Original Article

Anti-inflammatory Effect of *Myrtus communis* Hydroalcoholic Extract and Essential Oil on Acetic Acid–induced Colitis in Rats

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Abstract

Background: Colitis is an inflammatory bowel disease, many causes are involved in its pathogenesis and development. *Myrtus communis* (*M. communis*) contains anti-inflammatory and antioxidant ingredients that are useful for the treatment of inflammatory disease. **Objectives:** The purpose of this study was to investigate the effect of *M. communis* hydroalcoholic extract (MCHE) and essential oil (MCEO) on acetic acid–induced colitis model. **Materials and Methods:** MCHE (50, 100, 200, and 400 mg/kg) and MCEO (62.5, 125, 250, and 500 µL/kg) were given orally to rats, 2 h before induction of colitis and continued for further 4 days. Prednisolone (4 mg/kg) and mesalazine (100 mg/kg) were used as reference drugs. After 5 days, colitis markers and indices were investigated on isolated colons. Biochemical evaluation of inflamed colon was performed using assay of myeloperoxidase (MPO) activity. **Results:** Acetic acid caused significant inflammatory reactions as indicated by macroscopic and microscopic changes in control groups. Extracts with three doses and volatile oil with two lower doses were effective to reduce weight of distal colon (8 cm) as a marker of inflammation and tissue edema. Similarly, MCHE (50, 100, and 200 mg/kg) and MCEO (62.5 and 125 µL/kg) were statistically effective in dip of ulcer index, total colitis index, and MPO activity compared to control groups. **Conclusion:** The beneficial effect of *M. communis* was comparable with that of prednisolone and mesalazine; however, by its dose escalation, this activity tends to be diminished. This research showed the anti-inflammatory activity of MCHE and MCEO on experimentally induced acute colitis.

Keywords: *Colitis, essential oil, inflammation, Myrtus communis, plant extract, rats*

Introduction

Inflammatory bowel disease (IBD) is one of the most common diseases of the gastrointestinal (GI) tract, which is difficult to be diagnosed and treated.[1] IBD mainly consists of two categories of chronic illnesses: ulcerative colitis and Crohn's disease. The cause of IBD is not known yet in clear and obvious manner. Recent studies have shown that many factors including genetic, changes in the normal flora of the digestive tract, and environmental and immune factors, in particular, contribute to the disease.[2] 5-Aminosalicylates (5-ASA), steroids (e.g., topical formulations and budesonide), antibiotics (e.g., rifaximin and tinidazole), immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate, and cyclosporine), and monoclonal antibodies (e.g., infliximab, adalimumab, and natalizumab) could be a long list of IBD treatments.[1] Many of the aforementioned therapies, however, have limitations; for example, corticosteroids possess several metabolic adverse effects, which may limit their use, other drugs such as 6-mercaptopurine and azathioprine can lead to liver damage, bone marrow suppression, and pancreatitis.[3] Because of unpleasant side effects of current medications and lack of proper control of the disease that leads to patient dissatisfaction, more attention has been paid to alternative therapies.[4] In recent years, the use of medicinal herbs has been increased due to the lower drawbacks, cheapness, and easy access to them.[5] *Myrtus communis* is an evergreen shrub that is widely grown in Iran and elsewhere in the world.[6] Pharmacological researchers have shown that the plant has active compounds that possess antimicrobial,[6] anticoagulant, antidiabetic, antispasmodic, and vasodilator activities.[7] *M. communis* has been used traditionally for the treatment of diarrhea,[8] hemorrhoids, peptic ulcer, urethritis, inflammation, hemorrhagic ulcers, pulmonary, and skin diseases.[9] On the contrary, phenolic acids, tannins, flavonoids, glycosides, and terpenes are among the major components of this plant with different bioactivities.[7] Moreover, the essential oil of this plant is rich in monoterpene and sesquiterpene derivatives, which may

How to cite this article: Khosropour P, Sajjadi S, Talebi A, Minaiyan M. Anti-inflammatory effect of *Myrtus communis* hydroalcoholic extract and essential oil on acetic acid–induced colitis in rats. J Rep Pharm Sci 2019;8:204-10.

