

**Nutritional Supplementation with *Chlorella pyrenoidosa* for
Patients with Mild to Moderate Hypertension**

Final Report

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SUMMARY

Pharmacologic treatment of hypertension reduces the risk of cardiovascular disease, however, randomized controlled clinical trials and population studies have also both shown that abnormally high blood pressure can be lowered with diet modification and exercise. The basis for the present study was to show that daily dietary supplementation with natural "whole foods" such as the unicellular green alga, *Chlorella pyrenoidosa* which is rich in proteins, vitamins, and minerals may lower the blood pressure of individuals who otherwise ingest a normal, non-vegetarian diet. A total of 33 subjects with mild to moderate hypertension and taking no antihypertensive drugs were enrolled in the trial. Following the one-month placebo washout 24 patients were evaluable, seven were dropped because they no longer met eligibility criteria for mild to moderate hypertension and two withdrew because of side effects believed to be related to their not taking their anti-hypertensive drug treatment. The eligible consumed 10 g of "Sun *Chlorella*" tablets and 100 ml of liquid *Chlorella* extract each day for the next two months. Physical exams and ECGs did not change between the beginning (Visit 1) and end of the study period (Visit 5). Routine laboratory tests on blood, serum and urine were performed at Visit 1, the end of the placebo period (Visit 3), and at the end of the trial. All parameters were within normal limits of variation and no single variable significantly changed over the three-month course of the investigation. However, when the lipid components were analyzed the data suggested that the dietary supplementation of *Chlorella* used by the subjects in this study had a significant lowering effect on serum cholesterol. There was a significant drop in serum cholesterol both from the beginning and from Visit 3 until the end of the study; $p=0.003$ and $p=0.0001$, respectively. Also, high-density and low-density cholesterol both significantly dropped during the two months of dietary *Chlorella*.

The primary objective of the present study was to determine if there is a reduction in mean sitting diastolic blood pressure (SiDBP) in patients with mild to moderate hypertension who have added *Chlorella* to their daily diet for two months. At Visit 3, after one month of no anti-hypertension medicine and dietary supplementation with placebo, mean heart rates were 76.5 ± 9.9 , mean sitting systolic blood pressure (SiSBP) was 141.6 ± 14.4 mm Hg, and mean SiDBP 96.5 ± 6.6 . After one or two months of dietary *Chlorella* supplementation, the average heart rate, SiSBP, and SiDBP changed only slightly from the Visit 3 values. This suggests that coming off the anti-hypertension medicines for a month, alone was responsible for the increases in SiSBP and SiDBP at Visit 3 and that during dietary *Chlorella* supplementation there was essentially no significant worsening of the study population's average SiDBP. Based on standard criteria of the pharmaceutical industry, our results indicated that a quarter of the patients enrolled (6/24) had an excellent response to the dietary supplement (i.e. SiDBP was below 90 mm Hg) and that three patients whose SiDBP was above 90 mm Hg, still showed between a 4 and 9 mm Hg drop in their SiDBP. Almost two-thirds of our patients' SiDBP either rose during this period or fell by less than 4 mm Hg. However, when we used a 4 mm Hg change in SiDBP as an indicator of response and compared SiDBP at their first and last visits, five patients showed improvement, six patients had an unchanged SiDBP, and 13 had a worsening of their hypertension. The effect of the dietary supplement was more dramatic when these same criteria were applied to compare the SiDBP of Visit 3 (after one month off medication and placebo) and after two months of dietary *Chlorella* (Visit 5); nine patients showed improved SiDBP, seven a stable SiDBP, and only one-third showed a worsening of their hypertension. Questionnaires were administered to subjects at each clinic visit to determine whether or not dietary supplementation with *Chlorella* improved their quality of life. These results indicated that over the course of the entire study their

overall perception of health was significantly improved while their psychological well-being, social functioning, cognitive functioning, and sexual functioning was not significantly affected. The results of this pilot study indicate that daily dietary supplementation with *Chlorella* produces a significant reduction in serum cholesterol and suggest that some patients' can have their mild or moderate hypertension reduced or kept stable with the a daily dietary supplementation of *Chlorella* alone, eliminating the need of an anti-hypertensive medication.

I. INTRODUCTION

Hypertension is treated with the hope of lowering the patient's overall risk of cardiovascular disease and its consequences. There is now a substantial body of evidence that vegetarian dietary patterns lower blood pressure in normotensive and hypertensive subjects. These diets include "whole foods" such as fruits and vegetables which contain a complex of proteins, vitamins, and minerals which are believed to work in concert to lower blood pressure. **The present study was designed to test the hypothesis that daily dietary supplementation with *Chlorella* (10 g tablets and 100 ml Wakasa) would reduce the mean sitting diastolic blood pressure in patients with untreated mild to moderate hypertension within two months.** If dietary supplementation with *Chlorella* leads to a modest drop in blood pressure and a lowering of plasma lipid levels in patients with mild to moderate hypertension, this nonpharmacological treatment would then be expected to significantly reduce cardiovascular risk. This report describes the results of our trial which involved a total of 33 subjects with mild to moderate hypertension.

II. SUBJECTS

The study was open to patients with mild (mean sitting diastolic blood pressure (SiDBP) 90-104 mm Hg) to moderate (mean SiDBP 105-115 mm Hg) hypertension and who met all other entry criteria for enrollment. All subjects had to be willing to discontinue all medication given specifically for hypertension including diuretics although chronic therapies such as aspirin for myocardial infarction prevention, premarin, or thyroxine were allowed. Every effort was made, however, to maintain these at a constant dosage. Patients were also instructed not to add any new medications and/or treatments during the course of the study. The study design is presented in **Table 1**.

Table 1. Study Design and Schedule of Procedures.

