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Persian Medicine "Sahj" in Ulcerative Colitis Remedy: A before-and-after Clinical Trial

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Abstract

Ulcerative colitis (UC) is an inflammatory bowel disease and its etiology has not fully understood in conventional medicine. It also influences the quality of life as a result of its recurrence and progressive clinical course, then, it has been considered an important public health concern. This study aimed to evaluate the impact of prescription therapy based on the Persian Medicine as a complementary treatment for the mitigation of the symptoms of UC as well as improvement in the disease severity. A total of 30 UC patients with an age range of 15-70 years participated in this clinical trial. They were treated with the "Sahj" capsule containing: *Curcuma longa* L., Punica granatum L., and Terminalia chebula Retz. for 4 weeks. The "Sahj" capsule was prepared based on the Persian Medicine resources. The bowel frequency at day/night, urgency of defecation, general health, and blood in stool were assessed pre/post intervention and the results were compared before and after the clinical trial. The "Sahj" capsule significantly enhanced the clinical findings. There was a significant increase in simple clinical colitis activity index (SCCAI) score in response to the prescription of the "Sahj" capsule (7.73 ± 1.98 before and 4.30 ± 1.12 after the trial) in which general health condition of patients was increased by 50% after the clinical trial. Bowel frequency at day was remarkably decreased by totally 15 patients with the scores of 1, 2 and 3 were enrolled to score 0. Also, bowel frequency at night was not statically significant ($p = 0.267$) in spite of 7 patients were improved their score (changed their score from 2 to 1). Urgency of defecation ($p<0.003$) and blood in stool ($p<0.0001$) were significantly decreased compared with pre-intervention stage. These findings suggest an appropriate complementary treatment to reduce the symptoms of ulcerative colitis. However, further studies with larger sample size are warranted to assess the efficacy and safety of the "Sahj" capsule in the treatment of UC.

Keywords: Persian medicine; Ulcerative colitis; Inflammatory bowel disease; Herbal medicine

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Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease and affects the patients' quality of life associated with significant complications, including frequent diarrhea, urgent bowel movements, rectal bleeding, and fatigue [1,2]. The severity of the symptoms, as well as recurrent of UC, impact significantly on the ability to work and social life of patients [2]. It can also impose costs on developing or even developed countries, and its incidence is globally (35-100 cases per 100,000 people) and in the Iran 32.52 cases per 100,000 people increased; thus, it is considered an important public health concern [2,3].

However, the gold current therapies used for the treatment of UC such as surgery, immunosuppressive agents, and other medications [4] are relatively ineffective; therefore, alternative traditional and herbal agents have been widely investigated as complementary/remedy options for the treatment of a variety of disorders such as UC [5,6]. Major herbal medicines by natural active constituents have exhibited their efficacy and pharmacologic effects on UC through anti-inflammatory, antioxidant, anti-bacteria, anti-diarrheal, regulatory body requirements, and immunity properties [7,8]. In line with that, the previous clinical trial of the *Punica granatum* (*P. granatum*) peels aqueous extract on UC patients showed that the herb extract improved clinical symptoms, more than two times against placebo group and it was generally safe during follow-up time [9]. Also, *Curcuma* longa and its active ingredient curcumin exerted promising anti-inflammatory and antioxidant properties, which showed significant effects in the treatment of patients with inflammatory bowel diseases including Crohn's Disease (CD) and UC [6,10,11].

On the other hand, in Persian medicine terminology, "Sahj" has the closest relation to the UC and Crohn's disease [12,13] and "Sahj" has been introduced as a scratchor wound in the inner surface of the intestine, associated with abdominal pain and bloody diarrhea [14,15]. However, Persian medicine has introduced some preparations of herbal medicine to treat "Sahj". Thus far, this study aimed to evaluate Persian Medicine "Sahj" therapy using *Curcuma longa* L., *Punica granatum* L., and *Terminalia chebula* Retz. formulation on UC patients.

