

Table 7. Quality of life measures

Visit	Mean HAQ score	% Change in HAQ from visit 1	Mean hassles score	% Change in hassles from visit 1	Mean CES-D score	% Change in CES-D from visit 1
1	36	NA	50	NA	29	NA
2	37	NC	39	22%	21	28%
3	37	NC	41	19%	23	21%

HAQ, Health Assessment Questionnaire; CES-D, Center for Epidemiologic Studies-Depression; NA, Not applicable; NC, No change (defined as a less than a 2% change from visit 1).

Table 8. Results from daily diaries<sup>a</sup>

Symptom	Patients better (>5) <sup>b</sup> (n)	Patients unchanged (-5 to +5) <sup>b</sup> (n)	Patients worse (<-5) <sup>b</sup> (n)
Physical activity	6	8	2
Pain	5	3	8
Sleep	6	6	4
Stress	7	6	3
Fatigue	3	3	10
Headache	6	6	4

<sup>a</sup> 60 days of data available from 16 patients.

<sup>b</sup> Better defined as a net improvement of 6 points or more from baseline. Worse defined as a net decrease of -6 points or more negative from baseline. Unchanged is in between.

Table 9. Results based on comments of patients<sup>a</sup>

Change in symptoms	Number of patients	Percentage of patients
Improved	7	39
No change	6	33
Worse	5	28

<sup>a</sup>Based on the responses in PAQ and daily diary comments.

normal, everyday life, indicated that for our patient pool, there was already a 22% improvement in the average score at 1 month. This improvement which was sustained through the end of the study, however, was not statistically significant. A CES-D score of 13 or greater is interpreted as possible depression and 17 or greater as treatable depression (Radloff, 1977). The average baseline CES-D score for our subjects was 29 and there were improvements in the average scores at the midway point and end of the study; 28% and 21% respectively. Neither of these changes, however, was statistically significant.

In their daily diary, each patient was asked to comment on general level of physical activity, sleep quality, musculoskeletal pain, headache, and any stresses for that day simply by recording if there was a worsening, improvement, or no change from the previous day. One point was added if there was an improvement and one subtracted if there had been a worsening of a symptom in the past 24 h. Therefore, the highest possible number for the 2-month study was 60 and the lowest -60. A summary of recordings from complete 60-day diaries (available from 16 patients) is presented in Table 8. The daily recordings of data by the patient suggested that some felt their fibromyalgia symptoms had improved while others felt their symptoms were unchanged or had actually worsened over the day-to-day course of the study. No single symptom improved or worsened in all of the patients. A compilation of the results of each patient's

answers on PAQ and daily diaries is presented in Table 9. These summaries of patients led us to conclude that almost 40% of the patients believed the dietary supplements of *Chlorella* had significantly improved their symptoms of fibromyalgia. The other patients felt that they had experienced no change or some worsening of their condition.

## DISCUSSION

The objective of this pilot study was to determine if adding *Chlorella* to the diet of patients reduced pain and other symptoms of fibromyalgia as well as produced any improvements in their functional status. Eighteen patients with fibromyalgia syndrome supplemented their diet with 10 g of 'Sun *Chlorella*' tablets and 100 mL of liquid 'Wakasa Gold' each day for 2 months. The pure *Chlorella pyrenoidosa* tablets are approximately 60% protein, 20% carbohydrate and 11% unsaturated fats. The tablets contain chlorophyll (28.9 g/kg) as well as all the essential amino acids. Vitamins found in the *Chlorella* tablets include: vitamin C, provitamin A (β-carotene), thiamine (B1), riboflavin (B2), pyridoxine (B6), niacin, pantothenic acid, folic acid, vitamin B12, biotin, choline, vitamin K, lipoic acid, and inositol. Minerals include: phosphorus, calcium, zinc, iodine, magnesium, iron and copper. The Wakasa Gold contains CGF along with malic acid (apple acid), fructose, lemon essence, and water. The daily maintenance dosage of *Chlorella* recommended by manufacturers of Sun *Chlorella* and Wakasa Gold for normal people in good health is 15 tablets (3 g) and 30 mL, respectively.

