



# The Effect of *Bunium persicum* on Gastrointestinal Symptoms and Inflammatory Mediators in Irritable Bowel Syndrome Patients

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## Abstract

### Original Article

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**Introduction:** Irritable Bowel Syndrome (IBS) is a common condition characterized by abdominal pain, constipation or diarrhea, flatulence, nausea and varying degrees of anxiety or depression. IBS have high prevalence and it mainly occurs between the ages of 15-65 years. Medical cost for IBS is a heavy burden for individuals; also, the side effects of the drugs encouraged the scientists to evaluate other IBS treatment methods such as herbal remedy. Evidence suggests that herbal remedies containing antispasmodic and antioxidant agents may improve gastrointestinal symptoms.

**Methods:** 51 patients with irritable bowel syndrome were recruited after standardized diagnostic work-up into a double-blind, placebo-controlled and were randomly assigned to each group (*Bunium persicum* powder or placebo). Duration of intervention was 5 weeks. The main outcome variables were the changes in total abdominal pain, tenesmus, and feeling of inadequate defecation and C-reactive protein levels.

**Results:** Gender was not significantly different between intervention and control groups. Abdominal pain, tenesmus, and feel inadequate defecation were not changed either in the intervention group and control groups. Moreover, consumption of *Bunium persicum* powder had no effect on serum level of CRP in intervention group compared with the control group.

**Conclusion:** The results of this randomized, double blind, study indicate that *Bunium persicum* as an herbal remedy had no significant effect on symptoms and inflammatory marker of patients with irritable bowel syndrome.

**Keywords:** *Bunium persicum*, *Magliasa*, *Irritable bowel syndrome*, *C-Reactive Protein*, *Gastrointestinal symptoms*

## Introduction

Irritable bowel syndrome (IBS) is a disorder that affects the large intestine<sup>1</sup> and is characterized by special symptoms such as abdominal pain, constipation or diarrhea, flatulence, nausea and varying degrees of anxiety or depression<sup>2-4</sup>. IBS is the most common gastrointestinal disorder<sup>5,6</sup> diagnosed by gastroenterologists and commonly occurs between the ages of 15 and 65<sup>7</sup>. According to a survey done by Chang et al, it is estimated that 10 to 15 percent of adults suffer from IBS, the authors also claimed that 30 to 50 percent of all referrals to gastroenterologists are IBS patients<sup>8</sup>. Estimated worldwide prevalence of IBS among adults and adolescents is about 10%-20%<sup>9</sup>. A review reported that, the prevalence of IBS is between 1.1 to 25 percent and it is more common in women<sup>10</sup>. Management of patients with IBS is associated with a significant use of

healthcare resources. Medical cost for IBS is so expensive for individuals, due to its high prevalence and absence of curative therapy<sup>10,11</sup>. Moreover, most of the patients are given multiple drugs ranging from anticholinergic<sup>12,13</sup> to visceral analgesics and antidepressants<sup>14</sup>. Unfortunately, the side effects of these drugs are as undesirable as IBS. Hence, these issues encouraged the researchers to evaluate other IBS treatment methods such as herbal remedy<sup>15</sup>. In 2009, a digestive diseases nursing consultation, with availability of health telematic media showed that consultation can be effective in cost saving and IBS treatment<sup>16</sup> and nursing care and nutritional interventions can be effective in the management of many diseases such as IBS<sup>17</sup>. Zire Kermani (*Bunium persicum*) is a plant growing in arid region of Iran. Researchers believe that this herb contains antispasmodic and antioxidative agents<sup>18,19</sup>. Assessed the essential oil and different extracts of seeds of *B.*

*Bunium persicum* and its antioxidative elements via three complementary methods: 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay, beta-carotene bleaching and ammonium thiocyanate. The result acknowledged the antioxidant and radical scavenging activity of the essential oil and methanolic extract of *B. persicum*<sup>19</sup>. Also, Hajhashemi et al evaluated the effects of 0.1 to 1000 mg/ml elongate open-bored applicator (EOBP) on ruminal and abomasal smooth muscle of twenty-four healthy sheep and ileum of rats in vitro. The result indicated that the plant contains antispasmodic and antioxidative agents which cause EOBP change the gastrointestinal smooth muscle contraction<sup>20</sup>. In this study we want to assess the effect of *B. persicum* on gastrointestinal symptoms and inflammatory mediators in IBS patients.

