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Ameliorating effects of *Acacia arabica* and *Ocimum basilicum* on acetic acid-induced ulcerative colitis model through mitigation of inflammation and oxidative stress

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A R T I C L E I N F O

Keywords:
Acacia arabica
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Gum Arabic
Basil seed
Acetic acid-induced ulcerative colitis inflammation
Stress oxidative

A B S T R A C T

Introduction: Ulcerative colitis (UC) is a chronic recurrent inflammatory disease of the large intestine and rectum. The disease is characterized by oxidative stress and severe inflammation. Research has shown the anti-oxidative and anti-inflammatory effects induced by consuming the *Acacia arabia* and *Ocimum basilicum*. The present study aimed to evaluate the effect of treatment with *O. basilicum* together with *A. arabica* on healing, inflammation, and oxidative stress in the course of experimental colitis in rats.

Methods: A total number of 50 male rats were selected and randomly assigned to five groups of 10 rats each. Colitis was induced in rats by enemas with a 4 % acetic acid solution. Four days after the colitis induction, the rats were orally treated for the next 4 days with saline or a combination of A. arabica and O. basilicum (1000 mg/kg) or sulfasalazine (100 mg/kg).

Results: Acetic acid-induced colitis increased the colon's macroscopic and histopathological damage scores; increased colon levels of MDA (Malondialdehyde), MPO (Myeloperoxidase), TNF-α (Tissue necrosis factor α), IL6 (Interleukin 6), and IL17 (Interleukin 17); and decreased SOD (Superoxide Dismutase), GPx (Glutathione Peroxidase), and IL10 (Interleukin 10) levels in the treated rats compared with the control group ($P < 0.001$). Overall, a combination of *A. arabica* and *O. basilicum* reduced macroscopic and histopathological damage scores ($P < 0.01$) of the colon, and MDA, MPO, TNF-α, IL6 ($P < 0.001$), and IL17 ($P < 0.01$) levels of the colon. Furthermore, it increased SOD, GPx, and IL10 levels compared to the colitis group ($P < 0.01$).

Conclusion: A. arabica and *O. basilicum* have improving effects on UC by reducing inflammation and oxidative stress.

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Practical applications

Colitis is one of the most common digestive system diseases in the world. Herbal foods can be good options for treating diseases because of their fewer side effects than common drugs. Basil seeds and Arabic gum, having anti-inflammatory and antioxidant properties, can improve inflammation and oxidative stress in colitis. Therefore, these two plant foods can be used in patients with colitis.

1. Introduction

Ulcerative colitis is a chronic inflammatory disease of the large intestine characterized by mucous membrane inflammation with an unknown cause. Numerous factors, including genetic, environmental, and immune factors (e.g., increased proinflammatory cytokines), are involved in disease occurrence [1]. The disease is associated with symptoms of dysentery, abdominal pain, and weight loss. The prevalence of this disease varies in different geographical areas. The highest prevalence has been reported in Europe and North America, which also increases in industrial areas such as Latin America and Asia [2,3]. Although the exact mechanism of this disease is unknown, the dysfunction of immunological factors is among the most critical factors. UC is associated with an increase in inflammatory cytokines such as IL-4-5-10-13 due to an increase in TH2 and other immune cells (e.g., neutrophils and eosinophils). Thus, it leads to the production of metabolites of uric acid (COX), nitric oxide (NOS), and oxygen free radicals (ROS), all playing a role in causing inflammation and mucosal damage in the intestine [4,5]. Increased abnormal ROS activity in the tissue increases inflammation, oxidative damage, and mucosal damage. Increased MPO enzyme increases ROS in iterative bowel disease (IBD) [6]. Another influential factor in this disorder is oxidative stress. It has been found that IBD is associated with an imbalance between ROS and antioxidant activity, which induces oxidative stress and excessive ROS, and a decrease in antioxidant activity [7]. Reducing antioxidant factors following an increase in oxidative stress increases disease incidence [8]. In other words, in ulcerative colitis, the activation of arachidonic acid mediators due to the non-regulation of the immune system is followed by an increase in proinflammatory cytokines such as IL-6 and TNF-α. These factors, in turn, induce an increase in MPO, MDA, and iNOS [9]. Amino salicylates such as sulfasalazine are among the drugs of choice for treating inflammatory bowel disease. These drugs are used in mild to moderate cases of the disease. Corticosteroids such as prednisone are other effective drugs in treating severe to moderate diseases [10]. Other drugs, such as antibiotics, immunosuppressive drugs (cyclosporins), and anti-tumor necrosis drugs, have also been used to treat the disease [11]. Anti-TNF treatment is one of the newest methods based on intestinal immune response and inflammatory processes. As one of the most effective drugs in this category, infliximab significantly reduces steroids and induces improvement in these patients [12]. However, none of these drugs have entirely cured the disease. Moreover, these drugs have many side effects and are costly. Thus, finding an effective treatment with fewer side effects is necessary. Today, plants are used as a suitable alternative to chemical drugs because of their fewer side effects [13–16]. The use of medicinal plants has led to the development of adequate and appropriate treatment methods in treating diseases [17–22]. A. arabica is a polysaccharide obtained from the secretions of Senegal acacia and fluid acacia [23]. The plant belongs to the Leguminosae family [24]. Pharmacologically, several effects have been mentioned for this plant including antioxidant effects, which lead to the protection of rats against liver and kidney toxicity [25]. It also has anti-inflammatory activity [26], increases anti-inflammatory cytokines such as IL-10, and decreases proinflammatory cytokines such as TNF-α [27]. Another effect of this plant is the improvement of chronic kidney diseases after reducing inflammation and oxidative stress in the gastrointestinal tract [28]. It heals ulcers [29] and has protective effects on gastric ulcers [30]. Ocimum basilicum. L is a valuable medicinal plant of the Lamiaceae family [31]. This plant has many anti-inflammatory, antioxidant, anti-microbial, anti-cancer, and anti-aging effects [32–34]. It also has liver protective and neuroprotective effects [35]. The plant is used to treat various diseases such as fever, gastroenteritis, bloody diarrhea, and depression [36]. A. *arabica* plays a role in the treatment of inflammatory bowel diseases such as ulcerative colitis [37]. Other medicinal uses of this plant include: anti-cancer [38], anti-oxidant [33], anti-diabetic [39], and anti-arthritis [40] activity. This plant is also a moderator of the immune system and a preventive factor in cardiovascular diseases [41]. As mentioned, there are various drugs to reduce the inflammation caused by UC disease, although they have many side effects [42]. The present study aims to achieve a drug with the highest efficacy and negligible side effects. For this purpose, the therapeutic effects of a combination of *A. arabica*, and *O. basilicum* in the form of gavage on an animal model of ulcerative colitis are investigated.

