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A Randomized, Double-Blind, Placebo-Controlled, Clinical Study of the General Effects of a Standardized *Lycium barbarum* (Goji) Juice, *GoChi*™

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ABSTRACT

Background: This randomized, double-blind, placebo-controlled clinical trial is the first study reported from outside China that has examined the general effects of the orally consumed goji berry, *Lycium barbarum,* as a standardized juice (*GoChi*™; FreeLife International LLC, Phoenix, AZ) to healthy adults for 14 days.

Methods: Based upon the medicinal properties of *Lycium barbarum* in traditional Asian medicine, we examined by questionnaire subjective ratings (0–5) of general feelings of well-being, neurologic/psychologic traits, gastrointestinal, musculoskeletal, and cardiovascular complaints as well as any adverse effects. Also, measures of body weight, body–mass index, blood pressure, pulse rate, and visual acuity were assessed before and after consuming 120 mL of *GoChi*/day or placebo control solution. Data were statistically analyzed for changes between day 1 and day 15.

Results: Significant differences between day 1 and day 15 were found in the *GoChi* group ($N = 16$) in increased ratings for energy level, athletic performance, quality of sleep, ease of awakening, ability to focus on activities, mental acuity, calmness, and feelings of health, contentment, and happiness. *GoChi* also significantly reduced fatigue and stress, and improved regularity of gastrointestinal function. In contrast, the placebo group ($N = 18$) showed only two significant changes (heartburn and happiness). No significant changes in musculoskeletal or cardiovascular complaints were observed in either group. All parametric data (body weight, etc.) were not significantly different between groups or between day 1 and day 15 for either group.

Conclusions: These results clearly indicate that daily consumption of *GoChi* for 14 days increases subjective feelings of general well-being, and improves neurologic/psychologic performance and gastrointestinal functions. The data strongly suggest that further research is indicated to confirm and extend knowledge of the potential effects of *Lycium barbarum* upon human health.

INTRODUCTION

Lycium barbarum (goji) is in the family Solanaceae and its ripe fruit has been used in Asian countries, such as China, Korea, and Japan, for more than 2500 years as a traditional herbal medicine and functional food for its benefits to anti-aging, vision, kidney, and liver functions.[1–4] In his *Compendium of Medica*, Li Shi-zen named *L. barbarum* as a top-grade medicinal material that can nourish the liver and kidney, supplement energy, and improve eyesight. *Shennong's Classic of Materia Medica (Shennong Bencaojing)* also mentioned that "long term use of goji can contribute to agility and longevity." Ni Zhu-Mo, the renowned Chinese herbalist, also said in his *Ben Cao Hui Yan (Convergent Speech on the Materia Medica)* that "Goji can supplement energy, blood, adjust

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yin and *yang*, reduce internal heat and resist wind and humidity, and enjoys ten magic functions."[1]

In support of these traditional properties assigned to *L. barbarum*, recent studies indicate that extracts from *L. barbarum* fruit possess a range of biological activities, including effects on aging,[5,6] neuroprotection,[7–9] antifatigue/endurance,[10] increased metabolism,[11] glucose control in diabetics,[5,12–16] glaucoma,[12,17] antioxidant properties,[6,18–31] immunomodulation,[32–39] antitumor activity,[40–46] and cytoprotection.[7,12]

There are various chemical constituents found in *L. barbarum* fruit. Its reddish-orange color is derived from a group of carotenoids, which make up only 0.03–0.5% of the dried fruit.[47] The predominant carotenoid is zeaxanthin, mainly as dipalmitate (also called physalien or physalin), comprising about one-third to one-half of the total carotenoids. Also found are various small molecules such as betaine, cerebroside, β-sitosterol, *p*-coumaric acid, and various vitamins. Other minor components include glutamine; asparagine; stigmasterol; cholest-7-enol; campesterol; cholestanol; 24-methylene cholesterol; 28-isofucosterol; 24-methylcholesta-5,24-dienol; 24-ethylcholesta-5,24-dienol; 31-norcycloartanol; 31-norcycloartenol; cycloeucalenol; obtusifoliol; 4a,14a,24-trimethylcholesta-8′24-dienol; 4a-methylcholest-8-enol; 4-methylcholest-7-enol; 24-ethyllophenol; 4,24-methyllophenol; gramisterol; citrostadienol; 4a-methyl-24-ethylcholesta-7,24-dienol; lanost-8-enol; cycloartanol; lanosterol; b-amyrin; lupeol; 24-methylenelanost-8-enol; 24-methylenecycloartanol; taurine and -aminobutanoic acid. K, Ca, Zn, Fe, Co, Mn, Se, Mg, and other minerals are present in inorganic forms.[48]

Among the chemical constituents of *L. barbarum* fruit, the most valuable and well-researched components are a group of unique, water-soluble glycoconjugates—collectively termed *L. barbarum* polysaccharides (LBP)—which are estimated to comprise 5–8% of the dried fruits.[49] The LBP group has a molecular weight range of 24–241 kDa, and several LBP have been isolated and purified from aqueous *L. barbarum* extracts by methods such as diethylaminoethyl ion-exchange cellulose and gel permeation chromatography.[10,38,50,51] Their structural composition has been studied by sodium dodecyl sulfate–polyacrylamide gel electrophoresis, gas chromatography, amino acid automatic analysis, partial acid hydrolysis, periodate oxidation, and nuclear magnetic resonance spectrum, and they have been found to be complex glycopeptides consisting of acidic heteropolysaccharides and polypeptides or proteins. Although they differ somewhat in composition, the LBP contain six monosaccharides (Ara, Rha, Xyl, Man, Gal, and Glc), galacturonic acid, and 18 amino acids, and they share a Glycan-O-Ser glycopeptide structure.[50] The main chains of the glycan backbones of LBP have been found to be either alpha-(1 → 6)-D-glucans or alpha-(1 → 4)-D-polygalacturonans.[34]

