Comparison and Assessment of Flixweed and Fig Effects on Irritable Bowel Syndrome with Predominant Constipation: A Single-Blind Randomized Clinical Trial

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Background: Irritable bowel syndrome with predominant constipation (IBS-C) is a common digestive disorder. The current therapy is inadequate and evidence regarding the effect of herbal therapies on the relief of affected individuals is insufficient. The aim of this study was to investigate the beneficial effects of flixweed and fig consumption on IBS-C symptoms.

Methods: 150 patients with IBS-C were enrolled in this randomized, controlled trial. All patients were randomly assigned to three groups and received an intervention for four months. The IBS severity score system and quality-of-life questionnaires were used for evaluating IBS-C symptoms. C-reactive protein levels, frequency of defecation and hard stool were also assessed.

Results: Consumption of flixweed or fig, compared to a control group, caused a significant improvement in IBS symptoms including frequency of pain, distention, frequency of defecation and hard stool. Also, the findings showed a significant increase in quality of life, as well as satisfaction with overall bowel habits. However, flixweed and fig intake had no significant effects on abdominal pain severity and C-reactive protein levels.

Conclusions: In conclusion, consumption of flixweed or fig for four months would be a useful therapy for alleviating IBS-C symptoms and can be a beneficial option for first-line treatment.

Keywords: Descurainia sophia, Ficus carica, Irritable bowel syndrome, Herbal medicine, Clinical trial

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INTRODUCTION

Irritable Bowel Syndrome (IBS) is one of the most common functional gastrointestinal disorders, with a prevalence of 5–20%, depending on the diagnostic criteria selected.[1,2] IBS is characterized by bloating and abdominal pain or discomfort associated with changes in bowel habits in the absence of any specific mechanical, biochemical or inflammatory conditions.[3] Although this syndrome does not lead to mortality, it decreases productivity through work absence, increases healthcare costs, and has a substantial negative effect on patient quality of life.[4] Based on its symptoms, IBS is classified into three groups: diarrhea-predominant (IBS-D); constipation-predominant (IBS-C); and mixed type with diarrhea and constipation (IBS-M).[5] Of these types, IBS-C affects about 34% of patients and is generally defined by constipation associated with abdominal pain, which is generally relieved by defecation.[6] The pathology of this syndrome has not yet been clearly understood,[7] although there are some suggested mechanisms for IBS causation, including impaired gastrointestinal motility, visceral hypersensitivity, low-grade mucosal inflammation, and dysfunctions of the brain-bowel axis.[8] It has been shown that digestive organ dysfunction is mostly due to modifications in dietary habits. In this regard, plants and herbs have been reported as showing desirable effects, even playing an important role in the efficacy of pharmacological treatment.[9]

Descurainia Sophia (Flixweed) is an annual dicot, which has long been used in traditional medicine to relieve various conditions.[10] Different components, such as lipids, flavonoids, lignin, phytosterol and cardiac glycosides have been identified from this seed.[11] Also, it contains mucilage, which accounts for its laxative effects; thus flixweed can be beneficial for constipation.[12]

Ficus carica (Fig) has long been appreciated as a healthy food, and for its medicinal properties.[13] This fruit is a good source of bioactive compounds with an antioxidant, anti-inflammatory and antimicrobial effect.[14] Also, it contains high amounts of fiber, and is useful as a natural laxative.[15]

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Both flixweed and fig are widely used as traditional treatments for gastrointestinal disorders and constipation.[16,17] However, to the best of the authors' knowledge, there are no studies related to the effect of flixweed and fig consumption on symptom control in patients with IBS-C. Therefore, this study was conducted to examine the effect of flixweed and fig intake on abdominal pain, discomfort or cramps, defecation, hard stool, incomplete bowel movement and C-reactive protein blood levels among IBS patients.

METHODS

Setting

The study was a 4-month, single-blind, randomized, controlled trial. The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences (N: IR.MUI.REC.1394.3.197). Also, it was carried out based on the CONSORT statement recommendation, and registered on the clinicaltrial.gov website (ID: NCT02559245).

Subjects

Participants were selected from patients aged 18−70 who were referred to the gastrointestinal (GI) research center of Isfahan University of Medical Sciences and private medical practices in Isfahan. IBS-C was confirmed by GI specialists based on the ROME III criteria.[18] Subjects were excluded from the study if they had: significant cardiovascular, renal, hepatic, pulmonary, endocrine, metabolic or hematologic disorders; structural abnormalities of the gastrointestinal tract or diseases or conditions which affected bowel transition; recent surgery; prokinetic or laxative drug use during the past month; any medication use that may affect gastrointestinal motility; other therapeutic dietary advice use for IBS; flixweed or fig use during the past month; experienced diarrhea, pregnancy or breast-feeding. Participants per group sample size was calculated by G*Power software,[19] obtaining a type I error of 5% ($\alpha = 0.05$), type II error of 20% (power = 80%). After considering a potential 20% dropout rate, 150 subjects were recruited for this study. A statistician who did not participate in the study generated the randomization allocation sequence by a computer-generated blocked randomization list, and participants were divided to flixweed (D), fig (F) and control (C) study groups.

