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An Evidence-Based Study on Medicinal Plants for Hemorrhoids in Medieval Persia

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Abstract

Hemorrhoids is one of the most common gastrointestinal diseases. There are several therapeutic options associated with some complications. Therefore, researchers look for traditional medicines as a potential resource for introduction of new natural drugs. The current study reports an evidence-based review of herbal remedies for hemorrhoids in traditional Persian medicine. A comprehensive survey about hemorrhoids on the most important manuscripts of traditional Persian medicine was done. Then, scientific data banks were searched for possible related properties of each herb in the conventional medicine. We reported some historical aspects of traditional Persian medicine view on classification, examination, and predisposing factors of hemorrhoids. In addition, we have reported 105 medicinal plants belonging to 51 families. More than half of the reported herbs exhibited anti-inflammatory and analgesic effects. Although lack of human studies regarding the mentioned herbs is noted, positive results from experimental findings can be considered for new drug discovery supported by traditional and medieval experiences.

Keywords

hemorrhoids, traditional Persian medicine, medicinal plants, Avicenna, Rhazes

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Hemorrhoids or hemorrhoidal disease is often considered as one of the most common gastrointestinal diseases with a high prevalence.[1] In the United States, about 10 million people reported hemorrhoids.[2] The cause and etiology of this condition is not thoroughly clear.[3] Factors such as irregular bowel habits and low-fiber diets as well as genetics may lead the patient to this condition.[4] Bleeding from the lower gastrointestinal segments is most likely to be the main prevalent etiological reason of the incidence of hemorrhoids.[5] Anal pain and discomfort, itching, bleeding, swelling, and perceived mass in the perianal zone are considered as the main symptoms of hemorrhoids.[6,7]

Treatment lines for hemorrhoids are discussed as conservative approaches such as dietary fiber and oral fluids, rest, and nonsteroidal anti-inflammatory drugs as well as surgical techniques associated with degrees of complication.[4,8]

The first known description about hemorrhoids dates back to nearly 1700 BC, when Egyptians wrote on papyrus about the treatment of this disease. In the history of medicine, other traditional medical systems have discussed about hemorrhoids and related treatment. There are some historical investigations about the disorder.[9] Based on humoral theory, traditional Persian medicine is an ancient and popular medical paradigm with numerous therapeutic options for various diseases and complications.[10-12] Early Persian scholars and physicians have dedicated their experiences and knowledge to make this medical paradigm fluorish.[13,14] Reported therapeutic options in Persian medical manuscripts are mainly herbal remedies and could be defined as potential medicaments. Reviewing the herbal remedies for

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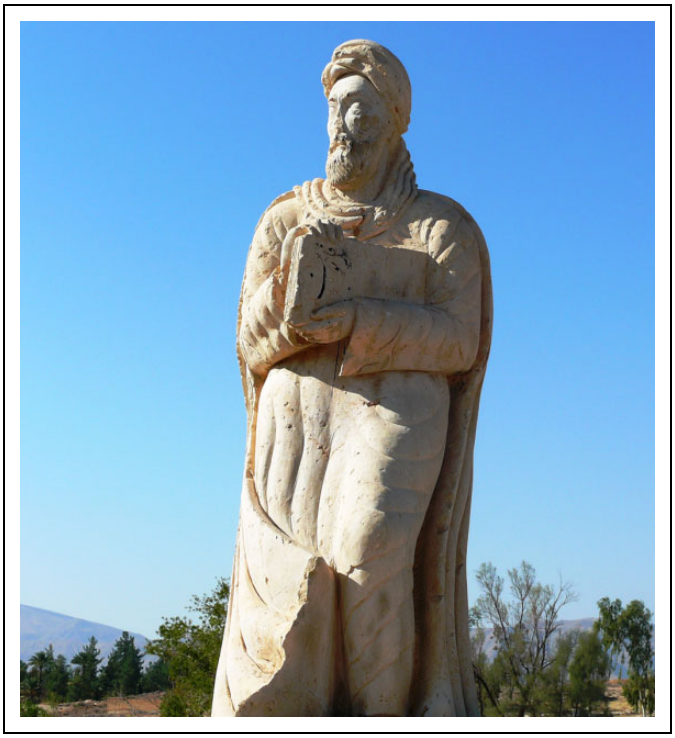

Figure 1. *Ibn-e Sina* (Avicenna) statue in the *Ibn-e Sina* square in front of Fasa University of Medical Sciences, Fasa, Iran (photo courtesy Abbas Khosravi).

each specific disease, by searching through main traditional Persian medicine references, could help the researchers to assess and introduce new and effective natural medicines.[15,16]

It is notable that oral and topical botanical preparations may effectively treat early stages of hemorrhoids. These medicaments can also be applied as adjuvant therapies in advanced stages.[17] Therefore, the current study aimed to compile herbal remedies for hemorrhoids in traditional Persian medicine and discuss their relevant pharmacologic properties in contemporary medicine.

Materials and Methods

Chapters related to hemorrhoids (*Bavāsir* in Persian) and medicinal plants were selected and studied from printed editions of *Kitāb al-hāwī fī al-tibb* (The Comprehensive Book on Medicine) by Rhazes (9th and 10th centuries AD), Canon of Medicine by Avicenna (Figure 1) (10th and 11th centuries), *Ikhtiyārāt-I Badī'ī* (Selections for Badī'ī) by *Hājjī Zayn al-'Attār* (14th century), *Tuhfat al-mu'minīn* (Present for the Faithful) by *Daylamī Tunakābunī* (17th century) and *Makhzan al-adviyah* (The Storehouse of Medicaments) by *Alavī Shīrāzī* (18th century).[18-22] These pharmacopeias are known as the most important and comprehensive resources in traditional Persian medicine, which are also repetitively used by natural healers in Iran.[23]

For concise nomenclature of herbal medicines, other textbooks such as *Dictionary of Medicinal Plants*,[24] *Matching the Old Medicinal Plant Names with Scientific Terminology*,[25] and *Dictionary of Iranian Plant Names*[26] as well as *Indian Medicinal Plants*[27] were used. Medicaments with unidentified scientific name were finally omitted from the results.