The LBP have been focused upon as the active compounds responsible for various efficacies listed above. According to Chinese understanding of *Lycium* spp. extracts and products, the content of LBP is important for the efficacy of *L. barbarum*. Many plant- and fungal-derived bioactive polysaccharides with a broad range of immunomodulatory activities are found in Traditional Chinese Medicine, and therefore, a high content of polysaccharides with proven pharmacologic activities is considered to be an indicator for the medicinal status of a natural product.[52,53]

Along with the growing number of studies of *L. barbarum*, we conducted this clinical study to examine the traditional effects of *L. barbarum*. To begin to address this, in the present study we examined directly the general effects of daily consumption of *L. barbarum* fruits provided in the form of a juice that is standardized for its main active constituents, LBP. The *L. barbarum* fruit juice or a placebo was provided daily for 14 days and changes in subjective ratings of feelings of general well-being, fatigue, stress, neurologic/psychologic traits, gastrointestinal and musculoskeletal complaints, cardiovascular effects (blood pressure and pulse rate), visual acuity, and any side-effects were determined at the end of the 14-day treatment period.

MATERIALS AND METHODS

L. barbarum preparation

A standardized *L. barbarum* fruit juice (*GoChi*™; lot no. ASA07120) was supplied by FreeLife International LLC, in Phoenix, AZ, and was kept refrigerated before use. This test material is a liquid dietary supplement containing reconstituted juice from fresh whole *L. barbarum* fruit with 10% of excipients by volume. It is standardized to contain, in a daily 120-mL serving, a content of LBP equivalent to that found in at least 150 g of fresh fruit, the amount customarily consumed in Traditional Chinese Medicine.[3,54] The types of analyses applied to the assay and identification of LBP are not standardized worldwide. We applied a general method based upon identification by Fourier transform near-infrared spectroscopy, the gravimetric assay of the isolated polysaccharide fraction, and a determination of sugars after hydrolysis using gas chromatography[55] and/or high-performance liquid chromatography with the glucan analysis reported.[56] Placebo control material (lot no. A198) was independently prepared by the third-party organization. The placebo solution matched the color, flavor, and taste of *GoChi* and was packaged in the same container as *GoChi*, but provided no nutritional value.

Study population

Subjects, 18 years old and older, were recruited for the study and participants selected for the trial were judged to

be healthy. Subjects were excluded from the study if they exhibited any evidence of heart, liver, lung, or kidney disease, if they had known allergies to *L. barbarum* or other fruit juices, were pregnant or breast feeding, were being treated for any immune, liver, or kidney-related conditions, were under anticoagulant therapy with Coumadin® (Bristol-Myers Squibb Company, Cincinatti OH, generic, warfarin), or had any acute or chronic medical or psychiatric condition. A total of 35 participants, of whom 69% were women, were selected for the study. Subjects were randomly assigned to either the *GoChi* treatment group ($n = 17$; average age = 32.2) or placebo control ($n = 18$; average age = 30.5). All subjects were fully informed of the purpose of the study, and signed Human Subjects Informed Consent forms approved by the Internal Review Board under the Helsinki Declaration. Female participants agreed to practice a recognized form of birth control during the course of the study. No participants were pregnant during the study based upon standard urine pregnancy test (Kurkel Enterprises, HCG Lot # 5-06257, Redmond, WA). One dropout occurred in the *GoChi* group because of missing intake for several days over a holiday weekend during the trial, and the final number of the subjects in *GoChi* group was 16. No dropouts occurred in the placebo group. After dietary background check, 1 vegetarian was found in the placebo group. All subjects enjoyed high-fat foods, such as hamburgers, dairy foods (milk, cheese, etc.), deep-fried foods including French fries, fried chicken, and sweets including chocolates, candies, snacks, and ice cream, consuming them about 3 times a week. The averages for length of *GoChi* consumption history, and the consumption of soda, coffee, tea and alcoholic beverages for the *GoChi* and placebo groups are shown in Table 1. There were 6 smokers in the placebo group and 2 in the *GoChi* group, whose cigarette use ranged from 1 pack in 2 weeks to 3 packs per day. There were no statistical differences between placebo and *GoChi* group in these dietary background parameters including smoking background (Table 1).

Study design

After enrollment in the trial, all participants were given a 2-week washout period during which time they were to discontinue use of any *L. barbarum* or *L. barbarum*-containing foods, any dietary supplements, energy drinks, or green tea, and this was continued throughout the study. After the washout period, subjects were randomly assigned to either the *GoChi* or placebo groups. All subjects were given a medical exam and physical measurements (body weight, body–mass index (BMI), blood pressure, heart rate, etc.) were assessed. Also, background information regarding dietary habits, smoking, and disease history was recorded for each participant. All subjects were then administered a written questionnaire consisting of 48 items for which the subjects provided a rating (scale of 0–5). The questionnaire consisted of 30 physical and psychologic fatigue-related symptoms, such as fatigue, feelings of physical weakness, short-term memory, mental acuity, and sleeping status, nine gastrointestinal questions, four musculoskeletal questions, three cardiovascular questions, and two questions regarding possible side-effects. Subjects consumed 120 mL of *GoChi* or placebo each morning after a meal for a period of 14 days. We established the dosage by following the daily amount of *L. barbarum* fruit customarily consumed in Traditional Chinese Medicine.[3,54] All participants were monitored daily to ensure full compliance with the protocol. At the end of the 14-day treatment period, subjects were again given a medical examination, morphometric data were recorded, and the questionnaire was completed again by each participant. Individuals administering the physical examination or questionnaire were blinded as to the treatment conditions, and the treatment codes were not broken until the study was completed.