Study design

All patients entered run-in for two weeks. Then they were randomly divided to 3 groups and received interventions or a normal diet for four months. Intervention groups were instructed to take 30 g of dried flixweed or 45 g of dried fig before breakfast and lunch with one glass of water every day, respectively (total consumption per day: flixweed 60 g/d and fig 90 g/d). Flixweed and fig were to be drenched in one glass of water for half an hour before consumption. The flixweed and fig used in this study were supplied by Shekoufeh (health license: 39/10387) and Mani (health license: 105/49673) food products, respectively. The control group were asked to continue their normal diet. IBS-C symptoms were assessed at the start, and at the end of every month. Anthropometric indices were measured before and after intervention. A dietary record table was completed by all subjects to determine adherence to flixweed and fig intake each week. During the follow-up, subjects were monitored for possible adverse intervention effects. Each participant's interview and data collection was carried out by professional staff, and blinding of researchers was guaranteed.

Assessment of intervention component

As these herbs have different ingredients, we assessed some of their component in the faculty lab. The crude and dietary fiber was evaluated by the crude fiber assessment tool and the AOAC 199/43 method respectively.[20] Also, carbohydrate (Fehling method),[21] protein (kjeldahl method)[22] and fat (Soksele methods)[23] of both flixweed and fig were assessed. The ingredients of flixweed and fig that we assessed in this study are shown in Table 1.

Assessment of dietary intake

A 3-day dietary record and the short International Physical Activity Questionnaire (IPAQ)[24] were used to evaluate of each subject's dietary intake and assess physical activity, respectively. Subjects were instructed to record everything that they consumed for 3 non-consecutive days (two weekdays and one weekend day). Additionally, subjects were asked to record any medication taken during intervention. The food record data was analyzed using Nutritionist 4 software.

Assessment of IBS symptoms

For assessing IBS-C symptom and severity, the IBS severity score system (IBSSS)[25] was used pre- and post-intervention. This tool has been validated for use in IBS patients, and assesses 5 clinically relevant items over the past 10 days, including severity of abdominal pain, frequency of abdominal pain, severity of abdominal distention, dissatisfaction with bowel movement and interference of IBS with life in general. Each item was scored on a 100 mm visual analogue scale (VAS). In this scale, 0 represents no symptoms and 100 indicates worst possible symptoms. Composite scores of the 5 items indicate the overall severity of IBS cases. Overall IBSSS scores of 75−175, 175−300, and >300 indicated mild, moderate and severe IBS cases, respectively. In addition, the frequency of defecation and hard stool was evaluated at baseline and at the end of every month using the same

Table 1. Amounts of nutrient analysis of dried flixweed and figs

Type of intervention	Dietary fiber %			Carbohydrate %	Protein %	Lipid %
	Total	Crude fiber %	Soluble fiber %			
Descurainia sophia (flixweed)	50	21	29	2	17	31
Ficus carica (fig)	21	12	9	64	12	3

VAS mentioned above. The Bristol stool chart was used due to distinguish between stool classifications. Also, quality of life in IBS-C patients was assessed pre-and post-intervention using a self-report IBS-QoL measurement. It contained 34 items with 8 sub-classifications, including dysphoria, interference with activity, body image, health concerns, food avoidance, social reaction, sexual concerns, and relationships.[26] The sum of response to these items by every subject were averaged and transformed into a 0−100 scale. Higher scores indicated better quality of life among IBS-C patients.

Assessment of other variables

Anthropometric indices, including body weight, height, body mass index (BMI) and waist circumference were measured at the baseline and at the end of intervention. C-reactive protein (CRP), as an inflammation marker, was measured by the immunoturbidimetric method (Pars Azmoon kit) at the baseline and at the end of the study. The palatability and tolerability of consuming flixweed and fig at the aforementioned dosage were also evaluated using VAS, in order to assess the accessibility of both interventions at the end of the study.

Statistical analysis

The Kolmogorov−Smirnov test was used to ensure a normal distribution of the data. Paired-sample *t*- test and Wilcoxon paired ranked test were applied based on the normality distribution of data to assess and determine the difference between IBS variables, QoL and CRP values pre- and post-intervention in each groups. An analysis of Covariance (ANCOVA) test or Kruskal-Wallis test was used for comparing changes (endpoint minus baseline value) in variables after the 4-month intervention among the 3 groups. Repeated-measure ANCOVA was used for comparing the evolution of bowel habit symptoms in the 4-month treatment among the groups. The results of the analysis were reported in terms of mean and standard deviation. Data were analyzed by SPSS (SPSS Inc, Chicago, IL, USA), and in all statistical procedures, p values <0.05 were considered statistically significant.