2. Materials and methods

The study was conducted following the Basic & Clinical Pharmacology and Toxicology Policy for experimental and clinical studies [43].

2.1. Animals

This investigation was verified with Ethical Number IR.KMU.AH.REC.1399.127 at Kerman University of Medical Sciences, Kerman, Iran. In this study, 50 male Wistar rats weighing approximately 250 g were purchased from Kerman University of Medical Sciences. The animals were kept in standard conditions at 24 ± 1 °C, light control (12 h of light: 12 h of darkness), and proper ventilation in the animal husbandry of Kerman Medical School. There was also free food and water for the animals. After adapting to the environment, the animals were randomly divided into five groups: 1) The sham group: The healthy and colitis-free rats that received saline (as a vehicle) orally; 2) the colitis group: the rats received acetic acid rectally; 3) the saline group: colitis rats that received saline (as a

vehicle) orally; 4) the drug group: rats with colitis received 1000 mg/kg body weight from the combination of Acacia arabica and basil as a gavage; and 5) the positive control group: rats with colitis received 100 mg/kg sulfasalazine orally. Each group included ten animals. Furthermore, the ethical principles of working with animals were observed in all experiment stages.

2.2. Colitis induction

The animals were kept hungry for 36 h with access to water to drain their intestines. Then, under mild anesthesia, a 2-mm plastic tube with a length of 8 cm was injected intrarectally with 4 % acetic acid. The animals in the sham group received saline instead of acetic acid. Then, to prevent acid leakage, each animal was kept down for 5 min, and then was placed separately in wire cages for 24 h. After 4 days, colitis formed in the rats [44].

2.3. 2.3Preparation and prescription of foods

According to Persian medicine sources, the herbal product is prepared in equal proportions (weight-weight proportion) from *A. arabica* powder and roasted *O. basilicum* powder. Roasted *O. basilicum* seeds are ground and passed through a 40-mesh sieve. *A. arabica* powder was purchased from the German Merck Factory, and *O. basilicum* seeds were gathered from farms in Kerman Province. *O. basilicum* seeds powder was mixed in equal proportions with *A. arabica* powder and used at a dose of 1000 mg/kg (or 1 mg/g) [42] of animal weight suspended in distilled water. The mixture was prepared fresh on the day of administration. Then, it was administered fresh immediately after preparation. This substance was administered rectally after completion (day 5 after the operation) and was given to the animal every day at 8 a.m. This process continued for about 4 days. Also, sulfasalazine, as a gold standard drug, was administered at a dose of 100 mg/kg orally.

The compounds in *A. arabica* can be measured using liquid chromatography. In a previous investigation, the bioactive compounds of *A. arabica* leaf and bark extract were detected by preparative HPLC and LC-MS methods. The results showed caffeic acid phenethyl ester, ferulic acid, 4-*p*-coumaroylquinic acid, palmitic acid, myristic acid, oleic acid, and methyl 3,4,5-trimethoxybenzoate as the main compounds of *A. Arabica* [45]. Also, the HPLC analysis of *O. basilicum* extract in a previous study revealed the presence of phenolic compounds. The amount of these compounds in ethanolic and methanolic extracts was higher than other fractions [46].

2.4. Disease activity index (DAI)

This index was calculated using the presence of 3 symptoms in animals, including weight loss, diarrhea, and anal bleeding, through the following formula. Then, occult blood in the stool was evaluated using the benzidine test [42,47].

$$DAI = \frac{\text{Body weight loss score} + Diarrhea\ score + rectal\ bleeding\ score}{3}$$

2.5. Determination of the ulcer area and ulcer index (UI)

A lens with a magnification of 10 was used to examine the surface lesions of the colon. The images were stored and examined using Image J. The UI index was measured according to the following formula [47]:

$$UI = \frac{\text{The total area of the ulcer } (\text{mm}^2)}{\text{The total area of the colon specimen } (\text{mm}^2)}$$

2.6. Macroscopic examination

All animals were anesthetized on day 9 with ketamine and xylazine and then killed. After cutting the lower abdomen, an 8-cm long piece of colon tissue was extracted from the animal's body. After a longitudinal incision, it was washed with normal saline. After calculating the weight, the tissue edema ratio of weight to length was also measured: (0) Absence of wound, (1) swelling and redness and mucosal erythema, (2) mild mucosal edema and low bleeding, (3) moderate edema and wound with bleeding, and (4) severe wound and tissue necrosis [48].