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Access this article online

Website: www.jrpsjournal.com

DOI:10.4103/jrptps.JRPTPS_8_19

Quick Response Code:

exert beneficial effects on GI ailments.[7] So this study was performed to delineate the anti-colitis effect of *M. communis* hydroalcoholic extract (MCHE) and essential oil (MCEO) in a rat model of experimental colitis.

Materials and Methods

Plant material, preparation of extract and essential oil

Aerial parts of *M. communis*, collected from Lordegan area, 1700 m altitude from the sea level in Chaharmahal and Bakhtiari province, were purchased from a public market in Isfahan, Iran. Its genus and variety were confirmed by a specialist at Pharmacognosy Department of Isfahan School of Pharmacy, Isfahan, Iran, and its herbarium voucher numbered 1740 was deposited there. Aerial parts of *M. communis* were then ground to powder using an electric miller. MCHE was prepared by maceration method using ethanol/water solvent. For this reason, 400 g of grounded powder was macerated with 2640 mL of EtOH:H_2O (80:20) for 24 h. Then, solvent was evaporated in a rotary evaporator under reduced pressure and the yield of the extract was calculated. MCEO was obtained by hydrodistillation of the powdered plant during 3 h in a full glass instrument according to the method offered by European Pharmacopoeia.

Chemicals

Prednisolone and mesalazine powders were procured from Iran Hormone (Tehran, Iran) and Aboureyhan (Tehran, Iran), respectively. *O*-dianisidine dihydrochloride (ODZ) and hexadecyltrimethylammonium bromide (HTAB) were obtained from Sigma-Aldrich (St. Louis, Missouri). Formaldehyde, glacial acetic acid, ethanol, and diethyl ether oxide were purchased from Merck (Darmstadt, Germany).

Animals

In this study, 72 male Wistar rats weighted 200 ± 25 g and aged 3–4 months were used and kept in animal's nest of the School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran. Rats were acclimatized to the laboratory situation for at least 1 week before the experiments and preserved under the same and standard conditions of light, humidity, and nutrition that were in accordance with the internal regulations for working with laboratory animals. This project was approved by Isfahan University of Medical Sciences Ethics Committee and recorded as IR.MUI.RESEARCH.REC. 1397.369.

Grouping

The rats were randomly assigned in 12 groups of six rats as following:

Group 1 (normal group) received vehicle (normal saline plus 0.2% Tween 80, 5ml/kg/day orally (p.o.)) without colitis induction
Group 2 (control colitis group), received vehicle orally (p.o.), whereas colitis induction was carried out by acetic acid instillation via the rectum
Groups 3, 4, 5, and 6 (extract groups) received four doses of MCHE (50, 100, 200, and 400 mg/kg/day, p.o.)
Groups 7, 8, 9, and 10 (essential oil groups) received four doses of MCEO (62.5, 125, 250, and 500 µL/kg/day, p.o.)
Group 11 (prednisolone group) received prednisolone[10] (4 mg/kg/day, p.o.)
Group 12 (mesalazine group) received mesalazine[11] (100 mg/kg/day, p.o.)

All groups received the first dose of treatment 2 h before the induction of colitis and it was continued daily for 4 days thereafter. In normal group, normal saline (2 mL) was instilled intrarectally instead of acetic acid.

Induction of colitis

For inducing colitis, the rats were kept in a fasting state for 24 h and then under light ether anesthesia, 2 mL acetic acid (4%) was instilled within the colon by a plastic and flexible tube (2 mm inner diameter and 10 cm in length). Before taking the catheter out, the rats were maintained in a head-down position for 60 s to prevent solution spreading out.[12]

Evaluation of colon macroscopic damage

Twenty-four hours after giving the last dose (5th day of treatment), the rats were killed by an overdose of ether inhalation. Eight centimeter of the colon was excised (3 cm from the anus) and washed with normal saline and its wet weight was measured. Then, tissue was fixed on a white sheet and a suitable photo was taken for macroscopic analysis. Ulcerated area of distal colon was determined by Fiji-P Win32 software (Image Analysis Program, version 2). Ulcer score was determined using the following scoring system[13]:

0 = no macroscopic changes; 1 = mucosal erythema only; 2 = mild mucosal edema, slight bleeding, or slight erosion; 3 = moderate edema, bleeding ulcers, or erosions; and 4 = severe ulceration, erosions, edema, and even tissue necrosis. Ulcer index was measured by summing the ulcer score and the ulcer area.[14] After macroscopic assessment, the tissues were cut into two equal parts. One part was preserved in formalin (10%) for histologic examination and the other was frozen in a freezer (–70°C) for measuring myeloperoxidase (MPO) activity.[15]

Evaluation of microscopic colon tissue damage

After fixation of colonic tissues, they were dehydrated by alcohol, paraffin embedded, processed, sectioned as 4-mm thick slices, deparaffinized with xylene, hydrated, and stained with hematoxylin and eosin (H–E). Inflammation severity (0, none; 1, slight; 2, moderate; and 3, severe), inflammation extent (0, none; 1, mucosa; 2, mucosa and submucosa; and 3, transmural), crypt damage (0, none; 1, basal 1/3 damaged; 2, basal 2/3 damaged; and 3, surface epithelium intact only), and leukocyte infiltration (0, trace; 1, mild; 2, moderated; and 3, severe) were assessed in H–E stained and coded sections using a modification[16] of a validated scoring scheme described by Cooper *et al*.[17] Total colitis index was measured by summing the scores of inflammation severity, inflammation extent, crypt damage, and leukocyte infiltration. Histological damages were investigated using a Zeiss microscope

(Oberkochen, Germany) equipped with a Sony color video camera (Sony, Japan) for digital imaging.

Determination of myeloperoxidase activity

Tissue MPO activity, as a marker of polymorphonuclear leukocyte migration and oxidative stress, especially on cell membranes, was measured according to the method described by Motavallian-Naeini *et al.*[18] Briefly, colonic (0.1 g) tissue was homogenized in the presence of 50 mM potassium phosphate (pH, 6) and 0.5% HTAB for 3 × 45 s. Then more buffer solutions were added until the volume reached 5 mL. Next, the homogenate was sonicated in an ice bath for 20 s. The suspensions were centrifuged (15,000 rpm) and then, 2.9 mL of 50 mM phosphate buffer (pH, 6) containing 0.167 mg/mL ODZ and 0.0005% hydrogen peroxide was added to 0.1 mL of the supernatant. The absorbance was measured at 450 nm by UV-Vis spectrophotometer (LSI Model Alfa-1502) at zero and 3 min later. MPO activity was reported as U/100 mg of the weight of wet colon.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS, IBM Co, USA) 20.0 statistical software. Data were shown as mean value ± standard error of mean (SEM). One-way analysis of variance (ANOVA) test and Turkey's *post hoc* test were used to compare the data with each other and with the controls. To compare nonparametric data, they were presented as median (range) and Mann–Whitney *U* test was used. $P < 0.05$ was reported as a significant difference level.

Results

Yield value of extract and essential oil

The yield values of MCHE and MCEO were found to be 21% (w/w) and 0.45% (v/w), respectively.

Effect of *M. communis* hydroalcoholic extract and essential oil on macroscopic parameters

Data showed that no changes appeared in normal group indicating that handling and surgical procedure had no interference with the results of the experiment. Treatment with prednisolone and mesalazine as reference drugs reduced the ulcer score ($P < 0.01$), ulcer area (cm^2), ulcer index, and the wet weight of 8 cm of distal colon (g) ($P < 0.001$) compared to that of the control group [Table 1] [Figure 1]. This revealed that this method was responsive to both main current therapies of IBD including corticosteroids and 5-ASA derivatives.

On the contrary, almost all test doses of MCHE and MCEO could diminish the severity of lesion scores, ulcer area, and ulcer index (at least $P < 0.05$) compared to that of the control group; however, for weight of distal colon parameter, the greatest applied doses of both fractions (MCHE, 400 mg/kg and MCEO, 250 and 500 µL/kg) were insignificant ($P > 0.05$) [Table 1], Figure 1].