RESULTS

A total of 150 patients with IBS-C were enrolled and randomly assigned into three groups. Among individuals in group D, two patients [not interested in completing the study ($n = 1$), influenza ($n = 1$)] withdrew. In group F, four subjects [did not consume fig according to schedule ($n = 1$), not interested in completing the study ($n = 3$)] dropped out, while in group C, two people [migration ($n = 1$), not interested in completing study ($n = 1$)] were excluded. Finally, 142 participants completed the trials (Fig. 1). No adverse reactions were reported for flixweed or fig consumption among patients throughout the intervention. Moreover, there were no reports of using IBS-C-related medication among subjects during the study.

The baseline patient information is presented in Table 1. The mean age of total subjects was 57.56 ± 6.23, and 75% of participants were female. 65% of participants were classified as having moderate IBS severity. No statistically significant difference was found in terms of their dietary intake, physical activity and anthropometric measurements between the three groups at baseline and the end of intervention (Tables 2 and 3).

Flixweed and fig consumption resulted in a significant improvement in IBSSS scores from baseline, and compared with the control group ($P < 0.05$; Table 4). Each of the 5 items of the IBSSS scale, except abdominal pain severity, showed significant differences in both intervention wings, compared to baseline and control, after the 4-month intervention ($P < 0.05$; Table 4). Abdominal pain severity at the end of the trial was reduced in D and F groups, compared to their pre-intervention values, but this reduction was not significant

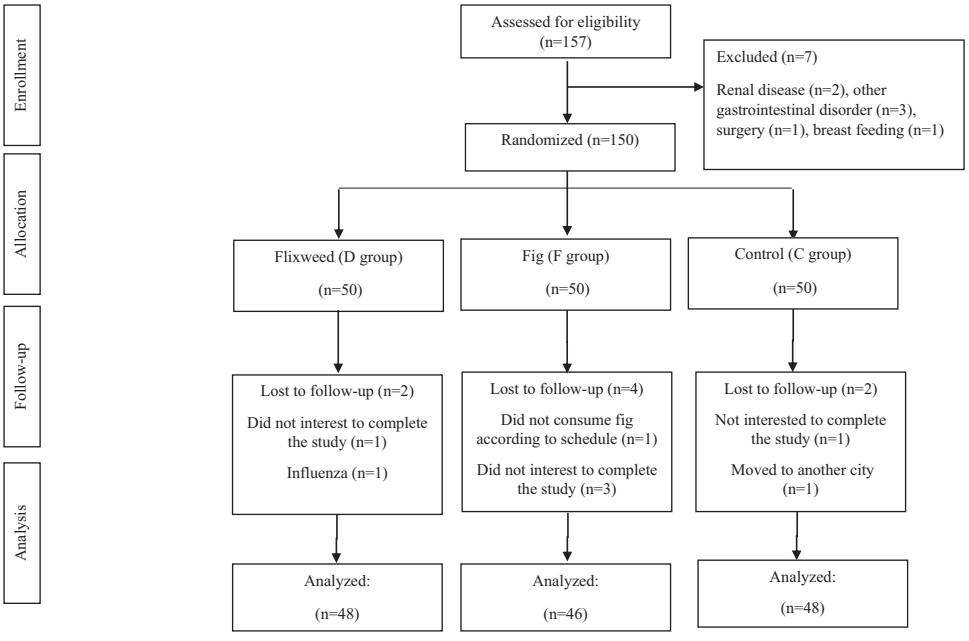

Fig. 1. Participant flow diagram.

Table 2. Baseline anthropometric measurement

		D. group (flixweed) n:48	F. group (fig) n:46	C. group (control) n:48	*P*-value
Sex (Number %)		Female: 75%	Female: 80.44%	Female: 79.17%	
		Male: 25%	Male: 19.56%	Male: 20.83%	
IBS severity (Number %)	Mild	14.5%	13.0%	14.5%	
	Moderate	68.7%	67.3%	73.9%	
	Severe	16.6%	19.5%	14.5%	
Age (Year)		59.16 ± 3.33	55.65 ± 6.68	57.73 ± 7.6	0.11
Weight (Kg)		78.88 ± 7.68	79.68 ± 5.34	76.64 ± 4.87	0.17
BMI		28.08 ± 2.84	29.14 ± 3.42	29.26 ± 3.01	0.30
Waist Circumference (Cm)		95.73 ± 4.52	97.74 ± 3.7	97 ± 3.8	0.18

Values are presented as means ± SD
P values were computed by the ANOVA test.

Table 3. Dietary intakes and physical activity of study participants.