Procedure	Visit 1 Screening	Visit 2 Baseline	Visit 3 Initiation	Visit 4 Interim	Visit 5 Final*
Interview**	X	X	X	X	X
Quality of Life Questionnaire	X	X	X	X	X
Physical Examination & ECG	X				X
Blood Pressure & Other Vitals	X	X	X	X	X
Dispense Diet Supplement	Placebo		Chlorella	Chlorella	
Hematology	X		X		X
Serum Chemistry & Lipids	X		X		X
Urinalysis	X		X		X

* or when patient leaves the trial

** to determine if there have been any adverse events

Screening Visit (Visit 1). Study candidates had their medical records reviewed for eligibility and once deemed eligible, signed the informed consent. They then completed a quality of life questionnaire, had a complete medical history taken, and underwent a physical examination, blood pressure measurement, laboratory assessment, and an ECG. If all eligibility criteria were met, they received 1500 placebo tablets and three bottles placebo liquid and were instructed to begin taking 50 tablets and 100 ml of the liquid every day. None of the patients were aware that the tablets and liquid were placebos. Each patient was also instructed to discontinue any medication they were taking for their hypertension and to return to the clinic after four weeks.

Baseline and Initiation Visits (Visits 2 & 3). Following the placebo period, patients had to have a mean SiDBP of between 90 and 115 mm Hg confirmed on two occasions (i.e. Visits 2 & 3) at least 24 hours apart to remain in the study. On Visit 2 (approximately four weeks after Visit 1), patients completed the quality of life questionnaire and had their vital measurements taken. One to seven days later, at Visit 3, patients completed the quality of life questionnaire, had their vital measurements taken, and had laboratory assessments of blood cytology, serum (chemistry and lipids) and urine. At this Initiation Visit, patients who still meet eligibility criteria, began daily dietary supplementation with *Chlorella*. They were given enough *Chlorella* tablets and liquid for four weeks.

Interim and Final Visits (Visits 4 & 5). After four weeks, patients returned to clinic for a brief consultation. At this time they completed the quality of life questionnaire, had their vital measurements taken, and were given enough *Chlorella* tablets and liquid for another four weeks. On Visit 5 (i.e. the end of the study), patients completed the quality of life questionnaire, had their vital measurements and an ECG taken, and had blood taken for laboratory assessments of their serum chemistry and lipids as well as cytology. A urinalysis was also performed.

A total of 33 subjects were enrolled in the trial between May and December, 1997. The demographic profile of the population is presented in **Table 2**.

Table 2. Patient Demographics.

Total Number of Subjects	33
Average Age	50 ± 11 (range 22-73)
Sex	20 Female, 13 Male
Ethnicity	18 White, 15 Black
Mean Education (yrs)	15 ± 2 (range 12-17)
Duration of Hypertension (yrs)	11 ± 11 (range 0-47)

All but six of the patients were taking some type of daily medical treatment for their hypertension when they were enrolled. Each patient's weight (Wt), blood pressure (BP), heart rate (HR), and hypertension medicines on Visit 1 are listed in **Table 3**. The average weight of the population was 208.5 ± 35.3 , their mean heart rate was 73.7 ± 10.2 , and their SiSBP was 136.8 ± 11.5 and mean SiDBP was 90.8 ± 6.2 .

Table 3. Patient Vitals and Hypertension Medicine(s) at Screening.

Patient #	Date	Wt	HR	BP	Hypertension Medication	Dose (mg/day)
01	23-May-97	168	76	121/92	Triamteren	50/25
02	27-May-97	178	53	152/99	None	--
03	02-Jun-97	216	76	134/94	Vasotec	5
04	04-Jun-97	255	72	125/79	Primivil	10
05	09-Jun-97	247	58	131/91	Maxicle	0.25
06	09-Jun-97	286	71	143/92	Verapamil	180
					Furosemide	40
					Metoprolol	25
07	11-Jun-97	222	63	141/95	Verapamil	180
08	13-Jun-97	192	64	149/89	Hydrochlorothiazide	25
09	24-Jun-97	233	76	131/89	Lopressor	50
10	25-Jun-97	203	88	140/89	Felodipine	10
11	25-Jun-97	249	88	147/102	Norvasc	5
12	25-Jun-97	194	68	121/87	Zesteril	20
13	27-Jun-97	168	80	138/85	HCTZ	12.5
14	22-Jun-97	166	86	170/98	Hyzaar	50/12.5
15	02-Jul-97	250	80	135/77	HCTZ	25
16	02-Jul-97	228	64	154/101	None	--
17	02-Jul-97	238	20	143/99	None	--
18	03-Jul-97	226	83	143/83	HCTZ	50
					Capoten	40
19	07-Jul-97	208	84	147/98	Benazepril	40
20	08-Jul-97	213	76	150/99	HCTZ	20
21	09-Jul-97	175	88	126/85	Procardia-XL	60
					HCTZ	25
22	09-Jul-97	270	88	126/88	Zestril	10
23	09-Jul-97	218	64	135/91	None	--
24	06-Aug-97	180	60	135/96	None	--
25	06-Aug-97	126	55	129/92	HCTZ	25
26	06-Aug-97	206	81	142/93	HCTZ	25
					Procardia-XL	60
28	13-Aug-97	164	62	127/91	Verapamil	250
29	26-Aug-97	174	76	137/89	Dilacor	240
30	29-Aug-97	192	80	135/86	Captopril	50
31	30-Oct-97	175	76	122/92	None	--
32	14-Nov-97	229	64	133/86	Zestril	10
33	25-Nov-97	211	76	141/85	Verapamil	250
34	02-Dec-97	176	80	114/83	HCTZ	25

