Immunomodulatory Effects of a Standardized *Lycium barbarum* Fruit Juice in Chinese Older Healthy Human Subjects

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ABSTRACT  *Lycium barbarum* has been traditionally used in combination with several herbs for medicinal properties, but systematic modern clinical evaluation as a single herb has not been reported. To examine the systematic effects of *L. barbarum* on immune function, general well-being, and safety, we tested the effects of a standardized *L. barbarum* fruit juice (GoChi®). FreeLife International, Phoenix, AZ, USA at 120 mL/day, equivalent to at least 150 g of fresh fruit, the amount traditionally used, or placebo for 30 days in a randomized, double-blind, placebo-controlled clinical study in 60 older healthy adults (55–72 years old). The GoChi group showed a statistically significant increase in the number of lymphocytes and levels of interleukin-2 and immunoglobulin G compared to pre-intervention and the placebo group, whereas the number of CD4, CD8, and natural killer cells or levels of interleukin-4 and immunoglobulin A were not significantly altered. The placebo group showed no significant changes in any immune measures. Whereas the GoChi group showed a significant increase in general feelings of well-being, such as fatigue and sleep, and showed a tendency for increased short-term memory and focus between pre- and post-intervention, the placebo group showed no significant positive changes in these measures. No adverse reactions, abnormal symptoms, or changes in body weight, blood pressure, pulse, visual acuity, urine, stool, or blood biochemistry were seen in either group. In conclusion, daily consumption of GoChi significantly increased several immunological responses and subjective feelings of general well-being without any adverse reactions.

KEY WORDS: • general well-being • humans • immunomodulation • *Lycium barbarum* • polysaccharides • safety

INTRODUCTION

*Lycium barbarum* is a Solanaceous defoliated shrubbery, and the fruit is a famous traditional medicine in Asian countries where it has been used for medicinal purposes and as a functional food for over 2,500 years. The ancient herbalist classics recorded that *L. barbarum* has the efficacy to nourish the liver and kidney and brighten the eye. In support of such traditional properties, modern studies indicate that extracts from *L. barbarum* possess a range of biological activities,1–5 including immunomodulation,6–13 anti-aging, neuroprotection, antifatigue/endurance, increased metabolism, control of glucose and other symptoms in diabetics, glaucoma, antioxidant efficacies, antitumor activity, and cytoprotection.

Various chemical constituents are 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.14 The predominant carotenoid is zeaxanthin, mainly as dipalmitate (also called physalen or physalin), making up about one-third to one-half of the total carotenoids. Also found are various small molecules, such as betaine, cerebroside, β-sitosterol, and *p*-coumaric acid, and various vitamins, amino acids, taurine, and γ-aminobutanoic acid, among others. K, Ca, Zn, Fe, Co, Mn, Se, Mg, and other minerals are also present in inorganic forms.15,16

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 (LBPs), which are estimated to make up 5–8% of the dried fruits.17 The LBP group has a molecular size range of 24–241 kDa, and several LBPs have been isolated and purified from aqueous *L. barbarum* extracts by methods such as diethylaminoethyl ion-exchange cellulose and gel-permeation chromatography.14,16–20 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 LBPs contain six monosaccharides (Ara, Rha, Xyl, Man, Gal, and Glc), galacturonic acid, and 18 amino acids. They also share a glycan-O-Ser
glycopeptide structure. The main chains of the glycan backbones of LBPs have been found to be either \( \alpha- (1 \rightarrow 6) \)-d-glucans or \( \alpha-(1 \rightarrow 4)-d \)-polygalacturonans. LBPs have been focused upon as the active component responsible for various effects reported for \( L. \) barbarum. According to Chinese understanding of \( Lycium \) extracts and products, the content of LBPs is important in the efficacy of \( L. \) barbarum. Other plant- and fungal-derivative bioactive polysaccharides with a broad range of immunomodulatory activities are found in traditional Chinese medicine, and therefore a high content of polysaccharides with proven pharmacological activities is considered to be an indicator of the medicinal status of the natural product.

Along with an increasing number of studies of \( L. \) barbarum, our recent randomized, double-blind, placebo-controlled clinical study showed that daily consumption of \( L. \) barbarum for 14 days, provided in the form of a fruit juice, GoChi® (FreeLife International LLC, Phoenix, AZ, USA), standardized for its LBP content, increased subjective feelings of general well-being, neurological/psychological assessment, and gastrointestinal function. In the present study, we have extended the clinical analysis of GoChi as an individual herbal treatment to include measures of immune function as well as its general subjective effects and safety in older healthy human subjects.