	Period	D. group Flexweed (28)	F. group Fig (26)	C. group Control (28)	p-value
Energy (kcal/d)	Initial	2204 ± 206	2174 ± 173	2216 ± 166	0.68
	End	2273 ± 216	2192 ± 233	2118 ± 320	0.09
	Diff	69 ± 297	18 ± 323	−98 ± 341	0.14
Carbohydrate (g/d)	initial	258 ± 42	267 ± 40	270 ± 43	0.57
	End	245 ± 61	274 ± 58	250 ± 58	0.16
	Diff	−13 ± 77	7 ± 74	−19 ± 79	0.42
Total fiber (g/d)	Initial	15.17 ± 2.62	16.26 ± 3.82	14.97 ± 1.90	0.21*
	End	17.02 ± 3.21	16.15 ± 2.67	16.66 ± 3.50	0.59*
	Diff	1.85 ± 4.14	−0.11 ± 5.20	1.69 ± 3.52	0.18*
Insoluble fiber (g/d)	Initial	10.32 ± 2.25	11.65 ± 2.30	11.18 ± 1.78	0.70*
	End	10.42 ± 2.64	10.88 ± 2.93	10.24 ± 2.48	0.67*
	Diff	0.09 ± 3.64	−0.77 ± 3.02	−0.93 ± 2.45	0.40*
Soluble fiber (g/d)	Initial	4.85 ± 3.71	4.61 ± 2.27	3.79 ± 2.47	0.47*
	End	6.60 ± 4.21	5.27 ± 4.05	6.42 ± 4.10	0.44*
	Diff	1.75 ± 5.86	0.66 ± 5.94	2.62 ± 4.03	0.73*
Water (ml/d)	Initial	1414 ± 347	1613 ± 476	1464 ± 255	0.12*
	End	1516 ± 380	1646 ± 488	1763 ± 492	0.13*
	Diff	102 ± 515	32 ± 793	299 ± 551	0.27*
Physical activity (met-min/week)	Initial	349.66 ± 167	328.75 ± 179	314.63 ± 172	0.61
	End	325.04 ± 181	301.30 ± 179	308.07 ± 170	0.66
	Diff	−24.62 ± 230	−27.45 ± 267	−6.55 ± 230	0.89
Weight (kg)	Initial	78.88 ± 7.68	79.68 ± 5.34	76.64 ± 4.87	0.17
	End	79.19 ± 6.71	79.84 ± 6.06	76.60 ± 4.73	0.10
	Diff	0.31 ± 4.01	0.16 ± 3.88	−0.04 ± 3.58	0.92

Values are presented as means ±SD.
P values were computed by the ANOVA test.
* *P* values were calculated by the Kruskal−Wallis test.

($P = 0.054$, $P = 0.068$, respectively; Table 4). The result of defecation and hard stool frequency analysis indicated a significant improvement in both intervention groups, compared with the control ($P < 0.05$; Table 4). Additionally, the result from the repeated measured ANCOVA showed a significant reduction in terms of abdominal distention and hard stool frequency, and a decrease in hard stool frequency in both intervention groups, compared with the control group, during the 4-month intervention ($P < 0.05$; Fig. 2). Overall QoL score was significantly improved in D and F groups after 4 months, when compared to both baseline and the control group ($P < 0.05$; Table 4). However, the comparison of mean change in each variable between F and D groups failed to detect a significant difference between the effect of flixweed and fig on overall IBSSS score, IBS symptoms variables, and QoL results. Also, no significant change was observed in CRP levels between the 3 groups ($P = 0.25$; Table 4).

DISCUSSION

The present study indicates that supplementation for IBS-C patients with flixweed or fig for 4 months has a significantly beneficial effect on IBS-C symptom severity and on patients' quality of life, compared to a control group who consumed their usual diet. These findings support the general notion that dried

Table 4. The effect of daily consumption of flixweed and fig on IBS-C symptom

		Flixweed *n:48*	Fig *n:46*	Control *n:48*	*P***
QoL	Before	61.62 ± 12.27	60.30 ± 9.51	60.72 ± 11.60	
	After	70.04 ± 11.25	69.52 ± 11.96	62.50 ± 10.44	
	change	8.42 ± 15.07	9.21 ± 15.34	1.7 ± 13.89	0.026
	*P**	<0.001	<0.001	0.423	
Abdominal pain severe	Before	41.97 ± 6.65	48.83 ± 7.05	40.84 ± 7.44	
	After	38.56 ± 11.25	45.46 ± 11.79	38.91 ± 9.80	
	change	−3.50 ± 11.94	−3.37 ± 12.23	−1.94 ± 12.66	0.802
	*P**	0.054	0.068	0.292	
Abdominal pain frequency	Before	53.71 ± 12.66	54.08 ± 11.31	46.77 ± 8.53	
	After	45.60 ± 13.31	46.71 ± 12.84	45.40 ± 10.95	
	change	−8.11 ± 13.76	−7.36 ± 13.02	−1.69 ± 13.22	0.040
	*P**	<0.001	<0.001	0.379	
Interference of life	Before	51.64 ± 10.59	56.07 ± 13.02	53.20 ± 12.53	
	After	36.21 ± 12.39	40.80 ± 14.12	51.82 ± 11.90	
	change	−15.56 ± 16.47	−15.26 ± 18.85	−1.38 ± 19.34	<0.001
	*P**	<0.001	<0.001	0.623	
Dissatisfaction with bowel habit	Before	54.62 ± 9.61	56.13 ± 8.99	53.98 ± 9.08	
	After	39.37 ± 13.34	39.63 ± 13.09	53.27 ± 11.92	
	Change	−15.24 ± 15.01	−16.50 ± 13.42	−0.68 ± 15.31	<0.001
	*P**	<0.001	<0.001	0.758	
IBSSS	Before	249.98 ± 20.25	264.15 ± 24.52	242.09 ± 17.24	
	After	198.52 ± 27.78	213.52 ± 34.03	236.81 ± 24.60	
	change	−51.46 ± 27.41	−50.62 ± 34.37	−5.27 ± 30.19	<0.001
	*P**	<0.001	<0.001	0.092	
CRP	Before	2.31 ± 0.36	2.96 ± 0.74	2.62 ± 0.80	
	After	2.45 ± 0.56	2.72 ± 0.46	2.51 ± 0.42	
	change	0.14 ± 0.46	−0.23 ± 0.71	−0.11 ± 0.73	0.256
	*P**	0.369	0.159	0.476	
tolerability		89%	89%		
palatability		86%	93%		