Although 33 subjects were enrolled in the trial, ten did not complete the four-month study. Nutritional supplementation with placebo or *Chlorella* was discontinued and the patients removed from the study if one of the following occurred: 1) Mean SiDBP went above 115 mm Hg or below 90 mm Hg on two consecutive measurements taken 1-7 days apart; 2) patient developed side effects (e.g. nausea, abdominal cramps, or diarrhea) or clinically significant laboratory abnormalities that, in the judgement of the investigators, warranted their discontinuation in the study; 3) patient withdrew consent or was unable to comply with the requirements of the study. **Table 4** lists the patients and their reasons for not completing the clinical trial. A total of seven subjects were discontinued at the end of the placebo period (Visits 2 & 3) because their mean SiDBP was either too high (three patients) or too low (four patients). Two other patients were also withdrawn at this time because of side effects which were believed attributable to the removal of their anti-hypertensive medication. Finally, one patient was discontinued after Visit 4, because his mean SiDBP was more than 115 mm Hg and we felt it was necessary that he resume taking his medication for hypertension. This patient, however, remains in the data analysis for determining the effects of *Chlorella* on hypertension such that results use data acquired from 24 patients.

Table 4. Reasons for Early Discontinuation From the Trial.

Patient #	# Visits Completed	Reason for Not Completing Trial
402	3	Mean SiDBP below 90 mm Hg on two consecutive measurements taken at Visits 2 & 3
404	3	Mean SiDBP below 90 mm Hg on two consecutive measurements taken at Visits 2 & 3
406	2	Mean SiDBP below 90 mm Hg on Visit 2
415	3	Mean SiDBP below 90 mm Hg on two consecutive measurements taken at Visits 2 & 3
418	2	Mean SiDBP above 115 mm Hg on Visit 2
421	3	Mean SiDBP above 115 mm Hg on Visits 2 & 3
422	1	Swelling in feet and ankles
425	2	Headaches
426	1	Mean SiDBP above 115 mm Hg before Visit 2
432	4	Mean SiDBP above 115 mm Hg on Visit 4

A total of 24 subjects remained eligible for the trial following their Visit 3 (Initiation) and all were started on the *Chlorella* tablets and Wakasa. The demographic profile of this population is presented in **Table 5**. This population did not differ significantly in any parameter from the original group of 33 subjects who were screened and enrolled.

Table 5. Demographics of Patients Who Completed Trial.

Total Number of Subjects	24
Average Age	49 ± 10 (range 22-73)
Sex	13 Female, 11 Male
Ethnicity	12 White, 12 Black
Mean Education (yrs)	15 ± 2 (range 12-17)
Duration of Hypertension (yrs)	10 ± 10 (range 1-40)

All but five of the patients were taking some type of daily medical treatment for their hypertension at the time they were enrolled. The average weight of the population was 203 ± 27, their mean heart rate was 73.4 ± 9.1, SiMBP was 137.3 ± 12.3 and mean SiDBP was 92.0 ± 5.5.

III. CLINICAL MEASUREMENTS

At all clinic visits the mean trough SiSBP, SiDBP and heart rate were determined. Blood and urine were also analyzed at the screening, initiation, and final clinic visit (i.e. Visits 1, 3, & 5) (Tables 6-9). Physical examinations and ECGs were performed at the beginning (Visit 1) and end (Visit 5) of the study period. There was no significant changes in the patients' physical exams, weights, and ECGs between the beginning and end of the study period. Laboratory values at the three principal visits during the study period are presented in Tables 6-9.

Table 6. Blood Cytology During *Chlorella* Supplementation.

Parameter	Visit 1 Screening	Visit 3 Initiation	Visit 5 Final	Normal Values
WBC	5.95 ± 1.57	6.12 ± 1.65	6.03 ± 1.58	4.1-10.1 x 10 ³
RBC	4.78 ± 0.51	4.80 ± 0.58	4.82 ± 0.6	4.2-5.4 x 10 ⁶
HGB	13.5 ± 1.68	13.6 ± 1.89	13.7 ± 1.9	12-16 g/dL
HCT	40.5 ± 4.45	40.5 ± 4.93	40.6 ± 5.17	37-47%
MCV	84.9 ± 6.13	84.7 ± 6.33	84.7 ± 6.65	81-99 fl
MCH	28.4 ± 2.44	28.4 ± 2.66	28.6 ± 2.53	27-31 pg
MCHC	33.5 ± 0.71	33.5 ± 0.94	33.8 ± 0.78	33-36 g/dL
RDW	14.5 ± 1.44	14.5 ± 1.44	14.4 ± 1.54	11.5-14.5%
Platelets	276 ± 78	278 ± 83	269 ± 73	130-400 x 10 ³
MPV	10.0 ± 2.0	9.8 ± 1.5	10.2 ± 2.2	7.4-10.4 fl
%Granulocytes	59.8 ± 8.2	58.7 ± 9.7	60.2 ± 8.7	42-75%
%Lymphocytes	32.4 ± 8.1	31.5 ± 8.8	29.7 ± 9.4	20-51%
%Monocytes	5.13 ± 2.11	5.33 ± 1.81	5.78 ± 2.39	2-9%
%Eosinophils	2.17 ± 1.61	3.08 ± 1.61	2.65 ± 2.66	0-5%
%Basophils	0.08 ± 0.28	0.04 ± 0.21	0.17 ± 0.39	0-1%

The mean and standard deviation for the formed elements in the blood of our study subjects at Visits 1, 3, and 5 are presented in **Table 6**. All parameters were within normal limits of variation and no single variable significantly changed over the three-month course of the investigation. The results of serum chemistry analyzes at these same time points are presented in **Table 7**. As was the case for the formed elements, all values were within normal limits and none of them changed significantly from the beginning and end of the study.

Table 7. Serum Chemistry During *Chlorella* Supplementation.

