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Review Article

Medicinal Plants for Hemorrhoid Therapy: Mechanistic Insights, Bioactive Compounds, and Preclinical-to-Clinical Evidence

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Abstract

Hemorrhoid is a multifactorial condition involving inflammation, venous stasis, degeneration of supporting tissue, and vascular fragility. It requires safer adjunctive therapy options for long-term use. This narrative review seeks to comprehensively examine potential anti-hemorrhoidal medicinal plants by linking bioactive compounds, pharmacological targets, and evidence from *in vitro*, *in vivo*, and clinical trials. Literature searches were conducted using PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar, focusing on original research articles that documented anti-inflammatory, antioxidant, venoprotective-venotonic, hemostatic-astringent, analgesic, and wound healing activities. The articles were further synthesized qualitatively according to the pathophysiology of hemorrhoids. A total of 90 articles met the inclusion criteria and were classified based on the predominant mechanism, namely anti-inflammatory–antioxidant agents (14 plants; 41 articles), vasoprotective–venotonic agents (6 plants; 10 articles), astringent–hemostatic agents (6 plants; 14 articles), and analgesic and wound healing acceleration (7 plants; 25 articles). The findings showed that medicinal plants operate through a multitarget manner by suppressing inflammatory mediators, increasing endogenous antioxidant defenses, improving venous tone and microvascular stability, supporting local hemostasis, and accelerating mucosal regeneration. Nonetheless, the evidence remains predominantly derived from preclinical studies, with variations in extraction methods, formulations, routes of administration, and dosages. Overall, medicinal plants have potential as adjuvant therapy for hemorrhoids; nevertheless, standardization of extracts and controlled clinical trials are necessary to ensure efficacy and safety.

Keywords

Anti-inflammatory, hemorrhoids, hemostatic, medicinal plants, venotonic, wound healing

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Introduction

Hemorrhoidal disease is characterized by pathological structural changes and distal displacement of the normal hemorrhoidal cushions within the anal canal.[1,2] Reported prevalence estimates vary according to the characteristics of the study population and the diagnostic or ascertainment methods employed.[2] Colonoscopy-based studies reported a prevalence of 38.9% among adults undergoing colorectal cancer screening in Austria[3] and 16.6% among apparently healthy young and middle-aged Korean adults undergoing routine health screening.[2] A recent meta-analysis estimated a global prevalence of 25.92%, highest in Africa (28.07%), followed by the Americas (26.40%), Europe (26.03%), and Southeast Asia (23.37%).[4] Lifestyle factors, including chronic constipation, low-fiber diet, and sedentary lifestyle, contribute to an

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increased risk and severity of hemorrhoids. Several studies indicated that smoking, alcohol consumption, and obesity did not show a significant correlation with the occurrence of hemorrhoids.[5]

Despite the development in hemorrhoid treatment strategies, conventional approaches remain clinically limited, particularly in achieving long-term control, as prolonged use of opioid analgesics may induce side effects, such as urinary retention and constipation.[6,7] Non-invasive procedures such as rubber band ligation, photocoagulation, and sclerotherapy provide initial improvement in 70%–90% of patients, but less than 50% remain asymptomatic after 4 years of follow-up.[6] Milligan–Morgan hemorrhoidectomy has been proven effective for long-term disease control. Nonetheless, it frequently occurs alongside postoperative pain and complications, including urinary retention, bleeding, and anal stenosis.[6,7] In addition, the high cost, protracted recovery period, and risk of recurrence further emphasize the need for the development of safer and more sustainable alternative and adjuvant therapies.

The use of medicinal plants has been practiced for centuries and is typically reported to have a good safety profile. A systematic review in Ethiopia identified at least 50 plant species from 33 families traditionally used for hemorrhoid therapy.[8] Experimentally, *Acacia ferruginea* bark extract showed anti-inflammatory, analgesic, and antioxidant activities through cyclooxygenase inhibition and proinflammatory cytokine reduction, with efficacy comparable to the commercially prepared Pilex granules.[9] Similarly, the water extract of *Pithecellobium dulce* seeds significantly suppressed Tumor Necrosis Factor-alpha (TNF-a) and Interleukin-6 (IL-6) production, reduced nitric oxide (NO) and MDA, and restored endogenous antioxidant activity, including superoxide dismutase (SOD) and catalase (CAT), in a castor oil-induced hemorrhoid model.[10] These findings confirm that medicinal plants exert therapeutic effects through multitarget mechanisms relevant to the pathophysiology of hemorrhoids.

To date, reviews of herbal therapies for hemorrhoids have predominantly been descriptive and have not yet mapped out active compounds, molecular targets, and the consistency of experimental-clinical evidence. Therefore, this article reviews anti-hemorrhoidal plants based on their mechanisms by analyzing their bioactive content, main pharmacological routes, and evidence from *in vitro, in vivo*, and clinical studies. This method is anticipated to assist in mapping potential plant candidates for the development of hemorrhoid adjuvant therapies.

Pharmacological Target Mechanism in Hemorrhoid Therapy

The pathophysiology of hemorrhoids is not simply a case of varicose veins, but rather a complex process involving distal displacement of the anal cushion due to weakening of the supporting tissue (Treitz muscle) and increased sphincter tone that inhibits venous reflux.[11,12] These changes are triggered by extracellular matrix degradation mediated by matrix metalloproteinases (MMPs), inflammation through increased cyclooxygenase-2 (COX-2), and fragile neovascularization due to increased vascular endothelial growth factor (VEGF).[11,13] Since it is multifactorial, modern therapy adopts a multimodal approach to suppress inflammation, reduce venous stasis, and improve tissue integrity. Conceptually, the mechanisms of anti-hemorrhoidal agents can be classified into four categories: (a) anti-inflammatory and antioxidant agents, (b) vasoprotective and venotonic agents, (c) astringent and hemostatic agents, and (d) analgesic and wound healing accelerators.

