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Original Research

Formulation, Standardization, and Evaluation of the Anti-Colitis Activity of Qurs-e Gol, a Persian Polyherbal Formulation in Acetic Acid-Induced Colitis in Rats

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Abstract

Inflammatory bowel disease (IBD) is a long-life disease with increasing global incidence, especially in children. In addition to the economic and social costs imposed by this disease, the progression of the disease over time can also increase the risk of developing colon cancer. Recent studies have shown the positive effects of natural products, especially herbal medicines, in controlling the signs and symptoms of IBD. This study explored the anticolitic effects of Qurs-e Gol, a traditional polyherbal formulation in Persian Medicine, in male Wistar rats suffering from colitis induced by acetic acid. *Rosa damascena* Mill. (Damask rose), *Rumex conglomeratus* Murray (clustered dock), starch, *Senegalia senegal* (L.), Britton gum (gum Arabic), and *Astragalus* L. subgenus. Tragacanth gum (gum Tragacanth) was separately ground, sifted, and then mixed with suitable excipients to formulate Qurs-e Gol tablets. To induce colitis, animals were administered 4% acetic acid intrarectally. The 14-day experiment involved six groups of rats, including a sham group that received normal saline; a second group that received normal saline postinduction; a third group that received dexamethasone postinduction; and three treatment groups that received Qurs-e Gol at doses of 200, 400 and 800 mg/kg for 14 days. Macroscopic evaluation revealed that, compared with the control, Qurs-e Gol at doses of 400 and 800 mg/kg significantly reduced inflammation and ulcers (p<0.001), with effects similar to those of dexamethasone. Microscopic examination of colon tissue confirmed these results, revealing a decrease in lesion depth with the 400 and 800 mg/kg doses (p<0.001). The most significant reduction in serum tumor necrosis factor (TNF-α) levels was noted at 800 mg/kg (p< 0.001), although the 200 and 400 mg/kg doses were also effective (p<0.01). This study highlights the effectiveness of Qurs-e Gol, a traditional Persian polyherbal remedy, in easing colitis symptoms in rats, resulting in impressive anti-inflammatory effects. When administered at doses of 400 mg/kg and 800 mg/kg, there was a notable decrease in inflammation, ulcers, and lesion depth, with results that rival those of dexamethasone. Moreover, the most significant decrease in the serum TNF-α concentration occurred at the highest dosage. These results indicate that Qurs-e Gol might be a promising natural option for treating ulcerative colitis, and further research in both animal and human trials is needed to fully explore its therapeutic potential.

Keywords: Ulcerative colitis; Inflammation; Traditional Persian medicine; Damask rose

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Introduction

Inflammatory bowel disease (IBD) is a long-life disease with increasing global incidence, especially in children. IBD is a term that primarily refers to two main conditions: a) Ulcerative colitis which involves inflammation and ulcers in the lining of the colon and rectum. b) Crohn's disease that causes inflammation in the digestive tract lining, which can affect any area from the mouth all the way to the anus [1]. While both conditions share some similar symptoms, there are also distinct differences. General symptoms of IBD include diarrhea, one of the most frequent symptoms, often accompanied by an urgent need to defecation, abdominal pain and cramping, following the inflammation caused by the disease, rectal bleeding, showing up as blood in the stool, fatigue, and weight loss. Some symptoms are more common in ulcerative colitis including the urgency to defecate and tenesmus. Symptoms may also differ based on where the inflammation is located and how severe it is. There can be extraintestinal manifestations as well, such as arthritis, skin issues, and eye inflammation [2].

A study investigating the incidence of IBD in the pediatric population has shown that it increased from 9.4 per 100,000 in 1994 to 13.2 per 100,000 in 2009 (p<0.0001) [3]. Reducing the age of onset means that patients spend more time with the disease and its complications. In addition to the economic and social costs imposed by this disease, the progression of the disease over time can also increase the risk of developing colon cancer. Thirty-year engagement with IBD makes the incidence rate of colorectal cancer approximately 18% [4]. However, more effective drugs that have recently been added to the medical regimen for IBD have decreased the risk of colorectal cancer and increased the surveillance of these patients [5].

