Effectiveness of great burdock essence compounds in the adjuvant treatment of gastric ulcer patients infected with Helicobacter pylori

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Abstract Helicobacter pylori commonly infects the human stomach lining is one of the risk factors that can lead a gastric ulcer to develop into gastric cancer. Studies have found that burdock can enhance the protection of gastrointestinal mucosa with antibacterial property that can reduce the damage of the stomach by \textit{Hp y l o r i}. Great burdock essence compounds are prepared using a nanomicell formulation, which contains \textit{Arctium lappa Linn}, \textit{Arnebia euchroma}, and \textit{Angelica sinensis}. This study aims to assess the effectiveness of great burdock essence compounds in the adjuvant treatment of \textit{H pylori} infected clinical patients. Forty-four patients with gastric ulcers, 21 of whom were taking great burdock essence compounds and 23 taking placebo, were included in this study. After taking great burdock essence compounds or placebo for 1 month, \textsuperscript{13}C-Urea Breath Test showed 20 (20/21) patients with negative results and only one person with positive results among the burdock group; in addition, it also indicated that there were 16 (16/23) with negative results and seven (7/23) patients with positive results among the placebo group. The statistical results also showed that the positive \textsuperscript{13}C-Urea Breath Test results in patients who took great burdock essence compounds were significantly different from those who took placebo.
Introduction

*Helicobacter pylori* (*H. pylori*), a gram-negative microaerophilic bacterium first isolated from human gastric mucosa by Marshall and Warren in 1982, is a type of microaerophilic rod-shaped bacteria that commonly infects the human stomach lining. More than one-half of the world’s population have had *H. pylori* infection. The adult infection rate in Taiwan is about 54.4%. Generally, *H. pylori* infection happens in early childhood. If not treated, *H. pylori* will persist lifelong in the infected human stomach. The infection is most likely transmitted orally through the mouth during eating, and excreted out with feces. Thus, the infection rate is closely related to the hygiene of the living environment. In developing countries, its prevalence in adults and children is quite high, reaching almost 80%–90%. *H. pylori* is one of the risk factors that can lead to a gastric ulcer to develop into gastric cancer. According to the literature, groups with *H. pylori* stomach infection are at two to six times higher risk of having gastric cancer as compared to groups that are uninfected. Epidemiologic studies suggest that *H. pylori* infection is directly related to chronic atrophic gastritis, and it may develop into early malignant lesions.

Great burdock essence compounds are prepared using a nanomicell formulation, which contains several major components such as *Arctium lappa* Linn, *Arnebia euchroma*, and *Angelica sinensis*. *Arctium lappa* Linn belongs to a composite of herbaceous plants that contains various ingredients such as inulin, polyphenols, and chlorogenic acid. Studies have found that burdock can enhance the protection of gastrointestinal mucosa with antibacterial property that can reduce the damage of the stomach by *H. pylori*. It can also prevent mucosal damage caused by alcohol. In addition, burdock also has antimutagenic property, which lowers the possibility of turning a gastrointestinal damage into cancer. The main active ingredients in *Arnebia euchroma* include shikonin and naphthoquinone class compounds. Modern studies have shown that shikonin possesses numerous pharmacologic properties such as anti-inflammation, inhibition of local acute inflammatory response, antitumor, promotion of granulation tissue formation and wound healing, inhibition of angiogenesis, inhibition of platelet activity, inhibition of bacterial growth, and inhibition of pathogenic fungi growth. The main active ingredient in the angelica for the *Umbelliferae* is the fumeric acid, which is an antioxidant capable of eliminating free radicals and keeps them from doing tissue damage.

The purpose of this study is to assess the effectiveness of great burdock essence compounds in the adjuvant treatment of *H. pylori* infected clinical patients.

