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Scientific Evaluation of the Prescribed Herbs by Avicenna for the Management of Post Hemorrhoidectomy Complications

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Abstract

Hemorrhoidectomy is an impressive surgery that relieves discomfort in patients who suffer from grade 3 or 4 hemorrhoids. This review is designed to investigate useful herbs for managing post-surgery complications by presenting an overview of *Avicenna*'s view compared to new scientific evidences. The herbs with anti-inflammatory, analgesic, anti-bleeding, antispasmodic, and wound-healing properties may be important for managing patient discomfort. Avicenna's most frequently prescribed herbs were selected using *Bavasir* as a keyword (traditional term for hemorrhoids) from volumes 2 and 5 of the *Canon of Medicine* textbook, and they were investigated in scientific databases including Scopus, PubMed, Web of Science, Science Direct, and Cochrane Library to obtain researches that confirmed their efficacy. Among the different herbs, *Hypericum perforatum* and *Portulaca oleraceae* were the most supported in scientific databases. Other herbs including *Anethum graveolens*, *Cocos nucifera*, *Ferula assa-foetida*, *Myrtus communis*, *Ocimum basilicum*, and *Plantago major* were next in order, while *Artemisia absinthium*, *Solanum melongena*, and *Trigonella foenum-graecum* exhibited few related pharmacological effects. The results established *Avicenna*'s claims regarding the importance of these herbs in post hemorrhoidectomy complications. Although there were many in vitro and/or in vivo researches on the selected herbal medicines, there were no obtained clinical studies on patients after their hemorrhoidectomy surgeries. So, the aforementioned herbs, especially *H. perforatum* and *P. oleraceae*, are recommended for future clinical studies. Among the different classes of compounds, flavonoids were the most responsible phytocomponents for displaying pharmacological effects.**[GMJ.2017;6(3):166-84] DOI:10.22086/gmj.v0i0.774**

Keywords: Herbal medicines; *Hypericum perforatum*; *Portulaca oleracea*; Hemorrhoidectomy

Introduction

Hemorrhoids is the most prevalent rectal disease and is described as the enlargement and distal dislocation of rectal cushions [1, 2]. Intensified pressure on the vascular plexus of hemorrhoids, mainly due to straining or pregnancy, seems to play a major role

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in the development of hemorrhoids [3]. A hemorrhoidectomy is an impressive surgery that relieves discomfort in patients suffering from grade 3 or 4 hemorrhoids [4]. This surgery is also used in situations like non-operative therapy failures, patient preference, and concomitant anorectal diseases including anal fistulas or fissures [2].

The main complications after a hemorrhoidectomy can include inflammation, acute and chronic pain, unhealed wounds, fecal urgency, and rectal bleeding [5, 4]. The main cause of post hemorrhoidectomy pain is ascribed to the spasmodic condition of the internal anal sphincters [6]. *Avicenna* is a famous ancient physician who wrote the well-known book "*Canon of Medicine*" [7, 8]. He thoroughly described "*Bavasir*" (the traditional term for hemorrhoids) in his book. He also recommended surgery for severe conditions of hemorrhoids and proposed different herbal medicines to manage post-surgery complications [9]. The herbs with anti-inflammatory, analgesic, anti-bleeding, antispasmodic, and wound-healing properties may be important in managing post hemorrhoidectomy complications.

Materials and Methods

In this review study, volumes 2 and 5 from the *Canon of Medicine* were investigated using the key terms from the *Bavasir* (hemorrhoids) chapter. The search terms in this chapter were *Zede varam* (anti-inflammatory), *Zede vaja/dard* (pain reliever), and *Zede khoon rizi/sayalan* (means anti-bleeding). Then, most of the prescribed herbs were collected in individual or polyherbal formulations. Afterward, the scientific name of each herb was found in textbooks that matched traditional plant names to their scientific names [10-12].