### MATERIALS AND METHODS

\( L. \) barbarum and placebo preparation

FreeLife International LLC supplied a commercially available, LBP-standardized \( L. \) barbarum fruit juice (GoChi; lot number ASA07120), which was produced from fresh ripe \( L. \) barbarum fruit grown in Ningxia Province, China. Botanical identification was performed by Jianguo Li, the director of the Ningxia Goji Institute (Yinchuan, China). The yield of juice as a percentage weight of the starting fresh plant material is about 35%. Juice was processed in an aseptic manner and kept refrigerated before use at 2–8°C. Description and standardization procedures for the test material were previously described. In brief, GoChi is standardized to contain a content of LBP equivalent to that found in at least 150 g of fresh fruit, the amount customarily consumed in traditional Chinese medicine.

Placebo control material (lot number A198) was carefully prepared to match the color, flavor, and taste of GoChi in a formulation of sucralose (10 mg), artificial fruit flavor (30 mg), citric acid (60 mg), and caramel color (12 mg) in 30 mL of purified water. It was packaged in the same type of container; however, it provided no nutritional value or LBP.

Study population

All recruited subjects were healthy Chinese residents of Hunan Province, China. Subjects were men and women between 55 and 72 years of age. All subjects had no obvious brain, heart, liver, lung, kidney, or blood diseases, no history of long-term medication, and no experience of GoChi intake. Subjects were to discontinue use of any \( L. \) barbarum or \( L. \) barbarum-containing foods at least 2 months before the trial and throughout the study. A total of 60 participants were selected for the study and were randomly assigned to either the GoChi treatment group \(( n = 30 \); average age = 58.70 ± 5.32 years) or placebo control \(( n = 30 \); average age = 59.03 ± 5.62 years). All subjects were fully informed of the purpose of the study and signed the Human Subjects Informed Consent forms approved under the Helsinki Declaration by the Internal Review Board of the Hunan Provincial Center for Disease Control and Prevention in China. No participants were pregnant during the study. All subjects consumed their normal Chinese foods, and their original dietary habits were not changed during the trial period. Their normal diet included digestible foods, such as milk, egg, soybean milk, noodles, gruel, vegetable, fruit, and others, which constituted over 80% of the daily intake, as well as small amount of deep-fried, greasy foods. Abdominal B-ultrasound, electrocardiogram, and chest X-ray exams of these subjects diagnosed right before the intervention trial were all within normal ranges. Mood and sleep parameters of the subjects were all normal.

### Trial design

Subjects were randomly assigned to either the GoChi or placebo groups. No dropouts were observed during the trial. All subjects were given a medical exam, and physical measurements (body weight, blood pressure, pulse rate, abdominal B-ultrasound, electrocardiogram, and chest X-ray exam) were assessed. Also, all subjects completed questionnaires and provided background information, including disease history. Finally, 10 mL of venous blood was collected at pre- and post-intervention, allowed to clot, and centrifuged, and the serum was stored at −70°C for subsequent assays.

Subjects consumed 60 mL of the GoChi or placebo twice daily (total, 120 mL/day) in the morning and evening after a meal every day for a period of 30 days. The dosage was based upon the quantity recommended in traditional Chinese medicine as previously described. All participants were monitored daily to ensure full compliance with the protocol. At the end of the 30-day intervention period, subjects were again given a medical exam, morphometric data were recorded, the questionnaire was completed again by each participant, and venous blood samples were collected. Individuals administering the physical exam or questionnaire were blinded as to the treatment conditions, and the treatment codes were not broken until the study was completed. Randomization information was concealed from the investigators and the subjects until the end of the study.

### Observation indicators

Each observation indicator was tested once upon commencement of the trial and at the end of the 30-day intervention period.

**General physical exam.** Questionnaire and physical exam were used to assess the subjects’ energy, sleep, diet,
urine, stool, body weight, blood pressure, and pulse rate collected at pre- and post-intervention.

**Urine panel.** The urine panel tests were done with a urine analyzer (Shanghai Precison Instruments Co., Ltd., Shanghai, China) for pH (5.5), leukocytes (±15 cells/μL), and urine glucose (mmol/L).

**Stool panel.** Stool test was determined by yellow color indication, and its characterization was analyzed by strip; no blood clots, purulence, or helminths were safety indications. Microscopic examination was done, and criteria were absence of erythrocytes or ovum and only a few plant cells and muscle fibers.