A number of studies in animals and humans have suggested that *Chlorella pyrenoidosa* in the diet has many beneficial effects for the consumer; the most important with regard to the present study probably being its capacity to promote healing and to non-specifically enhance immunologic reactions. Several years ago, we conducted an investigation to determine if the addition of Sun *Chlorella* and Wakasa Gold to the diets of patients with primary malignancies of the brain improved their immune system so that anti-tumour activities might be manifested which, in turn, would lead to some relief of symptoms and/or increase length and quality of survival (Merchant *et al.*, 1990). The dietary supplement was offered to 21 patients whose tumour may or may not have ever been treated and was given as an adjunct to any other treatment the patients might otherwise receive for their tumour. Patients consumed 20 g of Sun *Chlorella* and 150 mL of Wakasa Gold daily for up to 2 years. While this dietary *Chlorella* supplementation did not significantly affect tumour progression or survival, we did observe that the immune systems of these patients

functioned at near-normal levels; being less adversely affected by chemotherapy and immunosuppressive medications.

The present study was undertaken in patients with fibromyalgia in order to determine if dietary supplementation with 10 g of pure *Chlorella* and 100 mL of liquid containing CGF normalized body functions, relieved symptoms, and improved quality of life. The investigation was designed and carried out according to current conventional methodologies for clinical trials in which these patients are involved. We used the tender point exam to accurately diagnose and characterize each patient's fibromyalgia syndrome. The mean TPI for the 18 participants who completed the study was 32 at baseline. After 1 month of dietary supplementation with *Chlorella*, the average TPI had decreased by four points and at the end of 2 months, the mean TPI was 25. This seven-point drop in the TPI represented 22% average decrease in the intensity of pain from baseline and was statistically significant. Eight patients experienced at least a 25% decrease in pain intensity and two patients' pain decreased by more than half.

In addition to their physical examinations, patients also completed a self-administered PAQ that consisted of 10 cm visual analogue scales for pain and other symptoms of fibromyalgia. They were also asked to maintain a daily diary and to note any change in their general level of physical activity, sleep quality, musculoskeletal pain, headache and any stresses for that day. According to the PAQ, the majority of patients noted improvements in nervousness, activity, pain, good feeling, and constipation by the end of the 2-month study. The daily recordings of data by the patients also indicated that there was a great variability in how patients had perceived changes in their fibromyalgia symptoms. By combining the results of the PAQs and diaries, we were able to collect an overall self-assessment for each patient. According to these compilations, nearly 40% of the patients felt their symptoms had improved overall while a third of the subjects believed their symptoms had not changed. Five patients' comments led us to conclude that they felt their symptoms had worsened over the course of the study.

At each monthly clinic visit, subjects also completed a series of self-administered questionnaires dealing with 'quality of life' issues. The results of the HAQ which measures the functional abilities or limitations of the patients, indicated there was essentially no change in the average score over the course of the study. The Hassles Scale which measures how well a patient deals with various hassles of everyday life indicated a trend on average toward improvement after both 1 and 2 months of dietary supplementation. Although these improvements were not statistically significant, they suggest that perhaps with less pain, the hassles of life became not as noteworthy in these patients. The results of the baseline CES-D scale indicated that the average patient was clinically depressed. After 1 month in the study, however, a 28% improvement on average score was seen among the participants. This improvement was for the most part sustained through the second and final month.

