Effect of Descurainia sophia (L.) Webb ex Prantl on Adult Functional Constipation: A Prospective Pilot Study

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Abstract
Chronic constipation is a common gastrointestinal disorder that affects an estimated 12% to 30% of general population worldwide. Descurainia sophia L. known commonly as flixweed acts as first-line medical treatment for constipation in Iranian traditional medicine. The aim of this study was to assess the efficacy and safety of this remedy for treating functional constipation by standard assessments. The Rome III criteria for functional constipation were the basis for diagnosis. All participants underwent a 4-week treatment. The primary end point was the proportion of patients achieving ≥3 complete spontaneous bowel movements per week. Secondary outcome measures included Patient Assessment of Constipation–Symptom items, Bristol Stool Form Scale, numbers of laxatives/week used by patients, and reported adverse effects. Thirty-five patients completed the program with no important adverse effect. Fifty-four (4%) patients had ≥3 complete spontaneous bowel movements per week. Descurainia sophia is safe and effective in the treatment of chronic functional constipation.

Keywords
Descurainia sophia, functional constipation, PAC-SYM, Bristol Stool Form Scale, complete spontaneous bowel movements per week

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Chronic constipation is a very common gastrointestinal problem with minimal data available about its true epidemiology. This condition affects different population groups ranging from a low of 0.7% to a high of 81%.¹ In the general population, the mean value of chronic constipation prevalence including patient-reported or based on various existing definition criteria is estimated at 12% to 30% of the population,¹,⁴ and for its subtype functional constipation, it is 4.6% to 17%.²,⁵ Although functional constipation prevalence has not been globally investigated in Iran, recently in Kerman, the biggest city in the Southeast of Iran, it has been estimated at over 9.4%.⁶ Functional constipation is a heterogeneous condition that, beyond generally decreased frequency of defecation, includes a diversity of symptoms such as bloating, straining, abdominal pain, a feeling of incomplete evacuation, and hard or lumpy stools.⁷ Despite constipation not being a life-threatening condition, because of its negative effect on patients’ quality of life that subsequently leads to great economic consequences,¹ its treatment is considered very important by health providers.

Conventional treatment such as lifestyle changes such as increasing regular physical activity and fiber and fluid intake in the diet or pharmacological intervention such as using laxatives do not satisfy all patients with their treatment. Complementary and alternative medicine has introduced many remedies to ameliorate constipation symptoms.⁸ Similarly, Iranian traditional medicine introduces some therapeutic methods for treating constipation such as lifestyle changes especially in dietary intake and pharmacological intervention.⁹⁻¹¹ Descurainia sophia L. is commonly known as flixweed, herb-Sophia, and tansy mustard. Sisymbrium sophia L. is

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considered as its synonym. It belongs to the Brassicaceae family. This plant is native to Asia, Africa, and Europe and is generally used as a food additive and a medicinal herb in Iranian, Chinese, and Indian traditional medicines. In traditional Chinese medicine it is commonly used to manage cough and asthma. This plant in the largest traditional pharmacopeia of Iranian (Persian) traditional medicine, Makhzan-al-adviyah (The Storehouse of Medicaments), is known as Khob-bah, and among folk medicine practitioners it is famous as Khaksheer. In Iranian traditional medicine, Descurainia sophia is used as an antipyretic, antipruritic, purgative, helminthic, aphrodisiac, appetizer, digestive tonic, cardiotonic, astringent, and expectorant. The most frequent use of Descurainia sophia is the cold syrup of Descurainia sophia with sugar for cooling; the hot syrup of Descurainia sophia with sugar is used as laxative for constipation treatment. So we hypothesized that Descurainia sophia is useful for functional constipation. In modern pharmacology, Descurainia sophia has anti-inflammatory, analgesic, antipyretic, and anticancer activity. These pharmacologic properties get more interesting when it is noticed that Descurainia sophia is a highly safe herbal medicine. Despite its broad administration in traditional and folk medicines, there are few clinical trials evaluating its pharmacological activities. A study conducted in Iran showed that a combination of Descurainia sophia and prune (Prunus domestica L.) could prevent constipation in adult Hajj pilgrims. A similar study from another part of our country showed that Descurainia sophia can be used as a cheap and safe alternative to conventional polyethylene glycol in the management of functional constipation in children. The aim of this study was to assess the efficacy and safety of Descurainia sophia for treating functional constipation by standard assessments.