Anti-inflammatory and Antioxidant Agents

Inflammation plays an important role in hemorrhoids by metabolizing arachidonic acid into prostaglandins and leukotrienes, which increase vascular permeability and leukocyte infiltration.[14] The activation of the TLR4/MyD88/IKK pathway subsequently stimulates NF-κB, thereby increasing the production of proinflammatory mediators, such as TNF-α, IL-6, iNOS, and COX-2.[15] In addition, oxidative stress intensifies tissue damage through excessive production of reactive oxygen species (ROS). Endogenous antioxidant defenses neutralize ROS via SOD, further converting hydrogen peroxide by CAT and glutathione peroxidase (GPx).[16] GPx1 and GPx2 also contribute to suppressing ROS-induced NF-κB activation via redox mechanisms, thus aiding in the disruption of the connection between oxidative stress and inflammatory responses.[15]

Vasoprotective and Venotonic Agents

From a vascular perspective, vasoprotective and venotonic mechanisms support venous wall integrity, extracellular matrix homeostasis, and vascular tone. These effects are mediated through several complementary pathways, including enhancement of sympathetic-mediated venous contractility in vascular smooth muscle cells, protection of endothelial function and glycocalyx integrity to reduce capillary hyperpermeability, and modulation of MMP activity to limit excessive extracellular matrix and collagen degradation.[17]

Astringent and Hemostatic Agents

Astringent and hemostatic agents are pivotal in controlling local bleeding. Astringents function by precipitating mucosal surface proteins, leading to tissue contraction and reduced exudation. Stronger hemostatic agents, such as ferric chloride, induce coagulation of blood and tissue proteins, facilitating clot formation that helps in stopping capillary hemorrhage, often accompanied by local vasoconstriction.[18]

Analgesics and Wound Healing

In addition to controlling inflammation and bleeding, accelerating mucosal wound healing is a vital component of hemorrhoid therapy. This process involves angiogenesis, cell

proliferation, and tissue remodeling. VEGF plays a role in the formation of new capillaries, with bFGF activating the RAS/MAPK and PI3K/AKT pathways, while EGF promotes cell proliferation through EGFR activation. TGF-β supports re-epithelialization and collagen production through the Smad pathway, while CTGF helps regulate collagen remodeling by balancing MMP and TIMPs.[19]

Methods

This narrative review sourced literature from PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar using Boolean combinations of keywords (e.g., "hemorrhoid," "medicinal plants," and "pharmacological activity"). Following title, abstract, and full-text screening, eligible data regarding plant species, bioactive constituents, and experimental models were qualitatively synthesized. Data extraction specifically focused on anti-inflammatory and antioxidant agents, venoprotective and venotonic agents, astringent and hemostatic agents, and analgesic and wound healing activities, which were subsequently arranged into comparative tables and discussed descriptively.

Inclusion criteria comprised original *in vitro, in vivo*, or clinical studies that demonstrated biological outcomes affecting pathways directly involved in hemorrhoid pathogenesis, including anti-inflammatory and antioxidant activity, venoprotective and venotonic effects, astringent and hemostatic properties, analgesia, and wound healing. Studies using non-hemorrhoid models were included only if their pharmacological effects could be scientifically justified as relevant to one or more of these mechanistic pathways of hemorrhoids. Articles had to be published from 2015 onwards in peer-reviewed English or Indonesian journals indexed in Scopus, Web of Science, or Sinta 2. Reviews, non-original publications, and studies lacking accessible full texts or clear experimental evidence were excluded. The literature search initially identified 3,280 records. After removing 174 duplicate records, 3,106 articles were subjected to preliminary screening. Following title and abstract screening, 2,971 records were excluded because they were review articles, editorials, opinion papers, conference proceedings, books, patents, or publications without accessible full texts. A total of 135 reports were subsequently sought for retrieval and further evaluation. Of these, 45 reports were excluded because they were considered irrelevant to the objectives and eligibility criteria of the review. Ultimately, 90 studies were assessed for eligibility and included as the main references in this narrative review.

Results

A total of 90 articles that met the criteria were incorporated into the review and further summarized based on the main pharmacological mechanisms. Fourteen plant species exhibiting anti-inflammatory and antioxidant activities were documented in 41 articles (Table 1); six species with vasoprotective and venotonic mechanisms were reported in 10

Table 1. Medicinal Plants with Potential Anti-hemorrhoidal Activity Through Anti-inflammatory and Antioxidant Mechanisms.

No.	Plant Name	Sample	Chemical Compounds	Bioactivities Methods	Ref.
1	*Graptophyllum pictum*	Leaves; 96% ethanolic extract	Flavonoids, tannins, alkaloids, steroids, saponins, alcohol compounds, calcium oxalate	*In vitro*; *in vivo*	20
		Leaves; 70% ethanolic extract	Alkaloids, glycosides, pectin, formic acid, steroids, saponins, tannins, flavonoids	*In vivo*	21
		Leaves; Methanolic extract (1:10)	Alkaloids, flavonoids, terpenoids, phenols, eicosane, 2,4-di-tert-butylphenol	*In vitro*	22
		Leaves; 70% ethanolic extract	Flavonoids, phenolics, essential oils, phytol, myricetin, kaempferol	*In vitro*; *in vivo*	23
		Leaves; 96% ethanolic extract	Flavonoids, phenolics, alkaloids, tannins, saponins, glycosides, steroids, anthraquinones	*In vitro*	24
2	*Curcuma longa*	Rhizome; Hot-water extract	Curcumin, quercetin	*In vivo*	25
		Rhizome; Curcuminoid extract (capsules)	Curcumin, demethoxycurcumin, bisdemethoxycurcumin	Clinical	26
		Rhizome; Supercritical CO_2 dry extract	Curcuminoids, essential oils, mono- & polyunsaturated fatty acids	*In vitro*	27
3	*Aloe vera*	Leaves; 70% ethanolic extract	Anthraquinones (barbaloin, emodin), polysaccharides, glucomannan, phytosterols	*In vivo*	28
		Leaves; Aloe juice and gel	Amino acids, vitamins, enzymes, lipids, carbohydrates	*In vivo*	29
		Leaves; Gel	Vitamins C and E	Clinical	30
4	*Ageratum conyzoides*	Leaves; Methanol, ethyl acetate, chloroform, and hexane extracts	Alkaloids, tannins, flavonoids, phenols, glycosides, saponins	*In vitro*	31
		Leaves; Aqueous and methanolic extracts	Total phenolics, flavonoids, ascorbate	*In vitro*	32
		Leaves; Ethanolic extract	Flavonoids	*In vitro*; *in vivo*	33

(Table 1 continued)

(Table 1 continued)