Dependent measures

On the 1st and 15th day of the study, height, body weight, BMI, body fat, total body water content, blood pressure (sys-

Table 1. Dietary Background of the Subjects

Variable	N: *Placebo*	N: *GoChi*	*Mean placebo*	*Mean GoChi*	p<
Months Goji intake	18	15	10.28	11.10	**0.5629**
High fat food[a]	17	16	3.18	2.31	**0.0517**
Frequency (per week)					
Sodas (can/day)	18	16	0.67	1.13	**0.2339**
Coffee (cup/day)	18	16	1.39	1.14	**0.4687**
Tea (cup/day)	18	14	0.94	0.43	**0.6760**
Alcohol (a can of beer or a glass of wine/day)	18	16	0.50	0.26	**0.6537**
Cigarettes (pack/day)	18	16	0.39	0.09	**0.2771**

[a]Includes hamburgers, dairy foods (milk, cheese, etc.), deep-fried foods, such as French fries, fried chicken, sweets, such as chocolates, candies, snacks, ice cream.

Data were analyzed with nonparametric Mann–Whitney *U* test (placebo vs. *GoChi*,™ FreeLife International LLC, Phoenix, AZ). No significant group differences on dietary factors were found.

tolic and diastolic), and pulse rate were measured. The visual test indicators included reports of any eye fatigue, and a vision test was performed. Subjects also completed the 48-item clinical survey/questionnaire, which included any adverse effects. On both test days, subjects were asked to skip breakfast prior to completing the test protocol. The study was noninvasive, and subjective results were collected with the graded scores through questionnaire sheets and interviews. Quantitative data collected included body weight, height, BMI, body fat, total water content (Tanita BF-679W; Tokyo, Japan), pulse rate, and blood pressure (Omron HEM-637; Vernon Hills, IL). The vision tests included conscious eye-fatigue and distance vision, as checked by Graham Field #1264, 10-feet chart.

Statistical analysis

Dietary background data were analyzed with the nonparametric Mann–Whitney *U* test (placebo vs. *GoChi*). All parametric data (body weights, BMI, etc.) were analyzed by *t*-test for independent and for dependent groups. Descriptive statistics were calculated for placebo and *GoChi* for all dependent measures and summarized as means and standard errors. For all clinical symptom questions under all categories (well-being, gastrointestinal, etc.), each question was graded and the scores were analyzed for changes between day 1 and day 15 with the nonparametric Wilcoxon matched-pairs tests. Differences were considered significant at $p < 0.05$.

RESULTS

Parametric data

All parametric data, such as body weights, BMI, etc., were analyzed by *t*-test for independent and for dependent groups, and there were no significant changes in any of these dependent measures between day 1 and day 15 for either group or any group differences, as shown in Tables 2 and 3.

Clinical symptoms

Significant differences ($p < 0.05$) between day 1 and day 15 were found for the *GoChi* group for multiple questions in several categories as shown in Table 4, Table 5, Table 6 and Figure 1. *GoChi* significantly increased athletic performance, quality of sleep, focus on activities, calmness, and

Table 2. Parametric Data (Body Weight, etc.) Means ± SEM on Day 1 and Day 15[a]

Placebo (N = 18)	*Day 1*		*Day 15*	
Variable	*Mean*	*SEM*	*Mean*	*SEM*
Body weight (kg)	76.2	4.09	76.2	4.13
Height (cm)	167.4	2.72	169.3	2.79
BMI (kg/m^2)	27.0	0.98	26.4	0.96
Body fat (%)	32.9	2.19	31.9	2.35
Water content (%)	47.2	1.41	47.7	1.50
Systolic blood pressure (mm Hg)	119.2	3.20	115.9	2.06
Diastolic blood pressure (mm Hg)	78.6	2.26	74.8	2.60
Pulse	76.3	2.84	71.7	1.99
Left eye (/20)	43.0	8.28	40.1	7.98
Right eye (/20)	43.3	6.76	35.0	5.31
GoChi™[b] *(N = 16)*	*Day 1*		*Day 15*	
Variable	*Mean*	*SEM*	*Mean*	*SEM*
Body weight (kg)	88.7	17.36	88.7	17.51
Height (cm)	171.2	11.53	171.9	11.85
BMI (kg/m^2)	30.4	4.15	29.9	4.05
Body fat (%)	33.1	9.29	31.5	9.97
Water content (%)	47.3	5.98	48.0	6.36
Systolic blood pressure (mm Hg)	125.2	13.56	124.0	8.72
Diastolic blood pressure (mm Hg)	80.6	9.60	78.8	11.07
Pulse	75.7	12.04	70.6	8.44
Left eye (/20)	44.7	35.14	41.5	33.87
Right eye (/20)	44.0	28.68	38.5	22.53

[a]No statistical difference has been detected between these days.
[b]FreeLife International LLC, Phoenix, AZ.
BMI, body–mass index.

Table 3. Statistical Analysis with *t*-Tests for Differences Between Placebo ($N = 18$) and GoChi ($N = 16$) for Each Variable[a]

Variable	*Placebo mean*	*GoChi mean*	p
Body wt, day 1	76.2	88.7	0.1139
Body wt, day 15	76.2	88.7	0.1106
Height, day 1	167.4	171.2	0.3608
Height, day 15	169.3	171.9	0.5191
BMI, day 1	27.0	30.4	0.1463
BMI, day 15	26.4	29.9	0.1209
Fat, day 1	33.0	33.1	0.9555
Fat, day 15	31.9	31.5	0.9003
Water content, day 1	47.2	47.3	0.9792
Water content, day 15	47.7	48.0	0.8902
SBP, day 1	119.2	125.2	0.2801
SBP, day 15	115.9	124.0	0.0528
DBP, day 1	78.6	80.6	0.5533
DBP, day 15	74.8	78.8	0.3226
Pulse, day 1	76.3	75.7	0.8687
Pulse, day 15	71.7	70.6	0.7113
Left eye, day 1	43.0	44.7	0.8973
Left eye, day 15	40.1	41.5	0.8983
Right eye, day 1	43.3	44.0	0.9532
Right eye, day 15	35.0	38.5	0.6936

[a]No statistical difference has been detected.