Patients and Methods

Trial Protocol

The trial was conducted in compliance with Declaration of Helsinki Good Clinical Practice guidelines at the Department of Gastroenterology in Shariati Hospital and Shariatpanahi Iranian Traditional Medicine Clinic in Tehran. The protocol of this trial was approved by Office of Research Affairs, Deputy of Research and Technology, Shahid Beheshti University of Medical Sciences (Reference Number: 150). The trial was registered at the Iranian Registry of Clinical Trials (www.irct.ir/; unique registration number: IRCT2016030515408N2). Patients provided written informed consent before trial entry. This trial was conducted from December 2014 to December 2015.

Study Population

The enrolled patients included patients aged 18 to 75 years with chronic functional constipation defined based on Rome III criteria for functional constipation. Patients should have had 2 or more of the following symptoms during 25% or more of their bowel movements for at least the past 6 months: less than 3 spontaneous complete bowel movements per week (CSBMs/week), hard/lumpy stools, straining during defecation, and sensation of incomplete evacuation. Secondary constipation to cases such as surgery, bowel pathology, or medication use was the main exclusion criteria of the trial. All patients had no red alarm of serious disease and patients above 40 years were ruled out of serious disease especially colon cancer by coloscopy. All eligible patients passed 1 week of washout period of their laxatives. They all were allowed their own laxatives during the study if a patient, despite increasing medication as directed by the researcher, had not had a satisfied bowel movement for 3 consecutive days.

Assessments

The primary efficacy endpoint was the proportion of patients reaching 3 or more CSBMs/week. The secondary end points were the number of laxatives used, the type of stool according to Bristol chart, and the score of a checklist of Patient Assessment of Constipation–Symptom (PAC-SYM). For evaluating the constipation-related symptoms, we did not have any Persian-version validated questionnaire of any kind up to the time of study initiation. So we decided to use the items of the PAC-SYM questionnaire to evaluate patients’ constipation-related symptoms. Similar to a validated original questionnaire we designed a checklist with abdominal, stool, and rectal symptoms subscales. Each item of this list like in the PAC-SYM questionnaire items was scored on a 4-point Likert-type scale with higher scores indicating greater severity. It was completed at baseline and 4 weeks later by patients. The overall score was classified into 4 categories: mild (<1), moderate (>1 to ≤2), severe (>2 to ≤3), and very severe (>3 to ≤4). We considered ≥ 1 point reduction of overall score and its subscores as improvement from baseline, according to previous studies. To analyze the effect of Descurainia sophia on each subscales of our checklist, the mean changes were standardized as “effect size”: the mean change from baseline divided by baseline score standard deviation.

We calculated body mass index using the followed equitation: body mass index = weight (kg)/height (m²)² and categorized them according to the World Health Organization body mass index principal cutoff points. Although current cutoff points of overweightness and obesity may be not suitable in the Persian population, as it is not in many Asian populations, with regard to minimal data about the suitable cutoff points for Iranian population, we decided to use aforementioned points as a general standard.

Herbal Preparation

The Descurainia sophia seeds were bought from a local famous market in Tehran, Iran, and were authenticated by Dr Homa Hajimehdipoor, analyzed for physicochemistry quality control and microbial restriction tests. The sample passed all the necessary laboratory items according to the Iran Herbal Pharmacopeia and the World Health Organization. Then the seeds were filled into plastic boxes and with a measure were offered to the cooperative patients.

With regard to high safety of Descurainia sophia seed use as a medication up to 2500 mg/kg of body weight, for this study we asked patients to increase the dose to provide their satisfaction up to 60 mL by the measure (±50 g). Starting dose was 30 mL (∼25 g) of Descurainia sophia. They should make hot syrup of dry Descurainia sophia seeds with a teaspoon of sugar and drink 30 minutes before breakfast once daily. If the dose of drug was not sufficient to generate complete bowel movement, they were recommended to increase the Descurainia sophia dose every 3 days to reach a satisfactory level.
Safety Assessments

We monitored and recorded all adverse events. They mainly were reported by the patients and rarely were discovered by researcher.

Statistical Methods

All statistical tests were performed using SPSS version 21.0, and a value of $P < .05$ was taken to indicate statistical significance. All data were first tested by 1-sample Kolmogorov-Smirnov test. Means of data with normal distribution were tested by paired $t$ test and the others by Wilcoxon signed-rank test.