No.	Plant Name	Sample	Chemical Compounds	Bioactivities Methods	Ref.
5	*Pithecellobium dulce*	Seeds; Methanolic extract	Fatty acids (hexadecenoic, eicosatrienoic)	*In vitro*; *in vivo*	34
		Seeds; Aqueous extract	Polyphenols, flavonoids, saponins, tannins, alkaloids	*In vitro*; *in vivo*	10
		Aril; Methanolic extract	Phenolic acids, catechins, flavonoids, tannins	*In vitro*	35
		Fruits; Hydroalcoholic extract	Flavonoids, phenolics, saponins, triterpenes	*In vivo*	36
		Leaves; Methanolic extract	Flavonoids, phenolic acids, sterols, alkaloids	*In vitro*; *in vivo*	37
6	*Capsella bursa-pastoris*	ND; Hot-water extract	Luteolin-7-O-glucoside, isoorientin, isoquercitrin	*In vitro*; *in vivo*	38
		Whole plant; Ethanolic & aqueous extracts; precipitated fraction of the aqueous extract	Organic acids (citric, malic, quinic)	*In vivo*	39
		Whole plant; Herbal tea	Flavonoids, polypeptides, choline, acetylcholine	*In vivo*	40
		Whole plant; 80% methanolic extract	Sesquilignan & phenolic glycosides	*In vitro*	41
7	*Acacia ferruginea*	Bark & leaves; Hydroalcoholic extracts	Flavonoids, tannins, terpenoids, alkaloids, saponins	*In vivo*	42
		Bark; Aqueous & ethanolic extracts	Alkaloids, flavonoids, sterols	*In vitro*	43
		Bark; Hydroalcoholic extract	Alkaloids, flavonoids, tannins	*In vivo*	9
		Aerial parts; methanolic extract	Flavonoids, terpenoids, steroids	*In vivo*	44
8	*Allium iranicum*	Leaves; Fresh leaf extract cream	Flavonoids, steroidal saponins	Clinical	45
		Leaves; Methanolic extract	Fatty acid methyl esters	*In vivo*	46
9	*Rheum ribes*	Fruits; Syrup	Total flavonoids, total phenolics	Clinical	47
10	*Vitis vinifera*	Leaves; Methanolic extract	Flavonoids, stilbenes (resveratrol), anthocyanins	*In vitro*	48
11	*Vaccinium macrocarpon*	Fruits; Hydroalcoholic extract	Proanthocyanidins, flavonols, resveratrol	*In vitro*; *in vivo*	49
		Fruits; Ethanolic extract	Polyphenols, anthocyanins, vitamin C	*In vitro*	50
12	*Justicia gendarussa*	Leaves; Aqueous, ethanolic, methanolic, diethyl ether, dichloromethane, and ethyl acetate extracts	Alkaloids, flavonoids, tannins	*In vitro*	51
		Roots; Methanolic extract	Apigenin	*In vitro*; *in vivo*	52
13	*Thymus vulgaris*	Flowers & leaves; Essential oil	Thymol, carvacrol	*In vitro*; *in vivo*	53
		Leaves; Essential oil	Thymol, carvacrol	*In vitro*; *in vivo*	54
		Aerial parts; Hydroalcoholic extract	Thymol, carvacrol	*In vivo*	55
		Leaves; Aqueous extract	Thymol, luteolin, apigenin	*In vivo*	56
14	*Coleus scutellarioides*	Leaves; Ethanolic extract	Flavonoids, phenolic acids	*In vitro*	57
		Leaves; Methanolic extract	Rutin, kaempferol	*In vitro*	58

articles (Table 2); six species with astringent and hemostatic mechanisms were detailed in 14 articles (Table 3); and seven species with analgesic and wound healing acceleration activities were referenced in 25 articles (Table 4). This mechanism-based presentation aimed to map the correlation between bioactive compound content, biological targets, and preclinical and clinical evidence, thereby providing a comprehensive overview of the potential of medicinal plants as adjuvant therapy for hemorrhoids.

Plants with Anti-inflammatory and Antioxidant Mechanisms

Graptophyllum pictum (L.) Griff

G. pictum belongs to the family Acanthaceae and has been traditionally used to treat hemorrhoids, relieve pain, reduce fever, and promote wound healing.[20–22] *G. pictum* contains alkaloids, flavonoids, tannins, saponins, glycosides, steroids, anthraquinones, and coumarins.[21–24] The total phenol content was recorded at 41.17–428.3 mg GAE/100 g extract, while the total flavonoids were 16.3–26.52 mg QE/g extract,[21,22] with larger concentrations observed in the ethyl acetate fraction.[24] Its flavonoid and phenolic content are responsible for the plant's antioxidant and anti-inflammatory effects. Antioxidant activity was demonstrated with IC_{50} values of 72.312–143.0 μg/mL (DPPH) and 49.00 μg/mL (ABTS), with the ethyl acetate fraction showing the highest activity (IC_{50} = 17.23 μg/mL).[20,22,24]

In a writhing test on rats, *G. pictum* ethanol extract at a dose of 100 mg/kg BW showed an analgesic efficacy of 129.64%, surpassing that of mefenamic acid (100%).[20] The anti-inflammatory effects were confirmed by a reduction in TNF-α, IL-6, and COX-2 levels in rats at a dose of

Table 2. Medicinal Plants with Potential Anti-hemorrhoidal Activity Through Vasoprotective/Venotonic Mechanisms.

No.	Plant Name	Sample	Chemical Compounds	Bioactivities Methods	Ref.
1	*Aesculus hippocastanum*	Young bark; Methanolic extract	Esculin, fraxin, epicatechin, procyanidin A2, total phenolics	*In vitro*	59
		Seed; Aqueous gel extract, 20% ethanol gel, 20% glycerol gel	Aescin, flavonoids, polyphenols	*In vivo*	60
		Seed; Escin	Escin	*In vitro*	61
2	*Ruscus aculeatus*	Rhizome and roots; Dry extract standardized in sterolic heterosides	Sterolic heterosides, flavonoids	*In vitro*; *in vivo*	62
		Rhizome and roots; Dry extract standardized in sterolic heterosides	Sterolic heterosides	*In vivo*	63
3	*Centella asiatica*	90% pure compound from the extract; The extract was ultrasonically dissolved in double-distilled water and diluted	Asiaticoside	*In vivo*	64
4	*Vitis vinifera*	Seed; Grape Seed Proanthocyanidin Extract (GSPE) tablets	Proanthocyanidins (~85%), flavan-3-ol monomers (catechin, epicatechin, epicatechin gallate)	Clinical	65
5	*Vaccinium Macrocarpon*	Fruit; Cranberry juice	Proanthocyanidins, anthocyanins, phenolic acids	Clinical	66
6	*Thymus vulgaris*	Leaves, flowers, stems; Methanolic extract	Thymol, carvacrol, 1,8-cineole, p-cymene, linalool	*In vitro*	67
		Flowering tops; Essential oil	Thymol, carvacrol, p-cymene, terpine	*In vitro*	68

Table 3. Medicinal Plants with Potential Anti-hemorrhoidal Activity Through Astringent and Haemostatic Mechanisms.