Clinicians treating patients with fibromyalgia typically resort to psychotropic drugs such as amitriptyline in an attempt to improve sleep and relieve symptoms. Non-pharmacological means are also usually employed and

include light exercise and psychological support. Nutritional approaches to treatment, however, have received little attention. The design of the present study was modelled after earlier clinical trial of Super Malic in fibromyalgia patients (Russell *et al.*, 1995). Super Malic tablets which contain two naturally occurring compounds, malic acid (200 mg) and magnesium hydroxide (50 mg), had been shown in open label trials to dramatically relieve the pain of fibromyalgia (Abraham and Flechas, 1992). In the Russell study, 24 patients consumed 6-12 tablets per day for up to 8 months. Patients were first randomized to placebo and active compound groups for 4 weeks, were then crossed over for another 4 weeks, and finally all were offered open label Super Malic for 6 months. As we did in the present study, their primary outcome measure was pain as indicated by the TPI and also, secondarily they examined changes in functional and psychological measures. In the blinded, crossover segment of the study, the primary outcome measures of tenderness and pain showed no treatment benefit. Significant reductions in pain, however, were observed in the 6-month open label phase of the trial. Functional and psychological measures such as the CES-D, HAQ, and Hassles were not significantly improved in any phase of treatment. The results obtained in patients consuming Super Malic thus appear similar to our own with *Chlorella*.

No toxicity in laboratory animals or humans has ever been observed after consuming *Chlorella pyrenoidosa* regardless of whether the alga's cell walls were intact or broken. In clinical studies other institutions, amounts of *Chlorella* similar to that our group of patients consumed were given without any adverse effects (Merchant *et al.*, 1990). Temporary changes in the general state of health, however, have been attributed to the addition of broken cell wall preparations of *Chlorella pyrenoidosa* to a diet. In our earlier study with brain tumour patients, about half reported temporary irregularity of bowel movements and/or mild nausea during the first few days of *Chlorella pyrenoidosa* supplementation (Merchant *et al.*, 1990). Abdominal cramping and flatus were also reported. Any intestinal discomforts these patients experienced spontaneously cleared within a few days to a week after attaining the maintenance daily dosages of *Chlorella* tablets and extract.

In the present study in which 20 patients were enrolled, two voluntarily withdrew. One withdrew because she felt nausea after taking the *Chlorella* while the other just chose to no longer participate. Responses in each subject's PAQ as well as notations in their the daily diaries suggested that episodes of diarrhoea and abdominal cramping were the most common adverse events. Both side effects are probably related to the high fibre content from the *Chlorella*'s cell walls which may significantly increase peristalsis in some patients. Neither effect was ever so severe as to require any medical intervention.

The results of this small pilot study in 18 fibromyalgia patients suggest that the addition of *Chlorella* to their diet produced a significant reduction in their pain after only 2 months. Almost half of the patients also expressed that some of their other symptoms had also improved. It must be recognized that these patients were given open-label *Chlorella* and that such data are subject to substantial risk of bias on the part of both the subject and the investigator. Nevertheless, the possibility that patients with fibromyal-

since the subjective outcome measures relied on questionnaires and interviews.

**Dietary supplementation with Chlorella.** Each patient consumed two components; solid tablets, 'Sun Chlorella', and a liquid, 'Wakasa Gold' (provided by the YSK International Corporation, Kyoto, Japan). On day 1 of the study, patients began daily supplementation of their diet with 10 g (50 tablets) of Sun Chlorella and 100 mL of Wakasa Gold. The patient consumed each supplement daily for a total of 2 months. They also recorded the count of Chlorella tablets and total volume of Wakasa Gold consumed each day in their study diary (see below).

**Study diary.** Each patient was given a log book and instructed to record the following information each day: (1) total number of Sun Chlorella tablets taken; (2) total volume of Wakasa Gold liquid drunk; (3) name and total daily dose of any concomitant drugs; (4) list any symptoms of fibromyalgia which have either improved or worsened; and (5) comment on general level of physical activity, sleep quality, musculoskeletal pain, headache, and any stresses for that day.

**Plan and design.** The following methodologies were utilized at baseline and after the first and second months of dietary supplementation with Chlorella.