Values are presented as means ± SD.

* *P* values were computed by Paired-sample *t*-test.

** *P* values were computed by the ANCOVA test and adjusted for energy, sex and BMI.

flixweed or fig, which are widely consumed, can be useful in alleviating IBS-C symptoms. However, this study failed to reveal any significant effect on the reduction of abdominal pain severity and CRP levels. Additionally, the results showed that flixweed was no more effective than fig, statistically.

Abdominal pain is one of the most important discomforting symptoms in patients with IBS-C, and gives rise to hospital referrals.[27] According to the Food and Drug Administration (FDA) recommendation, it is crucial to focus on the treatment of abdominal pain and defecation disorder,[28] as this treatment may reduce the utilization of healthcare resources.[29] Therefore, in order to improve therapeutic methods, there is a need for better understanding of factors which may affect these disorders. In the present study, it was shown that consumption of flixeed and fig can reduce the frequency of abdominal pain. In addition, the results indicated a trend toward abdominal pain severity reduction due to flixweed intake. Existing evidence has revealed the advanced effect of soluble fiber on the overall symptoms of IBS-C.[30] Also, a few studies on insoluble fiber have shown a beneficial effect on overall symptoms.[31,32] However, previous studies have demonstrated that soluble fiber is generally more effective than insoluble fiber in treating IBS-C symptoms.[33] Similarly, it was found that consuming flixweed or fig can be effective on overall IBS-C symptoms. In contrast to those previously reported,[30,34–36] the current study's findings demonstrated no adverse effects due to increased dietary fiber intake—notably gas, bloating and pain that have been previously reported. This result can be seen as support for consuming fiber twice per day, or another component of flixweed and fig.

This study demonstrated that a daily intake of 60 g of flixweed and 90 g of fig can be effective in terms of bowel habit frequency of defecation and hard stools. The recommended adult daily fiber intake ranges between 20 and 35 g/d,[37] and the fiber intake of participants in this trial was less than recommended. It is possible fiber intake shortage resulted in this finding. However, the decrease in symptom frequency continued after the first month.

Quality of life is one of the indicators frequently used for measuring health care effectiveness.[38] IBS occasionally leads to health worries, food avoidance, interference with activity, social reaction, and relationship concerns, and consequently can have a negative effect on QoL.[39] Evidence has suggested that anxiety and depression have high prevalence among IBS patients, and thus a negative impact on QoL in these patients.[40,41] This study found that flixweed and fig consumption ameliorated QoL in

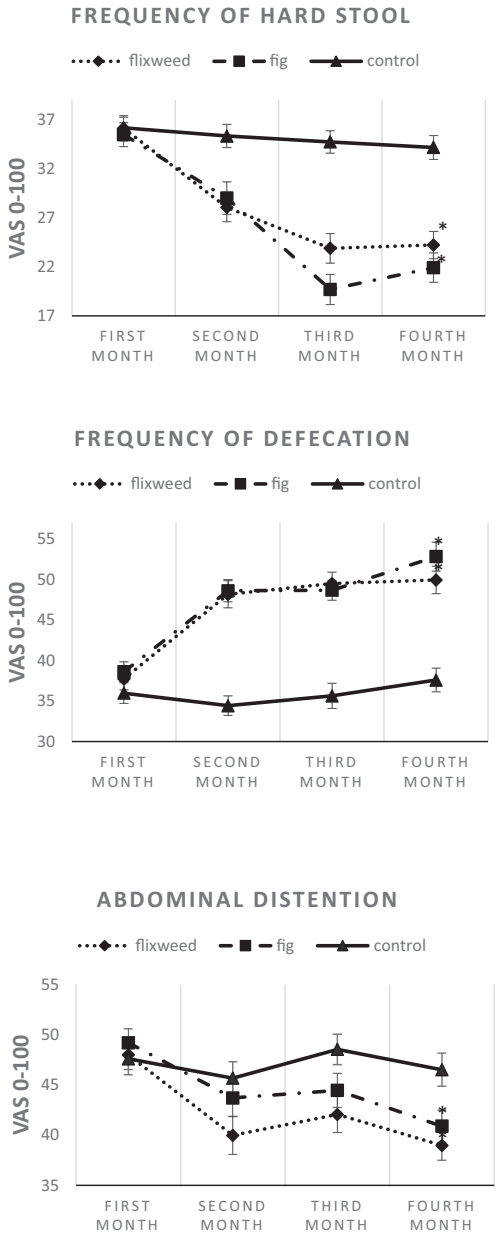

Fig. 2. IBS-C bowel habit trend during 4-months intervention with flixweed and fig. Repeated-measured ANCOVA was applied for comparing between three groups evolution during four-month intervention and adjusted for sex, BMI and energy. * $P<0.05$ in comparing to control. Data was mean ± SE.

patients suffering from IBS-C, which is potentially due to improvements in IBS-C symptoms.