Results

Subjects

Forty-two patients enrolled in the study with confirmed functional constipation from the Department of Gastroenterology in Shariati Hospital and Shariatpanahi Iranian Traditional Medicine Clinic. Four patients dropped out of the program after the first visit, because they changed their mind about participating. Two patients did not continue the program because they had to travel to other places. One patient reported an increase in severity of her constipation and withdrew from the study. With the exception a few patients, reported mild adverse events mainly included headache, nausea, and increased bloating, which were very mild and did not lead to discontinuation from the study; the other patients tolerated the drug easily. So 35 patients completed the program and their data were available for analysis.

Baseline Characteristics

The demographics of these patients are displayed in Table 1. Patients were predominantly female and the mean age was 47.8 years. As illustrated in Table 1, the mean body mass index of patients was 27.2 kg/m². A total of 48.6% of patients were in normal range of body mass index, but 51.4% were overweight or obese (Table 1). The constipation severity in 91.5% of the patients was recorded as moderate to severe (Table 1).

Response to Treatment

Primary Efficacy Endpoint. Before intervention approximately 62.9% of the patients reported that they had no CSBMs/week in the previous 6 months (data not provided), and all of them had ≤2 CSBMs/week in the same time (Table 2).

A total of 28.6% of the patients did not have any CSBMs/week and 54.4% had ≥3 CSBMs/week (data not provided). The means of frequency of CSBMs/week before and after treatment are shown in Table 3 (0.51 and 3.49, respectively, $P < .001$ by Wilcoxon signed-rank test). We also calculated the proportion of patients that had ≥1 change in their average CSBMs/week. A total of 71.4% of the patients had ≥1 change in their average CSBMs/week.

Secondary Efficacy Endpoints. As mentioned previously, we accumulated the information from a checklist of PAC-SYM items as overall, abdominal, rectal, and stool subscales. At the screening, before intervention, PAC-SYM items scores (average of 12 items) were predominantly (in 91.5% of patients) moderate to severe (overall score >1, ≤3; Table 1). The overall and subscale score changes are illustrated in Table 2. The proportion of patients that had ≥1 point reduction in their scores, considered as “improved,” is also illustrated. Nineteen percent of patients had an improvement in the total score after 4 weeks. For its subscales scores, the proportions of patients that had ≥1 point reduction were 12% for abdominal, 14% for rectal, and 23% for stool symptoms. The mean change from baseline in overall scores and their subscales are also illustrated in Table 2. These changes were 0.94, 0.61, 0.64, and 1.37 in total, abdominal, rectal, and stool PAC-SYM items scores, respectively ($P < .001$ by paired $t$ test). The results of calculation of effect sizes of the total and its subscales showed that Descurainia sophia had a large effect (>0.8) on rectal and stool symptoms (0.81 and 1.70, respectively) and a moderate effect (>0.5 to 0.8) on abdominal symptoms. Globally, Descurainia sophia had a large effect on overall symptoms (1.61; Table 3).

Patients’ satisfaction score and physician’s satisfaction score in visual analogue scale were both >66 mm (Table 3).

The mean types of their stools, according to the Bristol chart, before and after intervention, are displayed in Table 3 (1.83 and 3.34, respectively, $P < .001$ by Wilcoxon signed-rank test). Before treatment, 82.9% of the patients reported that they had the stool type of 1 and 2 according to the Bristol chart in the previous 6 months and only 14.3% of them reported they had the stool type of 3 and 4. After treatment, 17.1% of the patients reported that during the treatment period they had the stool type...
of 1 and 2 and 74.3% reported they had the stool type of 3 and 4 (data not provided). Before the start of treatment, 62.9% of the patients did not use any laxatives and 25.7% of them used 1 or 2 laxatives/week (data not provided). The mean numbers of laxatives/week used by patients, before and after 4 weeks treatment, are displayed in Table 3 (2.89 and 0.95, respectively, $P = .002$ by Wilcoxon signed-rank test). After treatment, 94.3% of the patients did not use any laxatives and 5.8% of them used 1 or 2 laxatives/week (data not provided).