Next, scientific databases including Scopus, PubMed, Web of Science, Science Direct, and Cochrane Library were searched to obtain reports of any related pharmacological effects including anti-inflammatory, analgesic/antinociceptive, anti-bleeding, antispasmodic, and wound healing, as well as any active constituents and possible mechanisms of each herb. Data were collected from 1987 to August 2016.

Results

The proposed herbs' scientific and traditional names, parts used, and routes of administration are presented in Table-1.

Table-2 summarizes the reported scientific studies' results regarding the herbal medicines, their used parts, extracts, and pharmacological models. These results are also discussed below.

Table 1. Main Herbs Prescribed by Avicenna for the Management of Post Hemorrhoidectomy Complications

Scientific name	Traditional name	Family	Used part(s)	Route of administration(s)
Anethum graveolens L.	*Shebet*	Apiaceae	Aerial part	Topical
Artemisia absinthium L.	*Afsantin*	Asteraceae	Aerial part	Oral
Cocos nucifera L.	*Narjil*	Arecaceae	Fruit	Oral
Ferula assa-foetida L.	*Anjodan*	Apiaceae	Fruit	Topical
Hypericum perforatum L.	*Hofarighoon*	Hypericaceae	Seed	Oral
Myrtus communis L.	*Murta*	Myrtaceae	Leaf	Topical
Ocimum basilicum Willd.	*Faranjamoshk*	Lamiaceae	Aerial part	Oral, topical
Plantago major L.	*Lesan-ol-haml*	Plantaginaceae	Root, leaf	Oral
Portulaca oleraceae L.	*Baghlat-ol-homgha*	Portulacaceae	Aerial part	Oral
Solanum melongena L.	*Badenjan*	Solanaceae	Fruit	Topical
Trigonella foenum-graecum L.	*Holbe*	Fabaceae	Seed	Topical

Anethum graveolens L.

The aqueous extract of *A. graveolens* fruits exhibited more potent antinociceptive effects than its volatile oil in vivo [13]. *A. graveolens* revealed significant analgesic effects in the late phase of formalin tests. Further, its aerial parts demonstrated potent analgesic activity during hot plate tests in vivo [14]. Sabinene, the most active constituent in the essential oil, may be responsible for the plant's notable anti-inflammatory effects due to its inhibitory effects on inducible nitric oxide synthase [15]. Moreover, Naseri *et al*. attributed this species' anti-inflammatory effects to its monoterpenoid constituents including carvone and limonene [16]. In addition, the herb exerted its antispasmodic properties via its inhibitory effect on calcium channels [17].

Artemisia absinthium L.

A. absinthium revealed its anti-inflammatory and analgesic effects in different in vivo models [18, 19]. The fresh leaves' essential oil in 4 and 8 mg/kg doses considerably reduced edema in rats. The presence of phytochemicals like neradiol, santolina triene, α-piene and trans-β-farnesene may have an important role in the plant's pharmacological effects [19].

Cocos nucifera L.

C. nucifera exhibited anti-inflammatory and analgesic effects in various in vivo models [20-23]. During a hot plate test on rats, a 200 mg/kg dose of an aqueous extract of husk fiber significantly prolonged the reaction time to heat stimulants. This effect was reversed by naloxone (an opioid antagonist). So, it can be concluded that opioid receptors mediate this analgesic effect [20]. The presence of phytoconstituents like polyphenols, saponins, and flavonoids can be important for a plant's antinociceptive and anti-inflammatory properties [21]. *C.nucifera*'s water extract displayed a significant inhibition during the second phase of a formalin-induced licking test in mice through a dose-dependent manner [23]. In the burn wounds model, after 16 days of a *C.nucifera* oil topical application, improvements in the wound contractions were seen. However, this effect was more powerful when *C. nucifera* was combined with silver sulfadiazine cream [24].

Ferula assa-foetida L.