Methods

Capsule preparation

The herbals were purchased from an herbal market in Mashhad and approved by the School of Persian and Complementary Medicine, Mashhad University of Medical Sciences. The "Sahj" capsule is composed of; the root of *Curcuma longa* L. (50 mg), the flower of *Punica granatum* L. (500 mg), and the fruits of *Terminalia chebula* Retz. (200 mg). During the process, the samples were ground separately, sifted, and after confirming microbial and physicochemical tests, and standardized based on total phenols, then, these were transformed into capsule in the environment of laboratory.

Participants

Female and male patients with UC with an age range of 15-70 years were enrolled. The diag-

nosis of ulcerative colitis was made by a trained gastroenterologist. The inclusion criteria were disease activity index scores greater than or equal to 5 (Table 1 SCCAI) and no need for hospitalization. Besides, smokers, patients with dyspepsia, abdominal pain, epigastric pain and sensitivity to plants, pregnant women, and other patients with high-risk disorders were excluded from the study. The study took place at outpatient who were referred to the Sayyad Medical and Educational Center, Gorgan, Golestan, between 2017 and 2018. All patients read and signed informed consent before enrollment and undergoing to trial procedures. Patients were free to exclude from the study at any time that they want. The patients were enrolled in accor-

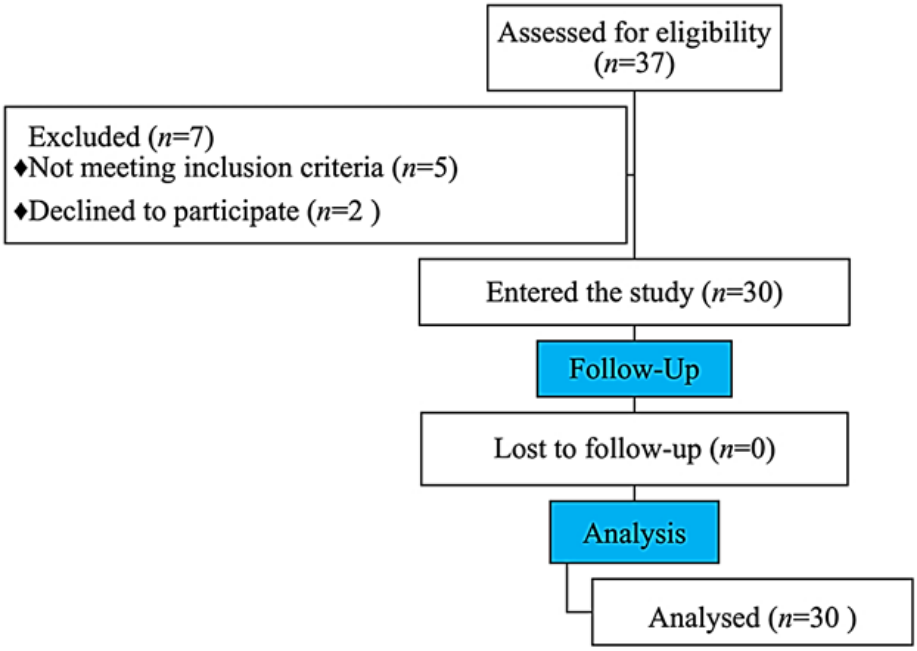

Figure 1. The consort diagram of participant flow.

Study design

The study was a non-randomized, uncontrolled, before and after clinical trial. This study was approved by the ethics committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1395.329) and by the Regional Committee on Health Research Ethics for Iran (IRCT201705201264N10). The outcomes were measured at the beginning of the study as a face-to-face visit (bowel frequency at day/night, urgency of defecation, general health, and blood in stool) and the data were recorded in the patient's file; then, patients received the "Sahj" capsules (2 capsules/8 h/ 3 times daily an hour before a meal) along with the routine medication (Sulfasalazine) for 4 weeks, and medicine consumption was followed-up by telephone. At the end of the 4 weeks, outcomes were assessed by face-to-face visit and recorded in the patient's file. Telephone calls were used to follow the patient complications or unexpected side effect every week and then subjected to statistical analysis.

Table 1. simple clinical colitis activity index (SCCAI) [27].