Flixweed and fig have been traditionally used for constipation treatment. They are good sources of both soluble and insoluble fiber. However, their beneficial effects may be not only a result of their fiber, as flixweed and fig have other components which might be effective in IBS-C treatment. Flixweed is a cheap, available and safe medication, which has been widely used in the treatment of constipation.[42] The underling mechanism of flixweed's action is unclear. It might soften the stool and relax bowel smooth muscles by acting through the mucilage component and the absorption of water in the colon. Further, the relaxing effect of Allyl Disulfide in flixweed can be beneficial for facilitating stool defecation.[43] On the other hand, fig components, like cellulose, act as an osmotic laxative and can elevate viscosity and increase stool defecation.[15] In addition, the fermented fiber of flixweed and fig can increase the production of short chain fatty acids, which provide energy for colonic cells, and might have an anti-inflammatory effect.[44] Like other dietary fiber sources, both flixweed and fig can increase stool bulk and defecation frequency, and consequently decrease symptoms in IBS patients.[45,46] Another possible mechanism might be related to their ability to act as a prebiotic, thus altering the gut microbial community profile. Previous studies have shown that prebiotics and probiotics can be effective in IBS treatment via modifying the expression of pain receptors in the gut,[47] alleviating inflammation marker levels,[48] and visceral sensory and motor functions.[49] However, further studies focused on the mechanism of flixweed and fig action are needed in order to assess the ability and alternation of probiotic bacteria after flixweed and/or fig consumption. Also, the present study showed that both flixweed and fig have high tolerability and palatability among patients. This quality can make them be seen as a priority treatment, compared to other fiber sources that lead to increased gas or bloating.

Studies have indicated that patients with IBS have low-grade inflammation.[50] Although CRP levels in these patients were in the normal range, they demonstrated higher CRP levels than in healthy people.[51] The current study was not able to demonstrate any significant effects of flixweed and fig consumption on CRP levels. This might be because of unexpected confounders.

Although this study observed beneficial effects of flixweed and fig on IBS-C symptoms, it did not find any significant difference between the two groups. Thus, this study could not give priority to either flixweed or fig in the treatment of IBS-C symptoms.

IBS-C has a relapsing and remitting nature, and nearly a 47% placebo effect rate. This highly undesirable effect decreases after 12 weeks.[52] One strength of the current study was its 4-month duration, which minimized this effect. In addition, several studies reported IBS might be associated with energy intake and obesity. They showed that IBS symptoms were more severe in obese patients and symptoms severity alleviated after bariatric surgery.[53,54] In present study, due to restricting the effect of energy intake and weight as confounders on results, we measured them at the baseline and after intervention, assessed statistical changes and present adjusted model. However, there are some potential limitations which should be considered. First, there was no placebo in this trial. Due to the special conditions of IBS-C patients, it was difficult to find a proper placebo, similar in size and texture to flixweed and fig, which had been proven ineffective on the syndrome. Hence, successful double-blinding of dietary interventions in the research was not achievable. Second, in the current study, only CRP was considered as a surrogate marker of inflammation. However, other inflammatory markers might better represent inflammatory conditions in patients with this syndrome. Finally, as mentioned before, both of the interventions have many

ingredients, such as polyphenol and antioxidants, which might affect IBS-C symptoms. This study focused on fiber and did not assess the other components of flixweed and fig. The assessment of other components in future studies may be valuable for understanding the mechanism.

CONCLUSION

In conclusion, the current study's findings suggested that consumption of flixweed and fig among IBS-C patients may have positive effects on IBS-C symptoms, and that these natural products could be considered as a safe therapy for this syndrome. However, more studies with high-quality design are suggested.