2.7. Microscopic examination

A piece of the colon was isolated and fixed in a 10 % formalin solution to examine the microscopic changes. Next, incisions with a thickness of 3–4 μm were prepared using microtomes. After preparing the slides and staining hematoxylin and eosin (H&E), the slides were examined and reported by a pathologist for the severity of inflammation and the penetration of immune cells: (−) No inflammation, (+) Mild inflammation, (++) Moderate inflammation, and (+++) Severe inflammation [49].

2.8. Oxidative stress evaluation

The colon tissue was homogenized with phosphate buffer for tests. After centrifugation, the supernatant was isolated to measure

Glutathione peroxidase (Gpx) and Malondialdehyde (MDA). MDA was also measured via spectrophotometry (TBARS) with thiobarbituric acid reactive species at 532 nm. Superoxide dismutase (SOD) activity was also measured using the kit (Navandsalamat Co.). MPO activity was evaluated by the relevant kit (Navandsalamat Co.) to assess the extent of colitis inflammation. In this process, peroxidase activity is caused by the infiltration of immune cells, including neutrophils [50].

2.9. Inflammation evaluation

In this study, the colon tissue level of TNF-α (Lot N: KPG-RTNFka; CN: KPG-RTNFk) and the levels of IL-6 (Lot N: KPG-RIL6Ka; CN: KPG-RIL6K), IL-10 (Lot N: KPG-RIL10Ka; CN: KPG-RIL10K), and IL-17 (Lot N: KPG-RI17Ka; CN: KPG-RI17K) were evaluated using enzyme-linked immunosorbent assay [ELISA] according to the kit protocol. The results were reported in Pg/mg. The colon tissue was homogenized in 6 buffer volumes of 10 mM HEPES, 10 mM KCl, 0.5 mM sucrose, 1 mM EGTA, 1 mM DTT, and 250 μl lysis buffer. The homogenates were then centrifuged at 750 g for 10 min, and the supernatant was stored at −70 °C for evaluations [51].

2.10. Statistical analysis

In this study, the results are expressed as mean ± SEM. The statistical analyses were performed using SPSS-23 software and one-way ANOVA and Tukey post hoc. Here, the significance level was considered less than 0.05 [52].

3. Results

3.1. The effects of oral administration of A. arabica and O. basilicum on body weight change, diarrhea, rectal bleeding, and hematocrit

Weight loss is a prominent feature of ulcerative colitis. In the Sham group (i.e., without colitis induction), no weight loss was observed. The body weight of the rats decreased after colitis induction. The highest weight loss was observed in the colitis and saline

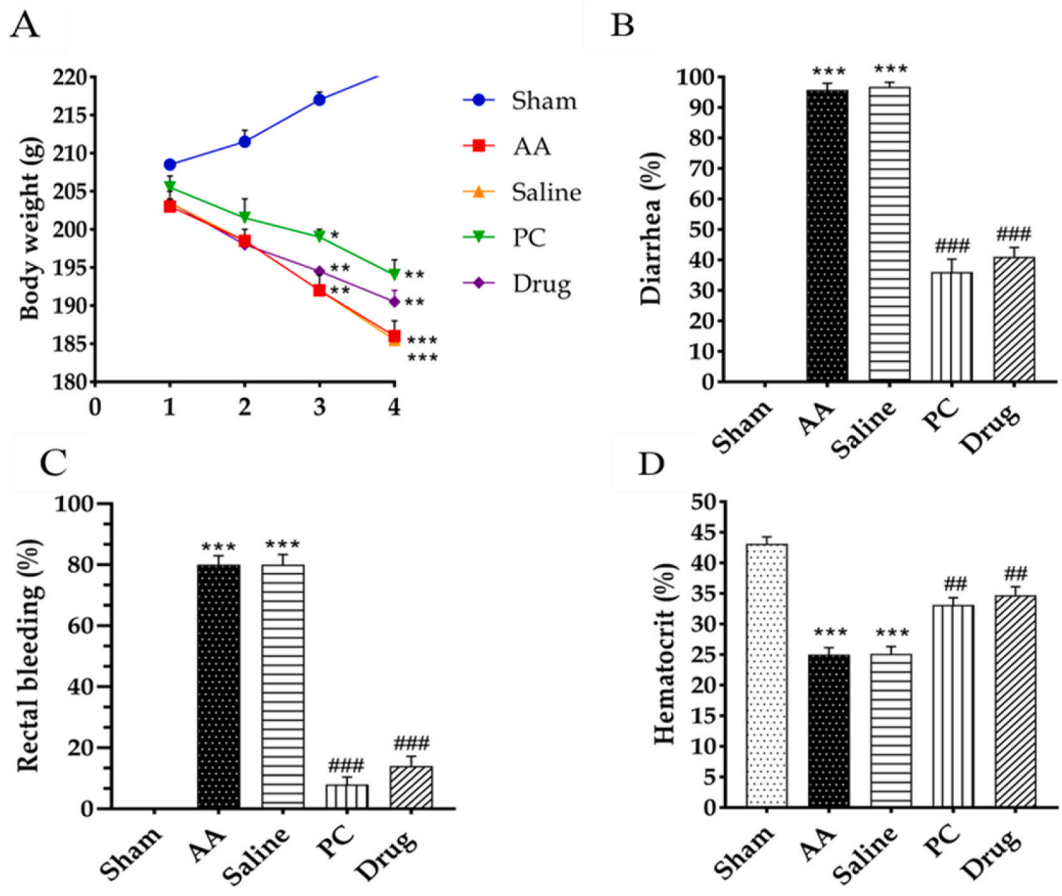

Fig. 1. The effects of gavage administration of *A. arabica* and *O.basilicum* on A: body weight, B: diarrhea, C: rectal bleeding, and D: hematocrit in rats. Sham, Sham group, AA, Acid Acetic Group, Saline, Saline group, PC, positive Control group, Drug, *A. arabica*, and *O. basilicum*. Data are shown as Mean ± SEM (n = 10 per group). *P < 0.05, **P < 0.01 and ***P < 0.001 vs. control group. ###P < 0.001 vs. AA and saline groups.