Medications play a vital role in managing IBD, bringing several important benefits to the table. One of the main perks is their ability to cut down inflammation in the digestive tract. When inflammation decreases, patients often experience relief from symptoms like diarrhea, rectal bleeding, and abdominal pain, which can greatly enhance their overall quality of life [6]. Nevertheless, it is not entirely positive; medications for IBD present their own array of challenges. A major concern is the potential side effects, which can differ based on the specific medication. Corticosteroids serve as an effective means to diminish inflammation and attain short-term remission; however, prolonged use may result in various adverse effects, including weight gain, mood fluctuations, an increased susceptibility to infections, and the potential development of osteoporosis. Additionally, it is important to note that no single medication is a one-size-fits-all solution for everyone with IBD. People can react quite differently to various treatments, and finding the right medication or combination often requires some trial and error. This underscores the fact that medications might not be the best fit for every symptom or every patient. On top of that, the financial aspect of IBD treatment can be quite heavy [7]. Many of the medications, especially the newer biologic therapies, come with a hefty price tag. These costs can encompass not only the medications themselves, but also the expenses related to their administration (like infusions), monitoring, and follow-up care. The steep cost of treatment can pose significant hurdles for patients trying to access and stick to their prescribed therapies [8]. Although IBD is worldwide prevalent, its socioeconomic impacts on low- and middle-income countries are more destructive [9]. Therefore, finding inexpensive, more potent medications with fewer adverse effects is the way to control this disease.

Recent studies have shown the positive effects of natural products, especially herbal medicines in controlling the signs and symptoms -and even in improving the pathological factors- of IBD. The results of using herbal therapy for managing IBD look quite encouraging. This approach works through several mechanisms, including blocking leukotriene B4, providing antioxidant benefits, modulating the immune system through nuclear factor-kappa B (NF-κB), and offering antiplatelet effects. In addition, it is worth noting that there have not been any reported negative side effects linked to this treatment [10]. There are several studies indicating the activity of different plants against IBD. Rahimi et al. in a meta-analysis showed that different herbal medicines including *Andrographis paniculata*, *Boswellia serata*, and *Plantago ovata* are comparable with 5-aminosalicylic acid (5-ASA) in the induction of clinical responses and remission. Nevertheless, it was only the Chinese polyherbal formulations that demonstrated significant results, surpassing even those of 5-ASA medications [11]. When it comes to treating ulcerative colitis, *Aloe vera* L. gel, *Triticum aestivum* L., *Andrographis paniculata* (Burm.f.) Nees extract, and enema of a Chinese polyherbal formulation, Xilei-san have shown to be more effective than a placebo in helping patients achieve remission or a positive clinical response. Moreover, curcumin has been found to be better than a placebo at maintaining remission. *Boswellia serrata* Roxb. gum resin and *Plantago ovata* L. seeds have effectiveness that rivals mesalazine, while *Oenothera biennis* L. has relapse rates that are quite similar to those of omega-3 fatty acids [12] .

Traditional Persian Medicine (TPM) as one of the oldest schools of medicine has well-described many such natural products. This information has been documented during a 1000-year period in a pile of manuscripts and books, many of which such as Avicenna's Canon of Medicine and Rhazes's Al-Hawi are now well-known worldwide [13,14]. In TPM therapeutic books, a comprehensive list of foods, monoherbal and polyherbal drugs has been listed under the title of each disease to introduce nutrition and pharmacotherapy. Based on this information, many investigations –including both experimental and clinical- have been done recently to examine the efficacy and safe-

ty of TPM treatments [15-17].
In TPM, IBD is known as "*Sahaj ul-Am'a*". From the point of view of TPM, this disease is caused by some harmful substances, which are mainly endogenous, called abnormal humors. These substances cause scratches and wounds on the surface of the intestines by causing tissue damage. This damage can develop to cover the entire intestinal wall, causing perforation of the intestinal wall [18]. TPM sources state that the destructive effect of these substances can be controlled by medicaments such as Qurs-e Gol.
Qurs-e Gol (literally means rose tablet) is one of the traditional drugs that has been frequently mentioned and prescribed for IBD [19,20]. It consists of *Rosa damascena* Mill. (damask rose petals), *Rumex conglomeratus* Murray (clustered dock) fruits, starch, gum Arabic, and gum Tragacanth. Recent investigations have shown antioxidant and anti-inflammatory activities for most of these ingredients [21-23]. However, there has been no investigation on the whole combination. *R. damascena*, commonly known as the damask rose, has a rich history of being used for medicinal purposes. Researchers have looked into various products and extracted compounds from its flowers, petals, and hips (those are the seed pods), studying their effects through numerous *in vivo* and *in vitro* experiments [24]. Numerous compounds derived from *R. damascena* include terpenes, glycosides, flavonoids, and anthocyanins. A significant therapeutic advantage of *R. damascena* in traditional medicine is related to its capacity to alleviate inflammation by suppressing the mediators associated with acute inflammation [25,26]. Just like many aromatic and medicinal plants, it has some impressive antioxidant properties. The key players behind these natural antioxidants are phenolic compounds, found in different parts of the plant, such as the fruits, vegetables, seeds, leaves, roots, and bark [27]. In a study by Kumar et al. (2009), they looked into the antioxidant properties of *R. damascena* extract, comparing it to the well-known antioxidant L-ascorbic acid using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free-radical assay. The results showed that *R. damascena* has impressive antioxidant activity. Additionally, this plant is a great source of vitamin C, which is celebrated for its antioxidant and anti-inflammatory perks [28].
A research study carried out by Kilic et al. in 2013 revealed that *R. conglomeratus* is rich in naturally occurring antioxidant compounds and exhibits significant antioxidant activity. This activity appears to arise from its capacity to neutralize free radicals and bind to metals. The researchers concluded that *R. conglomeratus* has the potential to serve as a valuable source of antioxidants [29]. Also a review study by Vasas et al. (2015) showed that some *Rumex* species have emerged as a good source of traditional medicine for the treatment of inflammation [30].
Research by Jhundoo et al. (2021) highlighted a significant anti-inflammatory effect of acacia and guar gum in a mouse model of experimental colitis. The findings showed that when these gums were combined with 5-ASA, there were generally better outcomes across various pathophysiological measures. Important indicators, such as myeloperoxidase (MPO) levels and the activity of NF-κB in the *in vivo* model, revealed a strong anti-inflammatory response linked to acacia. With their gentle anti-inflammatory properties in experimental colitis, acacia and guar gum offer exciting possibilities for delivering 5-ASA to the colon in the treatment of IBD. This potential could pave the way for creating a combination dosage form that boosts therapeutic effectiveness [31].
This study aimed to investigate the anti-ulcerative colitis activity of a traditional formulation, Qurs-e Gol, on acetic acid-induced colitis in rats. It also aimed to update the dosage form of this traditional formulation and to standardize it using pharmaceutical techniques.