BMI, body–mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

feelings of good health, contentment, and happiness, along with a tendency to increased energy level and mental acuity. The *GoChi* group also showed a significant reduction in feelings of fatigue and stress. Compared to the day 1 results, more than 80% of people who consumed *GoChi* reported better quality sleep. About 70% of people in the *GoChi* group experienced easier awakening, improved mental acuity, and better ability to focus on their activities. More than 50–60% of the subjects in the *GoChi* group felt healthier, happier, and more content. Around 50% of people who took *GoChi* reported less fatigue, more energy during the day, and increased athletic performance.

Several subjects who were consuming *GoChi* prior to the washout period reported verbally at the end of the washout period that they had lost energy and had felt tired. During the test period, several subjects reported that they could stay awake later in the evening because of increased energy, and they therefore found it unnecessary to take a nap. Several others in the *GoChi* group reported more vivid dreams.

In terms of gastrointestinal symptoms, the *GoChi* group showed a significant increase in bowel regularity (Table 5). Finally, several subjects in the *GoChi* group stated that they had less interest in sweets and ate less.

In contrast to the *GoChi* group, the placebo group ($N = 18$) showed only two statistically significant changes during the 14-day treatment period: heartburn and feeling happy (Tables 4 and 5). No significant changes were found for any questions regarding musculoskeletal or cardiovascular symptoms in either group (Table 5). Significant changes in clinical symptoms are summarized in Table 6 and Figure 1.

Additional verbally reported clinical effects

Additional information provided by subjects in the *GoChi* group during the Day 15 interview was as follows: Of the 9 female subjects in the *GoChi* group, 5 reported a decrease in nonspecific complaints and pain during their menstrual cycle. Several subjects in the *GoChi* group reported an increase in their sexual activity and ability during the trial. Two (2) male subjects in the *GoChi* group noted improvements in skin conditions, and 1 female subject reported harder nails. Importantly, none of the subjects in the placebo-treated group volunteered any information regarding any noticeable changes during the treatment period. Finally, there were no adverse effects reported by any subjects in either the *GoChi* or placebo control groups during the study period.

DISCUSSION

The present study has shown that, relative to a placebo control group, daily consumption of *GoChi* for 14 days produces significant changes in the subjective rating of feelings of general well-being, improves neurologic/psychologic performance and gastrointestinal regularity. These significant effects are consistent with previously published experimental studies as well as with the prescribed uses of *L. barbarum* as practiced in traditional Asian medicine.

A purified LBP was shown to increase adaptability to an exercise load, to enhance resistance to fatigue, and to accelerate the elimination of lactic acid in mice.[10] The study also found that LBP enhanced the storage of muscle and liver glycogen, increased the activity of lactate dehydrogenase (LDH) before and after swimming, inhibited the increase of blood urea nitrogen (BUN) after strenuous exercise, and accelerated the clearance of BUN after exercise. In the present study, subjects reported an increase in endurance/energy in the daytime and reduced fatigue within 14 days of consuming *GoChi*.

In the psychologic and neurologic area, the extract from *L. barbarum* has been shown to have effects on the brain and neuronal function. *L. barbarum* is traditionally regarded as exhibiting anti-aging effects in traditional Asian medicine. Experimentally, LBP protects neurons against β-amyloid (Aβ) peptide-induced apoptosis.[7] The extract from *L. barbarum* protected neurons through mechanisms independent of its anti-oxidative effects. This extract also exhibits cytoprotective effects against cytotoxic actions of dithiothreitol (DTT) by lowering the DTT-induced LDH release and caspase-3 activity. It has neuroprotective effects against toxicity of fibrillar Aβ [1–42] and Aβ [25–35] fragments,