Materials and methods

Participant recruitment and specimen collection

For the gastric ulcer patient information collected from Fooyin University Hospital, the patients who show positive *Campylobacter*-like organism (CLO) test results were included. The exclusion criteria were the patients who have congenital heart failure, chronic obstructive pulmonary disease, serious systemic diseases and malignant tumors, and patients with no breath test results. Patients were given antibiotics to take for a week in accordance with the original treatment process. All the randomly given great burdock essence compounds or placebos were taken twice daily after morning and evening meals, each time taken orally through a bottle (10 ml). They were taken continuously for four weeks before tested for breath test results.

Preparation of great burdock essence compounds

Preparation of burdock powder

Great burdock was provided by Dong Yuan Biotechnology Pharmacy Co., Ltd (Kaohsiung, Taiwan). Take a burdock plant and cut it into blocks before adding water to be mixed. Then, heat it to 95 °C and filter it twice while it is still hot. Freeze dry the filtrate to obtain dried burdock powder.

*Arnebia euchroma* and *Angelica sinensis* extraction

Prepare 90 g of *Arnebia euchroma*, 90 g of *Angelica sinensis*, and 300 g of Sesame oil (Young Full Food Co., Ltd, Yunlin, Taiwan). *Arnebia euchroma*, and *Angelica sinensis* were purchased from traditional Chinese herb store. Place the Chinese angelica in Sesame oil and soak it for 24 hours before heating to 130–140 °C. Then add the *Arnebia euchroma*, heat it, and filter it before pouring the filtrate into the glass bottle ready for use.

Burdock compound essence homogenization

Dissolve burdock powder in water until it has reached saturation point and set it aside. Heat Lithospermum anglica extract and glycerol using double boiling method to 80 °C and set them aside. Dissolve lecithin (Sigma-Aldrich Corporation, MO, USA) in alcohol before placing double boiling. Wait until alcohol evaporates before use. Sequentially add *Arnebia euchroma* and *Angelica sinensis* extract, glycerine (Sigma-Aldrich Co. LLC, USA), and burdock extract and mix well before stirring at high-speed using a high-speed emulsion homogenizer for about 3 minutes. Then, homogenize the mixture in a high-pressure homogenizer (EmulsiFlex-C3,
**Preparation of placebo**

Placebo preparation method is much the same as that used to prepare great burdock essence compounds, except that water is used in place of Arctium lappa, Arnebia euchroma, and Angelica sinensis ingredients.

**CLO test**

Use Pronto Dry reagent (Medical Instruments Corporation, Solothurn, Switzerland) for urease test. Use a stomach endoscope to obtain an appropriate amount of tissue and place it on the test strip, and observe the color change. If the color of the specimens changes from yellow to pink or red within 24 hours, then it is positive; if it stays yellow, then it is negative.

**Statistical analysis**

Results were analyzed using SPSS software (SPSS Inc., Chicago, IL, USA) and the positive / negative $^{13}$C-urea breathe test results were analyzed using chi-square test. If the analyzed results show a $p < 0.05$, then the difference is significant.

**Results**

The study recruited a total of 44 patients, 21 of whom were taking great burdock essence compounds and 23 were taking placebo. The great burdock essence compounds group included 13 men and 8 women, with an average age of 46.80 ± 9.65 (mean ± standard deviation); the placebo group included 14 men and nine women, with an average age of 48.00 ± 9.48 (mean ± standard deviation; Table 1).

After taking great burdock essence compounds for 1 month, $^{13}$C-Urea Breath Test showed 20 patients with negative results and one patient with positive results; the placebo group showed 16 with negative results and seven patients with positive results. The $^{13}$C-Urea Breath Test value distribution diagram showed that the positive $^{13}$C-Urea Breath Test results of the placebo group were significantly greater than that of the great burdock essence compounds group (Fig. 1). Statistical results confirm that the positive $^{13}$C-Urea Breath Test results in patients who took great burdock essence compounds were significantly lower than that of the control group ($p = 0.027$; Table 2).