F. assa-foetida showed significant analgesic properties in vivo [25, 26]. This effect was most potent in 10 mg/kg doses. In a dose of 2.5 mg/kg, the plant significantly reduced edema in vivo. These pharmacological effects were not reversed by antagonists like naloxone, glibenclamide, theophylline, etc. Phytochemicals including monoterpens, flavonoids, and phenolic constituents had notable lipoxygenase inhibitory effects [26]. Furthermore, *F. assa-foetida*'s essential oil and oleo gum resin exhibited antispasmodic activity through a remarkable reduction in acetylcholine-induced contraction method [27].

Hypericum perforatum L.

Although its antinociceptive effects were confirmed by different in vivo models [28-30], there were no significant properties observed in the acetic acid-induced writhing test [29]. Further, *H. perforatum* hydroethanolic extract revealed dose-dependent antinociceptive effects that were reversed by naloxone [30]. Phytochemicals including pseudohypericin, hypericin, and flavonoids may be responsible for its anti-inflammatory effects due to its iNOS, COX-2, and PGE-2 inhibitory effects [31-33]. Among the different extracts and pure compounds of *H. perforatum* that were investigated on mice with croton oil-induced ear edema, liophilic extract and amentoflavone demonstrated the most considerable anti-inflammatory properties [34]. This plant exerted wound-healing effects in vivo and in vitro [35-38]. Enhancements in polygonal fibroblasts and collagen granules were seen in the cultured NIH3T3 fibroblast model [36]. *H. perforatum* exerted its wound-healing effects via an increase in the wound closure percentage and wound contraction and tissue regeneration in vivo [35]. Wound-healing effects of the species' aerial parts can be attributed to its quinoids, flavonoids, tannins, xanthones, and naphtaquinones [35-38]. The species also exerted its smooth muscle relaxant properties by releasing phytochemicals such as hyperforin and kaempferol. However, this effect was potently reduced by

naloxone [39]. In addition, the herb showed calcium antagonistic and phosphodiesterase inhibitory properties in vitro [40, 41].

Myrtus communis L.

M. communis displayed its analgesic and anti-inflammatory effects in in vitro and in vivo models [42-45]. Tannins, alkaloids, and flavonoids play an important role in these pharmacological effects [42]. Acylphloroglucinol phytoconstituents including myrtucommulone (MC) and semimyrtucommulone, which were isolated from plant leaves, displayed cyclooxygenase-1 and 5-lipoxygenase inhibitory effects in vitro [45]. In addition, MC showed anti-inflammatory properties in carrageenan-induced paw edema and pleurisy models [44]. Moreover, the plant acts as an antispasmodic agent by blocking the calcium channels in vitro [46].

Ocimum basilicum L.

The leaves of *O. basilicum* revealed antinociceptive effects in vivo [44,45]. The presence of linalool in the essential oils and flavonoids of the species' ethanolic extract is ascribed to its antinociceptive properties [47, 48]. It seems that the possible mechanisms of its antinociceptive properties are its inhibitory effects on prostaglandins and prostacyclins synthesis, as well as its interaction with opioid receptors [47]. Its robust anti-inflammatory effects were confirmed using in vitro and in vivo models [49-51]. Aqueous extracts showed more potent anti-inflammatory properties than ethanol extracts in vitro [49]. The species demonstrated anti-inflammatory effects via its reductive action in producing inflammatory mediators such as tumor necrosis factor-α (TNF-α), Interleukin-1β, IL-2, and NO [50]. Phytoconstituents such as eugenol, rosmarinic acid, and estragole may play a significant role in its anti-inflammatory effects [49, 51]. Moreover, the species manifested antispasmodic properties in vitro [52, 53].

Plantago major L.

P. major ethanol extracts with a polyphenol composition at a 1 mg/mL concentration demonstrated powerful wound-healing effects ex vivo [54]. There were no significant antinociceptive properties observed during the tail flick test [55]. While its notable anti-inflammatory effects were proven using different in vitro and in vivo methods [55-57], there were no observed significant anti-inflammatory effects using a dextran-induced edema [55]. Among the herb's various extracts, P. major's methanol and ethanol extracts were the most potent reductions in the inflammatory cytokines levels in vitro [57].