Table 4. Well-being, Means, and Errors

	Placebo			*GoChi*		
Questions	N	*Mean*	*SEM*	N	*Mean*	*SEM*
Fatigue, day 1	18	1.11	0.267	**16**	**1.63**	**0.407**
Fatigue, day 15	18	1.22	0.329	**16**	**0.81**	**0.245**
Tiredness, day 1	18	1.33	0.291	16	1.71	0.398
Tiredness, day 15	18	1.33	0.352	14	1.25	0.296
Physical complaints, day 1	18	0.50	0.232	16	1.20	0.428
Physical complaints, day 15	18	0.33	0.198	15	0.50	0.274
Weakness, day 1	18	0.83	0.316	16	1.33	0.433
Weakness, day 15	18	0.72	0.226	15	0.88	0.340
Procrastination, day 1	18	1.56	0.372	16	0.93	0.286
Procrastination, day 15	18	1.17	0.326	14	0.75	0.266
Muscle stiffness, day 1	18	1.78	0.440	16	1.21	0.381
Muscle stiffness, day 15	18	1.28	0.331	14	0.94	0.322
Athletic performance, day 1	17	1.18	0.386	**16**	**2.20**	**0.380**
Athletic performance, day 15	18	1.00	0.280	**15**	**0.94**	**0.249**
Eye fatigue, day 1	18	1.17	0.381	16	1.44	0.508
Eye fatigue, day 15	18	1.11	0.332	16	0.60	0.335
Dizziness, day 1	18	0.17	0.121	15	1.13	0.427
Dizziness, day 15	18	0.11	0.076	16	0.40	0.235
Headache, day 1	18	1.17	0.381	15	0.87	0.291
Headache, day 15	18	0.83	0.283	15	0.75	0.296
Depression, day 1	17	0.88	0.283	16	0.25	0.144
Depression, day 15	18	0.67	0.256	16	0.27	0.153
Stress, day 1	18	2.28	0.411	**15**	**2.00**	**0.329**
Stress, day 15	18	2.33	0.370	**16**	**1.38**	**0.352**
Mental acuity, day 1	17	1.41	0.344	16	2.19	0.458
Mental acuity, day 15	18	1.61	0.380	16	0.94	0.392
Memory loss, day 1	18	1.11	0.312	16	0.75	0.266
Memory loss, day 15	18	1.22	0.319	16	0.81	0.292
Quality of sleep, day 1	18	1.94	0.431	**16**	**2.07**	**0.403**
Quality of sleep, day 15	18	1.39	0.293	**16**	**0.56**	**0.241**
Easy awakening, day 1	18	1.72	0.321	**16**	**2.06**	**0.370**
Easy awakening, day 15	18	1.72	0.289	**16**	**0.87**	**0.291**
Daydream, day 1	18	0.67	0.214	15	1.13	0.375
Daydream, day 15	18	1.56	0.390	16	0.73	0.300
Chest pain, day 1	18	0.33	0.229	15	0.47	0.336
Chest pain, day 15	18	0.33	0.198	15	0.13	0.085
Numbness, of limbs, day 1	18	0.33	0.181	16	0.81	0.379
Numbness of limbs, day 15	18	0.22	0.152	16	0.53	0.274
Cold foot and hand, day 1	18	0.61	0.270	15	1.38	0.464
Colf foot and hand, day 15	18	0.56	0.217	16	1.31	0.395
Shortness of breath, day 1	18	0.83	0.283	16	0.81	0.306
Shortness of breath, day 15	18	1.00	0.280	16	0.50	0.158
Frequent urination, day 1	18	0.83	0.218	16	1.06	0.335
Frequent urination, day 15	18	1.22	0.319	16	0.69	0.326
Allergy, day 1	18	1.00	0.323	16	1.31	0.489
Allergy, day 15	18	1.06	0.400	16	0.69	0.338
Stamina, day 1	18	1.22	0.298	16	1.86	0.417
Stamina, day 15	17	1.47	0.355	14	1.50	0.387
Calmness, day 1	18	1.33	0.352	**16**	**2.63**	**0.386**
Calmness, day 15	17	1.76	0.369	**16**	**0.94**	**0.232**
Energy in a day, day 1	18	1.72	0.331	16	2.25	0.393
Energy in a day, day 15	18	1.94	0.338	16	1.13	0.301
Focus on activities, day 1	18	1.17	0.345	**16**	**2.69**	**0.472**
Focus on acitivites, day 15	18	1.44	0.345	**16**	**1.00**	**0.224**
Feel healthy, day 1	18	1.39	0.389	**16**	**2.25**	**0.359**
Feel healthy, day 15	18	1.22	0.367	**16**	**0.81**	**0.209**
Feel content, day 1	18	1.56	0.364	**16**	**2.19**	**0.400**
Feel content, day 15	18	1.17	0.381	**16**	**0.80**	**0.296**
Feel happy, day 1	**18**	**1.72**	**0.386**	**15**	**2.38**	**0.455**
Feel happy, day 15	**18**	**0.78**	**0.263**	**16**	**0.88**	**0.328**

Bold indicates significant day 1 versus day 15 effect by nonparametric Wilcoxon matched pairs test.

Table 5. Descriptive Statistics: Means/Errors, Gastrointestinal, Diarrhea, and Musculoskeletal/Cardiovascular Questions

	Placebo			*GoChi*™[a]		
Variable	N	*Mean*	*SEM*	N	*Mean*	*SEM*
Body weight, day 1	17	1.29	0.427	16	1.69	0.481
Body weight, day 15	17	1.06	0.277	16	1.31	0.405
Constipation, day 1	18	0.89	0.301	16	0.81	0.332
Constipation, day 15	18	0.72	0.253	16	0.63	0.315
Diarrhea, day 1	18	0.22	0.129	16	0.81	0.356
Diarrhea, day 15	18	0.44	0.217	16	0.94	0.433
Regularity, day 1	18	1.28	0.378	**16**	**2.00**	**0.516**
Regularity, day 15	18	1.22	0.358	**16**	**0.69**	**0.299**
Stomach discomfort, day 1	18	0.83	0.318	16	1.69	0.416
Stomach discomfort, day 15	18	0.72	0.253	16	1.44	0.438
Nausea, day 1	18	0.33	0.229	16	0.75	0.348
Nausea, day 15	18	0.06	0.056	16	0.63	0.301
Heartburn, day 1	**18**	**0.72**	**0.311**	16	1.00	0.342
Heartburn, day 15	**18**	**0.11**	**0.076**	16	0.38	0.155
Abdominal discomfort, day 1	18	1.00	0.379	16	1.31	0.425
Abdominal discomfort, day 15	18	0.33	0.181	16	1.00	0.398
Stomach complaints, day 1	18	0.78	0.329	16	1.06	0.392
Stomach complaints, day 15	18	0.44	0.201	16	0.98	0.433
Muscle pains, day 1	18	0.94	0.392	16	0.88	0.315
Muscle pains, day 15	18	0.83	0.355	16	0.63	0.287
Physical discomfort, day 1	18	0.67	0.333	16	1.13	0.289
Physical discomfort, day 15	17	0.65	0.296	16	0.75	0.310
Backache, day 1	18	1.56	0.444	16	1.75	0.392
Backache, day 15	18	1.39	0.354	16	1.31	0.326
Joint pain, day 1	18	0.56	0.271	16	1.13	0.364
Joint pain, day 15	18	0.56	0.246	16	0.56	0.288
Rapid heart rate, day 1	18	0.33	0.162	16	0.75	0.359
Rapid heart rate, day 15	18	0.33	0.181	16	0.38	0.221
Circulation, day 1	18	1.39	0.397	16	2.06	0.423
Circulation, day 15	18	0.83	0.246	16	1.38	0.352
Cold peripheral under A/C, day 1	18	1.61	0.363	16	1.88	0.523
Cold peripheral under A/C, day 15	18	1.17	0.398	16	1.44	0.447

[a]FreeLife International LLC, Phoenix, AZ.
Bold indicates significant difference day 1 versus day 15 by nonparametric Wilcoxon matched-pairs test.
A/C, air conditioner.

which are associated with age-related neurodegenerative diseases. Aβ peptides induce a rapid activation of c-Jun N-terminal kinase (JNK) by phosphorylation. Pretreatment with an aqueous extract of *L. barbarum* markedly reduced the phosphorylation of JNK-1 [Thr183/Tyr185] and its substrates c-Jun-I [Ser 73] and c-Jun-II [Ser 63].[8] These studies support the anti-aging properties of *L. barbarum* claimed by traditional Asian medicine, and may be related to the psychologic and neurologic effects found in the present study.