**Clinical measures.** Clinical assessments were made on the occasions of the three clinic visits by asking patients to complete a general patient questionnaire (PAQ) which consisted of a number of questions and several 10 cm horizontal visual analogue scales. The patient's perceived pain was quantified using a visual analogue scale (VAS) on which the left end was marked 'No Pain' while the right end was marked 'Severe Pain' (Russell *et al.*, 1991). Since patients with fibromyalgia usually report worsening of their symptoms by poor sleep, a VAS was used to assess the patient's quality of sleep. The terminal anchors indicated 'Very Poor' on the left and 'Very Good' on the right. A separate 10 cm VAS was used to determine the sense of restfulness the patient perceived in the morning. The terminal anchors indicated 'Fully Rested' on the left and 'Very Fatigued' on the right.

Functional abilities or limitations were assessed by the Stanford Health Assessment Questionnaire (HAQ) (Russell *et al.*, 1991). This instrument has been applied to fibromyalgia patients in a number of studies (Russell *et al.*, 1991). In addition, a brief questionnaire was used to assess the level of actual physical activity the patient exerted within the past week. A series of four questions was also asked to determine whether the patient suffered from pyrrhosis, abdominal cramping, pain, constipation, excessive flatus, or diarrhoea.

Depression was identified by the Center for Epidemiologic Studies-Depression (CES-D) scale (Radloff, 1977). The level of anxiety was assessed using a 10 cm line VAS asking the level of anxiety with terminal anchors indicating 'Never Feel Anxious' on the left and 'Always Feel Very Anxious' on the right. Another measure used for anxiety was the Hassles Scale (Dailey *et al.*, 1977).

**Physical assessment.** A brief history and physical examination was performed at every clinic visit in order to assess the status of the patient's fibromyalgia

Table 3. Patient demographics

Average age	47 (range 32-59)
Sex	17 females, 1 male
Ethnicity	16 white, 2 black
Currently employed	8
Mean education (y)	13 (range 9-17)

syndrome and if any new medical condition was present which would contraindicate continuing on the study's dietary supplement. A careful musculoskeletal assessment was made to determine the number and location of tender points as well as the TPI. On each of the three clinic visits, approximately 20 mL of venous blood was collected into vacutainer tubes for analysis of serum chemistry, haematology with differential, and T lymphocyte subset analysis by flow cytometry. All samples were analysed by MCV Hospital Clinical Laboratory.

**Statistical considerations.** The sample size for this pilot study of Chlorella was based on the results of the double-blind placebo controlled ibuprofen-alprazolam study conducted with fibromyalgia patients (Russell *et al.*, 1991). In that study, 15 patients receiving active ibuprofen and active alprazolam experienced an average 7 point (30%) drop in TPI from an average baseline value of 23.1 to 16.1 after 6 weeks, i.e. the end of the blinded treatment period. A parallel group of 14 patients receiving placebo ibuprofen and placebo alprazolam experienced an average 4.4 point (17.5%) drop in TPI from baseline to week 6. For the present open-label study, we used a similar sample size. Furthermore, in order to be eligible, patients were required to show 2+ tenderness at 11 tender points. It was hoped that such rigorous selection would ensure a study sample with potential for a greater magnitude of improvement so that an average drop in TPI of 7 or more after 2 months of dietary Chlorella supplementation would be indicative of statistically significant improvement in pain level. The results of the tender point exams as well as those obtained from the other physical and clinical measures at baseline and after 1 and 2 months of dietary supplementation with Chlorella were statistically compared using paired *t*-test.

## RESULTS

Twenty patients, 19 females and one male, with fibromyalgia syndrome were enrolled in this study of dietary Chlorella supplementation. Two of the women, however, voluntarily withdrew early on in the study; one because she felt some nausea after taking the Chlorella and the other because she decided she no longer wanted to participate. Eighteen patients, therefore, completed the entire 2-month trial and their baseline demographics are presented in Table 3.

### Physical assessments

Patients were interviewed and examined in the clinic after 1 and 2 months of dietary supplementation with Chlorella. The investigator (CMW) who conducted the baseline physical and tender point examinations also

Table 4. Average changes in tender points and TPI

Visit	Mean total tender points*	% Change in tender points from visit 1	Mean TPI*	% Change in TPI from visit 1
1	17 (12-18)	NA	32 (23-45)	NA
2	16 (8-18)	4%	28 (8-42)	14%
3	15 (9-18)	8%	25 (10-44)	22% <sup>b</sup>

\* Tender Point Index with range in parenthesis.