No.	Plant Name	Sample	Chemical Compounds	Bioactivities Methods	Ref.
1	*Capsella bursa-pastoris*	Whole plant; 96% hydroalcoholic extract	Tannins, flavonoids, choline, acetylcholine, sterols, amino acids, fatty acids, vitamin K, iron	Clinical	69
		Aerial parts; 96% hydroalcoholic extract	Tannins, choline, acetylcholine, flavonoids, sterols, amino acids, fatty acids	Clinical	70
2	*Bletilla striata*	Tuber (rhizome); Bletilla striata micron particles (BSMP)	Polysaccharide	*In vitro*; *in vivo*	71
		Tuber (rhizome); Polysaccharide extract (hot-water extraction)	Glucomannan polysaccharide (glucose & mannose)	*In vitro*; *in vivo*	72
		Tuber (rhizome); Freeze-dried polysaccharide sponge (92.6%)	Polysaccharide	*In vitro*; *in vivo*	73
		Tuber (rhizome); Fermented and purified polysaccharide extract	Glucomannan polysaccharide	*In vitro*; *in vivo*	74
		Tuber (rhizome); Water extract, 80% ethanol precipitation	Polysaccharide (RBp)	*In vitro*	75
3	*Aloe vera*	Leaf; Gel	Polysaccharides, saponins, enzymes	*In vitro*; *in vivo*	76
		Leaf; *Aloe vera* gel extract	Polysaccharides, saponins, enzymes	*In vitro*	77
4	*Curcuma longa*	Rhizome; CEFs aqueous extract	Serine protease	*In vitro*	78
5	*Terminalia chebula*	Dried fruit; Hydroalcoholic extract	Tannins, phenolics, flavonoids, glycosides, luteolin, terpenoids, gallic acid	*In vivo*	79
6	*Musa paradisiaca*	Stem; Stem extract	Saponins, flavonoids, tannins, anthraquinones, lectins	*In vivo*	80
		Stem internode latex; Latex in DMSO	Alkaloids, tannins, saponins, flavonoids, phenolics, steroids	*In vitro*	81
		Stem; Stem extract	Flavonoids, tannins, saponins	*In vivo*	82

Table 4. Medicinal Plants with Potential Anti-hemorrhoidal Activity Through Analgesic and Wound Healing Mechanisms.

No.	Plant Name	Sample	Chemical Compounds	Bioactivities Methods	Ref.
1	*Bletilla striata*	Dried rhizome; Polysaccharide extract (BSP)	BSP polysaccharides, glucomannan	*In vitro*; *in vivo*	83
		Dried rhizome; Polysaccharide extract (BSP)	BSP polysaccharides, glucomannan	*In vitro*; *in vivo*	84
		Dried rhizome; Polysaccharide extract (BSP)	BSP polysaccharides, glucomannan	*In vitro*; *in vivo*	85
		Dried rhizome; Bletilla striata polysaccharide (BSP)	BSP polysaccharides	*In vitro*; *in vivo*	86
2	*Aloe vera*	Leaf; *A. vera* gel extract in gel foam	Polysaccharides (acemannan), vitamins, enzymes, amino acids, minerals, antioxidants	Clinical	87
		Leaf; *A. vera* gel	Acemannan, mannose-6-phosphate, aloin A/B, vitamin C	Clinical	88
		Leaf; *A. vera* gel	Polysaccharides (glucomannan, mannose), gibberellin	*In vivo*	89
		Leaf; *A. vera* gel	Mannose-6-phosphate, acemannan	Clinical	90
		Leaf; *A. vera* gel	Vitamins (A, C, E, B12), enzymes, minerals, polysaccharides, anthraquinones, hormones, salicylic acid, saponins	Clinical	91
		Leaf; Commercial hydrogel (Restauder®)	Acemannan, rhamnogalacturonan-like pectin, aloesin	*In vivo*	92
		Leaf; *A. vera* gel	Polysaccharides, glycoproteins, glucomannan, collagen, salicylates	Clinical	93
		Leaf; *A. vera* gel	Anthraquinones, polysaccharides, enzymes, vitamins, and amino acids	*In vivo*	94
3	*Conyza bonariensis*	Whole plant; Methanol, butanol, chloroform, hexane extracts	Flavonoids, sterols, cyanidin glycosides	*In vivo*	95
4	*Coptis chinensis*	Root/rhizome; Isolated alkaloids	Sanguinarine, chelerythrine	*In vivo*	96
		Root/rhizome; COP extract (99.36%)	Coptisine (COP)	*In vivo*	97
		Root/rhizome; Alkaloid fraction	Sanguinarine, chelerythrine	*In vivo*	98
5	*Terminalia catappa*	Leaf (green & brown); Ethanolic leaf extract	Alkaloids, triterpenoids, flavonoids, tannins	*In vivo*	99
		Leaf; Ethanolic leaf gel	Flavonoids, saponins, tannins, phenolics	*In vitro*	100
6	*Thymus vulgaris*	Aerial parts; tincture and syrup	Thymol and carvacrol	*In vivo*	101
		Aerial parts; Hydroalcoholic extract	Thymol, p-cymene, γ-terpinene	*In vitro*; *in vivo*	102
		Flower (nectar source); Thyme honey (100%)	Thymol, carvacrol, flavonoids	Clinical	103
7	*Musa paradisiaca*	Raw fruit peel; Methanol extract & n-hexane fraction	Cycloeucalenone	In silico; *in vitro*; *in vivo*	104
		Raw fruit peel; Gel extract	Flavonoids, tannins, gallocatechin	*In vivo*	105
		Stem sap; Ethanolic gel extract	Lectins, quercetin derivatives	*In vitro*; *in vivo*	106
		Fruit peel; Dried peel extract	Alkaloids, tannins, saponins, phenolics	*In vivo*	107

100 mg/kg BW, comparable to betamethasone.[21,22] In addition, ethyl acetate, hexane, and water fractions inhibited the LOX enzyme with IC_{50} values of 133.47, 153.8, and 162.84 µg/mL, respectively.[24]

Curcuma longa L.

C. longa is a member of the Zingiberaceae family, and has been used traditionally for hemorrhoids and various inflammatory and painful conditions.[25–27] Its pharmacological efficacy is primarily driven by curcuminoids and essential oils, supported by a high profile of unsaturated fatty acids.[27] Mechanistically, the specific functional groups of curcuminoids comprising hydroxyl groups, ketone groups, and double bonds act as potent scavengers that significantly inhibit the generation of ROS, such as superoxide anions and hydrogen peroxide.[27] Preclinically, this targeted antioxidant action significantly increases endogenous enzymes (SOD, CAT, and GPx) and reduces lipid peroxidation (MDA) in murine models.[25]

Concurrently, curcuminoids attenuate inflammation by downregulating COX-2 activity and exert analgesic effects through the inhibition of bTREK-1 potassium channels and

the reduction of the neurotransmitter substance P.[26] Clinically, these molecular anti-inflammatory and tissue-protective mechanisms translate into effective analgesia, with oral curcuminoids (1,000 mg/day) significantly reducing post-operative pain (VAS scores) at 24 and 72 hours.[26] Although this evidence was not derived from hemorrhoid-specific studies, its anti-inflammatory and antioxidant activities may offer indirect mechanistic insights that could be relevant to hemorrhoid-related pathophysiology.