Symptom	Score
Bowel frequency (day)	
1—3	0
4--6	1
7--9	2
>9	3
Bowel frequency (night)	
1—3	1
4--6	2
Urgency of defecation	
Hurry	1
Immediately	2
Incontinence	3
Blood in stool	
Trace	1
Occasionally frank	2
Usually frank	3
General well being	
Very well	0
Slightly below par	1
Poor	2
Very poor	3
Terrible	4
Extracolonic features	1 per manifestation

Statistical analysis

Data were expressed as means ± SEM and analyzed by SPSS 16. The differences between groups (per/post-treatment) were evaluated by using a paired t-test in normal distribution of data or non-parametric Wilcoxon test. Chi-square or Fisher test was used for comparing qualitative variables in the groups. P values < 0.05 were the considered significant levels.

Results

Basic demographical findings

37 participants were screened, 7 people were excluded from the study because 2 withdrew consent and 5 people did not meet inclusion criteria. Of the 30 patients who were entered in the trial, all the patients were treated by "Sahj" capsule for 4 weeks and completed the trial without losing. The consort diagram of participant flow is depicted in figure 1. Participants were 16 (53.3%) female and 14 (46.7%) male. Five of the 30 patients had a history of smoking (but, they were not smoker when enrolled to study) and twenty-three of them were employed. In term of race, 26 (86.7%) patients were Persian and 4 (13.3%) Turkmen.

Comparison of clinical findings

The "Sahj" capsule treatment analysis showed

significant reduction in the bowel frequency at day totally 15 patients with score 1, 2 and 3 were enrolled to score 0 ($p < 0.0001$), but reduction of bowel frequency at night not statically significant ($p = 0.267$) (Table 2) in spite of 7 patients were improved their score (changed score from 2 to 1). Urgency of defecation was diminished by 40% compared with pre-treatment by capsule at any subject point with score 2 or 3 before treatment (Table 2). As depicted in Table 2, blood in stool substantially improved after the treatment totally 16 patients to score 1 (all of patients with score 3 and 9 patients with score 2). By the end of the 4 weeks, very good general health was achieved in 50% of the patients and one patient was in very poor condition pre-treatment (SCCAI score=3) enhanced to poor symptom (SCCAI score=2) (Table 3). In addition, total SCCAI score was decreased from (7.73 ± 1.98) before treatment to (4.30 ± 1.12) after 4 weeks using "Sahj" capsule ($p < 0.0001$).

Side effects

During the study time, there was not reported any side effects of "Sahj" capsule consumption.

Table 2. effect of "Sahj" capsule on bowel frequency, urgency of defecation and blood in stool of the patients after 4 weeks' treatment.

Symptom	Frequency/Activity	Score	Before treatment N (%)	After treatment N (%)
Bowel frequency (day)	1-3 times	0	3 (10%)	18 (60%)*
	4-6 times	1	15 (50%)	11 (36.7%)*
	7-9 times	2	11 (36.7%)	1 (3.3%)*
	9 < times	3	1 (3.3%)	0
Bowel frequency (night)	1-3 times	1	22 (73.3%)	29 (96.7%)*
	4-6 times	2	8 (26.7%)	1 (3.3%)*
Urgency of defection	Rushing to defecate	1	14 (46.7%)	28 (93.3%)*
	Defecation immediately	2	14 (46.7%)	2 (6.7%)*
	Stool in continence	3	2 (6.7%)	0
Blood in stool	Rarely	1	7 (23.3%)	23 (76.7%)*
	Almost sometimes	2	16 (53.3%)	7 (23.3%)*
	Usually	3	7 (23.3%)	0*

N: Number of patient.
* $P < 0.05$ against before treatment.