<sup>b</sup> Statistically significant from visit 1 ( $p = 0.01$ ); NA, not applicable.

Table 5. Results based on change in TPI

Status based on change in TPI*	Number of patients	Percentage of patients
Very significantly improved (>50% drop in TPI)	2	11
Significantly improved (>25%-50% drop in TPI)	6	33
Moderately improved (>10%-25% drop in TPI)	3	17
Mildly improved (>5%-10% drop in TPI)	5	28
No change ( $\pm 5\%$ change in TPI)	1	6
Mildly worse (>5%-10% increase in TPI)	0	0
Significantly worse (>25%-50% increase in TPI)	1	6
Very significantly worse (>50% increase in TPI)	0	0

\* Tender point index and % change from baseline TPI.

Table 6. Patient questionnaire—changes from visit 1 to visit 3

Symptom	Patients better (n)	Patients worse (n)	Change from Visit 1* (%)
Nervousness	10	8	15%
Limited activity	9	4	16%
Headache	8	6	-5%
Pain	10	4	21%
Sleep	9	7	8%
General feeling	10	3	12%
Diarrhoea	6	10	-48%
Constipation	10	7	24%
Abdominal cramps	5	10	-17%

\* Positive number is the average % improvement while a negative number indicates the average % worsening of a symptom between the beginning and end of the study.

performed the same examinations for the two subsequent clinic visits. The general physical examinations indicated no significant changes had occurred over the 2-month course of the study. During this time also, the results of blood analyses indicated that values had remained within normal limits of variation (data not shown). The number of tender points and the severity of the tenderness at each point were measured at each visit. The average number of tender points and TPI for the entire group was calculated at each time point (Table 4). After 1 month of dietary supplementation with Chlorella, there was an average net decrease of one tender point and after 2 months, a drop of two points. The mean TPI, which was 32 at baseline, fell to 28 after 1 month and to 25 after 2 months. The seven-point drop after 2 months represented a statistically significant ( $p = 0.01$ ) decrease of 22% in the intensity of pain. Table 5 summarizes the patients' individual responses characterized according to the percentage change in TPI after 2 months in the study. Sixteen of the eighteen patients (88%) had a greater than 5% improvement in TPI and eight of these patients had a greater than 25% decrease in their pain intensity. One patient's TPI remained unchanged while another's TPI worsened over the 2-month study period.

### Clinical measures

On each visit, patients completed a series of four subjective assessments which included a general patient questionnaire (PAQ) that consisted of 10 cm visual analogue scales for pain and other symptoms, the Stanford HAQ disability questionnaire, the Hassles Scale, and the National Institute of Mental Health CES-D scale for depression. Comparisons of the various parameters obtained from the PAQ completed at baseline and at the end of the study are presented in Table 6. The results of the PAQ suggested that the majority of patients experienced at least a modest improvement in most of their symptoms of fibromyalgia. However, most patients also reported an increased frequency in episodes of diarrhoea and abdominal cramping. These two adverse events, however, were never so severe as to require medical intervention or to limit the activities of the patients involved.

The averaged results of the HAQ indicated that there had not been a significant change in the functional capabilities of the patients over the course of the study (Table 7). The Hassles Scale, which measures how well one deals with the various hassles one encounters in