**Abdominal B-ultrasound, electrocardiogram, and chest X-ray exam.** These tests were performed once immediately before the trial. All subjects were within normal ranges.

**Blood biochemical indicator tests.** Routine analysis of blood consisted of number of erythrocytes, number of leukocytes and their classification, and content of hemoglobin with a full automatic hemocyte analyzer (Tianjin Yixiangfa Technology Co., Ltd., Hebei, China). Standard clinical tests were used to measure serum total protein, albumin, alanine transaminase, aspartate transaminase, cholesterol, triglycerides, uric acid, blood urea nitrogen (BUN), creatinine, and blood glucose.

**General and adverse reaction observations.** Detailed questions of the patient’s medical history were asked to assess the patient’s physical condition; clinical symptoms were observed and scored as follows: severe, 3 points; moderate, 2 points; mild, 1 point; none, 0 points. Dizziness, physical fatigue, and quality of sleep were used to evaluate general feelings of well-being.

**Vision testing.** Because we are interested in the efficacy of GoChi in visual functions based on the reports that L. barbarum was effective in reducing the symptoms related to glaucoma and other eye diseases,25–27 vision was tested once at pre- and post-intervention. Subjects stood or sat 5 m from the international standard vision table and were asked to cover one eye and then recognize the smallest letter they could see on the table. Each eye was tested separately.

**Short-term memory test.** To begin, the subjects listened to a recording of a native speaker reading a paragraph in Chinese. Following the recording, the subjects took a 15-question test to see which words they remembered. Each question had four choices. The subjects had to circle the word they had heard in the recording. Some of the questions had four choices that sounded alike; in English, for example, weather, whether, wether, and wetter are four words that sound alike. Some of the questions had four choices that have the same meaning; in English, for example, method, way, manner, and system would be four words with the same meaning. Some of them had four unrelated choices. For instance, weather, method, love, and result could be used as four unrelated words.

**Focus testing.** In every line of figures, there are some figures with a neighbor, for which as a pair the two equal 10. Subjects were asked to focus attention on the line, find these numbers, and write the answer below the row. Every subject should be done within 7 minutes. An example is:

![2946119355](image)

**Tests of immunological indicators.** Venous blood samples were collected at pre- and post-intervention to measure numbers of CD4, CD8, and natural killer (NK) cells and lymphocytes and levels of interleukin (IL)-2, IL-4, immunoglobulin (Ig)G, and IgA. A flow cytometer (Beijing JunHeHua Technology Co., Ltd., Beijing, China) was used to measure the number of CD4, CD8, and NK cells and lymphocytes. Specific enzyme-linked immunosorbent assay kits (Zhengzhou AUTOBIO Co., Ltd. [Zhengzhou, China] and Chengdu Shuguang Biotech Co., Ltd. [Chengdu, China]) were used to measure the other immunological markers (IL-2, IL-4, IgG, and IgA levels) in serum.

**Statistical analysis**

Results were summarized as mean ± SEM values. For self-paired data t tests were used, and homogeneity of variance between the GoChi group and placebo group was a prerequisite. For mean comparisons group t tests were used. Otherwise, t tests were performed after homogeneity of variance was achieved through variable conversion. Rank-sum tests were used if the variance still lacked homogeneity. A nonparametric test was used to test for treatment effects on sleep and general feelings of well-being. The data were processed using Statistica version 8 (StatSoft, Inc., Tulsa, OK, USA). Differences were considered significant at P < .05.

**RESULTS**

**Safety observations**

After consumption of GoChi or placebo for 30 days, no abnormalities were observed in subjects’ energy, sleep, diet, urine, stool, body weight, blood pressure, or pulse rate measures.

**Parametric data**

As shown in Tables 1 and 2, at pre- and post-intervention, there were minimal changes in body weight, blood pressure, pulse rate, urine, stool, blood panel, and blood biochemistry for either the GoChi or the placebo control group. All parametric data, such as body weights, 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 pre- and post-intervention.
for either group or any group differences, as shown in Table 2.

*L. barbarum* is well known in traditional Chinese herbal medicine for treating diabetes, and this is supported by several reports showing an antidiabetic effect.25–30 Although we examined blood glucose levels in healthy older subjects, because of their general healthy condition and normal blood glucose levels, no changes were seen in the present study.

LBPs have been shown to inhibit the increase of BUN and accelerate its clearance after strenuous exercise,18 but in the present study GoChi did not influence BUN or other biochemical blood markers, possibly because of the absence of a strenuous exercise challenge.