Portulaca oleraceae L.

P. oleraceae exhibited analgesic effects in vivo [58]. The aqueous extract of its aerial parts exerted anti-inflammatory effects by inhibiting the effects on TNF-α action in vitro [59]. Alkaloid phytocompounds, especially oleracimine, exerted intense anti-inflammatory properties by inhibiting the effects on nitric oxide generation and suppressing the effects on IL-6, TNF-α, and PGE-2 secretions in vitro [60]. Additionally, crude extracts of aerial parts displayed potent wound-healing effects in doses of 50 mg/kg by reducing the in-wound surface and enhancing tensile strength in vivo [61]. The plant also manifested smooth muscle relaxant effects in vitro. Because phentolamine significantly reduced the herb's relaxant effects, it can be proposed that adrenergic receptors are involved in the herb's antispasmodic effects [62].

Solanum melongena L.

S. melongena demonstrated powerful analgesic properties using acetic acid-induced writhing tests in 500 mg/kg doses. Phytochemicals like flavonoids, alkaloids, and tannins were reported to be the most important agents for its analgesic property [63]. Lignanamides, which are presented in the ethanol extract of the roots, exhibited inhibitory effects on nitric oxide generation in vitro [64]. Additionally, 200 and 400 mg/kg doses of *S. melongena* displayed less inhibitory effects on paw edema (42.62%) compared to aspirin, which was used as a reference drug (64.5%) [65].

Trigonella foenum-graecum L.

There were many reports about anti-inflammatory and analgesic effects of the plant through in vitro and in vivo models [66-77].

The herb's leaves revealed significant antinociceptive effects at doses of 2000 mg/kg in vivo [66]. Mandegary *et al*. reported that alkaline chloroform and aqueous fractions of the seeds' methanolic extracts, which contained alkaloids and flavonoids, showed powerful antinociceptive and anti-inflammatory properties [67]. Moreover, the analgesic and anti-inflammatory effects of the seeds' methanolic extracts can be attributed to their glycoside and steroid constituents [69]. The presence of tannins and flavonoids in the leaves' methanol extract may antagonize the prostaglandin and bradykinin actions [68]. *T. foenum-graecum* may exert its robust anti-inflammatory effects by reducing COX-2 and 5-LOX activities and has a stabilizing effect on red blood cells against lyses due to its steroidal saponins, flavonoids, and polyphenols [72, 74, 77]. The pharmacological effects of the aforementioned herbs are summarized in Table-3. Reported phytoconstituents of each herb along with their observed pharmacological effects are illustrated in Table-4.

Table 2. Scientific Studies On the Main Prescribed Herbs by Avicenna for the Management of Post Hemorrhoidectomy Complications

Scientific name	Part / extract	Study type	Model	Results	Ref.
Anethum graveolens L.	Fruit / Aqueous extract and volatile oil	In vivo	Hot plate in mice	Antinociceptive activity	[13]
			Acetic acid-induced writhing test in mice		
	Seeds and aerial parts/ Aqueous ethanol extract	In vivo	Formalin test in mice	Analgesic activity	[14]
			Hot plate in mice		
	Aerial Parts / Essential oil	In vitro	RAW 264.7 macrophages	Anti-inflammatory activity	[15]
		In vivo	Formalin-induced inflammation in rat paw	Anti-inflammatory activity	[16]
	Seeds/ Hydroalcoholic extract	In vitro	Isolated rat ileum	Antispasmodic effect	[17]
Artemisia absinthium L.	Seeds and stems/ Methanol extract	In vivo	Tail immersion in mice	Analgesic activity	[18]
			Carrageenan-induced paw edema in rat	Anti-inflammatory activity	
	Fresh leaves/ Essential oil and aqueous extracts	In vivo	Acetic acid-induced writhing test in mice	Analgesic activity	[19]
			Formalin test in mice		
			Hot plate test in mice		
			Carrageenan-induced paw edema in mice	Anti-inflammatory activity	