Methods

Materials

The components of the Qurs-e Gol including damask rose (*Rosa damascena* Mill.), rumex (*Rumex conglomeratus* Murray), starch, gum Arabic, and gum Tragacanth were prepared from Tehran botanical market and authenticated by the Herbarium of School of Pharmacy, Alborz University of Medical Sciences, Karaj, Iran. Samples of each of the plants were kept in the Herbarium of Faculty of Pharmacy, Alborz University of Medical Sciences, Karaj, Iran (Herbarium number: Rosa damascena: R01-003; Rumex conglomeratus: R01-012; Gum Arabic: V01-014 ; Gum Tragacanth: A01-006). Microcrystalline cellulose (Avicel PH 101) was obtained from FMC Biopolymer (Ireland); Colloidal silicone dioxide was obtained from Mingtai Chemical (Taiwan); Lactose monohydrate 200M, Polyvinylpyrrolidone (PVP, k30) and magnesium stearate were obtained from Merck (Germany).

Tablet Preparation

Herbal components were separately ground and sifted, and then mixed using the geometric mixing method. Then, the mixture of herbal powders was mixed with lactose, PVP, and microcrystalline cellulose (Avicel 101). A cubic mixer (Erweka, Germany) was used to mix the powders. The mixing time was 10 minutes. Thereafter, magnesium stearate and colloidal silicon dioxide as lubricating agents were mixed with the previous mixture for 5 minutes. Finally, a single punch tableting machine (Korsch, Germany) was used to press powders. Each tablet of this formulation contains 500 mg of herbal powders.

Weight variation test

A weight variation test was performed according to 44th edition of the United State Pharmacopoeia (USP 44) [32].

Briefly, 20 tablets were weighed individually and the average mass was calculated. Then, the error for each tablet was calculated by using the equation:
% Error for a tablet= (difference between actual weight and average tablet weight/ average tablet weight) × 100

Hardness test
A hardness tester (Erweka, TBH30MD, Germany) was used to analyze the tablets' hardness. Ten tablets were taken for this measurement and the test was performed according to pharmacopoeial standard [32].

Friability test
The friability of the prepared tablets was determined by using a friability tester (Erweka, Germany). Briefly, ten tablets were randomly taken and de-dusted. De-dusted tablets were accurately weighted, then placed in the friability apparatus, after 4 minutes of rotating at 25 rpm tablets were deducted and weighted again. Mass loss was calculated the by initial mass of the tablets minus the final mass of the tablets and the following equation was used to calculate the percent of friability [32].
% Friability= (loss of mass/initial mass) × 100

Disintegration test
The disintegration test was performed according to USP 44 [32]. Briefly, six tablets were placed individually in each tube of the disintegration apparatus. The disintegration apparatus consists of six tubes with baskets at the end of each tube. Each basket was moved up and down by the machine inside the 37°C water to disintegrate the tablets. The disintegration time of the tablets was calculated.