**Discussion**

The findings of this study demonstrated that one month after consumption of Burdock essence, the gastric ulcer condition of patients with $H$ pylori infections was significantly better than that of the control group ($p = 0.027$). This shows that Burdock essence is effective in inhibiting the growth of $H$ pylori virus. Burdock essence consists of a mixed ingredient formula, including three Chinese herbs, namely, Arctium lappa, Arnebia euchroma, and Angelica sinensis. The active ingredient of Arctium lappa is chlorogenic acid, one of the polyphenols commonly found in foods. Past studies have shown that this substance is bioactive and has multiple functions such as antioxidant, anti-inflammatory, anti-cancer, antulcer, and antiviral effects. A study by Lou Z et al. found that chlorogenic acid increases the permeability of the outer and

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**Table 1** Clinical manifestation of burdock essence group and placebo group.

<table>
<thead>
<tr>
<th></th>
<th>Burdock essence solution (N = 21)</th>
<th>Placebo (N = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs) (mean ± SD)</td>
<td>46.80 ± 9.65</td>
<td>48.00 ± 9.48</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>F</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

SD = standard deviation.

**Table 2** $^{13}$C-Urea Breath Test results from burdock essence group and placebo group.

<table>
<thead>
<tr>
<th>$^{13}$C-Urea Breath Test</th>
<th>Burdock essence solution (N = 21)</th>
<th>Placebo (N = 23)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative (&lt;4)</td>
<td>20</td>
<td>16</td>
<td>0.027*</td>
</tr>
<tr>
<td>Positive (≥4)</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05 represents a statistically significant difference.
plasma membrane of a virus, causing the virus to lose its barrier protection and thus leading to its death.

The active ingredient of *Arnebia euchroma* is shikonin. Studies have shown that shikonin and its derivatives have antiviral effects against gram-positive viruses, gram-negative viruses, and mold. Shikonin itself, however, is more effective than its derivatives.\(^\text{13,21}\) Chen et al\(^\text{12}\) found that shikonin is effective in controlling inflammatory responses. It blocks regulated and normal T cells expressed and secreted (RANTES) from combining with macrophage inflammatory protein-1 alpha (MIP-1a) in monocytes. It can also block the combination of RANTES and MIP-1a with CC chemokine receptor-1 (CCR-1). In 1994, Ozaki et al\(^\text{14}\) found that shikonin and acetylsikokin can enhance the growth of granuloma tissues and that such growth is correlated with dosage.

The active ingredient of *Angelica sinensis* is ferulic acid, which has antilipid peroxidation activities. It is a free radical scavenger and may protect membrane lipids from being harmed by free radicals. The chemical structure of ferulic acid is such that its hydrogen atom can be easily released to form a free radical with strong resonance or high frequency stability. Unpaired electrons from peroxidized structures may then be steadily transferred on to ferulic acid, reducing the damage to the human body. The transfer of unpaired electrons to ferulic acid can directly eliminate free radicals and inhibit peroxidation responses and free radical reactions.\(^\text{15}\) Ferulic acid can also inhibit the formation of prostaglandin E2. It was found to significantly control carrageeinin-induced inflammatory responses such as edema, vasodilation, and pain in mice.\(^\text{22}\)

Burdock essence comprises three characteristics common to Chinese herbs: antiviral, antioxidant, and anti-inflammatory effects. In our past studies,\(^\text{13}\) it was found that Burdock essence is effective in repairing the gastric mucosa of gastric ulcer patients. In this study, however, it was found that Burdock essence has anti-*H pylori* properties.

In addition, patients with *H pylori* infections are usually given a 3-in-1 combination treatment of proton pump inhibitors, amoxicillin, and clarithromycin for one week. According to J Wu et al,\(^\text{24}\) patients taking the 3-in-1 combination treatment have an approximately 90% success rate in eradicating *H pylori*. This study found that the *H pylori* eradication rate was even higher in patients taking Burdock essence, at 95.2% (20/21). The *H pylori* eradication rate of the control group was approximately 69.6% (16/23). Burdock essence has antiviral, antioxidant, and anti-inflammatory properties and is an appropriate health supplement for gastric ulcer patients with *H pylori* infection.

**Acknowledgments**

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**References**