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Cocos nucifera L.	Husk fiber/ Aqueous extract	In vivo	Acetic acid-induced writhing response in mice	Analgesic activity	[20]
			Tail flick in mice		
			Hot plate in rat		
		In vivo	Formalin-induced licking model in mice	Anti-inflammatory activity	[23]
			Carrageenan-induced paw edema in rat		
	The bunch of spadix of coconut tree/ Hydromethanol extract	In vivo	Acetic acid-induced writhing response in mice	Antinociceptive activity	[21]
			Hot plate in mice		
			Carrageenan-induced paw edema in rat	Anti-inflammatory activity	
	Husk fiber/ Crude extract	In vivo	Acetic acid-induced abdominal writhing in mice	Antinociceptive activity	[22]
			Tail flick test in mice		
			Hot plate test in mice		
			Formalin test in mice		
			Carrageenan-induced paw edema in rat	Anti-inflammatory activity	
	Dried inner flesh / Oil	In vivo	Partial thickness burn wound in rat	Wound-healing property	[24]
Ferula assa-foetida L.	Oleo gum resin	In vivo	Hot plate test in mice	Analgesic activity	[25, 26]
			Acetic acid-induced writhing test in mice		
			Carrageenan-induced paw edema in mice	Anti-inflammatory activity	[26]
	Essential oil of seeds and oleo gum resin	In vitro	Isolated ileum of rat	Antispasmodic activity	[27]
Hypericum perforatum L.	Aerial parts / Aqueous and ethanolic extracts	In vivo	Acetic acid-induced writhing response in mice	Analgesic activity	[28]
			Hot plate in mice		
			Tail flick test in mice		
			Carrageenan-induced paw edema in rat	Anti-inflammatory activity	
			Cotton pellet-induced granuloma		

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Hypericum perforatum L.	Aerial parts / Hydroethanolic extract	In vivo	Acetic acid-induced abdominal constriction	Antinociceptive effect	[30]
	Aerial parts / Aqueous extract	In vivo	Tail electric stimulation in rat	Antinociceptive effect	[29]
			Hot plate in rat		
			Acetic acid-induced writhing test in rat	No significant antinociceptive activity	
	Aerial parts / Aqueous extract	In vivo	Carrageenan-induced paw edema in rat	Anti-inflammatory activity	[31]
		In vitro	Peritoneal macrophages		
	Flowering tops/ Hydroalcoholic, lipophilic, ethylacetic extracts and the pure compounds hypericin, adhyperforin, amentoflavone, hyperoside, isoquercitrin, hyperforin	In vivo	Croton oil-induced ear edema in mice	Anti-inflammatory activity	[34]
	Flower stems / Ethanol extract	In vitro	RAW 264.7 mouse macrophages	Anti-inflammatory activity	[32]
	Whole plant / Ethanol extract		RAW264.7 Mouse Macrophage Cells	Anti-inflammatory activity	[33]
	Aerial parts / Total extract	In vivo	Incision wound in rat	Wound-healing property	[35]
			Circular excision in rat		
		In vivo	Thermal burn in rat	Wound-healing property	[36]
		In vitro	Cultured NIH3T3 fibroblast		
	Flowering aerial parts / Ethanol extract	In vivo	Excision wound	Wound-healing property	[37]
			Incision wound		
	Aerial parts/ Ethanol extract	In vitro	Chicken embryonic fibroblast	Wound-healing property	[38]