### Materials and Methods

In the current study, participants were selected from patients with irritable bowel syndrome referred to gastroenterology clinic, Askarieh hospital in Esfahan in the last 2 months of 2012. We included patients with the following criteria : they had been diagnosed for IBS and age range between 18 and 70 years, able to provide consent and complete questionnaires, able to participate in all aspects of the study and IBS diagnosed by Rome III criteria (Recurrent abdominal pain or discomfort at least three days per month in the previous three months, symptom onset at least six months prior to diagnosis, pain or discomfort associated with two or more of the following: improvement with defecation, onset associated with a change in frequency of stool, onset associated with a change in appearance of stool<sup>7</sup>).

We excluded patients if they had been diagnosed for lactose intolerance, hypersensitivity to herbal medicine, pregnancy, lactating, likely to become pregnant during medication phase, abnormal full blood count, liver function test and renal function test. Recent history of alcohol or substance dependence use or abuse, past or present history of organic disease of gastrointestinal tract (e.g. colorectal cancer, advanced colonic polyp, celiac disease, inflammatory bowel disease, peptic ulcer and previous gastrointestinal surgery), systemic diseases that cause diarrhea or constipation (e.g. thyroid diseases, diabetic neuropathy), current or past history of psychotic disorder (schizophrenia, bipolar disorder) or recent or current use (within past 30 days) of select mood or pain or symptom altering medications, significant acute or chronic progressive neurologic, hepatic, renal, cardiovascular, respiratory or metabolic disease. Moreover, patients who took over-the-counter medication affecting GI motility or IBS-specific drugs

such as tegaserod (Zelnorm) and Lotronex (Alosetron) (within 30 days) and those who take antibiotics during run-in period (2 wks.) were excluded from this study. 51 patients who met inclusion criteria were randomly assigned into two treatment groups (intervention or control group). Patients were 24 men and 20 women with mean age and BMI of 43 and 28.2 respectively. Informed consent was obtained from all subjects. Ethical Committee of Isfahan University of Medical Sciences, Isfahan, Iran, approved this interventional study.

### Study design

This was a double-blind randomized clinical trial for 5 weeks. To allocate subjects into intervention group (*Bunium persicum*) and control group, we used a permuted block randomization method. 24 patients consumed 20 grams of powder in 150 ml of yogurt with lunch and dinner (total of 40 grams in 300 ml of yogurt) and received routine treatment (standard of care recommended). Intervention group included 24 patients (14 men and 10 Women) and control group included 24 patients (14 men and 10 women). Powders were packed in 20 grams packages and were given to participants in 3 stages (in the first day, 1<sup>st</sup> and 3<sup>rd</sup> week) and individuals should give back the empty or remaining packages at the end of study. To assess the effect of the powder at the beginning and at the end of the study, patients completed the questionnaire, 4 times and at each visit (in the first day, 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> week). Questionnaire variable including age, sex, previous medical history, history of medication, life habits and IBS symptoms such as: relief with defecation, onset associated with a change in stool frequency, onset associated with a change in form or appearance of stool, abnormal stool frequency (more than three times per day or less than three times per week), abnormal stool form (loose and watery or lumpy and hard), abnormal stool passage (urgency, frequency, feeling of incomplete evacuation), bloating or sensation of abdominal distension and each factor related to IBS disease. During the study, we asked patients not to alter their medication, usual diet and physical activity; moreover, they were asked to record any side-effects.

### Biochemical assessment

To evaluate the biochemical variables, we collected blood samples, 4 times after 12 hours of over- night fasting (in the first day, 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> week). C-reactive protein was measured using ELISA method (Millipore kit for CRP).

### Statistical analysis



Data analysis was conducted using SPSS statistical software (version 18.0; SPSS, Inc. Chicago, IL, USA). Results were expressed as mean±standard error of the mean (SEM) with significance defined as p-value of 0.05 or less. First, all variables were controlled in terms of normality. For normally distributed data, analysis of variance (ANOVA) followed by Tukey's HSD test was carried out. Kruskal-Wallis and Mann-Whitney tests were used for data that were not normally distributed. Within and between groups comparison was assessed using the paired t-test and independent sample t-tests, respectively.