Scientific data banks such as Medline and Scopus were searched to seek for possible related properties of each herb in the current medicine. According to the treatment lines and pathophysiology of hemorrhoid condition, the investigated pharmacologic effects were anti-inflammatory, analgesic, antinociceptive, and vasodilatory.

Results and Discussion

Hemorrhoids (*Bavāsir*) has been defined as a vascular mass in the anal canal that could be presented either internally or externally and may be associated with bleeding. Aspects of the examination of hemorrhoids have been categorized into factors such as bleeding, presentation, location, humoral etiology, and prognosis. With reference to traditional Persian medicine, the most important predisposing factors included intrinsic factors such as constipation, depression, inadequate sleep, intra-abdominal hypertension, and age >40 years as well as extrinsic factors like autumn season, dry climates, and bad food regimen. The main reason of the incidence has been remarked as blood aggregation near the anus and anal canal.[28]

Treatment approaches in traditional Persian medicine have been reported as lifestyle modification, management of the underlying diseases and topical or systemic drug administration as well surgery. Accordingly, natural remedies for hemorrhoids included laxatives, analgesics, and anti-inflammatory agents as well as medicines that affect the veins in the location. In these cases, remedies were administered according to their astringent or healing properties.[19]

By searching through pharmaceutical manuscripts of Persian medicine, 105 medicinal plants belonging to 51 families were derived and identified (Table 1). The most cited family was Fabaceae followed by Apiaceae and Lamiaceae. Similar to the current medicine, generally reported routes of administration in traditional Persian medicine for the management of hemorrhoids were oral and topical. In addition, dosage forms and preparations were decoction and maceration of the herbal parts for oral route and oil, ash, and enema for topical route. Moreover, some herbs were also used in an unusual topical dosage form as smoke.

Apart from the oral administration of medicinal plants for hemorrhoids, many medicinal herbs were used topically in an oil dosage form. In this regard, essential oil of the aromatic plants was being extracted under hydrodistillation procedure. On the other hand, oil-bearing seeds such as almond and castor oil plant were subjected to direct compression to extract the fixed oil. It is remarkable that in traditional Persian medicine the oil dosage forms containing nonoily parts have also been prepared. To do this, soft parts of a plant were soaked in heated sesame or olive oil for a certain time. The resulting oil sample was defined as the finished product. On the other hand, the plants' hard tissues such as roots or barks were boiled in water. Subsequently, the resulting extract was boiled in combination with sesame or olive oil until its water part was lost.[29]

According to the current knowledge, management of hemorrhoids includes modification of the dietary and lifestyle, medications, and radical surgery. Remedies to treat hemorrhoids underlie analgesic, anti-inflammatory, and local anesthetic and venotonic properties.[30]

Table 1. Cited Medicinal Plants for the Management of Hemorrhoid Disease.