Effect of *M. communis* hydroalcoholic extract and essential oil on pathologic parameters

Acetic acid in control group induced edema, necrosis, hemorrhage, crypt damage, and vast leukocyte infiltration in the tissue. Prednisolone and mesalazine improved (at least $P < 0.01$) these injuries greatly, such that the microscopic images of them represented much better presentation than that of the control colitis group [Figures 2 and 3]. Treatment with increasing doses of MCHE and MCEO orally reduced the incidence of pathological features of colonic damage, although it seemed that improvements were not statistically meaningful with the greatest doses of MCHE and MCEO ($P > 0.05$). So the microscopic and macroscopic results were mostly consistent with each other [Table 2] [Figure 2].

Table 1: Effect of *Myrtus communis* hydroalcoholic extract and essential oil on the macroscopic parameters of colitis induced by acetic acid in rats

Group/dose (mg/kg)	Ulcer score (0–4)	Ulcer area (cm^2)	Ulcer index (0–12)	Colon weight (g)
Normal	0.0 (0–0)	0.00 ± 0.0	0.00 ± 0.0	0.63 ± 0.1
Control	4 (4–4)****	7.48 ± 0.8****	11.48 ± 0.8****	1.56 ± 0.4****
MCHE50	2 (1–3)**	2.84 ± 0.7***	4.84 ± 1.2***	0.88 ± 0.2**
MCHE100	2 (1–3)**	1.91 ± 0.3***	3.91 ± 1.0***	0.94 ± 0.1**
MCHE200	2.5 (1–4)*	4.72 ± 0.5***	7.05 ± 1.6***	1.05 ± 0.3*
MCHE400	3.0 (1–4)*	5.85 ± 0.7*	8.35 ± 1.9*	1.16 ± 0.2
MCEO62.5	2.0 (1–3)**	2.03 ± 0.6***	4.03 ± 1.3***	1.04 ± 0.5*
MCEO125	1.5 (0–2)**	0.86 ± 0.3***	2.19 ± 1.1***	1.02 ± 0.2*
MCEO250	2 (1–3)**	3.47 ± 0.6***	5.47 ± 1.3***	1.1 ± 0.2
MCEO500	2.5 (2–4)*	5.55 ± 1.2*	8.02 ± 1.8*	1.25 ± 0.2
Prednisolone 4	1.0 (1–2)**	0.49 ± 0.5***	1.82 ± 1.0***	0.76 ± 0.1***
Mesalazine100	1.5 (1–2)**	0.63 ± 0.5***	2.13 ± 0.92***	0.86 ± 0.1**

Normal = normal rats received normal saline (5 mL/kg/day), control = rats with colitis received normal saline (5 mL/kg/day), MCHE = *M. communis* extract (50, 100, 200, and 400 mg/kg), MCEO = *M. communis* essential oil (62.5, 125, 250, and 500 µL/kg)
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ denote significant difference versus control, whereas ****$P < 0.001$ denote significant difference versus normal group
Data are expressed as mean ± standard error of mean (SEM) or median (range) for scoring parameter, $n = 6$

Myeloperoxidase activity measurement

Results of this study indicated that the activity of MPO enzyme was significantly diminished in MCHE (50, 100, and 200 mg/kg) and MCEO (62.5, 125, and 250 µL/kg) groups as well as prednisolone and mesalazine (at least $P < 0.01$); however, with dose escalation of both fractions, this effect was blunted in MCHE (400 mg/kg) and MCEO (500 µL/kg) groups [Figure 3].