Parameter	Visit 1 Screening	Visit 3 Initiation	Visit 5 Final	Normal Values
Sodium	143 ± 1.8	143 ± 1.6	142 ± 2.1	140-148 mmol/L
Potassium	4.1 ± 0.3	4.2 ± 0.3	4.2 ± 0.3	3.6-5.2 mmol/L
Chloride	105 ± 2.2	104 ± 1.8	105 ± 2.1	100-108 mmol/L
Carbon Dioxide	26.0 ± 2.0	26.7 ± 1.8	24.5 ± 2.5	21-32 mmol/L
Glucose	99 ± 36.9	102 ± 31.2	103 ± 45.5	70-100 mg/dL
BUN	13.6 ± 4.4	12.7 ± 3.6	12.1 ± 4.4	7-18 mg/dL
Creatinine	1.0 ± 0.2	1.0 ± 0.2	1.0 ± 0.2	0.6-1.0 mg/dL
Urate	5.5 ± 1.1	5.4 ± 1.1	5.8 ± 1.5	2.6-6.0 mg/dL
Calcium	9.6 ± 0.4	9.2 ± 0.4	9.1 ± 0.6	8.8-10.5 mg/dL
Inorganic Phosphate	3.3 ± 0.5	3.4 ± 0.6	3.3 ± 0.5	2.5-4.9 mg/dL
Bilirubin	0.5 ± 0.3	0.5 ± 0.2	0.6 ± 0.3	0-1.0 md/dL
Alkaline Phosphatase	82.0 ± 20.6	81.0 ± 17.8	88.1 ± 20.3	50-136 U/L
AST (SGOT)	19.5 ± 5.8	18.9 ± 8.1	19.2 ± 7.4	15-37 U/L
ALT (SGPT)	39.5 ± 12.3	40.8 ± 14.3	40.8 ± 16.0	30-65 U/L
Total Protein	7.2 ± 0.4	7.1 ± 0.4	7.1 ± 0.4	6.4-8.2 g/dL
Albumin	3.8 ± 0.3	3.8 ± 0.3	3.8 ± 0.3	3.4-5.0 g/dL
Globulin	3.3 ± 0.5	3.3 ± 0.5	3.3 ± 0.4	2.3-3.5 g/dL

One of the purposes of this study was to define any effects dietary supplementation with *Chlorella* may have on blood lipids and to correlate any changes with SiDBP. So, in these same blood chemistry samples, we also examined the lipid profile (i.e. total cholesterol, triglycerides, high- and low-density cholesterol). The averages and standard deviations for each parameter are presented in **Table 8**. Although all four items were within normal limits of variation, there are numerous statistically significant changes over the course of the investigation. First, there was a significant drop in serum cholesterol both from the beginning and from visit 3 until the end of the study; $p=0.003$ and $p=0.0001$, respectively. There was also a significant drop in triglycerides from Visit 1 to Visit 3 ($p=0.04$) but this was not maintained such that there was no statistical difference between Visits 1 and 5. High-density cholesterol dropped after two months of dietary *Chlorella*. Between Visits 1 and 5 the difference was almost significant ($p=0.055$) but between Visits 3 and 5 the difference was significant ($p=0.03$). Low-density cholesterol showed a similar pattern; significantly dropping between Visits 1 and 5 ($p=0.05$) and Visits 3 and 5 ($p=0.003$). *These results suggest that the dietary supplementation of Chlorella used by the subjects in this study had a significant lowering effect on serum cholesterol.*

Table 8. Serum Lipids During *Chlorella* Supplementation.

Parameter	Visit 1 Screening	Visit 3 Initiation	Visit 5 Final	Normal Values
Total Cholesterol	202 ± 42.9	199 ± 38.9	188 ± 40.1	0-200 md/dL
Triglycerides	127 ± 81.8	109 ± 65.1	123 ± 77.6	30-200 mg/dL
High Density Cholesterol	48.5 ± 12.9	48.7 ± 12.3	46.2 ± 11.5	39-96 mg/dL
Low-Density Cholesterol	128 ± 40.7	129 ± 35.9	118 ± 37.2	74-190 mg/dL

A urinalysis was also performed on study subjects at Visits 1, 3, and 5. The mean and standard deviation for specific gravity and pH as well as all other parameters were within normal limits of variation and no single variable significantly changed over the three-month course of the investigation (Table 9).

Table 9. Urinalysis During *Chlorella* Supplementation.

Parameter	Visit 1 Screening	Visit 3 Initiation	Visit 5 Final	Normal Values
Specific Gravity	1.02 ± 0.007	1.019 ± 0.006	1.019 ± 0.008	1.0005-1.03
pH	6.1 ± 0.9	6.3 ± 1.0	6.2 ± 0.7	5.0-9.0
Protein	Negative	Negative	Negative	Negative mg/dL
Glucose	Negative	Negative	Negative	Negative mg/dL
Ketones	Negative	Negative	Negative	Negative mg/dL
Occult Blood	Negative	Negative	Negative	Negative
Bilirubin	Negative	Negative	Negative	Negative

The primary objective of the present study was to determine if there is a reduction in mean sitting diastolic blood pressure (SiDBP) in patients with mild to moderate hypertension who have added *Chlorella* to their daily diet for two months. The changes in heart rate and blood pressure for each patient are demonstrated in Table 10. At the first visit, the average heart rate for the 24 patients was 73.4 ± 9.1 and their mean SiSBP was 137.3 ± 12.3 mm Hg, and mean SiDBP was 92.3 ± 5.5 mm Hg. After a month off their hypertension medicine and dietary supplementation with placebo their mean heart rate rose to 76.5 ± 9.9 and their SiSBP rose to an average of 141.6 ± 14.4, and mean SiDBP rose by 4.3 mm Hg to 96.5 ± 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 our patients could be constructed (Table 11). After one or two months of dietary *Chlorella* supplementation, their heart rates, SiSBP, and SiDBP changed only slightly from the Visit 3 values. However, compared to Visit 1, the mean SiDBP increased by 4-5 mm Hg at the three subsequent visits; remaining statistically significant (p=0.02). We believe that this suggests that coming off the anti-hypertensive medications for a month, alone was responsible for the increase in SiDBP and that during dietary *Chlorella* supplementation there was essentially no increase (i.e. worsening) on average of the SiDBP.