Family	Scientific Name	Traditional Name	Part(s)	Administration	Dose	Text(s)[a]
Adiantaceae	*Adiantum capillus-veneris* L.	*Barsiavashan*	Aerial	Topical (oil)	—	3
Amaryllidaceae	*Allium cepa* L.	*Basal*	Root	Topical (oil)	—	3, 4
	Allium ampeloprasum L.	*Korras*	Leaves	Oral, topical	15 g	1, 2, 3, 4
Anacardiaceae	*Mangifera indica* L.	*Anbaj*	Fruit	Oral	—	3, 4
	Semecarpus anacardium Blanco	*Belador*	Fruit	Topical (smoke)	—	2, 3
	Pistacia terebinthus L.	*Habatol khazra*	Seed	Oral	18 g	3, 4
	Rhus coriaria L.	*Somagh*	Fruit	Topical	—	1, 3, 4
Apiaceae	*Pimpinella anisum* L.	*Anisoon*	Seed	Topical (oil)	—	4
	Ferula assa-foetida L.	*Anjedan*	Seed	Topical (boiled)	—	2, 3, 4
	Ferula persica Willd.	*Barzad*	Flower	Topical	—	3, 4
	Apium graveolens L.	*Hazza*	Leaves	Oral (decocted)	10.8 g	4
	Cuminum cyminum L.	*Kroya*	Seed	Topical (ASH)	—	2, 4
	Ferula gummosa Boiss.	*Sakbinaj*	Gum	Smoke, topical	3.6 g	1, 4
	Anethum graveolens L.	*Shebet*	Seed	Topical (oil)	—	1, 2, 3, 4
Araceae	*Dracunculus vulgaris* Schott	*Loof*	Leaves	Oral, topical	25 g	2, 3, 4
Arecaceae	*Phoenix dactylifera* L.	*Ghoore-e-khorrna*	Fruit	Oral	—	3, 4
	Cocos nucifera L.	*Narjil*	Fruit	Topical (oil)	10.8 g	1, 2, 3, 4
Aristolochiaceae	*Aristolochia rotunda* L.	*Zaravand*	Root	Oral	8.4 g	3
Asparagaceae	*Drimia maritima* (L.) Stearn	*Esghil*	Root	Topical (ash)	—	3
Asteraceae	*Artemisia absinthium* L.	*Afsantin*	Flower	Oral, topical	8 g	2, 3, 4
	Matricaria chamomilla L.	*Baboonaj*	Flower	Topical (oil)	—	3
	Achillea millefolium L.	*Hozonbol*	Root	Oral	8.4 g	3, 4
	Tanacetum parthenium (L.) Sch.Bip.	*Oghhavan*	Aerial	Topical (oil)	—	1, 4
Berberidaceae	*Berberis vulgaris* L.	*Ambarbaris*	Fruit	Oral	60 g	4
Brassicaceae	*Lepidium sativum* L.	*Horf*	Leaves	Smoke	—	4
Burseraceae	*Boswellia sacra* Flueck.	*Kondor*	Gum	Oral (with sugar)	4.2 g	4
	Commiphora mukul (Hook. ex Stocks) Engl.	*Moghl*	Gum	Oral, smoke, topical	3.6 g	1, 2, 3, 4
Capparaceae	*Capparis spinosa* L.	*Kabar*	Root	Smoke, topical (decocted)	—	1, 2, 3, 4
Colchicaceae	*Colchicum autumnale* L.	*Sooranjan*	Root	Topical	—	3
Combretaceae	*Terminalia chebula* Retz.	*Ahlilaj*	Fruit	Oral (jam)	30 g	1, 2, 3, 4
	Terminalia bellirica (Gaertn.) Roxb.	*Balilaj*	Fruit	Oral	10.8 g	3
Cucurbitaceae	*Bryonia alba* L.	*Fashra*	Root	Topical (OIL)	—	3
	Cucurbita pepo L.	*Gar'a*	Fruit	Oral	—	3, 4
	Ecballium elaterium (L.) A.Rich.	*Ghesa-ol-hemar*	Fruit	Topical (boiled in oil)	—	3, 4
	Citrullus colocynthis (L.) Schrad.	*Hanzal*	Fruit	Oral	1.8-3.6 g	4
Cupressaceae	*Juniperus sabina* L.	*Abhal*	Seed	Topical (oil)	40 g	3
	Tetraclinis articulata (Vahl) Mast.	*Sandroos*	Gum	Smoke	—	4
Cyperaceae	*Cyperus longus* L.	*Soad*	Root	Oral	8.4 g	1, 2, 3, 4
Euphorbiaceae	*Ricinus communis* L.	*Kherva*	Seed	Topical (oil)	5-10 g	3, 4
Fabaceae	*Senna tora* (L.) Roxb.	*Ashragh*	Seed	Oral	—	4
	Vigna unguiculata (L.) Walp.	*Habol ghallat*	Seed	Oral, topical	3.6 g	3, 4
	Alhagi maurorum Medik.	*Haj*	Flower	Oral, smoke	30 g	3, 4
	Trigonella foenum-graecum L.	*Holbeh*	Seed	Oral, topical	—	1,2, 3, 4
	Cicer arietinum L.	*Homas*	Seed	Oral	—	3, 4
	Ceratonia siliqua L.	*Kharnoob*	Seed	Oral	18 g	3, 4
	Senna alexandrina Mill.	*Sena*	Leaves	Oral (boiled)	4.2 g	3, 4
	Glycyrrhiza glabra L.	*Soos*	Root	Topical	—	3
	Tamarindus indica L.	*Tamr*	Fruit	Oral	120 g	4
	Lupinus albus L.	*Termes*	Seed	Topical (boiled)	—	3
Hypericaceae	*Hypericum perforatum* L.	*Hufarighoon*	Aerial	Topical	—	3, 4
Iridaceae	*Iris* × *germanica* L.	*Irsa*	Root	Topical (oil)	—	1, 2, 3, 4
Juglandaceae	*Juglans regia* L.	*Jowz*	Seed	Oral, topical (ash)	4 g	3, 4
Lamiaceae	*Vitex agnus-castus* L.	*Aslagh*	Aerial	Oral	4.2 g	4
	Ocimum × *africanum* Lour.	*Faranjmeshk*	Leaves	Oral, Topical	12 g	2, 4

(continued)

Table 1. (continued)