Determination of total phenolic content (TPC)
The total phenolic content of the Qurs-e Gol tablet was determined by the Folin–Ciocalteu method as previously described [33]. Briefly, 10 tablets were crushed, powdered, and mixed with a laboratory Mortar and pestle. One gram of the powder was mixed with two 2 mL of ethanol 70% in two separate steps to extract the phenolic contents of the tablets. After filtration, 2 mL of distilled water and 0.25 mL of Folin– Ciocalteu reagent were added to 0.2 mL of this ethanolic extract and the mixture was shaken well. After 2 minutes, 0.5 mL of sodium carbonate solution (20% w/v) was also added to the mixture, and the final volume was adjusted to 5 mL by adding distilled water. The samples were mixed thoroughly and allowed to stand at ambient temperature for 2 hours until the characteristic blue color developed. The absorbance of the reaction mixture was measured at 760 nm. Quantification of TPC was based on a standard curve generated with gallic acid at 760 nm using the following equation:
Abs = 0.98C+0.017
Where Abs is absorbance and C is the concentration (mg/mL) of gallic acid. All tests were conducted in triplicate and averaged. The results were expressed as a percentage of TPC in the sample as gallic acid equivalents.

Animal model and experimental groups

Animals
Adult male Wistar rats (225–275 g) were obtained from the breeding colony of the animal house of Faculty of Pharmacy, Alborz University of Medical Sciences, Karaj, Iran. The animals were accommodated in cages containing six individuals each, with unrestricted access to food and water. They were maintained under a 12-hour light/dark cycle at a temperature of 23 ± 1 °C. This study was conducted in compliance with ethical standards and guidelines for animal experimentation. The research protocol was approved by the Institutional Animal Care and Use Committee (IACUC) (ethical code: IR.IAU.PS.REC.1400.392). All methods employed in this study are reported in accordance with the ARRIVE guidelines (https://arriveguidelines.org) for the reporting of animal experiments, ensuring the transparent and comprehensive reporting of relevant experimental details.

Animal model and experimental groups
Before inducing colitis, all the rats were kept without food for 24 hours, but they had access to water. Once that time was up, the animals were put under anesthesia through an intraperitoneal injection of a mix that included 100 mg/kg of ketamine and 5 mg/kg of xylazine. After they were anesthetized, induction of colitis in male Wistar rats was performed by 1 mL intrarectal administration of 4% acetic acid. To prevent any leakage of the solution, the rats were placed in a supine Trendelenburg position (essentially head-down).
Twenty-four hours after induction of colitis, traditional formulation of Qurs-e Gol was suspended in normal saline and administered orally for 14 days. In the dexamethasone group, the drug was administered intraperitoneally for 14 days. Rats were randomized into 6 groups, each containing 6 animals (n=6):
Group I, Sham group: healthy rats without any colitis were treated with 1 mL normal saline (gavage).
Group II, Control group: Colitis induced by 4% acetic acid, rats were treated with 1 mL normal saline.
Group III, Dexamethasone: Colitis induced by acetic acid (4%), rats were treated with Dexamethasone 1 mg/kg intraperitoneally.
Group IV (Q-200): Colitis induced by acetic acid (4%), Qurs-e Gol was administrated at 200 mg/kg via gavage.
Group V (Q-400): Colitis induced by acetic acid (4%), Qurs-e Gol was administrated at 400 mg/kg via gavage.
Group VI (Q-800): Colitis induced by acetic acid (4%), Qurs-e Gol was administrated at 800 mg/kg via gavage.
Twenty-four hours after the last intervention, blood samples were taken from the heart to measure serum TNF-α, and then, animals were sacrificed to remove their colon for histopathologic studies. The tissue was fixed in 10% for-

malin until the day of the study. The blood serum was separated and stored in a -40°C freezer until the day of the study.

Evaluation of ulcer index

Macroscopic scoring was performed under a magnifying glass by an independent observer by means of the following criteria: 0, no macroscopic modifications; 1, localized hyperemia but no ulcer; 2, linear ulcer with no critical inflammation; 3, linear ulcer with inflammation at one location; 4, two or more sites of ulcer and inflammation; 5, two or more locations of ulcer and inflammation amplifying over 1 cm.

Microscopic Evaluation of ulcer

For microscopic characterization, the colon tissue was settled in phosphate-buffered formaldehyde, inserted in paraffin and 5 µm sections were provided. The tissue was stained with hematoxylin and eosin and assessed by a light microscope, being scored in a blinded way by a master pathologist. A histological grading scale was utilized and microscopic parameters were graded from 0–3 (crypt damage, inflammation seriousness, and irritation degree); 0, no alter; 1, mild; 2, direct; and 3, extreme. Histological assessment and scoring were performed by using a Zeiss® magnifying lens prepared with an Olympus® color video camera for digital imaging. Samples were prepared in a blindness manner by assigning a number to each sample.

Ulcer depth assessment

The tissue slides were prepared by hematoxylin and eosin staining. Two slides per group were evaluated. The depth of the wound at the middle and edges of the sample was photographed at a magnification of 40. Afterwards, the wound depth was calculated using Motic software which has a precision of micrometers. The average sizes for each group were calculated and finally, the groups were compared.