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	Flowering top/ Hydromethanolic extract	In vitro	Isolated urinary bladder	Antispasmodic activity	[39]
	Standardized HP extract	In vitro	Isolated rat aorta	Antispasmodic activity	[41]
Hypericum perforatum L.	Aerial parts/ Petroleum spirit, chloroform, ethyl acetate and aqueous and its phytocompounds hyperforin, hypericin, and hyperoside	In vitro	Rabbit jejunum, Guinea-pig trachea and rabbit aorta	Antispasmodic activity	[40]
	Aerial parts / Aqueous and ethanolic extracts	In vivo	Hot plate in mice	Antinociceptive activity	[42]
			Acetic acid-induced writhing in mice		
			Xylene-induced ear edema in mice	Anti-inflammatory activity	
			Cotton pellet in mice		
Myrtus communis L.	Leaves/ Essential oil	In vivo	Acetic acid-induced writhing test in mice	Analgesic activity	[43]
	Leaves	In vitro	Human platelets and PMNLs	Anti-inflammatory activity	[45]
		In vivo	Carrageenan-induced paw edema in mice	Anti-inflammatory activity	[44]
			Carrageenan-induced pleurisy in mice		
	Aerial parts/ Crude methanolic extract	In vitro	Isolated rabbit jejunum	Antispasmodic activity	[46]
Ocimum basilicum L.	Leaves/ Essential oil	In vivo	Acetic acid-induced abdominal writhing test in mice	Antinociceptive activity	[47]
			Hot plate in mice		
			Formalin test in mice		
	Leaves/ Ethanol extract	In vivo	Formalin test in rat	Antinociceptive activity	[48]
	Aerial parts/ Aqueous and methanolic extracts	In vitro	Mouse macrophage (RAW264.7) and human chondrosarcoma (SW1353) cell lines, and human primary chondrocytes	Anti-inflammatory activity	[49]

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	Whole plant/Crude methanolic extract	In vitro	Human peripheral blood mononuclear cells	Anti-inflammatory activity	[50]
Ocimum basilicum L.	Leaves / Essential oil	In vivo	Carrageenan-induced paw edema in rat	Anti-inflammatory activity	[51]
			Dextran-induced paw edema in rat		
			Histamine-induced paw edema in rat		
			Arachidonic acid-induced paw edema in rat		
			Cotton pellet induced-granuloma		
	Aerial parts/ Aqueous methanol extract	In vitro	Isolated rabbit jejunum	Antispasmodic effect	[53]
	Leaves/ Aqueous extract	In vitro	Guinea pig tracheal	Antispasmodic effect	[52]
Plantago major L.	Seed/ Water extract	In vivo	Burn wound in rat	Wound-healing property	[83]
	Leaves/Ethanol and water extracts	*Ex-vivo*	Porcine wound-healing model	Wound-healing property of both extracts	[54]
	Leaves/Aqueous extract	In vivo	Tail flick in mice	No significant antinociceptive activity	[55]
			Acetic acid-induced writhing in mice	antinociceptive activity	
			Croton oil-induced ear edema in mice	Anti-inflammatory activity	
			Carrageenan-induced paw edema in rat		
			Dextran-induced paw edema in rat	No significant anti-inflammatory activity	
	Seeds/ Methanol extract	In vivo	Carrageenan-induced paw edema in rat	Anti-inflammatory activity	[56]
	Leaves/Aqueous ,methanol and ethanol extracts	In vitro	Collected blood sample of rat following Acetaminophen-induced liver injury	Anti-inflammatory activity	[57]

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Portulaca oleraceae L.	Aerial parts / Ethanolic extract	In vivo	Hot plate in mice	Analgesic activity	[58]
			Tail-flick in rat		
			Carrageenan-induced paw edema in rat	Anti-inflammatory activity	
	Aerial parts / Aqueous extract	In vitro	Human umbilical vein endothelial cell (HUVEC)	Anti-inflammatory activity	[59]
		In vitro	Lipopolysaccharide stimulated macrophages	Anti-inflammatory activity	[60]
	Aerial parts/ Crude extract	In vivo	Excision wound in mouse	Wound-healing activity	[61]
	Leaves/ Aqueous extract	In vitro	Isolated rabbit jejunum, taenia coli and guinea pig fundus	Antispasmodic effect	[62]
Solanum melongena L.	Dry residue of leaf juice	In vivo	Acetic acid-induced writhing test in mice	Analgesic activity	[63]
	Roots/ Ethanol extract	In vitro	RAW 264.7 macrophages	Anti-inflammatory activity	[64]
	Leaves /Aqueous extract	In vivo	Carrageenan induced paw edema in rat	Anti-inflammatory activity	[65]
Trigonella foenum-graecum L.	Leaves/ Water extract	In vivo	Tail flick in rat	Antinociceptive activity	[66]
			Formalin test in rat		
	Seeds/ Methanol extract	In vivo	Formalin test in mice	Antinociceptive activity	[67]
			Carrageenan-induced paw edema	Anti-inflammatory activity	