# Nutritional Supplementation with *Chlorella pyrenoidosa* for Patients with Fibromyalgia Syndrome: A Pilot Study

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Fibromyalgia syndrome is a common, chronic musculoskeletal disorder of unknown aetiology. While available therapy is often disappointing, most patients can be helped with a combination of medication, exercise and maintenance of a regular sleep schedule. The objective of the present study was to determine if adding nutritional supplements derived from the unicellular green alga, *Chlorella pyrenoidosa*, produced any improvements in the clinical and functional status in patients with moderately severe symptoms of fibromyalgia syndrome. Eligible patients had 2+ palpable tenderness at 11 or more of 18 defined tender points and had a tender point index (TPI) of at least 22. Each day for 2 months, participants consumed two commercially available *Chlorella*-based products, 10 g of 'Sun *Chlorella*' tablets and 100 mL of liquid 'Wakasa Gold'. Any amelioration of symptoms was validated and quantified using semi-objective and subjective outcome measures systematically administered at clinic visits on days 0, 30 and 60 of the diet therapy. Eighteen of the 20 patients enrolled completed the 2 month trial. The average TPI for the group which at onset was 32, decreased to a mean of 25 after 2 months. This decrease was statistically significant ( $p = 0.01$ ), representing a 22% decrease in pain intensity. Blood samples taken on each occasion indicated no significant alterations in serum chemistries, formed elements, and circulating lymphocyte subsets. Compilations of the results of patient interviews and self-assessment questionnaires revealed that seven patients felt that the dietary supplement had improved their fibromyalgia symptoms, while six thought they had experienced no change, and five believed the symptoms had worsened over the time of the trial. The results of this pilot study suggest that dietary *Chlorella* supplementation may help relieve the symptoms of fibromyalgia in some patients and that a larger, more comprehensive double-blind, placebo-controlled clinical trial in these patients is warranted. Copyright © 2000 John Wiley & Sons, Ltd.

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## INTRODUCTION

Fibromyalgia syndrome is a disorder of unknown aetiology which affects an estimated 2%-4% of the general population (Wolfe, 1994). The major complaint of patients with fibromyalgia is that they ache all over but its definitive diagnosis is based on the presence of at least 11 of 18 tender points in characteristic locations (Russell *et al.*, 1986). Any number of other symptoms may also be present, particularly fatigue, morning stiffness, sleep disturbance, paresthesias and headaches.

Most patients with fibromyalgia syndrome respond favourably to gentle aerobic exercise, maintenance of an adequate amount and regular schedule of sleep, and low doses of amitriptyline or other medications known to improve deep sleep (Goldenberg *et al.*, 1986; Russell *et al.*, 1991). Amitriptyline, however, also has frequent side

effects such as weight gain, dry mouth and cognitive impairment when given in doses sufficient to keep symptoms well controlled. Also, some tolerance may develop to the sedative effect of the medication, necessitating dose increases in order to maintain its beneficial effects. Several other medications have been shown in controlled studies to help relieve symptoms, including cyclobenzaprine, fluoxetine and alprazolam (Russell *et al.*, 1991; Carotte *et al.*, 1994; Goldenberg *et al.*, 1996). Imipramine, steroids, and non-steroidal anti-inflammatory drugs have been found to be no more effective than placebo (Russell *et al.*, 1991) and no 'alternative' drug or herbal treatments have been proven effective in controlled studies.

*Chlorella pyrenoidosa* is a unicellular green alga that grows in fresh water. The principal components of *Chlorella* that have been shown to have certain health benefits are chlorophyll, the organism's cell walls,  $\beta$ -carotene, and *Chlorella* Growth Factor (CGF). *Chlorella pyrenoidosa* has the highest content of chlorophyll of any known plant and also contains high concentrations of many vitamins and minerals, as well as dietary fibre, nucleic acids, amino acids, enzymes and other substances. This alga has a strong cell wall that prevents its

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Table 1. Tender point sites

Number	Point
1,2	Occiput: at the suboccipital muscle insertions
3,4	Low cervical: at the anterior aspects of the intertransverse spaces at C5-C7
5,6	Trapezius: at the midpoint of the upper border
7,8	Supraspinatus: at origins, above the scapula spine near the medial border
9,10	2nd rib: at the second costochondral junctions, just lateral to the junctions on upper surfaces
11,12	Lateral epicondyle: 2 cm distal to the epicondyles
13,14	Gluteal: in upper outer quadrants of buttocks in anterior fold of muscle
15,16	Greater trochanter: posterior to the trochanteric prominence
17,18	Knees: at the medial fat pad proximal to the joint line

Table 2. Severity scale and tender point index (TPI)

Severity response to digital pressure	
0	No reported tenderness
1+	Tenderness reported, but La Belle indifference, no physical response
2+	Tenderness reported plus an objective physical response (wince, withdrawal)
3+	Tenderness reported with emphasis, plus an exaggerated, dramatic physical response (wince, jerk, withdrawal)
4+	Untouchable area. The anticipated pain so severe that the patient avoids the expected palpation.