groups compared to the healthy animals ($P < 0.001$). This decrease was reversed partly in the PC and food groups ($P < 0.01$) (Fig. 1A). After the colitis induction in rats, the intestinal wall became inflamed and ulcerated. Increased inflammatory cytokines led to clinical manifestations such as diarrhea, bloody stools, edema, and necrosis. The diarrhea rate in the colitis and saline groups was significantly increased compared to the Sham group ($P < 0.001$). Also, the treatment with foods and sulfasalazine reduced the mentioned index compared to the colitis and saline groups ($P < 0.001$) (Fig. 1B). Colitis leads to bleeding or hemorrhage in the large intestine, characterized by a decrease in Hematocrit in the colitis group compared to the Sham group ($P < 0.001$). The decline rate in Hematocrit in the PC and food groups was lower than in the colitis group (Fig. 1C and D).

3.2. The effects of oral administration of *A. arabica* and *O. basilicum* on the disease activity index

The disease activity index (DAI) is one of the evaluation criteria for colitis that was measured according to the severity of clinical symptoms such as diarrhea, bleeding, and weight loss in rats. DAI showed a significant increase in the colitis and saline groups compared to the sham group ($P < 0.001$). Food administration caused a considerable decrease in the DAI score compared to the colitis and saline groups ($P < 0.001$). Sulfasalazine also caused a significant reduction in DAI ($P < 0.001$) (Fig. 2).

3.3. The effects of oral administration of *A. arabica* and *O. basilicum* on inflammatory factors

Our results showed that colitis induction increased tissue concentration of TNF-α, IL-6, and IL-17 ($P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively) and decreased IL-10 tissue concentration ($P < 0.001$) compared to the sham group. Our observations revealed that oral administration of the combination of *A. arabica* and *O. basilicum* in the treatment group reduced tissue concentration of TNF-α, IL-6, and IL-17 ($P < 0.01$, $P < 0.05$, and $P < 0.01$, respectively) and increased IL-10 tissue concentration ($P < 0.001$) compared to the colitis group. The data also disclosed that IL-17 and TNF-α concentration was significantly higher in the treatment group compared to the PC group ($P < 0.05$). Our findings also indicated that IL-10 concentration was significantly higher in the treatment group than in the PC group ($P < 0.05$) (Fig. 3A–D).

3.4. The effects of oral administration of *A. arabica* and *O. basilicum* on oxidative factors

Our results showed that colitis induction increased tissue concentration of MDA and MPO ($P < 0.001$ and $P < 0.001$, respectively) and decreased SOD and Gpx tissue concentration ($P < 0.001$ and $P < 0.001$, respectively) compared to the sham group. Our observations also revealed that oral administration of the combination of *A. arabica* and *O. basilicum* in the treatment group reduced tissue concentration of MDA and MPO ($P < 0.01$ and $P < 0.001$, respectively) and increased SOD and Gpx tissue concentration ($P < 0.01$ and $P < 0.01$, respectively) compared to the colitis group (Fig. 4A–D).

3.5. The effects of oral administration of *A. arabica* and *O. basilicum* on histopathological changes, weight/length ratio, ulcer area, and UI

Compared to the sham group, the animals in the colitis and the saline groups showed a significant increase in the total scores of histopathological changes (Fig. 6A–F), weight/length ratio of the colon (Fig. 5 A), ulcer area (Fig. 5 C), and ulcer index (Fig. 5 B) ($P < 0.001$). Treatment with sulfasalazine reduced these negative changes compared to the colitis and saline groups ($P < 0.01$, $P < 0.001$, $P < 0.001$, and $P < 0.001$, respectively). Oral administration of *A. arabica* and *O. basilicum* significantly reversed all the above indices in comparison with colitis and saline groups ($P < 0.05$, $P < 0.05$, $P < 0.01$, and $P < 0.01$, respectively) (Figs. 5 and 6).

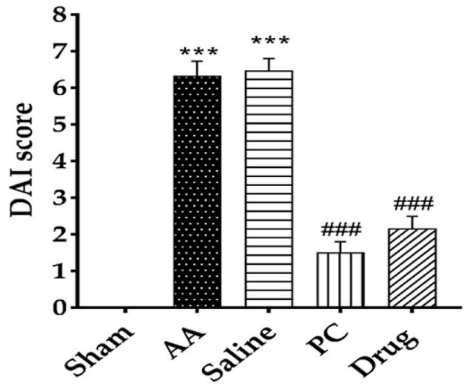

Fig. 2. The effects of gavage administration of *A. arabica* and *O. basilicum* on DAI score in rats. Sham, Sham group, AA, Acid Acetic Group, Saline, Saline group, PC, positive Control group, Drug, *A. arabica O. basilicum*. Data are shown as Mean ± SEM (n = 10 per group). ***$P < 0.001$ vs. control group. ###$P < 0.001$ vs. AA and saline groups.