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Trigonella foenum-graecum L.	Leaves and seeds / Petroleum ether, chloroform, ethyl acetate and methanolic extracts	In vivo	Hot plate in mice Acetic acid induced writhing test in mice	Antinociceptive activity	[68]
	Seed/ Methanolic extract	In vivo	Acetic acid-induced writhing in mice	Analgesic activity	[69]
			Hot-plate in mice	Analgesic activity	
			Carrageenan-induced paw edema in rat	Anti-inflammatory activity	
	Seed powder	In vivo	Hot immersion test in rat Formalin Test in rat	Analgesic activity	[70]
	Seeds/ Ethanolic extract	In vivo	Acetic acid induced writhing in mice	Analgesic activity	[71]
			Hot plate in mice		
			Carrageenan-induced paw edema in rat	Anti-inflammatory activity	
	Seed/ Methanolic extract	In vitro	Cultured human myeloma THP-1 cells	Anti-inflammatory activity	[72]
	Seeds/ Diethyl ether extract	In vivo	Carrageenan-induced paw edema in rat	Anti-inflammatory activity	[73]
	Seeds/ Ethanolic extract	In vivo	Carrageenan-induced paw edema in rat	Anti-inflammatory activity	[74, 75]
		In vitro	Peripheral blood mononuclear cells	Anti-inflammatory activity	[74]

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	Leaves/ Water extract	In vivo	Formalin-induced edema in rat	Anti-inflammatory activity	[76]
Trigonella foenum-graecum L.	Leaves/ Petroleum ether, benzene, chloroform, ethyl acetate, methanol, and water extracts	In vitro	Human RBCs	Anti-inflammatory activity	[77]
	Seeds/ Ethanol extract	In vivo	Cotton pellet-induced granuloma	Anti-inflammatory activity	[75]

Table 3. Pharmacological Effects of the Main Prescribed Herbs by Avicenna for the Management of Post Hemorrhoidectomy Complications

Scientific name	Analgesic (Antinociceptive)	Wound healing	Antispasmodic	Anti-inflammatory	Score
Hypericum perforatum L.	+	+	+	+	4
Portulaca oleraceae L.	+	+	+	+	4
Anethum graveolens L.	+	-	+	+	3
Cocos nucifera L.	+	+	-	+	3
Ferula assa-foetida L.	+	-	+	+	3
Myrtus communis L.	+	-	+	+	3
Plantago major L.	+	+	-	+	3
Ocimum basilicum L.	+	-	+	+	3
Artemisia absinthium L.	+	-	-	+	2
Solanum melongena L.	+	-	-	+	2
Trigonella foenum-graecum L.	+	-	-	+	2

-: there is no report.

Table 4. Reported Phytoconstituents of the Main Prescribed Herbs by Avicenna for the Management of Post Hemorrhoidectomy Complications