Evaluation of TNF-α in plasma

In order to evaluate TNF-α levels, blood samples were obtained from the cardiac apex. The blood samples were then centrifuged at 2000 rpm for 10 minutes, and 50 µL of the supernatant plasma was added to each well of a 96-well plate. A TNF-α kit (Karmania Pars Gen, Iran) was used to measure the absorption at 450 nm, and the amount of TNF-α was calculated accordingly.

Statistical analysis

The data were analyzed via SPSS version 21 software. To compare the groups, one-way analysis of variance (ANOVA) was employed. For qualitative data, a nonparametric statistical approach, specifically the Kruskal–Wallis test, was used. A significance level of $p < 0.05$ was established for this study.

Results

Formulation and standardization

Ingredients of Qurs-e Gol and the percentage of each ingredient in tablets are presented in table 1. The average weight of the 20 tablets was 1.04 ± 0.03 g. Table 2 shows the weight and the error percentage of each tablet. According to this table, no tablet's weight deviates from the average weight by more than 5%; thus, all tablets passed this test successfully. Figure 1 shows the appearance of formulated Qurs-e Gol tablets.

The average amount of tablet hardness was 8.56 ± 1.59 KP. This showed acceptable hardness to withstand other handling abrasions. The friability percentage was 0.83%, which was lower than 1%, indicating acceptable friability. Tablets disintegrated in less than 30 minutes, with an average disintegration time of 26.3 ± 1.7 minutes. Based on the Folin–Ciocalteu reaction, total phenolic compounds were measured at 0.02% (w/w) based on the gallic acid standard.

Evaluation of ulcer index

The results of macroscopic colon damage scoring are shown in table 3. In the sham group, no injuries were observed, and the respective data for surface area, severity, and wound index were zero. Meanwhile, the negative control group had the highest rates of ulceration, adhesion, and thickening of the intestinal wall. Moreover, the score was statistically different from all groups, except for Q-200 ($p<0.001$). In the Dexamethasone, Q-400, and Q-800 groups, significant decreases in the total macroscopic score were observed compared to the control group ($p<0.001$).

Microscopic evaluation of ulcer

In the sham group, no pathological or histological damage was observed. The mucosal layer, submucosa, and

Figure 1. The appearance of one-gram tablets of Qurs-e Gol.

colon muscles in this group were evaluated as completely healthy and normal. In the control group, colon mucosa, necrosis, severe intracellular inflammation, edema, bleeding, and congestion of the entire wall (mucosa, submucosa, muscle, and serosa) were observed along with damaged glands. In the Dexamethasone group, moderate inflammation was observed in the mucosal layer. In the Q-200 group, moderate focal inflammation was detected, along with a number of moderately damaged glands. In the Q-400 group, moderate inflammation was observed in the mucosal and submucosal layers. The intracellular glands were slightly damaged. Finally, in the Q-800 group, moderate central inflammation and healthy intracellular glands were observed (Figure 2).

Ulcer depth assessment

Exposure to intracolonic acetic acid led to ulcers with a mean depth of 250 μm in the control group. Ulcer depth was significantly lower in Dexamethasone, Q-400, and Q-800 when compared to the control group (p<0.001); while no difference was observed in Q-200 in comparison with the control (Figure 3).

Evaluation of TNF-α in plasma

Plasma TNF-α levels were significantly increased in the control group compared to the sham (p< 0.001). Administration of Qurs-e-Gol in all three doses resulted in a significant decline in TNF-α levels compared to the control group (p<0.001). Likewise, in the Dexamethasone group, the TNF-α level showed a remarkable decrease in comparison with the control group (p<0.001). Furthermore, no significant differences were detected between the treatment groups and the Dexamethasone group (Figure 4).

Table 1. Ingredients of Qurs-e Gol and their percentage in each tablet

Tablet ingredients	Percentage in formulation	Herbarium authentication code
Rosa damascena Mill.	14	R01-003
Rumex conglomeratus Murray	14	R01-012
Gum Arabic	7.5	V01-014
Gum Tragacanth	7.5	A01-006
Starch	7.5	---
Lactose monohydrate 200M	34	---
Microcrystalline Cellulose (Avicel® PH 101)	11	---
Polyvinylpyrrolidone (PVP, k30)	3.5	---
Magnesium Stearate	0.8	---
Colloidal silicone dioxide (Aerosil®)	0.1	---

Discussion

With increasing attention given to traditional Persian medicine in Iran, research on traditional Persian polyherbal formulations has increased significantly in the last decade. A significant number of pharmaceutical studies, as well as animal pharmacological studies and clinical trials, have been published on Persian herbal and traditional products. Although such studies are still lacking in the field of gastrointestinal diseases, especially IBD; these few studies have yielded promising results. Animal studies on traditional Persian formulations have shown considerable results on experimental colitis [34,35].