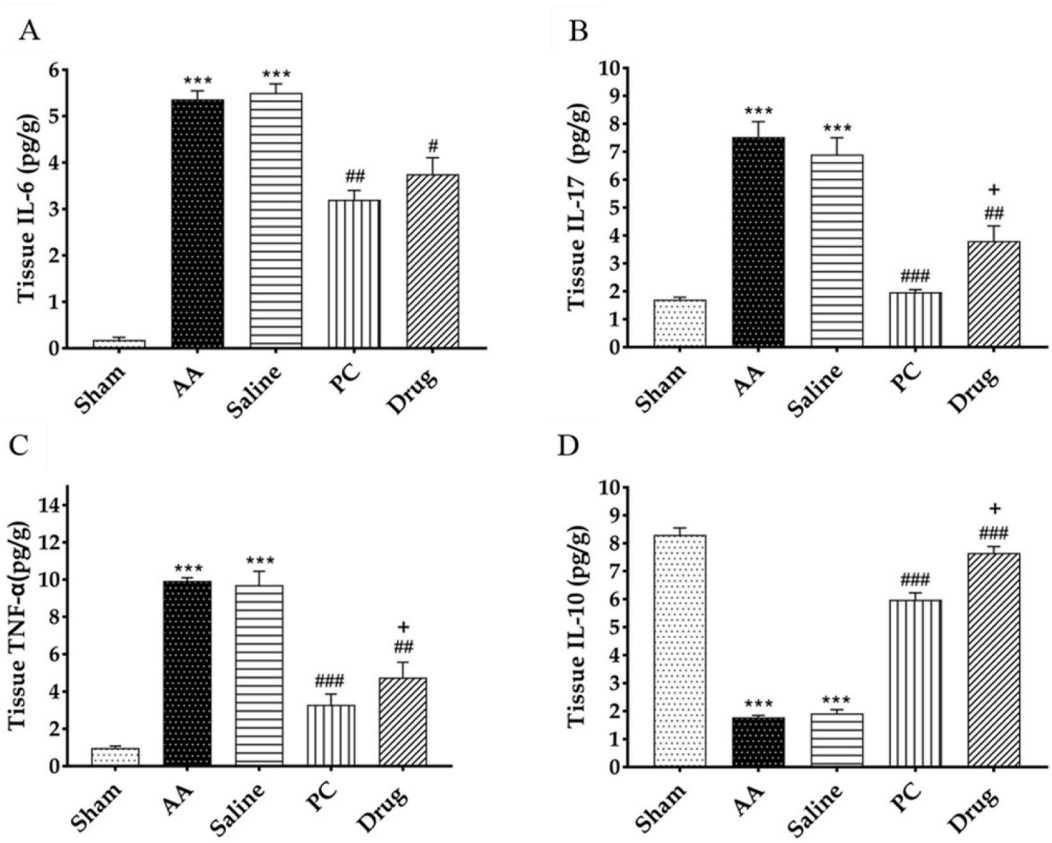

Fig. 3. The effects of gavage administration of *A. arabica*, and *O. basilicum* on A: IL-6, B: IL-17, C: TNF-α, DIL-10 in colon tissue. Sham, Sham group, AA, Acid Acetic Group, Saline, Saline group, PC, positive Control group, Drug, *A. arabica*, and *O. basilicum*. Data are shown as Mean ± SEM (n = 10 per group). ***P < 0.001 vs. control group. ##P < 0.01, ###P < 0.001 vs. AA and saline groups, + P < 0.05 vs. PC group.

4. Discussion

This study examined the anti-inflammatory, anti-oxidant, and anti-colitis effects of a combination of *A. arabica* and *O. basilicum* administered by gavage in an animal model of ulcerative colitis. After disease induction in rats, Hematocrit and weight decreased significantly. A significant increase was also observed in DAI, wound area, diarrhea index, and the weight-to-length ratio of the colon. The data also revealed that treatment with the mentioned plant composition by gavage decreased the number of macroscopic factors, including wound area, wound index, the length-to-weight ratio of the colon, enzymatic factors such as MPO, MDA, and the amount of proinflammatory cytokines such as IL-17, TNF-a, and IL- 6. Moreover, it increased antioxidants such as SOD, GPX, and anti-inflammatory cytokines such as IL-10 in rats with experimental colitis. In this study, drug delivery was performed through gavage. This method is used for rodents for more accurate delivery of volume and dose and maximum faster absorption of drugs [53]. Ulcerative colitis was also induced in rats using AA 4 %. In fact, AA acts on the epithelium, causing inflammation and tissue damage in rats [54]. Other models of colitis induction are performed using chemicals such as sodium dextran sulfate (DSS), oxazolone, and trinitrobenzene acid (TNBS) [55]. Although it was not possible to extract the effective ingredients of the combination of these two plants, other studies have pointed their therapeutic effects. *O. basilicum* is a valuable medicinal plant with many beneficial effects, including anti-inflammatory, antioxidant, anti-microbial, anti-cancer, and anti-aging properties [34]. Benedec et al. demonstrated the anti-inflammatory effects of *O. basilicum* [56]. Adel F. Ahmed et al. also confirmed the antioxidant properties of *O. basilicum* L [33]. Phenolic compounds present in the *O. basilicum* plant induce antioxidant properties [57]. Selvakkumar et al. reported declined levels of cytokines and proinflammatory mediators upon administration of *O. basilicum* [58]. Rashidian et al. examined the animal model of acetic acid-induced colitis. The results showed that basil administration in specific doses reduced the number of oxidative factors and UI and UA indices [59]. Many other studies have also reported this plant's anti-inflammatory and antioxidant effects [37,60,61].