LBP facilitated the recovery of peripheral red blood cells and platelets after mitomycin C–induced myelosuppression in mice.[9] These effects on blood cells may be related to the subjective reports of increased endurance and decreased fatigue with use of *GoChi*.

Because *L. barbarum* is reported in several animal studies to be neuroprotective against the loss of retinal ganglion cells in glaucoma[12] or age-related macular degeneration,[18] we tried to detect any changes in the visual functions in our subjects. However, the present study with healthy volunteers did not show any differences.

LBP is reported to enhance food conversion rate and the content of zinc and iron in female weanling mice, and to reduce their body weight after 21 days of consumption.[11] This shows that LBP can modulate metabolism *in vivo* and may correspond with the present study's result regarding the effects of *GoChi* on subjective assessments of physical performance and gastrointestinal function. In addition, LBP may be processed as prebiotics in the gastrointestinal tract, helping to increase regularity by improving quality and quantity of gut microflora.

There are several experimental reports showing an antidiabetic effect of *L. barbarum* because it is well known in traditional Chinese herbal medicine for diabetes. Animal studies have shown that oral intake of LBP can restore abnormal oxidative indices to near-normal levels in blood, liver, and kidney in rats made diabetic by intraperitoneal in-

Table 6. Summary of Statistical Analysis; Significant Differences Between Day 1 and Day 15 for Placebo and *GoChi*™[a] for the Multiple Questions are as Follows

Group	*Question*	N	t	Z	p
General well-being					
Placebo	Happy	18	8.0	2.432	0.015
GoChi	Fatigue	16	4.0	2.395	0.017
	Athletic performance	15	2.0	2.240	0.025
	Stress	16	7.0	2.090	0.037
	Sleep	15	4.0	3.045	0.002
	Wakeup	15	7.5	2.267	0.023
	Calm	16	1.5	2.801	0.005
	Focus	16	11.0	2.605	0.009
	Healthy	16	2.0	2.756	0.006
	Content	16	10.5	2.236	0.025
	Happy	16	7.7	2.267	0.023
Gastrointestinal					
Placebo	Heartburn	18	0.0	2.201	0.028
GoChi	Regularity	16	7.0	2.090	0.037
Musculoskeletal and cardiovascular					
Placebo	No significance for any questions				
GoChi	No significance for any questions				

[a]FreeLife International LLC, Phoenix, AZ.

jection of streptozotocin.[12] LBP reduces blood glucose levels, oxidative stress, and DNA damage in rats with non-insulin-dependent diabetes mellitus (NIDDM), decreases malondialdehyde and nitric oxide in serum of fasting rats, and elevates serum levels of superoxide dismutase. Furthermore, LBP reduced cellular DNA damage in peripheral lymphocytes of NIDDM rats.[13] These experimental results suggest that *L. barbarum* and LBP may be of benefit in the treatment of diabetes and possibly other metabolic diseases.

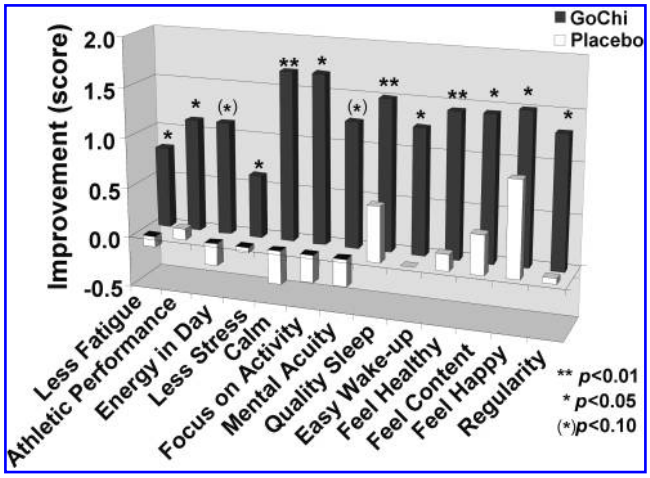

FIG. 1. Changes in clinical scores between days 1 and 15 for *GoChi*™ group (solid bars) and placebo group (open bars). Categories of questions are shown below graph.

Further studies including blood analysis on biochemical markers will clarify the detailed mechanisms of these actions of *GoChi* found in the present human clinical study.

CONCLUSIONS

The results shown in this randomized, placebo-controlled, double-blind clinical study clearly indicate that daily consumption of *GoChi* for 14 days increases subjective feelings of general well-being, neurologic/psychologic traits, and gastrointestinal functions. These are consistent with traditional uses.