Randomized controlled trials (RCTs) have confirmed the effectiveness of single and compounded drugs on inflammatory bowel disease. For instance, *Zataria multiflora* Boiss., *Artemisia dracunculus* L. (commonly known as tarragon), and *Ailanthus altissima* Mill. Swingle, all frequently prescribed in TPM have been previously explored for their impact on IBD. *Z. multiflora*, traditionally used to treat digestive issues, has shown promise in easing symptoms of ulcerative colitis and lowering inflammatory markers [36]. Likewise, tarragon, which is utilized in traditional Persian medicine for a range of ailments, has demonstrated benefits in reducing the severity of disease in experimental models of ulcerative colitis, showcasing the promise of these herbal remedies in managing IBD [37]. The protective benefits of *A. altissima* extract for ulcerative colitis in rats have been demonstrated, confirming its traditional role in Persian medicine. This plant has a long history in ancient Persian medicine, where it was used to address a range of health problems, such as dysentery and diarrhea, highlighting its promising therapeutic potential for gastrointestinal issues [38].

In a preliminary before-and-after clinical trial on the effectiveness of a polyherbal traditional Persian formulation, *Maqliasa*, in patients with moderate to severe colitis, 28 days of consumption of this drug significantly improved the signs and symptoms of the disease, including diarrhea, hematochezia, and abdominal pain (or cramping). Moreover, *Maqliasa* improved the patients' general well-being and reduced the need for anti-diarrheal medications [39]. Two different TPM polyherbal formulations, *Ramak* and *Sahj*, were also examined for their anti-colitis activities in RCTs, both of which reduced the symptoms of ulcerative colitis [40,41]. Therefore, it appears that focusing on TPM polyherbal formulations for anti-colitis treatment would be beneficial. The mechanical properties of pharmaceutical tablets are really important factors that usually make up a manufacturer's specifications. These properties can be measured through tablet hardness, which is more technically known as crushing strength, and the friability