Aloe vera (L.) Burm.f.

A. vera is a medicinal plant of the Asphodelaceae family.[28] It has traditionally been used to treat gastrointestinal disorders, including hemorrhoids, primarily for its analgesic, anti-inflammatory, and wound healing properties.[28–30] *A. vera* contains anthraquinones (e.g., aloin and aloesin), complex polysaccharides, saponins, vitamins, and minerals.[28–30] Mechanistically, its anthraquinones (such as barbaloin and emodin) and phytosterols act as potent antioxidants that inhibit free radical-mediated cytotoxicity and lipid peroxidation.[28] Concurrently, these bioactive compounds suppress the inflammatory cascade by inhibiting the COX-2 pathway and downregulating NF-κB DNA-binding activity, effectively reducing leukocyte adhesion and prostaglandin E2 production.[28,30] Preclinically, topical *A. vera* gel mitigates vascular permeability, edema, and proinflammatory cytokines (TNF-α, IL-6) in hemorrhoid models,[29] while rectal administration lowers oxidative stress markers (MDA and myeloperoxidase [MPO]) in colitis.[28] Clinically, *A. vera* 3% ointment significantly alleviates acute radiation proctitis symptoms, notably diarrhea, improving patients' quality of life.[30]

Ageratum conyzoides L.

A. conyzoides is an herbaceous plant from the Asteraceae family.[31,32] Traditionally, it has been used to treat inflammatory conditions, rheumatism, and wound healing.[33] Its pharmacological efficacy is primarily attributed to its high phenolic and flavonoid contents, reported up to 61.4 mg GAE/g and 42.2 mg QE/g, respectively.[31] Mechanistically, these compounds act as potent electron donors and Fe^{2+} chelators to scavenge ROS and prevent lipid peroxidation.[32] Concurrently, flavonoids stabilize cell membranes and suppress inflammation by inhibiting the NF-κB (p65) and p38 MAPK pathways.[33] Preclinically, this dual antioxidant-inflammatory modulation reduces leukocyte influx, MPO activity, and key mediators (TNF, IL-6, NO).[33] Consequently, its ethanol extract (45–90 mg/kg BW) exhibits *in vivo* anti-inflammatory and anti-edema efficacy comparable to sodium diclofenac.[33]

Pithecellobium dulce (Roxb.) Benth.

P. dulce, is a member of the Fabaceae family.[34,35] This plant is used ethno-medically for hemorrhoids and inflammatory conditions.[36,37] Its pharmacological efficacy is driven by a diverse metabolite profile, particularly seed extracts prominently featuring 9-hexadecenoic acid, polyphenols, and flavonoids.[10,34]

Mechanistically, specific bioactive constituents, particularly 9-hexadecenoic acid and polyphenol complexes act as potent free radical scavengers that restore endogenous antioxidant defenses by enhancing SOD, CAT, and reduced glutathione (GSH) activities, thereby inhibiting lipid peroxidation.[10] Preclinically, this targeted molecular inhibition translates into potent *in vivo* anti-inflammatory effects; extract administration (40 mg/kg) significantly reduced TNF-α, IL-6, IL-1β, COX-2, and iNOS levels, mirroring the efficacy of diclofenac.[36] Crucially, in a specific hemorrhoid murine model, seed extracts (100–400 mg/kg) effectively lowered the recto-anal coefficient, reduced local inflammatory mediators (PGE_2, NO), and restored endogenous antioxidant defenses (SOD, CAT, GSH) while decreasing lipid peroxidation.[10] Supporting evidence from a non-hemorrhoid model showed that the methanolic leaf extract reduced TNF-α, IL-1β, and MDA levels and increased GSH. Nevertheless, its relevance to hemorrhoid therapy remains indirect and requires further validation.[37]

Capsella bursa-pastoris L.

C. bursa-pastoris (shepherd's purse) is a cosmopolitan Brassicaceae species with traditional use in Anatolia, the Middle East, China, and Japan. It has been described as anti-inflammatory and antioxidant, with reported use in hemorrhoids in traditional medicine.[38–40] Phytochemical studies identified phenolic glycosides (e.g., (+)-pinoresinol-β-D-glucoside), flavonoid glycosides, and organic acids such as citric, malic, and quinic acids.[38–41]

Preclinical evidence shows that *C. bursa-pastoris* extracts reduce inflammation and oxidative stress. In a croton oil-induced hemorrhoid model, it decreased tissue damage, inflammatory cytokines, MPO activity, and lipid peroxidation while restoring antioxidant enzymes (GSH, CAT, GPx, SOD).[39] *In vitro* and non-hemorrhoid models further support NO inhibition and antioxidant activity of its phenolic and water extracts.[38,41] However, evidence from non-hemorrhoid models should be considered indirect, and clinical validation is still required.

Acacia ferruginea DC

A. ferruginea is a member of the Fabaceae family traditionally utilized for its anti-inflammatory, analgesic, and tissue-healing properties.[42,43] Mechanistically, these constituents suppress the inflammatory cascade by inhibiting NF-κB activation, thereby downregulating iNOS and COX-2 expression and halting the overproduction of NO, TNF-α, IL-1β, and IL-6.[42] The bark extract of *A. ferruginea* is rich in alkaloids, flavonoids, triterpenoids, saponins, tannins, and phenolic compounds, with a total phenolic content of 438.8 mg GAE/g extract, total flavonoids of 66.6 mg RE/g extract, and saponins of approximately 34% (w/w).[9]

Pharmacological studies showed that *A. ferruginea* extract has central and peripheral analgesic properties comparable to tramadol and aspirin, as well as strong anti-inflammatory effects, with 74.68% edema inhibition in the carrageenan

model, identical to indomethacin.[42] In a hemorrhoid model, the extract reduced TNF-α, IL-6, and PGE_2 with efficacy comparable to Pilex granules.[9] This mechanism involves the inhibition of iNOS and COX-2, alongside antioxidant activity (IC_{50} DPPH 51.27 μg/mL and IC_{50} NO 61.42 μg/mL), as well as the suppression of ROS formation and inflammatory pathways reliant on NF-κB and AP-1.[44]

Allium iranicum

A. iranicum (Afghan leek) belong the Amaryllidaceae family found in the Middle East.[45,46] In Traditional Persian Medicine, *A. iranicum* has been used for bleeding control and pain relief, including in hemorrhoids, epistaxis, and menorrhagia. This use is supported by a randomized double-blind clinical trial showing a significant reduction in bleeding severity and improved subjective outcomes in hemorrhoid patients treated with *A. iranicum* cream.[45] However, effects on pain, defecation discomfort, and itching were not significantly different among groups.[45] Bioactive compounds such as flavonoids, phenolics, and steroidal saponins may contribute to its antioxidant and anti-inflammatory properties.[46] In addition, preclinical evidence showed systemic antioxidant and hepatoprotective effects in a high-fat diet rat model, suggesting indirect mechanistic relevance to inflammatory processes.[46]

Rheum ribes L.

