a unicellular alga, *Chlorella vulgaris*, to *Escherichia coli* infection. *Infect Immun.* 1986;53:267-271.
- Umezawa I, et al. An acidic polysaccharide. chlon A, from *Chlorella pyrenoidosa*. *Chemotherapy* 1982;30:1041-1045.
- Wolfe F, et al. The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the multi-center criteria committee. *Arthritis Rheum.* 1990;33:160-172.
- Yamaguchi N, et al. Immunomodulation by single cellular algae. (*Chlorella pyrenoidosa*) and anti-tumor activities for tumor-bearing mice. Third Int Congress Dev Comp Immunol, Reims, France, 1985.
- Young HF, and Merchant RE. Brain tumors. *Curr. Opin Neurol. Neurosurg.* 1990;3:22-27.
- Young HF, et al. Immunocompetence of patients with malignant glioma. In: *Neurobiology of Brain Tumors*, M. Salzman (ed.), Williams and Wilkins, Baltimore, MD, pp.211-227,1991.