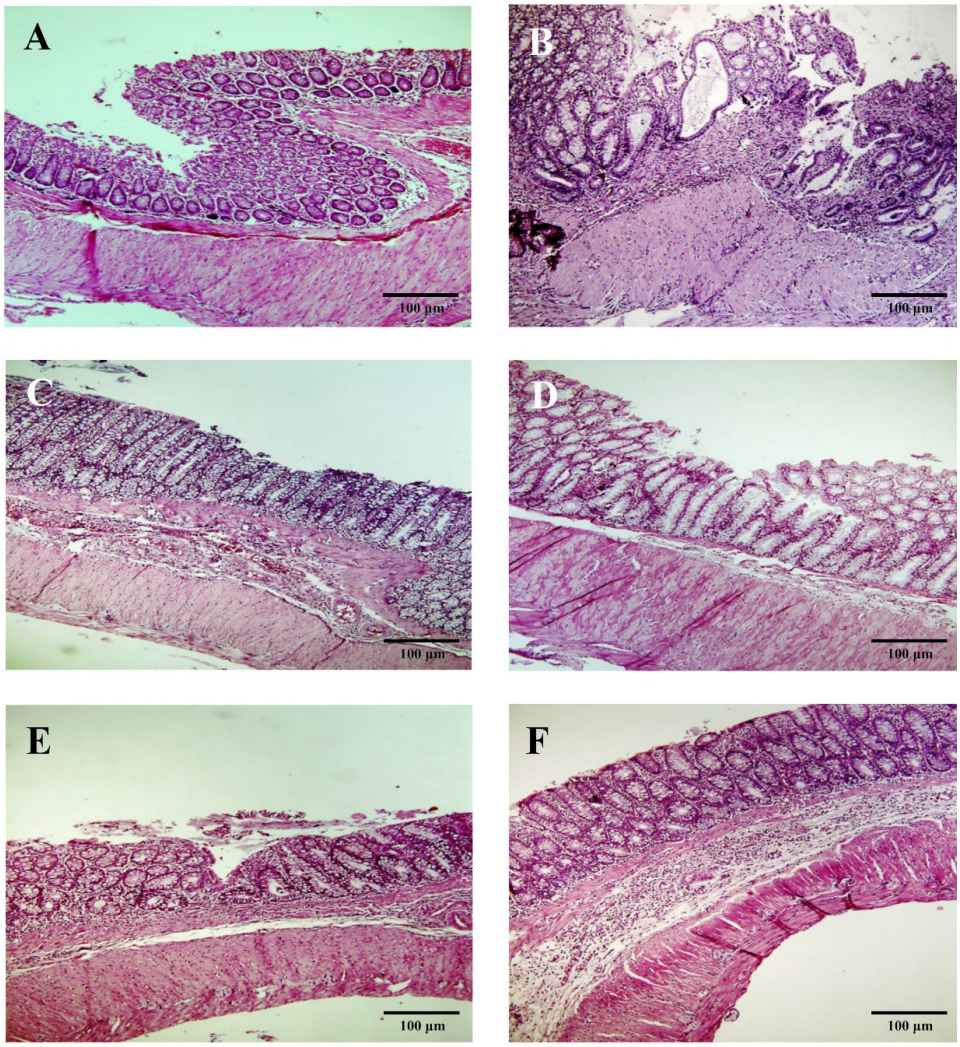

Figure 2. Microscopic illustration of rat colon tissue of different groups with H&E staining. A) Sham; B) Control; C) Dexamethasone; D, E, and F) Q-200, Q-400, and Q-800: the groups received 200, 400, and 800 mg/kg of traditional formulation of Qurs-e Gol.

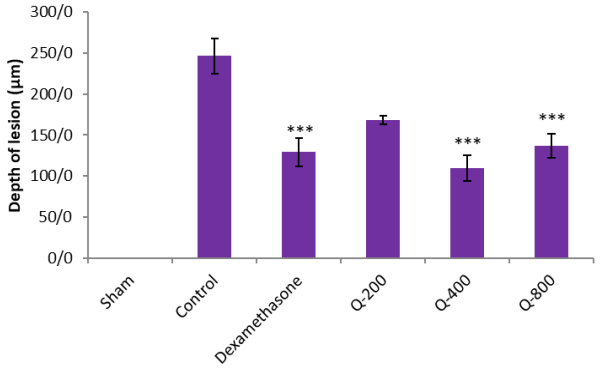

Figure 3. Depth of ulcers in the colon of rats with colitis. The results showed that the polyherbal formulation, Qurs-e Gol, at the doses of 400 and 800 mg/kg had the best wound healing activity comparable to dexamethasone. Significant differences in comparison with the control group are presented as *** (p<0.001).

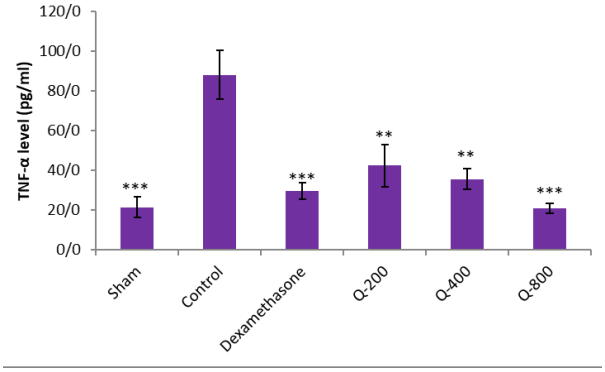

Figure 4. Plasma TNF-α levels of rats with colitis in different groups. The results showed that the polyherbal formulation, Qurs-e Gol, at the dose of 800 mg/kg had the best anti-inflammatory activity among the other two doses, which was comparable to dexamethasone. Significant differences vs. control were presented as *** (p<0.001) and ** (p<0.01).

Table 2. Weight and error percent of each tablet

Tablet number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Weight (g)	1	1.07	1.05	1.06	1.04	1	1.08	1.08	1.08	1	1.04	1.05	1.01	1.07	1.06	1.02	1.07	1	1.01	1
Error (%)	3.80	2.93	1.01	1.97	0.05	3.80	3.90	3.90	3.90	3.80	0.05	1.01	2.84	2.93	1.97	1.88	2.93	3.80	2.84	3.80

Table 3. Colon damage scoring in the macroscopic study

Groups[a]	Score (Mean ± SEM)
Sham	0.0 ± 0.0
Control	3.7 ± 0.75###
Dexamethasone	1.5 ± 0.22***
Q-200[b]	3 ± 0.40
Q-400	1.2 ± 0.25***
Q-800	1.0 ± 0.2***

*** Significant difference vs. control ($p < 0.001$)
Significant difference vs. sham ($p < 0.001$).
[a] All groups except the Sham group received 1 ml of acetic acid 4% intrarectally for colitis induction.
[b] Intervention groups receiving Qurs-e Gol:
Q-200: 200mg/kg traditional formulation of Qurs-e Gol.
Q-400: 400mg/kg traditional formulation of Qurs-e Gol.
Q-800: 800mg/kg traditio

of the tablets. Crushing strength gives us a sense of how durable the tablet is; while friability shows how prone it is to damage. Both of these aspects are key in figuring out how well the tablets can withstand breakage and wear during production and handling [42]. The standards set by pharmacopoeias for crushing strength largely depend on what the tablet is meant for; while for friability, conventional compressed tablets that lose less than 1% of their weight during testing are typically considered acceptable [43].