A. arabica has several benefits, including antioxidant, antibacterial, and anti-inflammatory effects [62]. It also affects lipid metabolism, especially animal cholesterol reduction [25]. Babiker et al. examined the effect of *A. arabica* on liver function. These authors reported a significant effect of *A. arabica* on the antioxidant activity of the liver [63]. Another study reported the protective effect of *A. arabica* against hepatic oxidative stress in an animal model of diabetes. Moreover, oxidative factors such as SOD, GPX, and GSH increased significantly, and MDA decreased significantly after *A. arabica* treatment [64]. AM Said et al. reported that the combination of *A. arabica* and lemongrass could effectively treat kidney disease due to their antioxidant and anti-inflammatory effects

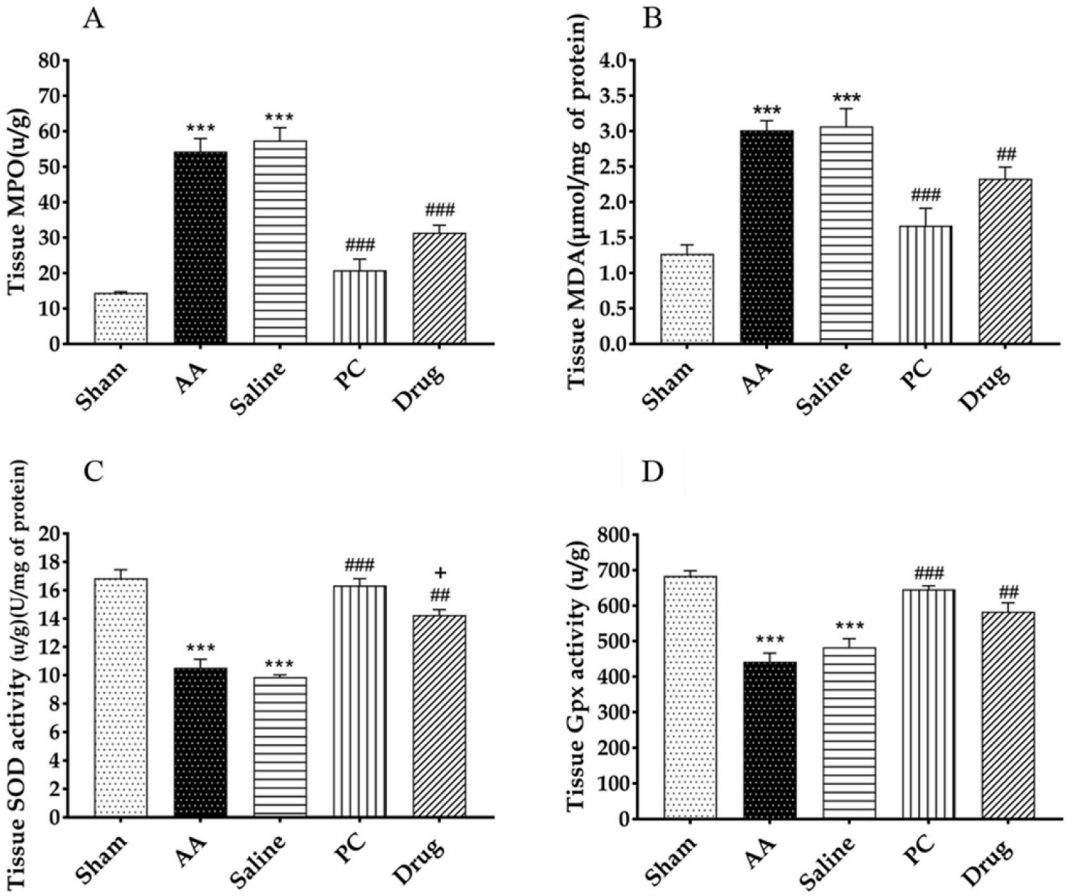

Fig. 4. The effects of gavage administration of Acaciais Arabica and basil on A: MPO, B: MDA, C: SOD, D: Gpx in colon tissue. Sham, Sham group, AA, Acid Acetic Group, Saline, Saline group, PC, positive Control group, Drug, *A. arabica*, and *O. basilicum*. Data are shown as Mean ± SEM (n = 10 per group). ***P < 0.001 vs. control group. ##P < 0.01, ###P < 0.001 vs. AA and saline groups, + P < 0.05 vs. PC group.

[65]. Nasir et al. showed the reducing effects of *A. arabica* on blood pressure in diabetic people [66]. Kamal et al. demonstrated the anti-inflammatory effects of *A. arabica* by reducing pro-inflammatory cytokine TNF-α in rheumatoid arthritis patients [26]. Another study reported AA's anti-inflammatory and antioxidant effects in improving kidney disease [27]. The results of this study also confirmed the anti-inflammatory and antioxidant effects of these two plants.

The present study assessed the rate of tissue inflammation. An increase in inflammation was observed in the colitis group. An important feature of ulcerative colitis is an increase in inflammation followed by an increase in inflammatory cells, including neutrophils [54]. One of the mechanisms underlying IBD is the increased transcription of inflammatory cytokines such as IL-6, TNF-α, and IL-1 [67]. Bamias et al. highlighted the importance of cytokines in the pathogenesis of ulcerative colitis [68]. In another study, Zhang et al. showed that proinflammatory cytokines, including IL-1β, IL-6, and TNF-a, increased in ulcerative colitis [69]. Other studies on the animal models of ulcerative colitis also showed an increase in proinflammatory cytokines [70]. De Oliveira et al. showed an increase in IL-17, TNF-α, and IL-1β in the animal model of colitis [71]. Palla et al. reported an increase in cytokines IL-17 and TNF-αwas after colitis induction [72]. Another study found that a decrease in TNF-α as a proinflammatory cytokine significantly reduced the disease symptoms [73]. Moreover, the level of anti-inflammatory cytokines such as interleukin 10 is reduced in this disease. This cytokine plays an important role in inhibiting immunoinflammatory responses [74]. IL10, as a regulatory cytokine, balances the function of inflammatory cells in the immune system. In fact, IL-10-deficient rats tend to develop chronic colitis following activation of the COX pathway and increased inflammation [75]. Fan et al. showed a decrease in interleukin 10 and an increase in proinflammatory cytokines following the induction of ulcerative colitis [76]. The results of the present study are consistent with all the above studies.