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REFERENCES

1. Wang Z. The Magic *Lycium barbarum* from Ningxia Province, China. 2006:58–128.
2. Chang HM, But PPH. *Gouqizi*. In: Pharmacology and Applications of Chinese Materia Medica, Vol. 2. Singapore: World Scientific, 2001:852–854.
3. Zhu YP. *Gou Qi Zi*. In: Chinese Materia Medica. Chemistry, Pharmacology and Applications. Amsterdam, The Netherlands: Harwood Academic Publishers, 1998:642–646.
4. Bensky D, Gamble A. *Gou Qi Zi*. In: Chinese Herbal Medicine, Materia Medica, rev. ed. Seattle, Washington: Eastland Press, 1993:333–334.
5. Deng HB, Cui DP, Jiang JM, et al. Inhibiting effects of *Achyranthes bidentata* polysaccharide and *Lycium barbarum* polysaccharide on nonenzyme glycation in D-galactose induced mouse aging model. Biomed Environ Sci 2003;16:267–275.
6. Li XM, Ma YL, Liu XJ. Effect of the *Lycium barbarum* polysaccharides on age-related oxidative stress in aged mice. J Ethnopharmacol 2007;111:504–511.
7. Yu MS, Ho YS, So KF, et al. Cytoprotective effects of *Lycium barbarum* against reducing stress on endoplasmic reticulum. Int J Mol Med 2006;17:1157–1161.
8. Yu MS, Leung SK, Lai SW, et al. Neuroprotective effects of anti-aging oriental medicine *Lycium barbarum* against beta-amyloid peptide neurotoxicity. Exp Gerontol 2005;40:716–727.
9. Hai-Yang G, Ping S, Li JI, et al. Therapeutic effects of *Lycium barbarum* polysaccharide (LBP) on mitomycin C (MMC)-induced myelosuppressive mice. J Exp Ther Oncol 2004;4:181–187.
10. Luo Q, Yan J, Zhang S. Isolation and purification of *Lycium barbarum* polysaccharides and its antifatigue effect. J Hyg Res 2000;29:115–117.
11. Zhang M, Wang J, Zhang S. Study on the composition of *Lycium barbarum* polysaccharides and its effects on the growth of weanling mice. J Hyg Res 2002;31:118–119.
12. Li XM. Protective effect of *Lycium barbarum* polysaccharides on streptozotocin-induced oxidative stress in rats. Int J Biol Macromol 2007;40:461–465.
13. Wu H, Guo H, Zhao R. Effect of *Lycium barbarum* polysaccharide on the improvement of antioxidant ability and DNA damage in NIDDM rats. J Pharm Soc Jpn 2006;126:365–371.
14. Zhao R, Li Q, Xiao B. Effect of *Lycium barbarum* polysaccharide on the improvement of insulin resistance in NIDDM rats. J Pharm Soc Jpn 2005;125:981–988.
15. Luo Q, Cai Y, Yan J, et al. Hypoglycemic and hypolipidemic effects and antioxidant activity of fruit extracts from *Lycium barbarum*. Life Sci 2004;76:137–149.
16. Xu M, Zhang H, Wang Y. The protective effects of *Lycium barbarum* polysaccharide on alloxan-induced isolated islet cells damage in rats. J Chin Med Materials 2002;25:649–651.
17. Cheng CY, Chung WY, Szeto YT, Benzie IF. Fasting plasma zeaxanthin response to *Fructus barbarum* L. (wolfberry; Kei Tze) in a food-based human supplementation trial. Br J Nutr 2005;93:123–130.
18. Li G, Yang J, Ren B, Wang Z. Effect of *Lycium barbarum* L on defending free radicals of mice caused by hypoxia. J Hyg Res 2002;31:30–31.
19. Wu SJ, Ng LT, Lin CC. Antioxidant activities of some common ingredients of traditional Chinese medicine, *Angelica sinensis*, *Lycium barbarum* and Poria cocos. Phytother Res 2004;18:1008–1012.
20. Luo Q, Li Z, Huang X, et al. *Lycium barbarum* polysaccharides: Protective effects against heat-induced damage of rat testes and H_2O_2-induced DNA damage in mouse testicular cells and beneficial effect on sexual behavior and reproductive function of hemicastrated rats. Life Sci 2006; 79:613–621.
21. Gong H, Shen P, Jin L, et al. Therapeutic effects of *Lycium barbarum* polysaccharide (LBP) on irradiation or chemotherapy-induced myelosuppressive mice. Cancer Biother Radiopharm 2005;20:155–162.
22. Huang X, Yang M, Wu X, Yan J. Study on protective action of *Lycium barbarum* polysaccharides on DNA impairments of testicle cells in mice. J Hyg Res 2003;32:599–601.
23. Ni H, Qing D, Kaisa S, Lu J. The study on the effect of LBP on cleaning hydroxygen free radical by EPR technique. J Chin Med Materials 2004;27:599–600.
24. Wang Y, Zhao H, Sheng X, et al. Protective effect of *Fructus Lycii* polysaccharides against time and hyperthermia-induced damage in cultured seminiferous epithelium. J Ethnopharmacol 2002;82:169–175.
25. Zhang X. Experimental research on the role of *Lycium barbarum* polysaccharide in anti-peroxidation. China J Chin Materia Med 1993;18:110–112, 128.
26. Zhang B, Zhang X, Li W. The injury of *Xenopus laevis* oocytes membrane and its acetylcholine receptor by free radical and the protection of *Lycium barbarum* polysaccharide. Chin J Appl Physiol 1997;13:322–325.
27. Huang LJ, Tian GY, Wang ZF, et al. Studies on the glycoconjugates and glycans from *Lycium barbarum* L in inhibiting low density lipoprotein (LDL) peroxidation. Acta Pharmaceut Sin 2001;36:108–111.
28. Zhao H, Alexeev A, Chang E, et al. *Lycium barbarum* glycoconjugates: Effect on human skin and cultured dermal fibroblasts. Phytomedicine 2005;12:131–137.
29. Ren B, Ma Y, Shen Y, Gao B. Protective action of *Lycium barbarum* L. (LbL) and betaine on lipid peroxidation of erythrocyte membrane induced by H_2O_2. China J Chin Materia Med 1995;20:303–304.
30. Huang Y, Lu J, Shen Y, Lu J. The protective effects of total flavonoids from *Lycium Barbarum* L. on lipid peroxidation of liver mitochondria and red blood cell in rats. J Hyg Res 1999;28:115–116.
31. Huang Y, Tan A, Shen Y, Lu J. Scavenging effect of total flavonoids of *Lycium barbarum* L on active oxygen radicals and inhibitory effects on heat output from L1210 cells. J Hyg Res 1998;27:109–111, 115.
32. Zhu J, Zhao LH, Zhao XP, Chen Z. *Lycium barbarum* polysaccharides regulate phenotypic and functional maturation of murine dendritic cells. Cell Biol Int 2007;31:615–619.
33. Gan L, Zhang SH, Liu Q, Xu HB. A polysaccharide-protein complex from *Lycium barbarum* upregulates cytokine expression in human peripheral blood mononuclear cells. Eur J Pharmacol 2003;471:217–222.
34. Duan CL, Qiao SY, Wang NL, et al. Studies on the active polysaccharides from *Lycium barbarum* L. Yao Xue Xue Bao (Acta Pharm Sin) 2001;36:196–199.