Family	Scientific Name	Traditional Name	Part(s)	Administration	Dose	Text(s)[a]
	Ajuga chamaepitys (L.) Schreb.	*Komafitoos*	Aerial	Oral (7 days)	10.8 g	4
	Mentha × *piperita* L.	*Na'na*	Leaves	Oral, topical	—	3, 4
	Nepeta menthoides Boiss. & Buhse	*Ostokhodus*	Aerial	Topical	—	3
	Ocimum basilicum L.	*Reyhan*	Leaves	Topical (oil)	—	2, 3
	Cinnamomum verum J.Presl	*Darsini*	Bark	Topical (in oil)	—	4
Lythraceae	*Punica granatum* L.	*Jolnar*	Flower	Oral, topical		4
Moraceae	*Ficus carica* L.	*Tin*	Leaves	Topical (enema)	—	1,3, 4
Moringaceae	*Moringa arabica* (Lam.) Pers.	*Habol ban*	Seed	Topical (oil)	—	3, 4
Myrtaceae	*Myrtus communis* L.	*Aas*	Leaves	Smoke, topical	—	1, 2, 4
Nitrariaceae	*Peganum harmala* L.	*Hormal*	Seed	Topical (Iris oil)	—	3, 4
Oxaliaceae	*Oxalis acetosella* L.	*Hommaz*	Seed	Oral	3.6 g	1, 3, 4
Papaveraceae	*Chelidonium majus* L.	*Mamiran*	Gum	Topical	—	4
Pedaliaceae	*Sesamum indicum* L.	*Samsam*	Seed	Oral (oil)	8.4 g	3, 4
Phyllanthaceae	*Phyllanthus emblica* L.	*Amlaj*	Fruit	Oral	20 g	1, 2, 3, 4
Plantaginaceae	*Plantago major* L.	*Lesan-ol-haml*	Leaves, seed	Oral, topical (enema)	42 g (leaves)	1, 2, 3, 4
Poaceae	*Panicum miliaceum* L.	*Javars*	Seed	Topical	—	3
	Triticum spelta L.	*Selt*	Seed	Topical (boiled)	—	3, 4
	Bambusa bambos (L.) Voss	*Tabasheer*	Gum	Topical	—	3
Polygonaceae	*Persicaria bistorta* (L.) Samp.	*Anjebar*	Root	Topical (boiled)	—	3, 4
	Rheum palmatum L.	*Ravand*	Root	Topical (oil)	—	3, 4
	Rheum ribes L.	*Ribas*	Leaves	Oral (in water)	120 g	1
Polypodiaceae	*Polypodium vulgare* L.	*Basfayej*	Root	Oral (boiled)	12 g	3
Portulacaceae	*Portulaca oleracea* L.	*Baghlat-ol-hamgha*	Leaves	Oral (fresh juice)	84 g	1, 2, 3, 4
Ranunculaceae	*Aconitum napellus* L.	*Khanegh-ol-namr*	Leaves	Topical	—	3, 4
	Nigella sativa L.	*Shooniz*	Seed	Topical (oil)	—	3, 4
Rosaceae	*Rubus vestitus* Weihe	*Olligh*	Leaves	Topical	—	1, 3
	Potentilla reptans L.	*Bantafelon*	Aerial	Topical (boiled)	—	3, 4
	Prunus persica (L.) Batsch	*Khookh*	Seed	Topical (oil)	—	3, 4
	Prunus armeniaca L.	*Meshmesh*	Seed	Oral, topical	4.2 g	2, 3, 4
	Rosa canina L.	*Nasrin*	Leaves	Topical	—	4
Rubiaceae	*Coffea arabica* L.	*Bon*	Seed	Oral	—	4
Rutaceae	*Aegle marmelos* (L.) Corrêa	*Bal*	Fruit	Smoke	—	3
	Citrus medica L.	*Otroj*	Peel	Oral, topical	—	2, 3, 4
	Ruta graveolens L.	*Sodab*	Leaves	Oral	12.6 g	3, 4
Salvadoraceae	*Salvadora persica* L.	*Arak*	Stem	Topical (in oil)	—	3, 4
Smilacaceae	*Smilax china* L.	*Choob-e-chini*	Root	Oral	2-3 g	4
Solanaceae	*Solanum melongena* L.	*Badenjan*	Fruit	Oral, topical	—	2, 3, 4
	Hyoscyamus niger L.	*Bazrolbanj*	Seed	Oral (with fig)	2 g	2, 3
	Withania somnifera (L.) Dunal	*Boozidan*	Fruit	Oral, topical	6.3 g	3, 4
	Lycium afrum L.	*Hozaz*	Aerial	Oral	3.6 g	1, 2, 4
	Datura stramonium L.	*Jowz masel*	Seed	Topical (oil)	7.2 g	3, 4
	Physalis alkekengi L.	*Kakanj*	Leaves	Topical	—	4
Tamaricaceae	*Tamarix aphylla* (L.) H. Karst.	*Asl*	Root	Smoke, topical	7 days	3, 4
Theaceae	*Camellia sinensis* (L.) Kuntze	*Chai-e-khataii*	Leaves	Topical (boiled)	—	4
Valerianaceae	*Nardostachys jatamansi* (D.Don) DC.	*Sonbol*	Aerial	Oral	4.2 g	3, 4
Vitaceae	*Vitis vinifera* L.	*Karam*	Fruit	Topical (ash)	—	2, 3, 4
Xanthorrhoeaceae	*Aloe vera* (L.) Burm. f.	*Sebr*	Gum	Topical	—	1, 2, 4
Zingiberaceae	*Curcuma zedoaria* (Christm.) Roscoe	*Jadvar*	Root	Topical	—	3
	Zingiber officinale Roscoe	*Zanjebil*	Root	Topical	—	3, 4

[a]Texts: 1—(MS A 17- NLM, NLM Microfilm Reel: FILM 48-115 no. 3) *Kitāb al-Hāwī fī al-Tibb* (*Liber Continens*) by Abū Bakr Muhammad ibn Zakarīyā' al-Rāzī (865-925), the 20th and 21st books of this encyclopedia are on *Materia Medica* containing 898 simple medicines; 2—*Kitāb al-Qānūn fī al-Tibb* (The Canon of Medicine), by Ibn Sīnā (Avicenna) with 800 natural medicines and their application and effectiveness; 3—(MS P 21, 22- NLM, NLM Microfilm Reel: FILM 48-136 no. 2) the book of *Tuhfat al-mu'minīn* (The Present for the Faithful), a Persian comprehensive pharmacopoeia of remedies (second half of 17th century) by Muhammad Mu'min Daylamī Tunakābunī with 763 simple natural medicines; 4—(MS P 12- NLM, NLM Microfilm Reel: FILM 48-133 no. 2) *Makhzan al-adviyah* (The Storehouse of Medicaments), the largest and one of the latest Persian pharmacopoeias written by Muhammad Hāshim Hādī Alavī Shīrāzī (18th century AD) containing 28 chapters and 1698 monographs on natural medicine.

Many of the contemporary medical strategies for treatment of hemorrhoids are similar to those mentioned by the medieval Persian practitioners. On the other side, many of the reported herbs (Table 1) may manage the disorder with the aforementioned mechanisms of action.