TPI = Sum of severities at the 18 tender point sites.

native form from being adequately digested so that only after Dyno-Mill processing to break its cell wall can the organism be digested by humans (Mitsuda *et al.*, 1977). *Chlorella* Growth Factor is a water soluble extract and contains a variety of substances including amino acids, peptides, proteins, vitamins, sugars and nucleic acids. Estimates of the CGF content in raw *Chlorella pyrenoidosa* is approximately 5%. A number of scientific reports from Japan have shown that broken cell wall preparations and extracts of *Chlorella pyrenoidosa* and other *Chlorella* species when either given orally or injected promote growth and healing, stimulates the immune system such that the host is protected from infection, and exerts significant anti-cancer activity (Konishi *et al.*, 1985; Yamaguchi *et al.*, 1985; Komiyama *et al.*, 1986; Tanaka *et al.*, 1986; Miyazawa *et al.*, 1988; Merchant *et al.*, 1990).

Although our findings and those of others who have suggested that there may be a health benefit from *Chlorella* in the diet for patients with cancer, there remains a clear need for more scientific research specifically directed at certain diseases, particularly those of a chronic, protracted nature. Therefore, the purpose of the present investigation was first to identify 20 patients with fibromyalgia syndrome who exhibited moderately severe symptoms and who agreed to add *Chlorella* to their daily diet for 2 months. Then, to document their clinical status at strategic intervals using validated, semi-objective and subjective outcome measures and finally, to determine the magnitude of any resultant change in clinical symptoms, particularly pain and outcome variables.

## MATERIALS AND METHODS

**Subjects.** The study was open to males and females between the ages of 18 and 65 years of age who met American College of Rheumatology (ACR) criteria for a diagnosis fibromyalgia syndrome (Wolfe *et al.*, 1990).

The treatment protocol was approved by the Virginia Commonwealth University Committee on the Conduct of Human Research and performed in accordance with their guidelines and regulations. All patients understood the role and responsibilities in the study and had granted their informed consent. The ACR criteria were used to achieve conformity with other fibromyalgia syndrome studies. These criteria are primarily based on the severity of a patient's tenderness at each of the typical tender points measured by palpation (Russell *et al.*, 1986, 1991). Tables 1 and 2 briefly summarize the anatomic locations of the 18 tender points and the severity scale used to define the severity of tenderness at each tender point and calculate the tender point index (TPI). In order to be eligible for the present study, patients were required to show 2+ tenderness at at least 11 sites; i.e. a TPI of 22 or higher (Russell *et al.*, 1986).

**Concomitant medications.** Each subject was asked to indicate from a list of choices, the medications he/she was currently using and had used in the prior 2 months. The choices were specially prepared to include psychotropic drugs, non-narcotic analgesics, and narcotic analgesics that might be used to treat chronic pain. Patients were asked to continue any medication given specifically for their fibromyalgia syndrome but not to add any new medications and/or treatments during the course of the study without notification and approval by one of the investigators. Subjects also recorded the name and total dose of any drug taken each day in their study diary (see below).

**Exclusion criteria.** Patients with fibromyalgia syndrome symptoms were excluded if they also met published criteria for systemic lupus erythematosus or rheumatoid arthritis. Patients were also excluded if they ever had previously consumed any dietary supplement containing *Chlorella*. They were not enrolled if the investigators had reason to expect that the patient would not be compliant with the dietary supplement or the follow-up schedule. Patients had to be able to read and understand English