35. Luo Q, Yan J, Zhang S. Effects of pure and crude *Lycium barbarum* polysaccharides on immunopharmacology. Zhong Yao Cai (J Chin Med Materials) 1999;22:246–249.
36. Cao GW, Yang WG, Du P. Observation of the effects of LAK/IL-2 therapy combining with *Lycium barbarum* polysaccharides in the treatment of 75 cancer patients. Zhonghua Zhong Liu Za Zhi (Chin J Oncol) 1994;16: 428–431.
37. Du G, Liu L, Fang J. Experimental study on the enhancement of murine splenic lymphocyte proliferation by *Lycium barbarum* glycopeptide. J Huazhong Univ Sci Technolog Med Sci 2004;24:518–520, 527.
38. Peng XM, Wang ZF, Tian GY. Physico-chemical properties and activity of glycoconjugate LbGp2 from *Lycium barbarum* L. Yao Xue Xue Bao (Acta Pharm Sin) 2001;36:599–602.
39. Xu Y, He L, Xu L, Liu Y. Advances in immunopharmacological study of *Lycium barbarum* L. Zhong Yao Cai (J Chin Med Materials) 2000;23:295–298.
40. Chao JC, Chiang SW, Wang CC, et al. Hot water-extracted *Lycium barbarum* and *Rehmannia glutinosa* inhibit proliferation and induce apoptosis of hepatocellular carcinoma cells. World J Gastroenterol 2006;12:4478–4484.
41. He YL, Ying Y, Xu YL, et al. Effects of *Lycium barbarum* polysaccharide on tumor microenvironment T-lymphocyte subsets and dendritic cells in H22-bearing mice. Zhong Xi Yi Jie He Xue Bao (J Chin Integr Med) 2005;3:374–377.
42. Zhang M, Chen H, Huang J, et al. Effect of *Lycium barbarum* polysaccharide on human hepatoma QGY7703 cells: Inhibition of proliferation and induction of apoptosis. Life Sci 2005;76:2115–2124.
43. Gan L, Hua Zhang S, Liang Yang X, Bi Xu H. Immunomodulation and antitumor activity by a polysaccharide-protein complex from *Lycium barbarum*. Int Immunopharmacol 2004;4:563–569.
44. Lu X, Xian X, Lu W, et al. The regulation of *Lycium barbarum* on apoptosis of rat spleen in vitro. Zhong Yao Cai (J Chin Med Materials) 1999;22:250–251.
45. Gan L, Wang J, Zhang S. Inhibition the growth of human leukemia cells by *Lycium barbarum* polysaccharide. Wei Sheng Yan Jiu (J Hyg Res) 2001;30:333–335.
46. Lu CX, Cheng BQ. Radiosensitizing effects of *Lycium barbarum* polysaccharide for Lewis lung cancer. Zhong Xi Yi Jie He Za Zhi (Chin J Mod Dev Trad Med) 1991;11:611–612, 582.
47. Peng Y, Ma C, Li Y, et al. Quantification of zeaxanthin dipalmitate and total carotenoids in *Lycium* fruits. Plant Foods Hum Nutr 2005;60:161–164.
48. National Health Information, NHIOnDemand, LLC. Gou Qi Zi, *Lycium* Fruit, *Lycii fructus*. Online document at: http://content.nhiondemand.com/moh/media/TCMH1.asp?objID=100832& ctype=tcmh#fn 111585 Accessed November 20, 2007.
49. Wang Q, Chen S, Zhang Z, et al. Determination of polysaccharide contents in *Fructus Lycii*. Chin Trad Herbal Drugs 1991;22:67–68.
50. Tian M, Wang M. Studies on extraction, isolation and composition of *Lycium barbarum* polysaccharides. Zhongguo Zhong Yao Za Zhi (China J Chin Materia Med) 2006;31:1603–1607.
51. Peng X, Tian G. Structural characterization of the glycan part of glycoconjugate LbGp2 from *Lycium barbarum* L. Carbohydr Res 2001;331:95–99.
52. Chang R. Bioactive polysaccharides from traditional Chinese medicine herbs as anticancer adjuvants. J Altern Complement Med 2002;8:559–565.
53. Wong CK, Leung KN, Fung KP, Choy YM. Immunomodulatory and anti-tumour polysaccharides from medicinal plants. J Int Med Res 1994;22:299–312.
54. Dharmananda S. Lycium Fruit, Food and Medicine. Institute for Traditional Medicine, Portland, OR. Online document at: http://itmonline.org/arts/lycium.htm Accessed January 17, 2008.
55. Food Analysis: Detection of natural thickeners in foodstuffs. In: Official Collection of Test Procedures under Section 35 of the German Foodstuffs and Commodities Act (Lebensmittel- und Bedarfsgegenstandsgesetz [LMBG]). Germany, November 1986.
56. AOAC International Official Methods of Analysis. Beta-D-Glucan in Barley and Oats. Method number 995.16. Online document at: http://eoma.aoac.org/methods/info.asp?ID=21738 Accessed January 15, 2008.

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