Scientific name	Chemical constituent	Effect(s)	Ref.
Anethum graveolens L.	Terpenoids	Anti-inflammatory activity	[15, 16]
Artemisia absinthium L.	Terpenoids	Analgesic activity, anti-inflammatory activity	[19]
Cocos nucifera L.	Tannins, flavonoids, saponins, and polyphenols	Analgesic activity/ antinociceptive activity, anti-inflammatory activity	[20, 21]
Ferula assa-foetida L.	Terpenoids, flavonoids	Analgesic activity, anti-inflammatory activity	[25, 26]
Hypericum perforatum L.	Naphtoquinones, phloroglucinols, flavonoids, polyphenols, and tannins	Anti-inflammatory activity, wound-healing activity, antispasmodic activity	[31-33, 35, 37, 39]
Myrtus communis L.	Tannins, alkaloids,flavonoids, and phloroglucinols	Antinociceptive activity, anti-inflammatory activity	[42, 45, 44]
Ocimum basilicum L.	Terpenoids, flavonoids, phenylpropenes, and polyphenols	Antinociceptive activity, anti-inflammatory activity	[47-49, 51]
Plantago major L.	Polyphenols	Wound-healing activity	[54]
Portulaca oleraceae L.	Alkaloids	Anti-inflammatory activity	[60]
Solanum melongena L.	Flavonoids, alkaloids, tannins, and lignanamides	Analgesic activity, anti-inflammatory activity	[63-65]
Trigonella foenum-graecum L.	Alkaloids, flavonoids, tannins, glycosides, steroids, and polyphenols	Antinociceptive/ analgesic activity, anti-inflammatory activity	[67-69, 72, 76, 77]

Discussion

Herbal medicines with vigorous historical backgrounds are great sources to discover novel drugs [78, 79]. The *Canon of Medicine* prescribed eleven important herbs for the management of post hemorrhoidectomy complications (Table-1). As it is apparent in Table-1, the plants used for the management of post hemorrhoidectomy complications belonged to different families, and they were equally utilized in oral and topical forms. Moreover, aerial parts and fruits were the most frequently used for the management of post-surgery complications. These herbal medicines exerted relieving effects on post hemorrhoidectomy complications using two or more pharmacological effects including anti-inflammatory, analgesic, antinociceptive, antispasmodic, and wound-healing activities (Table-3). As demonstrated in Table-4, different classes of phytoconstituents especially flavonoids, polyphenols, terpenoids, alkaloids, and tannins are responsible for the discussed pharmacological effects. Flavonoids displayed all of the mentioned pharmacological effects [67, 68, 77]. However, lignans had less importance, and there was only one report about their anti-inflammatory effects [64].

All of the phytocomponents displayed an anti-inflammatory effect [64-67, 72, 76, 77], while analgesic/antinociceptive effects were reported in terpenoids, tannins, flavonoids, saponins, polyphenols, alkaloids, glycosides, and steroids [19-21, 67-69]. Further, wound-healing properties were attributed to naphtoquinones, tannins, and flavonoids [35, 37,54]. Moreover, antispasmodic effects were ascribed to phloroglucinols and flavonoids [39].

Although there was no clinical study that observed the selected herbs' effects on patients after hemorrhoidectomy surgery, there are some clinical studies on hemorrhoid patients. For example, Mosavat *et al*. confirm *Allium ampeloperasum L.* cream's potent anti-bleeding effects on symptomatic patients [80, 81]. Moreover, Yousefi *et al*. revealed that *Commiphora mukul* can improve some patients' discomforts such as constipation and bleeding severity [82]. Our review study revealed that most of *Avicenna*'s prescribed herbs demonstrate potent related pharmacological effects in modern medicine. So, these herbs are good candidates for future clinical purposes. However, these plants need to be evaluated by scientists and go through clinical trial tests to confirm their efficacy and safety. The second suggestion is to examine the plant mixtures to observe their possible synergistic effects.

Conclusion

H. perforatum L. and *P. oleraceae L.* have revealed most support through scientific databases. They showed anti-inflammatory, analgesic, antinociceptive, antispasmodic, and wound-healing effects. All of the mentioned herbs displayed analgesic and anti-inflammatory effects. While 36% of medicinal plants displayed wound-healing properties, 54% of them exhibited antispasmodic activities. These results don't establish wound-healing or antispasmodic activities for all of the discussed plants; however, these species may not have been tested for their pharmacological effects, and future research on them are recommended. Among the various phytocomponents, only flavonoids exhibited all of the mentioned pharmacological effects.

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Conflict of Interest

None

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