The analysis of weight variation showed uniformity, as it was found through calculation that the mean tablet weight was 1.04 ± 0.03 g and that no single tablet had a weight deviation above 5% from this value; thus, fulfilling the requirements for USP 44 standards. The tablets had satisfactory hardness, as reflected by a total reading of 8.56 ± 1.59 KP, signifying adequate mechanical strength to survive handling. The friability test results revealed a minimal percentage of 0.83%, well below the 1% limit, suggesting minimal loss of tablet mass during handling and transportation.

In addition, disintegration time is crucial for making sure that the drug is released quickly and absorbed by the body as it should be. This measure tells us how fast and effectively a tablet breaks down into smaller particles in a liquid environment, which simulates conditions in the gastrointestinal tract [44]. The crushing strength and friability can negatively impact the disintegration time of the tablets, so it is important to assess these factors together [45]. The results of this study showed that the Qurs-e Gol tablet not only has the right hardness and friability, but also has an adequate disintegration time. The disintegration test indicated that the tablets disintegrated within the specified time, with a mean disintegration time of 26.3 ± 1.7 minutes.

To our knowledge, this is the first study to investigate the therapeutic effects of another TPM polyherbal formulation, Qurs-e Gol, on IBD. The mechanism of action of these medications is described in TPM manuscripts with processes such as reducing inflammation, clearing harmful substances from the walls of the intestines, detoxification, accelerating the repair processes, and forming a protective layer on the mucous membranes of the intestines [46]. Based on our results, Qurs-e Gol significantly reduced the tissue damage of the colon, the depth of lesions, and serum TNF-α. Perhaps all components of Qurs-e Gol play a role in this anti-colitis activity.

Previously, studies showed that *R. damascena* hydroalcoholic extract reduces inflammation in acetic acid-induced colitis in rats [21]. This medicinal plant also showed a therapeutic effect in IBD patients [47]. Flavonoids and polyphenols have been identified as the responsible ingredients for the anti-inflammatory, antioxidant, and anti-ulcer effects of Damask rose [21,47].

Several studies have been conducted on the chemical compositions of different species of the genus *Rumex*. These studies showed that this genus is rich in polyphenols, as well as terpenes and terpenoids which have strong antioxidant and anti-inflammatory activities [22,48]. Although there is no study on the anti-ulcer activity of *R. conglomeratus*, one study showed that the fruits of another species, *R. patientia*, have anti-ulcer activity in a

rat model of ethanol-induced gastric ulcer. In this study, the fruits of *R. patientia* inhibit ulcer formation based on macroscopic and histopathological evidence [49].

Another ingredient of Qurs-e Gol, starch, seems to have significant effects in controlling the inflammation of IBD. Qualified studies revealed that the administration of both dietary and resistant starch can reduce ileal and colonic inflammation and lesion development via interferon-gamma (IFN-γ) decrement [23]. It also provides a suitable environment in the colon by increasing the production of butyrate, maintaining a low pH in the lower parts of the colon, and inhibiting the growth of harmful bacteria [23,50]. Studies have shown that gum Arabic has anti-inflammatory and antifibrotic effects. A recent study conducted on a mouse model of colitis induced by dextran sodium sulfate, showed that gum Arabic alleviates the severity of colitis via a reduction in colonic fibrosis and transforming growth factor beta 1)TGFβ1(expression [51]. Another gum used in this polyherbal formulation was gum Tragacanth, which has recently been shown to have immunomodulatory activity [52]. Because IBD is considered a gastrointestinal immune disorder, immunomodulation may be fruitful in controlling the signs and symptoms of IBD and even its progression [53].

Overall, Qurs-e Gol appears to exert its therapeutic effects in IBD probably through a combination of anti-inflammatory, antioxidant, and immunomodulatory effects. *R. damascena* polyphenols and flavonoids assist in mitigating inflammation and oxidative stress; while *Rumex* species, being rich in polyphenols and terpenoids, provide supplementary anti-inflammatory effect. Starch assists in the regulation of gut inflammation by reducing IFN-γ levels and promoting a favorable colonic environment via increased butyrate production. Besides, gum Arabic reduces the severity of colitis via fibrosis and TGFβ1 inhibition, and immunomodulation of gum Tragacanth can be a complement to immune control in IBD. These synergistic effects suggest Qurs-e Gol eases colonic inflammation and damage with a multi-target mode of action, justifying its natural therapeutic potential in IBD.

Conclusion

In conclusion, Qurs-e Gol has considerable positive effects on the macroscopic and microscopic features of inflamed colons in rats. It also reduced serum TNF-α which means that its anti-inflammatory effect goes beyond the colon and affects the whole body. The formulation and standardization of this medicine have prepared the conditions for future trials.

Conflict of Interests

None.

Acknowledgments

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