REFERENCES

1. Siegfried W, Rao SS. Advances in the management of constipation-predominant irritable bowel syndrome: the role of linaclotide. *Int J Biol Macromol*. 2014;7:193–205.
2. Lee Y-T, Hu L-Y, Shen C-C, et al. Risk of psychiatric disorders following irritable bowel syndrome: a nationwide population-based cohort study. *PloS one*. 2015;10: e0133283.
3. Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. *JAMA*. 2015;313:949–958.
4. Amirimani B, Nikfam S, Albaji M, et al. Probiotic vs. placebo in irritable bowel syndrome: a randomized controlled trial. *Middle East J Dig Dis*. 2013;5:98.
5. Trinkley K, Nahata M. Treatment of irritable bowel syndrome. *J Clin Pharm Ther*. 2011;36:275–282.
6. Jadallah KA, Kullab SM, Sanders DS. Constipation-predominant irritable bowel syndrome: a review of current and emerging drug therapies. *World J Gastroenterol: WJG*. 2014;20:8898.
7. Layer P, Stanghellini V. Review article: linaclotide for the management of irritable bowel syndrome with constipation. *Aliment Pharmacol Ther*. 2014;39:371–384.
8. Furnari M, de Bortoli N, Martinucci I, et al. Optimal management of constipation associated with irritable bowel syndrome. *Ther Clin Risk Manag*. 2015;11:691.
9. Camilleri M, Tack JF. Current medical treatments of dyspepsia and irritable bowel syndrome. *Gastroenterol Clin N Am*. 2010;39:481–493.
10. Ara KM, Jowkarderis M, Raofie F. Optimization of supercritical fluid extraction of essential oils and fatty acids from flixweed (Descurainia Sophia L.) seed using response surface methodology and central composite design. *J Food Sci Technol*. 2015;52(7):4450–4458.
11. Lee YJ, Kim NS, Kim H, et al. Cytotoxic and anti-inflammatory constituents from the seeds of Descurainia sophia. *Arch Pharm Res*. 2013;36:536–541.
12. Golalikhani M, Khodaiyan F, Khosravi A. Response surface optimization of mucilage aqueous extraction from flixweed (Descurainia sophia) seeds. *Int J Biol Macromol*. 2014;70:444–449.
13. Tian J, Zhang Y, Yang X, et al. Ficus carica polysaccharides promote the maturation and function of dendritic cells. *Int J Mol Sci*. 2014;15:12469–12479.
14. Mawa S, Husain K, Jantan I. Ficus carica L.(Moraceae): phytochemistry, traditional uses and biological activities. *J Evid Based Complement Altern Med*. 2013;2013:974256.
15. Oh H-G, Lee H-Y, Seo M-Y, et al. Effects of Ficus carica paste on constipation induced by a high-protein feed and movement restriction in beagles. *Lab Anim Res*. 2011;27:275–281.
16. Ayoobi F, Kamali B, Shamsizadeh A, et al. Effect of aqueous extract of descurainia sophia on castor oil-induced diarrhea in male rat. *J Rafsanjan Univ Med Sci*. 2013;12:149–156.
17. Nimrouzi M, Sadeghpour O, Imanieh M-H, et al. Remedies for children constipation in medieval Persia. *J Evid Based Complement Altern Med*. 2014;19:137–143.
18. Wong RK, Palsson OS, Turner MJ, et al. Inability of the Rome III criteria to distinguish functional constipation from constipation-subtype irritable bowel syndrome. *Am J Gastroenterol*. 2010;105:2228–2234.
19. Faul F, Erdfelder E, Buchner A, et al. Statistical power analyses using G* Power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41:1149–1160.
20. Horwitz W. *Official methods of analysis of AOAC International*. AOAC international; 2000.
21. Chaira N, Ferchichi A, Mrabet A, et al. Chemical composition of the flesh and the pit of date palm fruit and radical scavenging activity of their extracts. *Pak J Biol Sci*. 2007;10(13):2202–2207.
22. Vinklárková B, Chromý V, Šprongl L, et al. The Kjeldahl method as a primary reference procedure for total protein in certified reference materials used in clinical chemistry. II. Selection of direct Kjeldahl analysis and its preliminary performance parameters. *Crit Rev Anal Chem*. 2015;45(2):112–118.
23. Babazadeh M, Kousha A, Safari R. Changes in nutritional factors of freezed kutum (Rutilus frisii kutum). *World J Zool*. 2008;3(2):51–53.
24. Lee PH, Macfarlane DJ, Lam T, et al. Validity of the international physical activity questionnaire short form (IPAQ-SF): a systematic. *Int J Behav Nutr Phys Act*. 2011;8:115.
25. Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Aliment Pharmacol Ther*. 1997;11:395–402.
26. Drossman DA, Patrick DL, Whitehead WE, et al. Further validation of the IBS-QOL: a disease-specific quality-of-life questionnaire. *Am J Gastroenterol*. 2000;95:999–1007.
27. Lembo A, Ameen VZ, Drossman DA. Irritable bowel syndrome: toward an understanding of severity. *Clin Gastroenterol Hepatol*. 2005;3:717–725.
28. Food Administration D: Guidance for industry: irritable bowel syndrome-clinical evaluation of products for treatment. Rockville, MD: US Department of Health and Human Services 2010.
29. Spiegel B, Bolus R, Harris L, et al. Measuring irritable bowel syndrome patient–reported outcomes with an abdominal pain numeric rating scale. *Aliment Pharmacol Ther*. 2009;30:1159–1170.
30. Prior A, Whorwell PJ. Double blind study of ispaghula in irritable bowel syndrome. *Gut*. 1987;28:1510–1513.
31. Cann P, Read N, Holdsworth C: What is the benefit of coarse wheat bran in patients with irritable bowel syndrome? Gut 1984;25:168–173.
32. Lucey M, Clark M, Lowndes J, Dawson A. Is bran efficacious in irritable bowel syndrome? A double blind placebo controlled crossover study. *Gut*. 1987;28:221–225.
33. Moayyedi P, Quigley EM, Lacy BE, et al. The effect of fiber supplementation on irritable bowel syndrome: a systematic review and meta-analysis. *Am J Gastroenterol*. 2014;109:1367–1374.
34. Hebden JM, Blackshaw E, D'Amato M, et al. Abnormalities of GI transit in bloated irritable bowel syndrome: effect of bran on transit and symptoms. *Am J Gastroenterol*. 2002;97:2315–2320.
35. Bijkerk CJ, de Wit NJ, Stalman WA, et al. Irritable bowel syndrome in primary care: the patients' and doctors' views on symptoms, etiology and management. *Can J Gastroenterol Hepatol*. 2003;17:363–368.
36. Longstreth GF, Fox DD, Youkeles L, et al. Psyllium therapy in the irritable bowel syndrome: a double-blind trial. *Ann Intern Med*. 1981;95:53–56.
37. Furnari M, de Bortoli N, Martinucci I, et al. Optimal management of constipation associated with irritable bowel syndrome. *Ther Clin Risk Manag*. 2015;11:691–703.