Discussion

The current study was a non-randomized before and after clinical trial of "Sahj" therapy on UC. Our data showed the "Sahj" capsule three times daily for 4 weeks diminished frequency and urgency of defecation, diarrhea, and rectal bleeding as the major clinical findings of UC. In Persian Medicine, there are evidence about the beneficial effects of *Curcuma longa*, *Punica granatum*, and *Terminalia chebula* Retz. in the treatment of "Sahj" digestive disorders,

particularly abdomenal pain and bloody diarrhea [16,12,17]. However, the present study is the first clinical trials that evaluated the effect of *C. longa, P. granatum,* and *T. chebula* combination on UC therapy. It seems that major secondary metabolism of *P. granatum* including flavonoids, tannins and alkaloids can explain its antioxidant, anti-inflammatory, and anti-diarrheal properties [9]. Additionally, *Punica granatum* juice (400 mg/kg/day) treatment attenuated levels NO, MDA, MPO, TNF-α, IL-18, IL-1β, and NF-κB, along with SOD level augmentation in 2,4-dinitrobenzene sulfonic acid-induced inflammatory bowel disease rats. On the other hand, *P. granatum* improved colon mucosal damage index (CMDI) and disease activity index (DAI) score as compared to control group. These findings suggested that several phytochemical of *P. granatum* synergistically exerted its anti-colitis effect due to their anti-inflammatory, antioxidant, and decreasing neutrophil infiltration [18].

Several studies have demonstrated that *Terminalia chebula* Retz. ameliorated the acetic acid-induced colitis in rat through inhibition of MPO activity, TNF-α, and prostaglandin E2 [19]. Also, its oral administration in combination remarkably improved the severity of colitis symptoms and regulated pro-inflammatory cytokines in 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis mouse model [20]. Collectively, *Terminalia chebula* Retz. through its antioxidant and anti-inflammatory effects such as rutin, catechin, caffeic acid, gallic acid, ellagic acid, epicatechin, and quercetin can be regarded as a therapeutic candidate for the treatment of UC [21].

Curcumin as a main active component of C. longa revealed its immunosuppressive actions in IBD patients through inhibiting expression of NF-κB, IL-1, IL-2, IL-6, IL-8, IL-12, TNF-α, IκBα, iNOS, COX-2, Lipoxygenase-5, oxidative stress, modulating p38 and JNK-MAPK, and suppressing mitogen activation and apoptosis [11]. Curcumin can change its activity from an antioxidant to a strong pro-oxidant by directly binds to thioredoxin reductase in response to NF-κB-promoted many antioxidant enzymes [6]. Moreover, it has been recently reported that UC patients assigned to curcumin (1,500 mg/day) for 8 weeks, significantly reduced C-reactive protein (hs-CRP), erythrocyte sedimentation rate values and enhanced the clinical outcomes of UC patients [22].

A growing body of evidence, many clinical studies indicated that there is a significant difference in the rates of clinical symptom reduction, and mucosal healing, in colic or UC patients during treatment by herbals [10, 23,24,25]. Thus, IBD treatment using curcumin will be cheap, effective and associated with safety as an accessible therapeutic approach to improving patient's quality of life. Therefore, improvement of UC parameters by the Iranian traditional "Sahj" treatment may be triggered via antioxidant and anti-inflammatory properties of these herbs rich in polyphenolic compounds as well as their multiple mechanisms of action which have been recently reported by Kamali et al. and Chandan et al. [10,26]. Besides, conventional medications with single target factors have failed in the treatment of patients

with long-term ulcerative colitis, and they also exhibit severe adverse reactions [1]. In this light, Persian medicine guide to "Sahj" therapy along with conventional therapy can attend as an effective complement in the treatment of UC. However, further studies with larger sample size in an enhanced setting, are needed to confirm multiple target therapy and/or synergistic combination like as "Sahj" formulation. We hope that the present study and the Persian medicine "Sahj" formulation will provide beneficial strategy for the treatment of UC.

Table 3. general health before and after 4 weeks' treatment by the "Sahj" capsule

Time	Very well N (%)	Slightly below par N (%)	Poor N (%)	Very poor N (%)	*P* value
Before	-	15 (50%)	14 (46.7%)	1 (3.3%)	
After treatment	15 (50%)*	14 (46.7%)	1 (3.3%)*	-	4.29E10

N: Number of patient.
* Significantly different, $P< 0.05$; when compared with before "Sahj" treatment.

Declaration of competing interest

There are no conflicts of interest.

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