R. ribes (Syrian rhubarb), from the Polygonaceae family, has been traditionally used for gastrointestinal disorders and bleeding.[47] Its pharmacological activity is mainly attributed to phenolic constituents, including chrysophanol, physcion, emodin, and quercetin, together with vitamins and minerals that may contribute to antioxidant and anti-inflammatory effects.[47] Mechanistically, these phenolic compounds may attenuate gastrointestinal inflammation by reducing oxidative stress and modulating inflammatory responses, thereby supporting mucosal protection. In a randomized, double-blind, placebo-controlled trial involving 96 children with shigellosis, *R. ribes* significantly reduced the duration of fever, diarrhea, and abdominal pain compared with placebo, without reported adverse effects.[47] Although this study was not conducted in hemorrhoid patients, its anti-inflammatory and antioxidant properties may provide mechanistic insights relevant to hemorrhoid therapy.

Vitis vinifera L.

V. vinifera (grape) contains key bioactive compounds such as hydroxybenzoic acid, flavonols (quercetin, kaempferol, morin), flavones, hydroxycinnamic acid, and stilbene derivatives (including pterostilbene, resveratrol isomers, and viniferin its pharmacological efficacy is driven by a high concentration of phenolics (25.03 mg GAE/100 mg) and flavonoids (7.05 mg QE/100 mg).[48] Mechanistically, these polyphenol complexes serve as exceptionally potent electron donors; *in vitro* assays demonstrate a hydroxyl radical scavenging ability 1.8 times higher than ascorbic acid (IC_{50} 155.77 vs. 279.53 μg/mL).[48] The synergy of this polyphenol complex produces multitarget biological activity, including inhibition of NO and lipoxygenase pathways. Although these studies were not conducted in hemorrhoid patients, the antioxidant and vasoprotective effects may provide mechanistic insights relevant to hemorrhoid therapy.

Vaccinium macrocarpon

V. macrocarpon (American cranberry) has traditionally been used for urinary and gastrointestinal disorders, including stomach ulcers.[49] Its therapeutic efficacy is driven by a highly concentrated polyphenol profile (1,041.9 mg/100 g), encompassing 32 active compounds prominently featuring anthocyanins, quercetin, and vitamin C.[50] Mechanistically, these polyphenols serve as potent free radical scavengers, demonstrated *in vitro* by exceptional DPPH (2,271.2 mg TE/100 g) and ABTS (1781.5 mg TE/100 g) inhibition values.[50] Preclinically, this targeted antioxidant capacity translates into the active reduction of ROS and the upregulation of endogenous defenses (SOD, CAT, and GSH).[49,50] Concurrently, the extract exerts strong anti-inflammatory effects by inhibiting COX-1/COX-2 enzymes and modulating the NF-κB/IκB signaling pathway to suppress TNF-α and IL-1β release.[49,50] Furthermore, it actively supports mucosal tissue regeneration by increasing TGF-β and PCNA expression.[49,50] The consistency of these biological effects across models provides a strong scientific basis for further development of *V. macrocarpon* in the treatment of hemorrhoidal disease.

Justicia gendarussa (L.) Griff.

J. gendarussa, a member of the Acanthaceae family, contains alkaloids, flavonoids, tannins, saponins, terpenoids, and steroids.[51] Apigenin isolated from this plant exerts anti-inflammatory effects by suppressing TLR/NF-κB signaling, reducing TNF-α, IL-1β, IL-6, COX-2, and PGE_2, and increasing IL-10.[52] In addition, the methanolic leaf extract demonstrated up to 76% protection in an HRBC membrane-stabilization assay, supporting its anti-inflammatory activity.[51] Although these findings were not obtained from hemorrhoid-specific models, they provide indirect mechanistic support for further investigation of *J. gendarussa* in hemorrhoid-associated inflammation.

Thymus vulgaris L.

T. vulgaris (thyme) has long been used for its antitussive, carminative, antimicrobial, and anti-inflammatory properties.[53] The essential oil is primarily composed of carvacrol (56.8%), p-cymene (12.8%), γ-terpinene (11.17%), and thymol (3.99%), with total phenol and flavonoid contents of 187.3 and 78.83 mg GAE/g extract, respectively.[53,54] The anti-inflammatory activity of thyme has been validated in various *in vivo* models, including experimental autoimmune encephalomyelitis, with a maximum clinical score drop from 3.6 to 1.5–1.7, accompanied by an increase in IL-10 and TGF-β and a decrease in IFN-γ and IL-6.[55]

In the croton oil-induced ear edema model, thyme inhibited edema by 65.69%–73.00%, comparable to diclofenac.[53] Strong antioxidant capacity was demonstrated by DPPH and

ABTS radical scavenging, increased GSH and CAT levels, and reduced lipid peroxidation. Mechanistically, these effects are mediated by inhibition of NF-κB and AP-1 pathways, regulation of T cells, and membrane stabilization by carvacrol and thymol, with synergistic action from minor compounds like linalool and rosmarinic acid.[53–56] The combination of strong anti-inflammatory and antioxidant effects, along with GRAS status and a long history of traditional use, positions *T. vulgaris* as a viable therapeutic agent for the development of hemorrhoid therapy, particularly in conditions with predominant inflammatory and vascular components.

Coleus scutellarioides (L.) Benth.

C. scutellarioides a member of the Lamiaceae family, is traditionally used in Southeast Asia for hemorrhoids and inflammatory conditions.[57] Its pharmacological efficacy is primarily attributed to the purple-leaved variety's flavonoid-rich profile, particularly quercetin and luteolin derivatives.[57] The anti-hemorrhoidal relevance of *C. scutellarioides* is mainly associated with its flavonoid-rich profile, which may contribute to antioxidant and anti-inflammatory effects through NO radical scavenging and suppression of oxidative stress-related inflammatory responses.[57] Comparative analysis within the Lamiaceae family shows that while *C. scutellarioides* has high antioxidant activity; it is less potent than *Plectranthus amboinicus*, which contains higher levels of rosmarinic acid and carvacrol.[58]

Plants with Vasoprotective and Venotonic Effects

Aesculus hippocastanum L.