Table 10. Heart Rate and Blood Pressure During *Chlorella* Supplementation.

Patient #	Visit 1 HR	Visit 1 BP	Visit 3 HR	Visit 3 BP	Visit 4 HR	Visit 4 BP	Visit 5 HR	Visit 5 BP
01	76	121/92	76	132/97	88	135/96	68	138/105
03	76	134/94	76	129/101	80	146/101	88	133/103
05	58	131/91	60	149/103	76	132/83	76	137/89
07	63	141/95	80	130/90	76	128/93	60	127/89
08	64	149/89	62	176/106	76	140/90	68	175/107
09	76	131/89	88	139/98	82	135/102	72	145/100
10	88	140/89	76	151/89	76	149/85	87	153/95
11	88	147/102	84	141/103	80	141/93	86	138/96
12	68	121/87	76	122/89	72	129/91	76	123/84
13	80	138/85	66	145/94	76	165/93	88	149/99
14	86	170/98	88	151/99	84	136/81	87	140/74
16	64	154/101	84	139/100	84	145/105	73	158/109
17	76	143/99	64	133/91	76	138/101	58	163/107
19	84	147/98	80	165/110	88	172/110	70	170/111
20	76	150/99	76	171/106	76	165/105	60	164/99
23	64	135/91	60	134/93	58	131/98	46	144/105
24	60	135/96	88	133/89	76	138/100	86	136/91
28	62	127/91	64	133/98	60	137/99	55	137/93
29	76	137/89	76	135/90	76	137/91	81	139/90
30	80	135/86	84	153/107	80	141/100	83	155/103
31	76	122/92	96	118/91	78	127/87	68	122/87
32	64	133/86	80	145/92	76	162/109	Withdrawn	Withdrawn
33	76	141/85	82	143/90	82	134/91	82	145/94
34	80	114/83	70	131/91	72	142/87	72	131/83

Table 11. Mean Heart Rate and Blood Pressure Changes During *Chlorella* Supplementation.

Visit #	HR	SiSBP	SiDBP	Change in SiDBP from Visit 1	Change in SiDBP from Visit 3
1	73.4 ± 9.1	137.3 ± 12.3	92.3 ± 5.5		
3	76.5 ± 9.9	141.6 ± 14.4	96.5 ± 6.6	+4.3	
4	77.0 ± 7.0	141.9 ± 12.4	95.5 ± 8.0	+4.6	-1.0
5	73.5 ± 11.9	142.4 ± 18.1	96.3 ± 9.5	+5.1	-0.2

Since only working with “average” changes in SiDBP might mask real responses (i.e. decreases in SiDBP) among the subjects, we characterized each patient’s response by three different criteria (Table 12). In the protocol, we had explained that we would characterize response based on standard criteria which have been used previously to assess responses to antihypertensive pharmacologic agents. These results which are presented in Table 12A, indicate that a quarter of the patients enrolled (6/24) had an excellent response to the dietary supplement; that is that after two months of taking *Chlorella*, their SiDBP was below 90 mm Hg. A further one-eighth of the patients (3/34) although having a SiDBP above 90 mm Hg, still showed between a 4 and 9 mm Hg drop in their SiDBP. Almost two-thirds of the subjects (15/24), however, were considered inadequately treated by stopping their anti-hypertensive medication and adding *Chlorella* to their diet. These patients SiDBP either rose during this period or fell by less than 4 mm Hg. Thus, following the conventional pharmacological criteria for assessing response, we can say that slightly more than a one-third (38%) of the subjects showed some improvement in their hypertension by adding *Chlorella* to their diet.

Table 12. Characterization of SiDBP Changes After *Chlorella* Supplementation.

A. Summary of Results by Standard Endpoints Used in Pharmacological Studies of Hypertension

Result	Description	# Patients
Excellent	SiDBP <90 mm Hg	6 (25%)
Good	SiDBP >90 mm Hg & reduction from baseline of at least 10 mm Hg	0 (00%)
Fair	SiDBP >90 mm Hg & reduction from baseline from 4 to 9 mm Hg	3 (13%)
Inadequate	SiDBP >90 mm Hg & reduction from baseline of <4 mm Hg or an increase	15 (62%)

B. Summary of Results Based on 4 mm Hg or more Change in SiDBP from Visit 1

Result	Description	# Patients
Improved	Final SiDBP reduced by 4 mm Hg or more from Screening (Visit 1)	5 (21%)
Stable	Final SiDBP less than 4 mm Hg change from Screening (Visit 1)	6 (25%)
Worse	Final SiDBP increased by 4 mm Hg or more from Screening (Visit 1)	13 (54%)

C. Summary of Results Based on 4 mm Hg or more Change in SiDBP from Visit 3

Result	Description	# Patients
Improved	Final SiDBP reduced by 4 mm Hg or more from Initiation (Visit 3)	9 (38%)
Stable	Final SiDBP less than 4 mm Hg change from Initiation (Visit 3)	7 (29%)
Worse	Final SiDBP increased by 4 mm Hg or more from Initiation (Visit 3)	8 (33%)