## Results

**Table1. The Effect of *Bunium persicum* and placebo on abdominal pain, tenesmus, feel inadequate defecation and CRP**

Sign		Control group			p-value	Intervention group			p-value
		1 <sup>st</sup> week	3 <sup>rd</sup> week	5 <sup>th</sup> week		1 <sup>st</sup> week	3 <sup>rd</sup> week	5 <sup>th</sup> week	
Abdominal pain (once a week)	Male	2.1±0.55	2.2±0.73	2.1±0.44	0.64	2.4±0.80	2.2±0.98	2.5±0.75	0.65
	female	2.4±1.02	2.3±0.76	2.3±0.87	0.45	2.5±0.81	2.4±0.77	2.7±0.91	0.86
	p-value	0.62	0.43	0.52		0.68	0.74	0.53	
Tensmus (times a day)	Male	4.2±1.1	4.1±1.3	4.3±1.5	0.16	4.1±1.1	4.0±1.6	4.2±1.3	0.33
	female	4.3±1.3	4.2±1.6	4.2±1.7	0.37	4.0±1.4	4.1±1.3	4.1±1.5	0.51
	p-value	0.74	0.97	0.63		0.35	0.52	0.61	
Inadequate defecation	Male	2.2±1.0	2.1±1.1	2.0±1.2	0.14	2.3±1.2	2.1±1.1	2.2±1.2	0.09
	female	2.3±1.5	2.0±1.2	2.2±1.0	0.22	2.3±1.0	2.2±1.2	2.3±1.1	0.15
	p-value	0.59	0.44	0.72		0.78	0.69	0.75	
C-reactive protein	Male	1.41±0.66		1.38±0.78	0.08	1.44±0.65		1.41±0.82	0.06
	female	1.43±0.42		1.41±0.49	0.1	1.43±0.86		1.40±0.96	0.09
	p-value	0.81		0.42		0.38		0.22	

## Discussion

This randomized, double-blind, placebo-controlled study indicates that the use of *Bunium persicum* as an herbal remedy, had no significant effect on some symptoms and on inflammatory marker (CRP) of patients with irritable bowel syndrome. Although different kinds of herbal preparations have been used extensively for the treatment of irritable bowel syndrome in many countries, few clinical studies have been performed on these remedies<sup>18</sup>. To our knowledge, this was one of the first randomized trials that investigated the effect of *B. persicum* on gastrointestinal symptoms and inflammatory mediators in IBS patients. In our study, we used two different parameters as the irritable bowel syndrome symptom scale includes symptoms associated with abdominal pain and changes in defecation. The abdominal pain scale includes information about pain sensation in irritable bowel syndrome patients. Previously, the results of two double-blind, placebo-controlled study demonstrated a significant improvement

Results of within and between groups comparisons and effects of powder (*Bunium persicum* and placebo) at the beginning and at the end of the study in terms of abdominal pain, tenesmus, feel inadequate defecation and CRP are shown in Table 1. Gender was not significantly different between intervention group and control group. Among men and women, abdominal pain, tenesmus, feel inadequate defecation and CRP level were not significantly different between intervention group and control groups at the baseline. Abdominal pain, tenesmus, feel inadequate defecation were not affected between and within groups ( $P>0.05$ ). Moreover, consumption of powder (*Bunium persicum* and placebo) had no effect on serum level of CRP compared with intervention or control group and baseline.

of symptoms in patients with irritable bowel syndrome after treatment with a traditional Chinese herbal medicine or herbal preparations<sup>18,21</sup>. Also, another study suggests that caraway, a common household plant grown in Iran with anti-inflammatory, spasmolytic, antioxidant, carminative and immunomodulatory properties, are both effective and possess anti-colic activity irrespective of the dose and route of administration<sup>22</sup>. But the effects of *B. persicum*, this new member of herbal remedies, in the treatment of irritable bowel syndrome were not investigated in previous studies. This study indicated no significant effect of *B. persicum* on symptoms or inflammatory markers of IBS patients. *B. persicum* is a kind of herbal remedy but the mechanism of action is not clear yet. Anti-inflammatory, spasmolytic, antimicrobial, antioxidant, carminative and immunomodulatory properties of *Carum carvi* L. (Caraway) and *B. persicum* suggest that it might exert beneficial effects on inflammatory diseases such as IBS. But in the present study we observed neutral effect of *B. persicum* on gastrointestinal symptoms and inflammatory mediators.

However, the precise mechanism of action is not clear, but we can hypothesize that herbal remedies are complex and consisted of numerous active ingredients possibly working together, rather than one specific active substance. The multiple effects of different active ingredients may be beneficial or detrimental for the variety of different symptoms that occur in functional gastrointestinal disorders. The complex interactions among *B. persicum* ingredients, can explained the neutral effects were seen in this trial. Generally, more studies are needed to identify the main ingredient which causes the precise effect.

### Conclusion

In conclusion, the results of this randomized, double blind, study indicate that *Bunium persicum* as an herbal remedy had no significant effect on symptoms and on inflammatory marker (CRP) of patients with irritable bowel syndrome.

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