**Observation of symptoms**

As shown in Tables 3 and 4, GoChi treatment produced significant changes (*P* < .05) in general feelings of well-being over the trial period. Over 60% of subjects in the GoChi group reported increased ratings of general well-being, which was statistically significantly different from the placebo group. Only 20% of the subjects in the placebo group showed increased ratings to these subjective questions, which were not statistically significant.

**Visual functions**

Neither group showed any significant differences or changes in their visual functions between pre- and post-intervention. *L. barbarum* has been reported to improve age-related visual functions.

**Table 1. General Effects and Safety Aspects of GoChi or Placebo on Various Indications Pre- and Post-Intervention**

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 30)</th>
<th>GoChi (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>60.91 ± 1.74</td>
<td>61.02 ± 1.73</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>118.33 ± 2.33</td>
<td>118.07 ± 2.18</td>
</tr>
<tr>
<td>Diastolic</td>
<td>73.60 ± 1.46</td>
<td>74.07 ± 1.25</td>
</tr>
<tr>
<td>Pulse (beats/minutes)</td>
<td>73.77 ± 1.21</td>
<td>74.13 ± 1.07</td>
</tr>
<tr>
<td>White blood cells (10^3/L)</td>
<td>6.36 ± 0.28</td>
<td>6.39 ± 0.35</td>
</tr>
<tr>
<td>Red blood cells (10^12/L)</td>
<td>4.33 ± 0.07</td>
<td>4.35 ± 0.09</td>
</tr>
<tr>
<td>Total protein (g/L)</td>
<td>134.90 ± 1.93</td>
<td>133.07 ± 1.76</td>
</tr>
<tr>
<td>Urine</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Stool</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Data are mean ± SEM values. Each indicator was tested once at pre- and post-intervention of the 30-day trial. Standard clinical tests and routine analysis of blood were used.

**Table 2. Biochemical Parameter Changes in Blood Pre- and Post-Intervention with GoChi or Placebo**

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 30)</th>
<th>GoChi (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention</td>
<td>Post-intervention</td>
</tr>
<tr>
<td>Alanine transaminase (U/L)</td>
<td>23.63 ± 1.91</td>
<td>18.70 ± 1.81</td>
</tr>
<tr>
<td>Aspartate transaminase (U/L)</td>
<td>26.47 ± 1.38</td>
<td>23.40 ± 1.33</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>4.99 ± 0.14</td>
<td>4.87 ± 0.16</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.41 ± 0.16</td>
<td>1.40 ± 0.20</td>
</tr>
<tr>
<td>Total protein (g/L)</td>
<td>75.08 ± 1.03</td>
<td>70.65 ± 0.66</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>46.70 ± 0.59</td>
<td>44.40 ± 0.45</td>
</tr>
<tr>
<td>BUN (mmol/L)</td>
<td>4.55 ± 0.20</td>
<td>4.62 ± 0.22</td>
</tr>
<tr>
<td>Creatinine (mmol/L)</td>
<td>75.07 ± 2.70</td>
<td>68.07 ± 3.56</td>
</tr>
<tr>
<td>Uric acid (mmol/L)</td>
<td>257.37 ± 12.0</td>
<td>255.30 ± 9.80</td>
</tr>
<tr>
<td>Blood glucose (mmol/L)</td>
<td>4.98 ± 0.09</td>
<td>5.02 ± 0.11</td>
</tr>
</tbody>
</table>

Data are mean ± SEM values.

All subjects were administered a written questionnaire for which the subjects provided a rating (scale of 0–3). The questionnaire consisted of physical and psychological fatigue-related symptoms, such as fatigue, dizziness, and sleep. These clinical symptoms were observed and scored as follows: severe, 3 points; moderate, 2 points; mild, 1 point; none, 0 points. Overall scores were obtained by summed each scores from symptoms and statistically analyzed by a nonparametric test. Data are mean ± SEM values.

Significant difference compared to placebo, *P* < .05.

Significant difference compared to pre-intervention, *P* < .05.
related macular degenerative disease, but subjects in the present study were all healthy and showed no symptom of age-related macular degenerative disease.

Short-term memory and attention capability

No statistically significant differences were found between the placebo and GoChi groups, as shown in Table 5, but there was a tendency for increased short-term memory and focus between pre- and post-intervention in the GoChi group ($P < .10$).