This improvement is shown even more dramatically if we use a 4 mm Hg change in SiDBP as an indicator of response. As is shown In **Table 12B**, when the first SiDBP of patients (when most are taking the antihypertensive medication) is compared to their last visit (after three months off medication and two months of taking *Chlorella*), five (21%) patients showed improvement, six (25%) patients showed an essentially unchanged SiDBP, and 13 (54%) had a worsening of their hypertension. *Therefore, according to these criteria, the SiDBP of almost half (11/24) the patients had as good or better control of their blood pressure with the dietary supplement as they had by taking an anti-hypertensive drug.* The effect of the dietary supplement is even more dramatic when these same criteria are applied to compare the SiDBP of Visit 3 (after one month off medication and placebo) and after two months of dietary *Chlorella* (Visit 5) (**Table 12C**). Here nine (38%) patients showed improved SiDBP, seven (29%) a stable SiDBP, and only one-third (8/24) showed a worsening of their hypertension. *This finding that the SiDBP of two-thirds of the study population either improved or was stable with the patients on no anti-hypertensive medications suggests that for most patients, dietary supplementation either improved or kept their hypertension under controlled.*

IV. QUALITY OF LIFE MEASURES

Another major purpose of the present trial was to determine whether or not dietary supplementation with *Chlorella* improved the quality of life of patients with mild to moderate hypertension. In order to obtain this information, questionnaires were administered at each regularly scheduled clinic visit, prior to any examination or test. Six domains of health-related quality of life were included in the questionnaires: overall health perceptions, psychological well-being, social functioning, cognitive functioning, and sexual functioning. A symptoms inventory also was used to assess disease- and treatment-related symptoms.

A single item from the RAND 36-Item Health Survey 1.0 was used to assess overall health perceptions. The response to this item was recorded so that a lower value represented better perceived health (**Table 13A**). The participants showed no statistically significant change in their own perceived state of health over the course of the study. *The trend toward improvement however suggests that the subjects in this trial perceived their general state of health to be better because of their participation in this trail.*

Table 13. Results of the RAND Health Survey

A. Perceived Health Perception

Parameter	Best/Worst Score	Visit 1 Screening	Visit 3 Initiation	Visit 4 Interim	Visit 5 Final
State of Health	1/5	2.46 ± 0.59	2.33 ± 0.64	2.33 ± 0.70	2.26 ± 0.62

The Psychological General Well-Being Index was used to assess psychological well-being. Items were recorded (where necessary) so that lower values represented better well-being. Responses were summed to create six subscales: anxiety (5 items), depressed mood (3 items), positive well-being (4 items), self-control (3 items), general health (3 items) and vitality (4 items) (Table 13B). An overall score was also calculated. The patient's perceived level of anxiety between Visit 1 and Visit 3 was slightly less and not statistically significant. The decrease in anxiety between Visits 3 and 5 were also not significant. However, a comparison of Visit 1 and 5, indicated a significant ($p=0.02$) drop in the patient's anxiety on average. Compared to Visit 1, depressed mood was significantly improved at both Visits 3 ($p=0.01$) and even more at Visit 5 ($p=0.02$). The improvement in mood between Visits 3 and 5 was not statistically significant. The patients' sense of well-being was significantly better at Visit 3 ($p=0.002$) and at the end of the study ($p=0.007$). The difference in well-being between Visits 3 and 5 was not statistically significant. Although all values indicated a trend for improvement over the course of the trial, none of the patients' perceived changes in self-control, general health were statistically significant. The overall scores for the general well-being index showed improvements at every time point. The differences between Visits 1 and 3 and Visits 1 and 5 were statistically significant; $p=0.04$ and $p=0.01$, respectively. The difference in overall score between Visits 3 and 5, however, was not significant. *These results suggest that our patients 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 they were supplementing their diets with Chlorella.*

B. Psychological General Well-Being Index

Subscales	Best/Worst Score	Visit 1 Screening	Visit 3 Initiation	Visit 4 Interim	Visit 5 Final
Anxiety	5/30	11.5 ± 5.45	10.8 ± 4.93	9.42 ± 4.30	9.30 ± 3.52
Depressed Mood	3/18	5.00 ± 2.86	5.04 ± 2.46	4.42 ± 2.04	4.04 ± 1.72
Positive Well-Being	4/24	10.1 ± 3.39	8.96 ± 3.44	9.42 ± 3.73	8.61 ± 3.17
Self-Control	3/18	4.67 ± 2.41	4.79 ± 2.36	4.50 ± 2.09	4.30 ± 2.16
General Health	3/18	6.08 ± 2.43	5.71 ± 2.65	5.63 ± 2.67	5.43 ± 2.35
Vitality	4/24	9.38 ± 4.16	9.21 ± 4.14	8.69 ± 4.86	7.91 ± 3.52
Overall Score	22/132	46.8 ± 17.8	45.4 ± 18.1	42.7 ± 18.2	39.6 ± 14.6

A two-item scale from the RAND 36-Item Health Survey 1.0 was used to assess social functioning. Responses were summed to form a single score, after recording so that lower values represented better functioning. A four-item scale was used to assess sleep disturbance. Responses were summed to form a single score, after recoding so that lower values represented better sleep. A seven-item scale from the Symptom Rating Test was used to assess cognitive functioning. Responses were summed to form a single score, after recording so that lower values represented better functioning (Table 13C). All of the values for social functioning, sleep, and cognition improved over the course of the study but these trends were not statistically significant. *There are at least two possible explanations which may or may not be occurring simultaneously that could account for these*

observations: improvement may have occurred because of 1) the withholding of antihypertensive drugs; and/or 2) dietary supplementation with *Chlorella*.