MPO enzyme is found in abundance in neutrophils. Hence, this enzyme is tested to measure the degree of inflammation in this disease [77]. MDA is another oxidative factor that is increased in ulcerative colitis. In contrast, antioxidants such as GPX and SOD are reduced in this disease [78]. Motawea et al. reported an increase in oxidative factors such as MPO and MDA and a decrease in antioxidants such as GPX and SOD in ulcerative colitis [79]. In addition, El-Abhar et al. showed an increase in two parameters of MPO and TNF-α in ulcerative colitis [80]. A decrease in SOD in this disease was also reported by Al-Rejaie [81]. Another research reported an increase in MPO and MDA and a decrease in GPX, and SOD after the colitis induction in the animal [82]. Consistent with the present study, Liu D-y et al. reported the relationship between the reduced concentration of antioxidant agents such as GPX, and SOD and

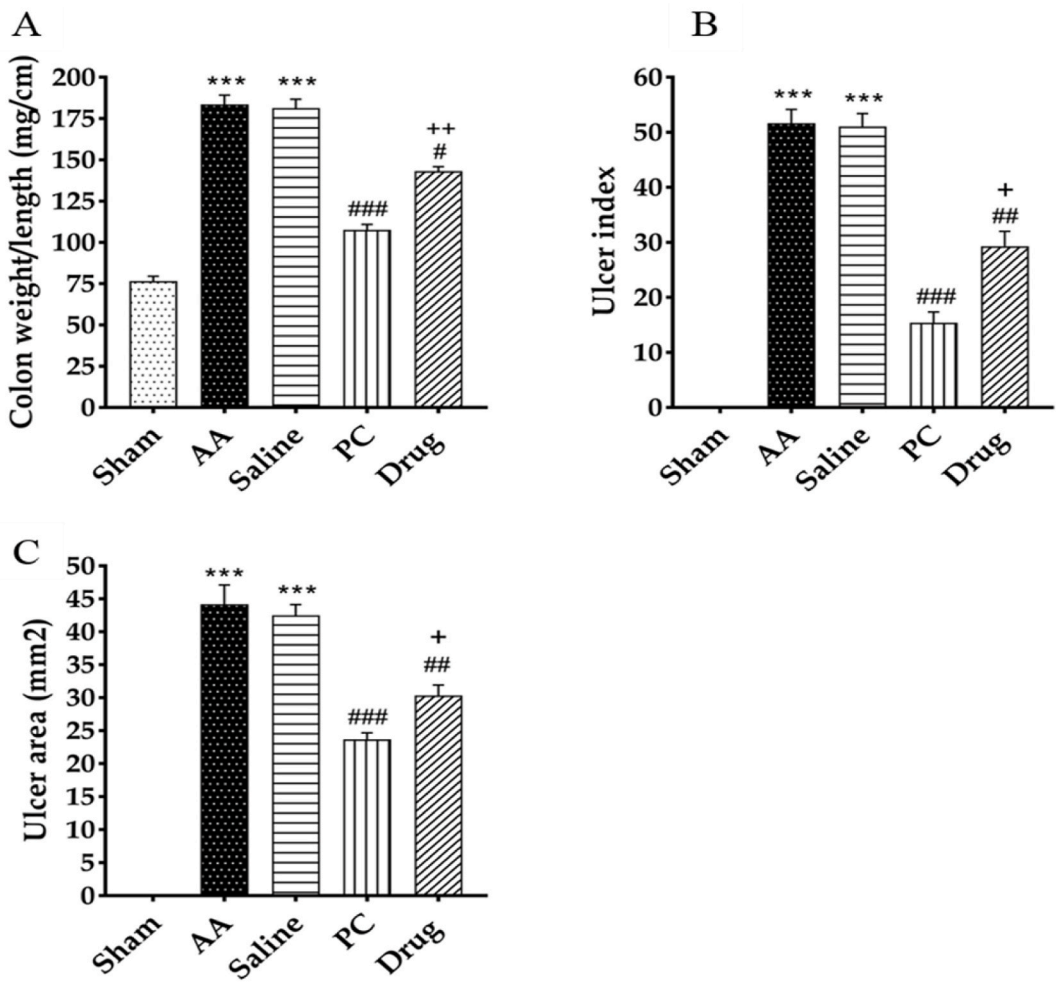

Fig. 5. The effects of gavage administration of *A. arabica*, and *O. basilicum* on A: Colon weight/length, B: UI, C: Ulcer area, D: total score of pathological changes in colon tissue. Sham, Sham group, AA, Acid Acetic Group, Saline, Saline group, PC, positive Control group, Drug, *A. arabica*, and *O. basilicum*. Data are shown as Mean ± SEM (n = 10 per group). ***P < 0.001 vs. control group. #P < 0.05, ##P < 0.01 and ###P < 0.001 vs. AA and saline groups, + P < 0.05, ++ P < 0.01 and vs. PC group.

increased intestinal damage in colitis [83].

Ulcerative colitis manifests itself with diarrhea, weight loss, and rectal bleeding, reflected by the increased DAI [84]. Abd Elmaksoud et al. observed a significant increase in DAI and an increase in the colon's weight-to-length ratio after colitis induction [85]. Moreover, da Silva et al. reported diarrhea and weight loss as features of colitis [86]. Consistent with other studies, the present research showed that colitis induction increased DAI and its related parameters (weight loss, diarrhea, and rectal bleeding).