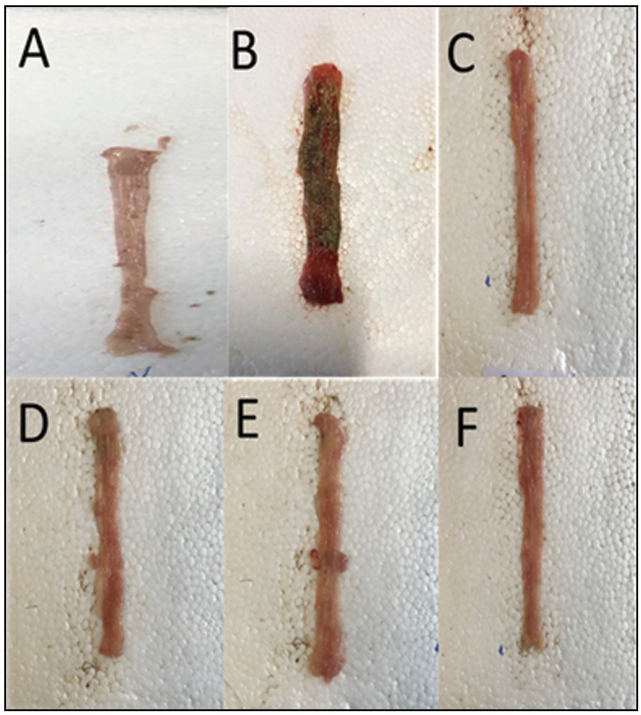

Figure 1: Photographs of colon tissue, 5 days after acetic acid–induced colitis in rats: (A) Normal colon treated with normal saline. (B) Control colitis treated with normal saline. (C) Colitis treated with *Myrtus communis* hydroalcoholic extract (MCHE, 100 mg/kg). (D) Colitis treated with *M. communis* essential oil (MCEO, 125 µL/kg). (E) Colitis treated with prednisolone (4 mg/kg). (F) Colitis treated with mesalazine (100 mg/kg)

Discussion

M. communis is an evergreen shrub, its extracts and essential oils have a lot of uses in traditional medicine.[19] In this research, we applied acetic acid–induced colitis for investigation of anti-colitis activity of *M. communis* extract and essential oil. Results of this study showed the protective activity of MCHE and MCEO through macroscopic, pathologic, and biochemical evaluations. Our results showed that edema and increase in the wet weight of distal colon segment in control groups were mainly due to the presence of inflammatory cells and neutrophils, which leads to the release of inflammatory cytokines and the surge of reactive oxygen species (ROS) within the cluster mucosa, causing pathological damage and weight gain of colon.[20,21] In addition, our results showed that MCHE (at 50, 100, and 200 mg/kg doses) and MCEO (at 62.5 and 125 µL/kg doses) could decrease the wet weight of distal colon segments compared to that of the control group. Attenuation in wet weight of distal colon segments could be due to *M. communis* effect on inflammatory cytokine release, tissue inflammation, and vascular extravasation.[22] Also, MCHE and MCEO with all test doses could decrease ulcer index in evaluated segments compared to that of the control group. In addition, microscopic examinations of colon tissue injuries indicated that oral administration of MCHE and MCEO, probably, due to anti-inflammatory and ulcer-healing effects, reduced the severity and extent of inflammation and crypt damage and at the same time improved the total index of colitis compared with that of the controls. This implies that active ingredients of oral MCHE and MCEO are capable to reach in enough amounts to the distal colon to exert their beneficial effect on colitis. An investigation carried out by

Table 2: Effect of *Myrtus communis* hydroalcoholic extract and essential oil on the microscopic parameters of colitis induced by acetic acid in rats

Group/dose (mg/kg)	Inf. severity (0–3)	Inf. extent (0–3)	Crypt damage (0–4)	Leuk. infiltration (0–3)	Total colitis index (0–13)
Normal	0.0 (0–0)	0.0 (0–0)	0.0 (0–1)	0.0 (0–1)	0 (0–0)
Control	3 (3–3)****	2 (2–3)****	3 (2–4)****	3 (2–3)****	11 (9–13)****
MCHE50	1 (1–2)**	1 (0–1)***	1 (0–1)***	1 (1–2)**	4 (3–5)***
MCHE100	1 (0–1)***	1 (0–1)***	1 (1–1)***	1 (1–2)**	3 (2–4)***
MCHE200	1 (1–2)**	1 (0–1)***	1 (1–2)***	1 (1–2)**	5 (4–7)***
MCHE400	3 (2–3)	2 (0–3)	2 (1–2)**	2 (2–3)	9 (9–11)
MCEO62.5	2 (1–2)**	1 (0–1)***	0 (0–1)***	1 (1–1)***	4 (2–5)***
MCEO125	1 (1–2)**	1 (1–1)***	0 (0–1)***	1 (1–2)***	3 (2–3)***
MCEO250	2 (2–3)*	1 (0–1)***	1 (0–1)***	1 (1–2)***	5 (3–5)***
MCEO500	2 (1–3)*	2 (1–2)	2 (0–4)*	3 (2–3)	9 (7–11)
Prednisolone4	0 (0–1)***	0 (0–1)***	1 (1–2)***	2 (1–2)**	1.5 (1–3)***
Mesalazine100	0 (0–1)***	0 (0–0)***	0 (0–1)***	1 (1–2)***	1 (1–2)***