Ethanol extract of *Adiantum capillus-veneris* aerial parts (200 μg) was evaluated for anti-inflammatory activities by evaluating the spleen index and tumor necrosis factor–related protein expression in lipopolysaccharide-induced mice. The extract could normalize the lipopolysaccharide-induced elevation of the spleen index as well as tumor necrosis factor and thus could be introduced as a natural anti-inflammatory resource.[31] Ethanol extract and ethyl acetate fraction of *Adiantum capillus-veneris* have also shown antinociceptive effects (300 mg/kg orally) by tail-flick method and writhing test.[32]

Anti-inflammatory activities of freeze-dried *Allium cepa* sprout have been evaluated by the lipoxygenase inhibitor screening assay. Results confirmed the respective activity with a dose-related response.[33] In another investigation, hydroalcoholic extract of *Allium cepa* peels was evaluated for antihypertensive and vasorelaxant properties. Outcomes revealed a reduction in the aorta contractions, which could be related to the quercetin content in the extract.[34] This finding can be considered for application of this plant in the management of hemorrhoids. In addition, antispasmodic activities of saponins from the polar extract of *Allium cepa* bulb in guinea pig isolated ileum have been confirmed.[35]

Concerning the anti-inflammatory properties of *Allium ampeloprasum*, steroidal saponins have been isolated and its effectiveness has been confirmed.[36]

Mangifera indica is another treatment modality for hemorrhoids. To assess the anti-inflammatory effects of *Mangifera indica* aqueous extract, an investigation has been carried out on dextran sulfate sodium–induced colitis in rats. In that study, the extract was administered either rectally for 7 days or orally over 2 weeks at a dose of 150 mg/kg. Anti-inflammatory effect of *Mangifera indica* was subsequently checked by myeloperoxidase activity. The extract showed anti-inflammatory effects by reduction of ulceration and myeloperoxidase activity.[37] In an investigation, vascular effects of *Mangifera indica* extract and mangiferin (a C-glucosylxanthone derivative) were evaluated in the vascular smooth muscle cells and mesenteric resistance arteries of Wistar Kyoto rats.[38] Another study proved the analgesic effect of *Mangifera indica* aqueous extract using acetic acid–induced abdominal constriction as well as formalin-induced licking.[39]

The anti-inflammatory activity of *Semecarpus anacardium* has been shown in a study by reduction in the carrageenan-induced paw edema and cotton pellet granuloma.[40] Also, a 3-oxotriterpene, namely oleanonic acid, has been isolated from *Pistacia terebinthus* and assessed for possible anti-inflammatory effects (50% inhibitory concentration [IC_{50}] = 17 μM) in another study.[41]

The vasorelaxant activity of *Rhus coriaria* leaves extract has been examined in an isolated rabbit's aorta ring with or without endothelium. Results confirmed the vasorelaxant effect, which was endothelium dependent.[42]

The analgesic and anti-inflammatory activities of *Pimpinella anisum* have been proved in animal models. An investigation showed that oral application of *Pimpinella anisum* essential oil (100 mg/kg) was as effective as aspirin with regard to the analgesic property.[43] Regarding the inhibitory activities on muscarinic receptors, *Pimpinella anisum* aqueous and ethanol extracts as well as essential oil showed muscle relaxant effects on isolated tracheal chains in guinea pig.[44] This could be considered as possible relaxant effects on veins.

Sesquiterpene dienones from *Ferula assa-foetida* showed nuclear factor-κB inhibitory activity which could be considered as agents for inflammatory disturbances.[45] The anti-inflammatory effect of the *Ferula assa-foetida* ethanol extract has been clinically assessed and confirmed in the irritable colon.[46] In an animal study, *Ferula assa-foetida* gum extract showed antispasmodic (3 mg/mL) and hypotensive effects (0.3-2.2 mg/100 g body weight) due to the presence of relaxant compounds.[47] Using hot plate and acetic acid induced writhing tests, analgesic activity of *Ferula assa-foetida* (25, 50, and 100 mg/kg) in comparison with sodium diclofenac (30 mg/kg) or morphine sulfate (8 mg/kg) was confirmed in animal model.[48]

Using acetic acid–induced writhing and hot-plate tests, *Apium graveolens* ethanol extract has shown analgesic effects in animal model.[49] Polar fraction of the plant also revealed to have anti-inflammatory activity in carrageenan-induced edema in rats.[50] *Apium graveolens* has also possessed hypotensive effect in animal model[51] and thus may be useful in the management of hemorrhoids.

Cuminum cyminum showed both antinociceptive and antihypertensive activities which can be useful for the current complications. Aqueous extract of *Cuminum cyminum* seeds was administered orally (200 mg/kg body weight for 9 weeks) in rats and it improved plasma nitric oxide, declined blood pressure and ameliorated inflammatory and oxidative stress.[52] *Cuminum cyminum* also possessed antinociceptive effects in animal models. *Cuminum cyminum* essential oil (0.0125 and 0.20 mL/kg) could exhibit a significant and dose-dependent analgesic effect in chronic and inflammatory pain model.[53]

Ferula gummosa has been evaluated for possible antispasmodic activity on the ileum contractions. Because of the presence of α-pinene and β-pinene, *Ferula gummosa* essential oil possessed relaxant effects.[54]

During 8 weeks of the intervention, *Anethum graveolens* showed anti-inflammatory effects in patients with diabetes type II (3.3 g/d dry powder) as compared to placebo.[55] Moreover, antinociceptive activity of the herb also showed antispasmodic effects on the rat ileum.[56] In that study, *Anethum graveolens* fruit hydroalcoholic extract could relax the ileum with cumulative concentrations (0.5-4 mg/mL).

Anti-inflammatory activities of *Phoenix dactylifera* have been proved in the rats with chronic inflammation model. Foot swelling was significantly reduced by the methanol and aqueous extracts by 67.8% and 61.3%, respectively.[57]

Antinociceptive and anti-inflammatory activities of *Cocos nucifera* have been evaluated in an animal study. The analgesic activity was assessed in comparison with morphine and anti-inflammatory effect was confirmed on the rat paw edema

induced by histamine.[58] *Cocos nucifera* also showed hypotensive and relaxant activities, which could be considered for hemorrhoids. In an investigation on salt-induced hypertensive rats, *Cocos nucifera* ethanol extract reduced the mean systolic blood pressure.[59]

As a popular medicinal plant, *Matricaria chamomilla* has been repeatedly evaluated for anti-inflammatory and antinociceptive effects. The α-bisabolol from *Matricaria chamomilla* essential oil was fed to animals and proved by inflammatory model of paw edema and model of nociception.[60]