A. hippocastanum (horse chestnut) has long been used for venous insufficiency disorders, including varicose veins and hemorrhoids.[59,60] Its pharmacological efficacy stems from a dual-action phytochemical profile: the bark is rich in vascular-protective coumarin glycosides (esculin, fraxin) and procyanidins, while the seeds contain escin, a potent venotonic and anti-edematous triterpene saponin.[59] Glycerol-extracted seeds have been shown to provide higher anti-edema and anti-inflammatory activity than ethanol extracts in animal models, making them more suitable for local therapeutic applications.[60,61]

Mechanistically, escin improves endothelial function by increasing the fluidity of pathological vein cell membranes, thereby aiding in the normalization of vein tone and potentially reducing the risk of stasis and thrombosis without cytotoxic effects at therapeutic doses.[61] The synergy between polyphenol-based vascular protection and the venotonic–anti-edema effects of escin establishes a strong scientific basis for the use of *A. hippocastanum* in hemorrhoid therapy.[59,61]

Ruscus aculeatus L.

R. aculeatus (butcher's broom) extract is a venotonic agent associated with chronic venous disease and hemorrhoidal symptoms.[62,63] Its effects are linked to microvascular modulation.[63,64] *In vitro*, it acts as a partial agonist at hM1 and hM3 muscarinic receptors with additional activity on hM5-mediated calcium signaling.[62,63] *In vivo* (hamster cheek pouch model), oral administration induced venular constriction, reduced macromolecular permeability, and inhibited leukocyte–endothelium interactions without affecting arteriolar diameter.[62,63] Compared with micronized diosmin, it showed stronger effects on several microcirculatory parameters.[63,64] These findings provide preclinical mechanistic support, while direct clinical evidence for acute hemorrhoidal treatment remains limited.[62,63]

Centella asiatica (L.) Urb.

C. asiatica (gotu kola) from the Umbelliferae family is a plant prevalent in tropical and subtropical Asia, traditionally used to accelerate wound healing and treat venous insufficiency and microangiopathy.[64] The main compound, asiaticoside, has angiogenic, anti-inflammatory, and antioxidant activities that facilitate the tissue repair process.[64] In a random skin flap rat model, asiaticoside (40 mg/kg/day) markedly increased tissue viability by increasing micro-vessel density (via VEGF induction), augmenting local blood flow, decreasing proinflammatory cytokines (TNF-α, IL-6), enhancing antioxidant defense (↑SOD, ↓MDA), and reducing edema and neutrophil infiltration.[64] These multimodal effects create an optimal environment for tissue healing and conceptually align with the mechanism of repairing vascular insufficiency in hemorrhoids. Despite robust preclinical results, the therapeutic application in hemorrhoids still requires controlled clinical trials and standardization of the extract, dosage, and formulation.

Vitis vinifera L.

V. vinifera (grape), particularly grape seed proanthocyanidin extract (GSPE), contains proanthocyanidins and flavan-3-ol monomers such as catechin and epicatechin, which exhibit strong antioxidant and vascular-protective activities.[65] Its proposed mechanisms include reducing ROS production, inhibiting proinflammatory mediators such as IL-1β, TNF-α, and PGE_2, suppressing platelet aggregation, limiting vascular smooth muscle cell proliferation, and inhibiting ACE activity.[65] In a clinical trial of prehypertensive individuals, a daily dosage of 400 mg of GSPE over 12 weeks reduced systolic blood pressure and significantly improved vascular elasticity, particularly among non-smokers.[65] Although this study had limitations in terms of sample size and population, the findings suggest that GSPE may improve vascular function and integrity. Conceptually, the combination of anti-inflammatory, antioxidant, and vascular wall-strengthening effects renders grape seed extract pertinent as an adjuvant therapy for conditions characterized by vascular fragility and dysfunction, including hemorrhoids.[65]

Vaccinium macrocarpon L.

V. macrocarpon (American cranberry) has long been used for urinary tract infections and cardiovascular support, with

further potential in normalizing venous function.[66] Clinical evidence from double-blind trials shows that cranberry extract improves endothelial function by increasing flow-mediated dilation in a dose-dependent manner, with peak vascular effects observed approximately 4 hours after intake and closely associated with circulating polyphenol metabolites.[66] Mechanistically, this effect may involve increased endothelial NO bioavailability through NADPH oxidase inhibition and/or AMPK pathway activation, leading to improved vascular elasticity and endothelial stability.[66]

Although these studies were not conducted in hemorrhoid patients, the vascular-protective effects of cranberries may offer mechanistic insights relevant to hemorrhoid therapy.

Thymus vulgaris L.

T. vulgaris (thyme) is an aromatic medicinal plant whose essential oil is rich in phenolic monoterpenes, mainly thymol and carvacrol, which contribute to its antioxidant, anti-inflammatory, and vascular-modulating.[67,68] Thymol and carvacrol are the primary phenolic components responsible for antioxidant and anti-inflammatory activity, with proportions ranging from 12% to 61% and 0.4% to 20.6% of the total essential oil, respectively.[68]

Mechanistically, the extract exerts a targeted biphasic vasodilator effect on vascular smooth muscle, inducing significant relaxation through both endothelium-dependent and endothelium-independent pathways.[67] At the molecular level, thymol directly modulates calcium homeostasis by reducing Ca^{2+}-ATPase activity and inhibiting sodium currents in the vascular smooth muscle, whereas carvacrol activates endothelial TRPV3 channels to induce the hyperpolarization of smooth muscle cell membranes.[68] Although these effects were not studied in hemorrhoid patients, the vascular-modulating properties may offer mechanistic insights relevant to hemorrhoid therapy.

Plants with Astringent and Hemostatic Effects

Capsella bursa-pastoris L.

C. bursa-pastoris (shepherd's purse; Brassicaceae) has traditionally been used for bleeding disorders. In randomized clinical studies, its hydroalcoholic extract reduced heavy menstrual bleeding when administered as an adjunct to mefenamic acid[69] and decreased early postpartum bleeding when combined with oxytocin.[70] These findings provide clinical evidence of bleeding-reducing activity in gynecological and obstetric settings; however, its mechanisms and efficacy in hemorrhoidal bleeding remain indirect and require specific validation.

Bletilla striata (Thunb.) Reichb. f.

B. striata belongs to the Orchidaceae family, known as baiji in traditional Chinese medicine. It has been used for over 2000 years as a hemostatic and wound healing agent to treat hematemesis, hemoptysis, traumatic bleeding, and ulcerative lesions.[71–73] Pharmacognostically, the main biological activity of this plant is associated with *B. striata* polysaccharide (BSP), a heteropolysaccharide composed mainly of glucose and mannose with a molecular weight ranging from 30 to 200 kDa and a total sugar content of >94%.[72,74,75]

Mechanistically, BSP exhibits a hemostatic effect through a dose-dependent increase in platelet aggregation at concentrations of 50–200 mg/L (EC_{50} 93.58 mg/L) via the ADP pathway involving the $P2Y_1$ and $P2Y_{12}$ receptors.[75] It also accelerates wound healing by reducing inflammation, as indicated by decreased IL-6 levels, and enhancing angiogenesis through increased VEGF expression, with histological findings confirming improved tissue repair.[73] Safety studies further indicate good biocompatibility, fibroblast-supporting activity, and low hemolytic potential.[72] Given the combination of direct hemostatic effects (platelet activation), anti-inflammatory, pro-angiogenic, and pro-regenerative effects, *B. striata* has significant potential as a hemorrhoid therapy candidate, particularly in cases dominated by mucosal bleeding and chronic wounds.