C. Functioning Assessments of Social Interactions, Sleep and Cognition

Subscales	Best/Worst Score	Visit 1 Screening	Visit 3 Initiation	Visit 4 Interim	Visit 5 Final
Social Functioning	2/10	2.88 ± 1.92	2.79 ± 1.50	2.67 ± 1.74	2.35 ± 0.98
Sleep Disturbances	4/24	9.33 ± 4.93	8.21 ± 3.88	8.08 ± 4.31	7.70 ± 3.31
Cognitive Functioning	7/42	9.54 ± 3.37	9.91 ± 3.30	8.75 ± 2.67	9.52 ± 3.17

A seven-item scale from the Trial of Antihypertensive Interventions and Management study was used to assess sexual functioning. Items were recorded so that lower values represented better functioning. Items were summed to obtain two subclasses: sexual satisfaction (4 items) and physical complaints (3 items) and an overall score was also calculated (**Table 13D**). Patients' responses too were quite varied (note the large standard deviations of the means). In both categories there was a trend toward a worsening of sexual functioning over the course of the trial. The change in sexual satisfaction were not statistically significant however physical complaints were between Visits 1 and 3 and Visits 1 and 5. The change between Visits 3 and 5 was not significant. *This pattern of changes suggests that physical complaints worsened as a consequence of dropping their anti-hypertension medication and that the dietary supplement had no effect on this parameter.*

D. Sexual Functioning Assessments

Sexual Functioning	Best/Worst Score	Visit 1 Screening	Visit 3 Initiation	Visit 4 Interim	Visit 5 Final
Sexual Satisfaction	4/24	14.0 ± 6.94	13.7 ± 7.26	14.5 ± 7.63	15.0 ± 6.75
Physical Complaints	3/18	8.17 ± 5.21	9.54 ± 5.87	9.75 ± 6.19	9.78 ± 5.98
Overall Score	7/42	22.2 ± 11.5	23.2 ± 12.4	24.3 ± 13.2	24.7 ± 12.1

A 35-item symptom inventory was used to assess disease- and treatment-related symptoms. These items were analyzed separately and results are presented in **Table 14**. The questionnaire asked subjects about how they had felt in the past week. For each question, subjects were asked to indicate which of the following statements best applied:

1 = Not at all 2 = A little 3 = Moderately 4 = Quite a bit 5 = Extremely

The numbers beside each comment indicates how it was scored for data entry and analysis. Responses to each question were averaged; the lower the value, the less of a problem was the symptom. Although for most items there was a slight trend towards improvement of symptoms over the course of the study, none of these changes was statistically significant.

Table 14. Disease Symptoms During *Chlorella* Supplementation.

Problem	Visit 1 (Screening)	Visit 3 (Initiation)	Visit 4 (Interim)	Visit 5 (Final)
Dry mouth	1.38 ± 0.82	1.13 ± 0.34	1.29 ± 0.75	1.30 ± 0.76
Headaches	1.79 ± 0.78	1.70 ± 0.76	1.71 ± 1.04	1.48 ± 0.51
Weakness in your limbs	1.38 ± 0.88	1.22 ± 0.42	1.38 ± 0.88	1.35 ± 0.78
Blurred vision	1.33 ± 0.70	1.22 ± 0.42	1.21 ± 0.41	1.17 ± 0.39
Shortness of breath	1.33 ± 0.64	1.17 ± 0.49	1.21 ± 0.59	1.22 ± 0.52
Swollen ankles	1.26 ± 0.69	1.26 ± 0.75	1.29 ± 0.69	1.30 ± 0.70
Constipation	1.29 ± 0.62	1.22 ± 0.52	1.46 ± 0.93	1.43 ± 0.95
Bad taste in mouth	1.33 ± 0.76	1.22 ± 0.60	1.25 ± 0.53	1.22 ± 0.42
Feeling of having burnt your	1.13 ± 0.63	1.09 ± 0.29	1.04 ± 0.20	1.04 ± 0.21
Blocked or runny nose	1.54 ± 1.06	1.48 ± 0.73	1.54 ± 0.83	1.32 ± 0.48
Nausea	1.21 ± 0.59	1.04 ± 0.21	1.25 ± 0.44	1.35 ± 0.83
Rash on body	1.13 ± 0.46	1.04 ± 0.21	1.13 ± 0.34	1.09 ± 0.42
Itching	1.35 ± 0.65	1.26 ± 0.54	1.33 ± 0.56	1.48 ± 0.73
Cramps in legs	1.39 ± 0.78	1.17 ± 0.39	1.33 ± 0.56	1.30 ± 0.56
Pain in joints of hands	1.57 ± 0.99	1.52 ± 0.59	1.29 ± 0.55	1.48 ± 0.73
Shaky hands	1.17 ± 0.50	1.17 ± 0.49	1.25 ± 0.74	1.17 ± 0.49
Racing heart	1.17 ± 0.49	1.13 ± 0.46	1.21 ± 0.59	1.17 ± 0.39
Stomach pain	1.22 ± 0.60	1.09 ± 0.29	1.33 ± 0.76	1.22 ± 0.52
Heartburn	1.22 ± 0.52	1.30 ± 0.70	1.38 ± 0.58	1.26 ± 0.54
Sore throat	1.27 ± 0.55	1.27 ± 0.55	1.17 ± 0.49	1.17 ± 0.39
Dry cough	1.45 ± 1.06	1.18 ± 0.39	1.13 ± 0.34	1.13 ± 0.34
Sweating more than usual	1.19 ± 0.51	1.27 ± 0.70	1.17 ± 0.65	1.13 ± 0.34
Wheezing	1.17 ± 0.65	1.04 ± 0.21	1.00 ± 0.00	1.09 ± 0.29
Dry eyes	1.05 ± 0.22	1.05 ± 0.21	1.04 ± 0.21	1.09 ± 0.29
Mouth ulcers	1.00 ± 0.00	1.05 ± 0.21	1.00 ± 0.00	1.00 ± 0.00
Light hurts your eyes	1.52 ± 1.03	1.27 ± 0.55	1.22 ± 0.52	1.30 ± 0.63
Cold hands and feet	1.24 ± 0.70	1.05 ± 0.21	1.13 ± 0.46	1.13 ± 0.34
Getting up at night to urinate	1.62 ± 0.97	1.59 ± 1.10	1.83 ± 1.07	1.74 ± 1.05
Diarrhea	1.24 ± 0.54	1.23 ± 0.43	1.13 ± 0.34	1.30 ± 0.76
Flushing of the face	1.14 ± 0.65	1.00 ± 0.00	1.04 ± 0.21	1.00 ± 0.00
Heart pounding or missing a beat	1.10 ± 0.44	1.14 ± 0.47	1.17 ± 0.49	1.09 ± 0.29