The anti-inflammatory activity of *Achillea millefolium* crude extract has also been confirmed experimentally via in vitro protease inhibition assays. Flavonoid-enriched fraction inhibited the human neutrophil elastase ($IC_{50} = 72$ μg/mL), which could represent it as a potent anti-inflammatory medicament.[61] Additionally, antinociceptive and hypotensive activities of *Achillea millefolium* were evaluated and proved in animal models.[62,63]

Tanacetum parthenium showed anti-inflammatory effects and made reduction in erythema in a methyl nicotinate-induced vasodilation model.[64] Sesquiterpene lactones and other components of *Tanacetum parthenium* inhibited the generation of thromboxane B_2 and leukotriene B_4.[65] Antinociceptive and anti-inflammatory effects of *Tanacetum parthenium* have been evaluated against acetic acid-induced writhing and carrageenan-induced paw edema in mice and rats, respectively.[66]

Anti-inflammatory properties of *Berberis vulgaris* have been assessed and proved in another study. Root ethanol extract was effective in a chronic inflammatory model of adjuvant arthritis.[67] Antinociceptive activity of isoquinoline alkaloids from *Berberis vulgaris* root significantly exhibited dose-dependent inhibitory activity against acetic acid-induced increase in vascular permeability via oral administration.[68] Fruits of BV possessed hypotensive effects on deoxycorticosterone acetate–induced hypertension in rats.[69]

Lepidium sativum showed anti-inflammatory and analgesic effects by inhibition of carrageenan-induced paw edema in rats and prolongation of the mice reaction time on hot plate.[70] Moreover, the antihypertensive activity of the *Lepidium sativum* aqueous extract was orally checked and proved in spontaneously hypertensive rats (20 mg/kg), revealing a significant reduction in blood pressure ($P < .01$) in 3 weeks.[71]

Via 5-lipoxygenase, boswellic acids from *Boswellia sacra* inhibited the leukotriene synthesis. Therefore, *Boswellia sacra* can be presented as a herbal medicament with anti-inflammatory activity.[72]

The anti-inflammatory effects of *Commiphora mukul* have been proved in 2 investigations via inhibitory activities on lipid peroxidation and cyclooxygenase in an experimental assessment,[73] and anti-arthritis activity in male and female patients.[74]

Some fractions of the fruits' aqueous extract of *Capparis spinosa* potently inhibited the carrageenan-induced paw edema in mice, which can prove *Capparis spinosa* anti-inflammatory activity.[75] *Capparis spinosa* aqueous extract also exhibited rapid vasorelaxant activity (10 mg/mL) during the plateau phase of contraction.[76]

Regarding the anti-inflammatory effects on knee osteoarthritis, significant improvement has been observed in the colchicines (from *Colchicum autumnale* L.) plus nimesulide group in comparison to placebo plus nimesulide. Visual analog scale for index knee pain showed 52.6% improvement in the colchicine group versus 17.6% for the placebo group.[77]

Anti-arthritic effects of *Terminalia chebula* hydroalcoholic extract was assessed and proved by modulatory effect of the extract on pro-inflammatory cytokine expression in experimental models.[78]

Ethanol extracts of *Terminalia bellirica* and *Terminalia chebula* showed antinociceptive effects at 200, 400, and 800 mg/kg on chronic pain due to the presence of saponins, triterpenoids, carbohydrates, tannins, and proteins.[79]

A lead compound isolated from the roots of *Bryonia alba* (<80 μM) effectively suppressed nitric oxide generation, which is responsible for inflammation.[80]

Cucurbitacin R (1 mg/kg, oral) from *Cucurbita pepo* has shown considerable anti-inflammatory effects on adjuvant-induced arthritis in rats by reduction in joint damage and footpad soft-tissue swelling.[81] Using formalin-induced inflamed method, methanol extract of *Cucurbita pepo* fruits showed analgesic activities as compared with indomethacin.[82] Compared with amlodipine (0.9 mg/kg), *Cucurbita pepo* seed oil (40 or 100 mg/kg) has exhibited antihypertensive effects on rats with hypertension induced by nitric oxide synthesis inhibitor in 6 weeks.[83]

Ecballium elaterium (EE) fruit juice showed analgesic activity in animal models.[84]

Analgesic and anti-inflammatory effects of *Citrullus colocynthis* root and stem aqueous extracts have been evaluated by carrageenan-induced paw edema test in rats and acetic acid writhing assay in mice.[85] Extracts revealed to possess inhibitory activities. The organic extracts of roots, seeds, and fruits of *Citrullus colocynthis* also underwent the previous tests and exhibited respective effects.[86]

Using writhing test in mice, the analgesic effect of *Cyperus longus* (10 and 20 mg/kg) has been proved in comparison with indomethacin (5 mg/kg).[87]

Methanol extract of *Ricinus communis* root has shown anti-inflammatory effects (250 and 500 mg/kg) in the carrageenan-induced hind paw edema model.[88] Furthermore, *Ricinus communis* leaves possessed antinociceptive activity via writhing test, paw licking, and tail immersion method in mice (100, 125, and 150 mg/kg).[89]

By reduction in abdominal constrictions in acetic acid–induced pain model, *Vigna unguiculata* revealed antinociceptive activities in an investigation.[90]

Antinociceptive and anti-inflammatory activities of *Alhagi maurorum* alcoholic extract have been evaluated and proved by hot plate and carrageenan-induced paw edema tests, respectively. Results were attributed to high flavonoid contents.[91] Relaxant effect of *Alhagi maurorum* aqueous-acetic acid extract on guinea pig ureter has also been evaluated and confirmed in a study.[92]

Trigonella foenum-graecum mucilage has exhibited maximum edema inhibition percentage and shown anti-inflammatory activity against arthritis-induced joints in rats (75 mg/kg for 21 days).[93] Also, alkaloid- and flavonoid-rich

fractions of the methanol extract of *Trigonella foenum-graecum* possessed antinociceptive activities (100 mg/kg) as effective as morphine (5 mg/kg).[94]