Other significant factors in colitis are the histopathological changes of the colon tissue that occur with an increase in indices such as UI and UA [87]. This disease is associated with an increase in UI and UA indexes. Many studies reported an increase in UI and UA in animal models of colitis [88–90]. Awaad et al. showed an increase in UI and UA indices following colitis induction in animals [91]. This study also confirmed the results reported in the mentioned studies.

5. Limitation of the study

The most important limitation of our study was not performing HPLC and referring to previous similar studies.

6. Conclusion

The results of the present study indicated an increase in inflammatory and oxidant mediators after the colitis induction in the colon tissue. We used the combination of *A. arabica* and *O. basilicum* to treat ulcerative colitis, considering their anti-inflammatory and antioxidant properties and multiple effects on the immune system. Overall, the data in this study showed that this combination has a protective effect and reduces pro-inflammatory cytokines and oxidative factors in colon tissue after treatment. The results also showed

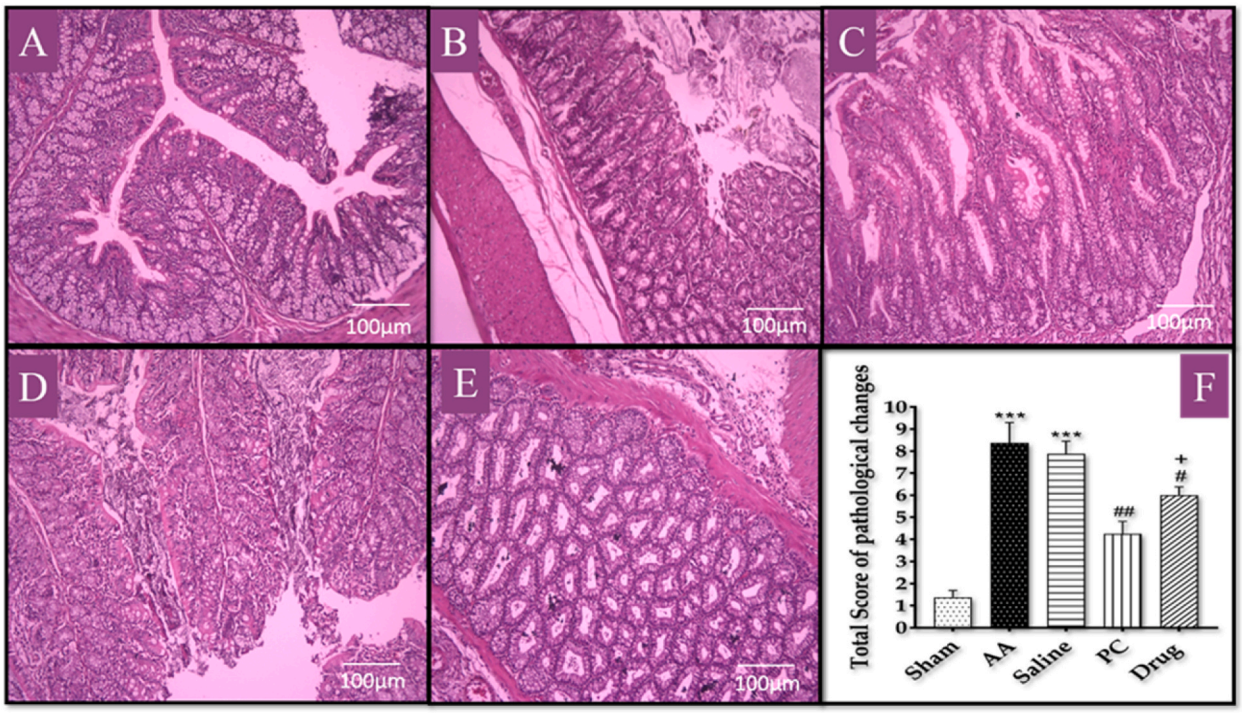

Fig. 6. Microscopic presentation of acetic acid–induced colitis in rats stained by hematoxylin and eosin (light microscopy, 10 X): (A) normal colon without any treatments, mucus layer, and crypts are normal and leucocyte infiltration is absent; (B) colitis in control group without any treatments, mucosal and submucosal inflammation, as well as crypt damage and leucocyte infiltration are evident; (C) colitis in control group treated with saline, mucosal and submucosal inflammation, as well as crypt damage and leucocyte infiltration; (D) Sulfasalazine treated colitis. (E) combination of *A. arabica*, and *O. basilicum* treated colitis.

an improvement in colitis. Thus, the combination of *A. arabica* and *O. basilicum* is effective in controlling ulcerative colitis. However, more studies are needed to reveal the mechanism of action of this combination.

Ethical approval

All experiments were conducted in accordance with the guidelines for animal experiments at the Kerman University of medical sciences, in accordance with the ethical rules regarding the use of experimental animals. This research was confirmed (Ethical Number IR.KMU.AH.REC.1399.127) in Kerman University of Medical Sciences, Kerman.

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Consent to participate

N/A.

Consent to publish

N/A.

Data availability statement

Data associated with this study has not been deposited into a publicly available repository. Data will be made available on request.

CRediT authorship contribution statement

Mohammad Abbas Bejeshk: Writing – original draft. **Amir Hashem Aminizadeh:** Writing – review & editing. **Mohammad Amin**

Rajizadeh: Writing – original draft. **Fahimeh Rostamabadi:** Methodology. **Fatemeh Bagheri:** Methodology. **Mohammad Khaksari:** Writing – review & editing. **Maryam Azimi:** Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Dr.Maryam Azimi reports administrative support was provided by Kerman University of Medical Sciences. Dr.Maryam Azimi reports a relationship with Kerman University of Medical Sciences that includes: board membership. Dr.Maryam Azimi has patent pending to N/A. N/A If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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