Immunological marker changes in human serum

As shown in Table 6 and Figure 1, the GoChi-treated group showed significant increases in number of lymphocytes and levels of IL-2 and IgG, relative to pretreatment levels ($P < .05$). The percentage of CD4, CD8, and NK cells and levels of IL-4 and IgA were not altered by GoChi treatment. None of the immune markers was changed following the 30-day treatment period in the placebo control group.

**DISCUSSION**

The present study is the first human clinical study reporting immunomodulatory and other effects of *L. barbarum* fruit in a form of juice (GoChi) as a single herb in healthy older human subjects. Lymphocyte numbers and IL-2 and

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**Table 4. Effect of GoChi compared to Placebo on General Well-Being, Such as Dizziness, Fatigue, and Sleep, and Total Indications**

<table>
<thead>
<tr>
<th></th>
<th>Placebo ($n=30$)</th>
<th>GoChi ($n=30$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects with positive response/total number of subjects (% positive)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>5/24 (20.8%)</td>
<td>12/24 (50.0%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2/18 (11.1%)</td>
<td>11/21 (52.4%)</td>
</tr>
<tr>
<td>Sleep</td>
<td>1/26 (3.9%)</td>
<td>8/25 (32.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>6/30 (20.0%)</td>
<td>19/30 (63.3%)*</td>
</tr>
</tbody>
</table>

Clinical symptoms were observed and scored as follows: severe, 3 points; moderate, 2 points; mild, 1 point; none, 0 points. Dizziness, physical fatigue, and quality of sleep were used to evaluate general feelings of well-being.

*Significant difference compared to placebo, $P < .05$.

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**Table 5. Effect of GoChi Compared to Placebo on Short-Term Memory and Attention Capability**

<table>
<thead>
<tr>
<th>Task, group (n)</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-term memory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>2.47 ± 0.16</td>
<td>2.53 ± 0.14</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>2.40 ± 0.12</td>
<td>2.67 ± 0.11*</td>
</tr>
<tr>
<td>Attention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>3.57 ± 0.31</td>
<td>3.70 ± 0.28</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>3.43 ± 0.26</td>
<td>3.87 ± 0.20*</td>
</tr>
</tbody>
</table>

In the short-term memory test, the subjects first listened to a recording of a native speaker reading a paragraph in Chinese. Following the recording, the subjects took a 15-question test to see which words they remembered. In focus attention testing, there are some figures in a line with a neighbor, for which as a pair the two equal 10. Subjects were asked to focus attention on the line, find these numbers, and write the answer below the row. Every subject should be done within 7 minutes. Data are mean ± SEM values.

*Trend compared to pre-intervention, $P < .10$.

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**Table 6. Immunological Changes After Consumption of GoChi Compared to Placebo**

<table>
<thead>
<tr>
<th>Immunological marker, group (n)</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>53.21 ± 2.03</td>
<td>52.76 ± 1.80</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>53.80 ± 1.86</td>
<td>54.95 ± 1.79</td>
</tr>
<tr>
<td>CD8 (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>34.54 ± 1.67</td>
<td>35.47 ± 1.89</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>33.22 ± 2.09</td>
<td>36.59 ± 2.18</td>
</tr>
<tr>
<td>NK (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>0.67 ± 0.02</td>
<td>0.67 ± 0.03</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>0.69 ± 0.03</td>
<td>0.73 ± 0.03</td>
</tr>
<tr>
<td>Lymphocytes ($\times 10^6$/mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>1.82 ± 0.03</td>
<td>2.09 ± 0.04</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>1.76 ± 0.05</td>
<td>2.23 ± 0.03ab</td>
</tr>
<tr>
<td>IL-2 (pg/mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>6.09 ± 0.44</td>
<td>7.48 ± 0.54</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>5.94 ± 0.53</td>
<td>9.36 ± 0.60ab</td>
</tr>
<tr>
<td>IL-4 (pg/mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>10.35 ± 0.66</td>
<td>11.42 ± 0.36</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>10.79 ± 0.88</td>
<td>12.24 ± 0.78</td>
</tr>
<tr>
<td>IgG (g/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>14.70 ± 0.58</td>
<td>14.98 ± 0.63</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>14.12 ± 0.52</td>
<td>16.78 ± 0.50ab</td>
</tr>
<tr>
<td>IgA (mg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (30)</td>
<td>2,586.33 ± 230.38</td>
<td>2,733.90 ± 191.66</td>
</tr>
<tr>
<td>GoChi (30)</td>
<td>2,709.23 ± 188.50</td>
<td>3,280.87 ± 375.60</td>
</tr>
</tbody>
</table>

Venous serum samples were collected at pre- and post-intervention of the trial. A flow cytometer was used to measure the number of CD4, CD8, and NK cells and lymphocytes. Specific enzyme-linked immunosorbent assay kits were used to measure the other immunological markers. Data are mean ± SEM values.