Compared with indomethacin (10 mg/kg), methanol and ethanol extracts of *Cicer arietinum* (500 mg/kg) were checked for possible anti-inflammatory effect and showed maximum effects from the second and fifth hours of administration.[95]

A flavonoid, isoliquiritigenin, from *Glycyrrhiza glabra* showed analgesic activity in acetic acid–induced writhing response and hot plate test at the high dose.[96]

The anti-inflammatory effect of hydroalcoholic extract of *Tamarindus indica* leaves was assessed by the carrageenan-induced hind paw edema. The antinociceptive activities of the extract were evaluated using tail-flick, acetic acid–induced writhing, and the hot plate models. The extract was effective at doses of 500, 750, and 1000 mg/kg body weight, with regard to both properties.[97]

Hypericum perforatum revealed to have anti-inflammatory effects against carrageenan-induced paw edema in mice regarding modulation of cyclooxygenase II expression.[98] *Hypericum perforatum* lipophilic extract showed topical anti-inflammatory and antiphlogistic effects in the mices ear edema induced with croton oil.[99]

Using spectrophotometric assay on activated human neutrophils, anti-inflammatory effects of isoflavonoids from *Iris germanica* rhizomes were assessed and confirmed.[100]

Methanol extract of *Juglans regia* has been evaluated for anti-inflammatory activity. The extract significantly decreased the tumor necrosis factor–α-induced endothelial expression in both vascular cell adhesion and intracellular adhesion molecule in human aortic endothelial cells.[101]

In a cell-based contemporary assay, some secondary metabolites from *Vitex agnus-castus* showed anti-inflammatory activity and lipoxygenase inhibition.[102] Methanol extract of *Vitex agnus-castus* revealed antispasmodic effects on the isolated rabbit's jejunum (3.0 mg/mL).[103]

Antinociceptive activities of *Mentha piperita* have been evaluated using acetic acid–induced writhing and hot plate tests in mice which were dose dependent. On the other hand, the herb possessed anti-inflammatory effects using xylene-induced ear edema.[49]

Ocimum basilicum aqueous extract (500 mg/kg body weight for 10 weeks) has exerted significant vasorelaxant effects on the rat's thoracic aorta.[104] By confirmed inhibition of pro-inflammatory cytokines and mediators, *Ocimum basilicum* methanol extract can be introduced as an anti-inflammatory agent.[105]

Among various types of *Ficus carica* extracts, ethanol extract (600 mg/kg) exerted maximum anti-inflammatory activity by using cotton pellet granuloma and carrageenan-induced rat paw edema methods.[106]

Antinociceptive and anti-inflammatory effects of *Myrtus communis* were confirmed by hot plate and writhing as well as xylene-induced ear edema and cotton pellet tests. Aqueous and ethanol extracts exhibited significant antinociceptive and anti-inflammatory effects.[107]

Alkaloid extract of *Peganum harmala* seeds possessed antinociceptive effect (12.5 and 25 mg/kg) against acetic acid intraperitoneal injection.[108] Bioassay-guided purification of *Peganum harmala* seeds resulted in isolation of vasorelaxant components active against phenylephrine-induced contraction of the rat's isolated aorta.[109]

Chelidonium majus has exerted anti-inflammatory effect in animal model. *Chelidonium majus* methanol extract was fed to collagen-induced arthritis mice (400 and 40 mg/kg/d for 4 weeks) and significantly suppressed the collagen-induced arthritis progression.[110]

Sesamum indicum seeds oil has been evaluated for possible antinociceptive and anti-inflammatory effects. Using paw licking (100, 200, or 400 mg/kg) and hot plate (200 or 400 mg/kg) as well as application of carrageenan, the oil revealed to be effective.[111]

Compared with that of the control group ($P < .05$), *Phyllanthus emblica* exhibited anti-inflammatory effect against acute inflammation models as acetic acid–induced mice peritonitis and carrageenan-induced rat paw edema.[112]

By using acetic acid–induced writhing and tail-flick tests, oral administration of methanol extract of *Plantago major* seeds showed antinociceptive effects in mice (400 mg/kg). Also, large doses of *Plantago major* leaves exerted some effect as compared with the controls.[113] In addition, *Plantago major* exhibited anti-inflammatory activity at 20 and 25 mg/kg as compared to indomethacin and placebo.[114] In another study, the aqueous extract of leaves (1 g/kg) could reduce acetic acid–induced writhing and carrageenan-induced paw edema and pleurisy.[115]

Portulaca oleracea was shown to have anti-inflammatory and antinociceptive effects in animal models. The antinociceptive effect of *Portulaca oleracea* petroleum ether extract was assessed and confirmed by acetic acid–induced writhing, formalin test, and tail immersion method in mice. The anti-inflammatory activity was proved by carrageenan-induced hind paw edema in rats.[116]

Nigella sativa oil (50-400 mg/kg) could dose dependently exert antinociceptive effects by hot-plate, acetic acid–induced writhing, and tail-pinch tests on oral administration.[117] The mentioned tests as well as carrageenan-induced paw and croton oil–induced ear edema tests were performed on *Nigella sativa* seed polyphenols. Intraperitoneally, *Nigella sativa* seed polyphenols exhibited dose-dependent inhibition in paw edema.[118]

A topical ointment from water extract of the roots of *Potentilla reptans* was applied on the mouse ear inflammation (2.5 mg/ear) induced by croton oil (10 μg/ear). *Potentilla reptans* ointment could significantly reduce the inflammation as compared with the controls' ear.[119]

The anti-inflammatory and analgesic effects of *Citrus medica* peel extract was observed by using carrageenan-induced inflammatory pain as well as plantar, hot plate, pin prick, and mechanical allodynia tests in rats (400 mg/kg).[120]

Ruta graveolens methanol extract showed potent edema inhibition (20 mg/kg for 21 days) in arthritis rat model,[121] and thus could be introduced as an anti-inflammatory agent.