38. Shahbazi K, Solati K, Hasanpour-Dehkordi A. Comparison of hypnotherapy and standard medical treatment alone on quality of life in patients with irritable bowel syndrome: a randomized control trial. *J Clin Diagn Res*. 2016;10:Oc01–Oc04.
39. Amouretti M, Le Pen C, Gaudin AF, et al. Impact of irritable bowel syndrome (IBS) on health-related quality of life (HRQOL). *Gastroenterol Clin Biol*. 2006;30:241–246.
40. Whitehead WE, Palsson O, Jones KR. Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications? *Gastroenterology*. 2002;122:1140–1156.
41. Rey de Castro NG, Miller V, Carruthers HR, Whorwell PJ. Irritable bowel syndrome: a comparison of subtypes. *J Gastroenterol Hepatol*. 2015;30:279–285.
42. Nimrouzi M, Sadeghpour O, Imanieh MH, et al. Flixweed vs. polyethylene glycol in the treatment of childhood functional constipation: a randomized clinical trial. *Iran J Pediatr*. 2015;25:e425.
43. Sun K, Li X, Liu J-M, Wang J-H, Li W, Sha Y. A novel sulphur glycoside from the seeds of Descurainia sophia (L.) note. *J Asian Nat Prod Res*. 2005;7:853–856.
44. Zimmerman MA, Singh N, Martin PM, et al. Butyrate suppresses colonic inflammation through HDAC1-dependent Fas upregulation and Fas-mediated apoptosis of T cells. *Am J Physiol Gastrointest Liver Physiol*. 2012;302:G1405–G1415.
45. Stevens J, Vansoest P, Robertson JB, Levitsky DA. Comparison of the effects of psyllium and wheat bran on gastrointestinal transit time and stool characteristics. *J Am Diet Assoc*. 1988;88(3):323–326.
46. Brandt LJ, Chey WD, Foxx-Orenstein AE, et al. An evidence-based position statement on the management of irritable bowel syndrome. *The American journal of gastroenterology*. 2009;104(Suppl 1):S1–35.
47. Rousseaux C, Thuru X, Gelot A, et al. Lactobacillus acidophilus modulates intestinal pain and induces opioid and cannabinoid receptors. *Nat Med*. 2007;13:35–37.
48. O ' Mahony L, McCarthy J, Kelly P, et al. Lactobacillus and bifi dobacterium in irritable bowel syndrome: symptom responses and relationship to cytokine profi les. *Gastroenterology*. 2005;128:541–551.
49. Andresen V, Baumgart DC. Role of probiotics in the treatment of irritable bowel syndrome: potential mechanisms and current clinical evidence. *Int J Probiotics Prebiotics*. 2006;1(1):11.
50. Abbasnezhad A, Amani R, Hajiani E, Alavinejad P, Cheraghian B, Ghadiri A. Effect of vitamin D on gastrointestinal symptoms and health-related quality of life in irritable bowel syndrome patients: a randomized double-blind clinical trial. *Neurogastroenterol Motil*. 2016;28:1533–1544.
51. Hod K, Dickman R, Sperber A, et al. Assessment of high-sensitivity CRP as a marker of micro-inflammation in irritable bowel syndrome. *Neurogastroenterol Motil*. 2011;23:1105–1110.
52. Miller LE. Study design considerations for irritable bowel syndrome clinical trials. *Ann Gastroenterol*. 2014;27:338.
53. Pickett-Blakely O. Obesity and irritable bowel syndrome: a comprehensive review. *Gastroenterol Hepatol*. 2014;10(7):411.
54. Austin GL, Dalton CB, Hu Y, et al. A very low-carbohydrate diet improves symptoms and quality of life in diarrhea-predominant irritable bowel syndrome. *Clin Gastroenterol Hepatol*. 2009;7(6):706–708.