*aSignificant difference compared to placebo, $P < .05$.

*bSignificant difference compared to pre-intervention, $P < .05$.

![FIG. 1. Immune-stimulating effect of GoChi on several immune markers in human serum. Data are mean percentage changes from the pre-intervention value. **$P < .01$, *$P < .05$. Color images available online at www.liebertonline.com/jmf.](image-url)
IgG levels were significantly increased by GoChi intake. These study results suggest that GoChi may have immunomodulatory effects, which is consistent with traditional usage and nonclinical studies of *L. barbarum*. These nonclinical studies have shown a wide variety of immunomodulatory functions, including activation of various immune cells with enhancements of both cell-mediated and humoral immune responses. Chemical analysis of LBPs has identified multiple-molecular-weight constituents. These LBPs are structurally similar to compounds isolated from medicinal mushrooms and from several herbs, including *Astragalus*, that have been shown to stimulate immune cells, have antioxidant properties, reduce gastric irritation, and may protect against neurological damage related to Alzheimer’s disease. One potential mechanism for the immunomodulatory action for these large molecules is that they share structural similarities with cellular components of microorganisms and can modulate immune cells via cell surface receptors. One clinical study has shown successful immunotherapy with the combination of lymphokine-activated killer cell/IL-2 therapy and LBP consumption in advanced cancer patients. Lymphokine-activated killer cell/IL-2 plus LBP treatment led to larger increases in NK and lymphokine-activated killer cell activity than lymphokine-activated killer cell/IL-2 without LBP. Although we did not observe an increase in the percentage of NK cells, NK cell activity was not assessed in the present study. However, we did observe an increase in IL-2 levels in the GoChi-treated group, as well as an increase in IgG levels and the number of lymphocytes.

The antioxidant properties of GoChi may contribute to the observed immune changes. Other dietary antioxidants have been shown to produce an increase in IL-2 and IgG levels as well as lymphocyte number. It is of interest that the same immune measures that were changed with GoChi treatment in the present study have been reported to show a decline with age. Given that the subjects in the current study were older healthy adults (55–72 years old), the GoChi-induced increase in IL-2 and IgG levels and lymphocyte number may indicate an anti-aging effect on the immune system. For example, the potentiation of IL-2 production and T-cell function by dietary antioxidants has been shown to be much more pronounced in older animals, relative to their younger controls.

Additional changes found in the GoChi-treated group, relative to placebo controls, were significant reductions in dizziness and fatigue and improvements of sleep with GoChi, results that are comparable to our previous study. The present study also found there was a tendency for increased short-term memory and focus. *L. barbarum* is regarded as exhibiting anti-aging effects in traditional Asian medicine as it has been shown to have effects on the brain and neuronal function associated with age-related neurodegenerative diseases. Whether the antioxidant properties represent a primary mechanism for the multiple effects of GoChi requires additional investigation.

The present and our previous study confirmed the safety of GoChi with daily consumption of 120 mL, equivalent to at least 150 g of *L. barbarum* fresh fruit for 14–30 days in humans. The safety of even high doses of GoChi has been confirmed in animal studies. There were two recent case reports of a possible interaction of *L. barbarum* fruit tea with warfarin, but the inhibition observed was weak, suggesting that the observed interaction may be caused by factors other than the cytochrome P450 system. Further, given the high frequency of use of *L. barbarum* fruit and of warfarin, the lack of more reports of interaction suggests that the incidence may be very low. An independent lab analysis has shown that atropine has not been detected in GoChi, even though it is in a family of Solanaceae. Thus, considering all the efficacy and safety information, GoChi may be safely taken without serious adverse effects.

In conclusion, a randomized, placebo-controlled, double-blind clinical study has shown daily consumption of LBP-standardized *L. barbarum* fruit juice, GoChi, for 30 days significantly increased subjective feelings of general well-being and increased lymphocyte number and IgG and IL-2 levels in Chinese normal healthy older human subjects without toxicity.

**AUTHOR DISCLOSURE STATEMENT**

All sources of support were from FreeLife International. H.A. is an employee of FreeLife International, and B.S. was supported by FreeLife for pursuing clinical study in China. D.M.N. is a member of FreeLife’s Independent Scientific Advisory Board.

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