Inf. = inflammation, Leuk. = leukocyte, normal = normal rats received normal saline (5 mL/kg/day), Control = rats with colitis received normal saline (5 mL/kg/day), MCHE = *M. communis* hydroalcoholic extract (50, 100, 200, and 400 mg/kg), MCEO = *M. communis* essential oil (62.5, 125, 250, and 500 µL/kg)

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, denote significant difference versus control, whereas ****$P < 0.001$ denote significant difference versus normal group

Data are expressed as median (range) for scoring parameter, $n = 6$

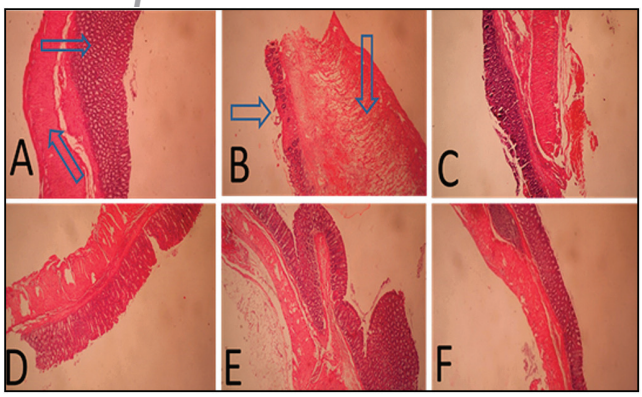

Figure 2: Microscopic illustration of colonic tissue in rats. (A) Normal tissue, treated with normal saline (5 mL/kg). (B) Colitis control group, which shows crypt damage, leukocyte infiltration, and mucus and submucusal layer edema and inflammation (blue arrows). (C) Colitis treated with *Myrtus communis* hydroalcoholic extract (MCHE, 100 mg/kg). (D) Colitis treated with *M. communis* essential oil (MCEO, 125 µL/kg). (E) Colitis treated with prednisolone (4 mg/kg). (F) Colitis treated with mesalazine (100 mg/kg)

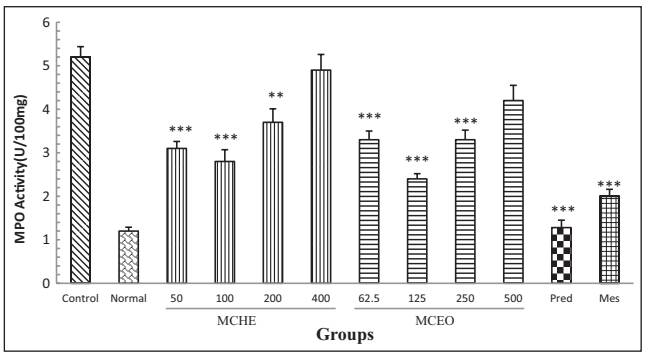

Figure 3: Myeloperoxidase (MPO) activity (U/100 mg) in colonic tissue of rats treated with normal saline (5 mL/kg), *Myrtus communis* hydroalcoholic extract (MCHE), *M. communis* essential oil (MCEO), prednisolone (Pred., 4 mg/kg), and mesalazine (Mes, 100 mg/kg). Data are presented as mean ± standard error of mean (SEM). **P* < 0.05, ***P* < 0.01, ****P* < 0.001 denote significant difference versus control

Sumbul *et al*.[23] showed that aqueous and alcoholic extract of *M. communis* reduced gastric acidity and increased mucosal barrier and dramatically improved healing of gastric ulcers in rats. We know that *M. communis* is rich in volatile oils, phenolic acids, flavonoids, and tannins, which at least for some of them GI absorption is not complete.[24]