The anti-inflammatory activity of *Salvadora persica* was assessed and confirmed in an animal study. According to the findings, ethyl acetate and hydroalcoholic extracts of *Salvadora persica* (100 mg/mL) significantly reduced the edema thickness and decreased secretion of inflammatory mediators.[122]

Ethyl acetate fraction of *Smilax china* revealed in vitro (IC_{50} = 38 μM) and in vivo (10 and 50 mg/kg) anti-inflammatory effects by lipoxygenase- and carrageenan-induced hind paw edema models, respectively.[123] Bioassay tests on isolated steroidal saponins from the *Smilax china* butanol extract showed the inhibitory effects of those isolates on cyclooxygenase II at 10^{-5} M.[124] *Smilax china* aqueous extract was evaluated for anti-inflammatory (egg albumin–induced edema) and antinociceptive (hot-plate test) activities (1000 mg/kg) and possessed significant effects.[125]

Solanum melongena showed dose-dependent analgesic activity (100, 250, and 500 mg/kg) by using the acetic acid–induced writhing test.[126]

Methanol extract of *Hyoscyamus niger* seeds has been assessed for in vivo analgesic and anti-inflammatory activities. *Hyoscyamus niger* showed dose-dependent analgesic effect by reduction in writhing response and was effective on inflammation (using carrageenan-induced paw edema).[127]

Withania somnifera aqueous fraction has been evaluated for possible efficacy to produce pro-inflammatory molecules from lipopolysaccharide-stimulated macrophage cell lines. Dose-dependently, *Withania somnifera* extract could inhibit the lipopolysaccharide-induced production of interleukin-1 and thus may be introduced as a treatment for inflammatory diseases.[128] Compared with that of the indomethacin, *Withania somnifera* root powder could suppress the increase in paw diameter and lysosomal enzyme activity to the normal level (1 g/kg).[129]

Using hot-plate or formalin tests, analgesic effect of ethanol extract of *Datura stramonium* seeds was experimented via oral and intraperitoneal administration in male NMRI rats. Intraperitoneally, *Datura stramonium* extract could potentially alleviate the pain in formalin and hot-plate tests (more than 100 mg/kg). The effective dose for oral administration was marked at >400 mg/kg.[130]

The chloroform fraction from the methanol extract of *Physalis alkekengi* demonstrated significant inhibitory effects on the production of nitric oxide, cyclooxygenase, and tumor necrosis factor. Therefore, it may be introduced as an anti-inflammatory medicament.[131]

Aloe vera has long been known as an anti-inflammatory agent. A study has evaluated the effects of *Aloe vera* aqueous, chloroform, and ethanol extracts on carrageenan-induced paw edema in rat. The chloroform and aqueous extracts could suppress the edema.[132] Anti-inflammatory properties of the aloe vera gel on inflammatory bowel disease has also been experimentally confirmed.[133]

Using different pain models, curcumenol and also a dichloromethane fraction from *Curcuma zedoaria* hydroalcoholic extract has shown potent but dose-dependent analgesic activity (ID_{50} from 12 to 29 μmol/kg).[134] Sesquiterpene compounds, furanodiene, and furanodienone from *Curcuma zedoaria* methanol extract exerted anti-inflammatory activity (0.1 μmol) by suppressing 12-*O*-tetradecanoylphorbol-13-acetate–induced inflammation of mouse ears.[135]

Zingiber officinale has demonstrated anti-inflammatory and analgesic activities in experimental studies. Using acetic acid and hot-plate tests as well as fresh egg albumin–induced pedal edema, *Zingiber officinale* ethanol extract (50-800 mg/kg intraperitoneally) exhibited significant but dose-dependent analgesic and anti-inflammatory effects, as compared with morphine (10 mg/kg) and diclofenac (100 mg/kg).[136] A main ingredient, 6-gingerol (25-50 mg/kg) could exert analgesic and anti-inflammatory activities by acetic acid–induced writhing and formalin-induced tests.[137]

Previously, a study has been carried out on medicinal herbs for hemorrhoids reported from different countries' folk and traditional medicine.[138] Those medicinal plants have been used to improve such symptoms as pain, bleeding, heaviness, and rectal prolapse. Mechanisms underlying those improvements were anti-inflammatory, venoprotective, analgesic, venotonic, and laxative. The current study reviewed anti-inflammatory, analgesic, venotonic, and vasorelaxant effects with regard to the medieval medicinal plants. The analgesic or anti-inflammatory effects of 64 out of 105 reported medicinal plants have been experimented and proved by previous investigations. Besides 2 reports on human studies, most investigations were performed as an animal study. Active secondary metabolites such as flavonoids, tannins, and terpenoids are responsible for the aforementioned properties. Among those classes of active compounds, flavonoids have been evidently used to treat hemorrhoids. These compounds, seemingly, suppress the progressive symptoms and reduce the pain and inflammation as well as bleedings.[139]

Conclusion

The current study aimed to evidently investigate the possible mechanism underlying the treatment effect of plants traditionally reported for hemorrhoids in traditional Persian medicine. More than half of the reported herbs exhibited anti-inflammatory and analgesic effects. Although lack of human studies regarding the mentioned herbs and pharmacological effects is observed, positive results from experimental findings can be considered for new drug discovery supported by traditional and medieval experiences.

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Author Contributions

The work presented in this article was carried out through collaboration between all authors. MHH made the initial hypothesis. MHH and MMZ defined the research theme. FKH, MR, and MMZ contributed to data gathering. MHH and MMZ drafted the manuscript. All authors revised and approved the final version of the manuscript.

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Ethical Approval

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