Problem	Visit 1 Screening No/Yes	Visit 3 Initiation No/Yes	Visit 4 Interim No/Yes	Visit 5 Final No/Yes
Unsteadiness, lightheadedness or faintness lasting for less than hour	23/1	22/2	24/0	22/1
Unsteadiness or faintness occurs only when standing and lasting for less than hour	23/1	22/2	24/0	22/1
Unsteadiness or faintness worse first thing in the morning and lasting for less than hour	24/0	23/1	24/0	23/0

Patients were also asked to complete a questionnaire about their physical activities during a typical day. They were asked if their health now limited any of the activities listed and if so, how much. They scored the form according to the following three responses: 1 = Not Limited at All, 2 = Limited a Little, or 3 = Limited a Lot (**Table 15A**). Very few of the patients expressed that they had any difficulties with these physical activities at any time over the course of the study. Therefore, we observed there were no statistically significant changes in any of the activities they had attempted during preceding week.

Table 15. Physical Activity Survey

A. Activities During the Past Week

ACTIVITIES	Visit 1 Screening	Visit 3 Initiation	Visit 4 Interim	Visit 5 Final
Vigorous activities such as running, lifting heavy objects, participating in strenuous sports	1.6 ± 0.8	1.6 ± 0.8	1.6 ± 0.7	1.5 ± 0.8
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1.2 ± 0.4	1.1 ± 0.3	1.0 ± 0.0	1.2 ± 0.4
Lifting or carrying groceries	1.0 ± 0.2	1.0 ± 0.2	1.0 ± 0.0	1.0 ± 0.2
Climbing several flights of stairs	1.4 ± 0.7	1.3 ± 0.6	1.2 ± 0.5	1.3 ± 0.7
Climbing one flight of stairs	1.2 ± 0.5	1.1 ± 0.4	1.1 ± 0.3	1.1 ± 0.3
Bending, kneeling, or stooping	1.3 ± 0.6	1.2 ± 0.5	1.2 ± 0.4	1.3 ± 0.6
Walking more than a mile	1.3 ± 0.6	1.2 ± 0.5	1.2 ± 0.5	1.3 ± 0.5
Walking several blocks	1.1 ± 0.4	1.0 ± 0.2	1.0 ± 0.2	1.0 ± 0.2
Walking one block	1.0 ± 0.2	1.0 ± 0.0	1.0 ± 0.2	1.0 ± 0.0
Bathing or dressing yourself	1.1 ± 0.4	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0

They were also asked if during the past month, if they had any of the following problems with their work or other regular daily activities as a result of their physical health. Data was recorded as a 1 for No and a 2 for Yes (**Table 15B**). As before, very few of the patients expressed that they had any difficulties with these activities at any time during the past month and over the entire course of the study. Again, there statistically significant changes in any of the activities listed during preceding month.

B. Activities during the Past Month

	Visit 1 Screening	Visit 3 Initiation	Visit 4 Interim	Visit 5 Final
Cut down on the amount of time you spent on work or other activities	1.1 ± 0.3	1.1 ± 0.3	1.0 ± 0.2	1.1 ± 0.3
Accomplished less than you would like	1.3 ± 0.5	1.2 ± 0.4	1.2 ± 0.4	1.1 ± 0.3
Were limited in the kind of work or other activities	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3
Had difficulty performing the work or other activities (for example, it took extra effort)	1.3 ± 0.4	1.1 ± 0.3	1.2 ± 0.4	1.1 ± 0.3

V. CONCLUSIONS

1. Of the 33 patients enrolled in the study, 24 were eligible to continue after the one-month placebo period. Of these 24, only one patient withdrew prematurely because it was felt he needed to resume taking an anti-hypertension drug.
2. Routine tests of blood and urine, performed at screening, initiation, and final clinic visit (i.e. Visits I, 3, & 5), showed the parameters analyzed remained within normal limits of variation throughout the three-month study period.
3. A significant lowering of serum cholesterol was observed from the beginning of the trial (Visit I) as well between Visit 3 until the end of the study. Both high- and low-density cholesterol also significantly dropped after two months of dietary *Chlorella*.
4. Following the conventional pharmacological criteria for assessing response, we observed that slightly more than a one-third (38%) of the subjects showed some improvement in their hypertension by adding *Chlorella* to their diet.
5. Using a 4 mm Hg change in SiDBP as an indicator of response, the SiDBP of almost half the subjects had as good or better control of their blood pressure with the dietary supplement than they had by taking an anti-hypertensive drug.
6. Using a 4 mm Hg change in SiDBP as an indicator of response, comparisons at Visit 3 (off medication and on placebo for a month) with those after two months of dietary *Chlorella*, showed that 38% of patients improved, 29% were stable, and one-third (33%) had a SiDBP that worsened.
7. Responses to quality of life and functional ability questionnaires suggested that our patients were feeling better overall and particularly their anxiety and depression improved significantly probably because of the combined effects of 1) no longer having to take their regimen of anti-hypertensive drug(s) and 2) supplementing their diets with *Chlorella*.
8. Overall, the results of this pilot study suggest that for some people, their mild or moderate hypertension can be controlled or reduced with a daily dietary supplement of *Chlorella* alone.