An experiment performed by Dejam and Farahmand[25] on essential oil composition of *M. communis* L. leaves from the south of Iran revealed that 1,8-cineole (26.91%), α-pinene (22.02%), linalool (12.74%), linalyl acetate (8.64%), α-terpineol (8.29%), and α-terpinyl acetate (4.58%) were the six most abundant oils in this fraction. Another study carried out by Mahboubi[26] indicated that MCEO and its decoction decreased the average time of pain relief and the size of ulcers in patients with minor recurrent aphthous ulcers without any adverse effects. Anti-inflammatory, immunomodulatory, and ulcer-healing qualities of MCEO are predominantly attributed to 1,8-cineol and linalool and α-pinene ingredients.[22] In MCHE, on the contrary, tannins are among the materials that can protect intestinal mucosal layers by precipitating their small proteins and also can protect the luminal layers against acid and pepsin injuries and proteolytic enzymes.[27] Flavonoids additionally have significant antioxidant and chelating attributes,[28] that some of them, especially in conjugated forms such as quercetin derivatives (quercetin 3-*O*-galactoside and quercetin 3-*O*-rhamnoside), naringin, and neohesperidin are sparingly absorbable in the GI tract and could reach the distal colon to exert a kind of relatively site-specific delivery.[29] They have strong antibacterial effect on pathologic microorganisms[30] and free radicals scavenging property and reduce the production of ROS, and hence reduce lipid peroxidation.[31] *M. communis*, because of polyphenolic compounds and flavonoids with many hydroxyl groups that have high ability to donate electrons, exerts good antioxidant activity as free radical inhibitors or scavengers.[32-34] Gonçalves *et al*.[35] and Kumar *et al*.[36] showed antioxidant and anti-inflammatory effect of *M. communis* exerted by lipid peroxidation inhibition. Because of the presence of flavonoids, tannins, and terpenoids, it is supposed that *M. communis* produced its antidiarrheal effects in rats, probably through reducing the amount of stool water and the frequency of defecation.[8] Besides, lotion and ointment were made from essential oil of *M. communis*, which effectively reduced pain, bleeding, and itching of the anus as hemorrhoid symptoms in patients.[37] Moreover, MCHE and MCEO showed a modulating impact on immune system activity and anti-inflammatory effects.[38] Results of this study also indicated that the activity of MPO enzyme was significantly diminished in MCHE (50, 100, and 200 mg/kg) and MCEO (62.5, 125, and 250 µL/kg) treated groups. The reduction of MPO activity within the targeted tissue supports the anti-inflammatory and antioxidant effects of the MCHE and MCEO made by diminishing leukocyte migration and infiltration.[33] Excessive ROS production can lead to many diseases such as endothelial dysfunction, IBD, atherosclerosis, and hypertension.[39] As there are some concerns about *M. communis* toxicity, we reviewed the literature to clarify this issue. Generally, if the lethal dose 50% (LD50) value of the test drug is more than three times greater than the maximum effective dose, it is supposed that the substance could be considered safe and applied in screening studies.[40] LD50 value for MCHE has been reported as greater than 2000 mg/kg p.o., so designated as "unlikely to be hazardous" in the World Health Organization hazard classification systems.[8] Therapeutic potential of *M. communis* on experimental colitis was previously shown by Sen *et al*.[41] and the authors had reported similar results for ethanol extract of aerial parts. In a recent study, however, essential oil component of *M. communis* at four increasing doses as well as two larger doses of extract (200 and 400 mg/kg) were examined for anti-inflammatory activity in distal colitis. So in this study, dose–response relationship was more clarified and the findings revealed that both examined fractions of *M. communis* were both effective and safe in reasonable manner. In addition, it should be noted that in recent study, by reducing the dose of MCHE and MCEO, the anti-inflammatory and anti-colitis effects were found to be strengthened. This might be due to

the presence of some ingredients that at higher concentrations counteract with the beneficial effects of extract and essential oil on colitis.[42] Further studies are recommended to delineate the mechanisms are involved and the active ingredients are responsible for these actions. Dose-response relationship could be additionally explored in more detail on trinitrobenzene sulfonic acid and dextran sulfate sodium models of colitis.

Conclusion

This study suggests that *M. communis* has anti-inflammatory and antioxidant effects, which ultimately resulted in colitis-healing activity. MCHE and MCEO were both effective, especially at lower doses, so clarification of dose–response relationship would be essential for introducing this plant for further basic and clinical trials.

Financial support and sponsorship

This study was financially supported by the Research Council of Isfahan University of Medical Sciences under project number 397082.

Conflicts of interest

There are no conflicts of interest.

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