### Discussion

The present study is the first to have been undertaken to investigate the potential efficacy of *Descurainia sophia* L. in the management of adult patients with chronic functional constipation by standard assessments. *Descurainia sophia* is considered as the first line of constipation management in Iranian folk medicine. The mechanism of *Descurainia sophia* has not yet been exactly known. *Descurainia sophia* seeds produce mucilage when wetted. This mucilage may relieve constipation.17 *Descurainia sophia* has a compound named allyl disulfidemay that may have a relaxant effect on bowel smooth muscles and facilitate defecation.26 Findings of the study conducted by Nimrouzi et al showed that there was no significant difference between the efficacy of *Descurainia sophia* and polyethylene glycol in the treatment of functional constipation in children.17 Considering the fact that many studies have confirmed the superiority of polyethylene glycol over other laxatives in the treatment of functional constipation,27-29 *Descurainia sophia* can be used as a safe alternative in the treatment of functional constipation in children. Despite the limitations of this study including its small sample size and the absence of a suitable conventional drug or placebo, we found noticeable effects of *Descurainia sophia* on adult functional constipation that can be a good reference for future studies.

The primary efficacy endpoint was the proportion of patients achieving 3 or more CSBMs/week. A high proportion of patients reported an average of $\geq 3$ CSBMs/week (54.3%), which was a good result in comparison with similar other studies.30-33 This study demonstrated a significant increase in CSBM frequency of 2.97 CSBMs. The results reported herein with *Descurainia sophia* are difficult to compare with other agents because of differences in study design. This endpoint reflects not only normalization of frequency of bowel movement and its function, but it also identifies those bowel movements that relieve a key symptom of chronic constipation in terms of sensation of incomplete evacuation. The proportion of patients that had an average increase $\geq 1$ CSBMs/week (71.4%) was also a noticeable result, compared with previous studies (<50%). In addition, compared with before treatment, patients reported using significantly fewer laxatives per week (Table 3).

The patients also reported a significant high improvement in their stool forms compared with before treatment. Recent data have shown that stool form scales, especially Bristol Stool Form Scale, are responsive to changes in gut transit time and can be used with certainty to monitor motility changes in intestinal function.34 In this research, only 14.3% of patients had a normal type of Bristol Stool Form Scale (type 3 or 4); a high percentage of them, 74.3% of the patients, achieved the normal type of stool form at the end of program. Although we did not access to Persian translated version of Bristol Stool Form Scale up to the time of study conduction, since Bristol Stool Form Scale...
Scale is a visual descriptive stool form scale, the above-mentioned result could be very near to a clear and standard report of data about the effect of Descurainia sophia on bowel function.

The aforementioned effect of Descurainia sophia on normalization of stool form conformed to the results of the PAC-SYM questionnaire items, especially the data calculated from the stool subscale score. An effect size of 1.70 showed a significant large effect of Descurainia sophia on stool symptoms of functional constipation. Its large effect was not limited to stool symptoms, and Descurainia sophia had a large effect on rectal symptoms and a moderate effect on abdominal symptoms (Table 2). The high proportion of patients that had an improvement of ≥1 point reductions on average, in overall, abdominal, rectal, and stool subscales was the most important result obtained from this research.

Either patients or investigator had a moderate satisfaction with the treatment (66 and 69, respectively, in visual analogue scale). Importantly, all the aforementioned differences between assessments before and after treatment were statistically significant (P ≤ .002 in Tables 2 and 3). These results get more interesting when considering its minimal side effects. The other major limitation of this study was its short period of treatment. So we could not answer the question if benefits of this plant would be maintained with longer treatment. No statistically significant difference was found between the efficacy of both interventions in the treatment of constipation at the end of the third and eighth weeks of intervention.

Conclusion

In conclusion, in patients with a mean age of 47 years, a history of moderate to severe constipation, 50% of whom were obese and over weighted, Descurainia sophia significantly improved frequency of CSBMs/week and symptoms associated with chronic constipation. The effect size of Descurainia sophia on stool symptoms and forms were prominent. Also Descurainia sophia was well tolerated. So, in conclusion, Descurainia sophia is safe and effective in the treatment of chronic functional constipation. However, there is a need for clinical trials with larger sample sizes, longer treatment periods, and a suitable conventional drug for real comparison.

Author Contributions

All authors discussed the concept of the study. AG drafted the first version. All authors edited and approved the final version of the article.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

The protocol of this trial was approved by Office of Research Affairs, Deputy of Research and Technology, Shahid Beheshti University of Medical Sciences (Reference Number: 150).

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