Aloe Vera (L.) Burm.f.

A. vera is traditionally used for wound healing and mild anorectal inflammation.[76,77] Its hemostatic and regenerative activities are primarily driven by polysaccharides, glycoproteins, and saponins (~3%).[76,77] Experimentally, *A. vera*-based hydrogels provide sustained mucosal adhesion, while composite scaffolds significantly accelerate blood clotting, achieving hemostasis in approximately 60 seconds.[76,77] Furthermore, these formulations demonstrate high biocompatibility (hemolysis <0.5% and ~100% cell viability) alongside near-perfect *in vitro* wound closure.[77] Consequently, *A. vera* serves as an ideal topical base for hemorrhoid therapy to control bleeding and accelerate mucosal regeneration.

Curcuma longa L.

C. longa (turmeric) rhizome has traditionally been applied to fresh cuts to control bleeding and support wound healing. *In vitro*, a dialyzed crude enzyme fraction obtained from its aqueous rhizome extract reduced human plasma clotting time from 172 to 84 s and completely hydrolyzed the α, β, and γ chains of fibrinogen. Its proteolytic activity was markedly inhibited by phenylmethylsulfonyl fluoride, suggesting the involvement of serine proteases. These findings indicate a protease-mediated procoagulant effect, while the associated fibrinogenolytic activity may contribute to subsequent clot remodeling. However, this evidence remains limited to an *in vitro* non-hemorrhoid model, and its topical efficacy and safety in hemorrhoidal bleeding require further validation.[78]

Terminalia chebula Retz

T. chebula is traditionally used for bleeding and inflammatory gastrointestinal disorders.[79] Its pharmacological activity relies on a tannin-rich profile (±32%) and major GC-MS

identified compounds like 4,4-dimethyl-2-(3-phenyl-2-thienyl) oxazoline (89.38%) and 4-cyclohexene-1,2-dicarboximide, N-butyl-(cis-) (10.62%).[79] Preclinically, the extract enhances both platelet-related hemostasis and intrinsic coagulation, evidenced by shortened bleeding time, increased platelet count, and reduced prothrombin and aPTT times.[79] Given this potent procoagulant activation, localized topical application is the most rational approach for treating hemorrhoidal mucosal bleeding to maximize local efficacy while avoiding systemic risks, pending further clinical validation.[79]

Musa paradisiaca

M. paradisiaca has been investigated in Indonesia for its haemostatic and wound-healing potential.[80,81] A 30% stem extract significantly shortened bleeding and clotting times without increasing platelet counts.[80,82] In addition, its latex enhanced NIH3T3 fibroblast proliferation and migration, accompanied by increased platelet-derived growth factor expression.[81] These complementary haemostatic and regenerative effects support its potential topical application for hemorrhoidal bleeding and tissue repair, although validation in hemorrhoid-specific models remains necessary.

Plants with Wound Healing and Analgesic Effects

Bletilla striata (Thunb.) Reichb. f.

B. striata (Chinese ground orchid) is a member of the Orchidaceae family that has long been used in traditional Chinese medicine as a hemostatic and wound healing agent, including for ulcerative gastrointestinal lesions.[83–86] Its wound healing efficacy is primarily attributed to BSP, a natural polysaccharide that exhibits anti-inflammatory and hemostatic properties, promotes fibroblast proliferation and collagen deposition, and accelerates wound healing, especially when used in combination with asiaticoside for scar inhibition.[86] Preclinically, BSP exhibits a robust, multitarget wound healing profile: it exerts anti-inflammatory effects by inhibiting the NLRP3 inflammasome (decreasing IL-1β and TNF-α), provides antioxidant protection by upregulating SOD activity, and promotes tissue repair through fibroblast proliferation and enhanced angiogenesis (increasing CD31 and VEGF expression).[83–85] By concurrently stopping bleeding, resolving anorectal inflammation, and accelerating mucosal regeneration, BSP directly targets the primary pathology of hemorrhoids while potentially preventing long-term complications like fibrosis and strictures.

Aloe Vera (L.) Burm.f.

A. vera, a xerophytic species from the Asphodelaceae family, is traditionally used for wound healing and tissue regeneration, driven by its rich composition of polysaccharides, anthraquinones, and phenolics.[87–90] Mechanistically, its gel suppresses inflammation and pain by inhibiting COX-mediated PGE_2 production and inactivating bradykinin and histamine.[88] Concurrently, it accelerates tissue repair by stimulating fibroblast proliferation, increasing collagen synthesis, and enhancing antioxidant defenses (SOD, CAT, and GPx).[88,89,91]

A. vera hydrogel possesses physicochemical properties conducive to wound healing, with a contact angle value of 43.11°, reflecting optimal hydrophilicity, a maximum swelling of 12.693%, and a porous microstructure that aids exudate drainage and tissue adhesion. This formulation accelerates wound closure by Day 15, in contrast to the control at Day 24.[92] Clinically, *A. vera* gel has improved healing outcomes in extraction sockets, burns, and pressure ulcers, including reduced pain scores and enhanced tissue repair.[87,90,93] In the diabetic wound model, the *A. vera* group showed a relative wound area of 0.24 on Day 7 with abundant fibroblast infiltration (Score 3), outperforming *Nigella sativa* oil, which showed a value of 0.58 with moderate fibroblast infiltration (Score 2).[94] Overall, the pharmacological profile of *A. vera*, particularly its potential to attenuate excessive inflammation, promote tissue regeneration, and support wound repair, suggests its relevance as a supportive therapeutic candidate for chronic inflammatory conditions and mucosal wounds, including hemorrhoids.

Conyza bonariensis

C. bonariensis, a member of the Asteraceae family, has traditionally been used for pain and inflammatory conditions.[95] In rodents, its methanolic extract and butanol, chloroform, and hexane fractions significantly inhibited acetic acid-induced writhing and reduced the late phase of formalin-induced nociception, suggesting a predominantly peripheral antinociceptive effect involving inflammatory pain mediators. The extract also attenuated carrageenan-induced paw edema, with activity comparable to indomethacin.[95] Although wound-healing and hemorrhoid-specific outcomes were not evaluated, these findings provide indirect mechanistic support for its potential relevance to hemorrhoid-associated pain and inflammation and warrant validation in disease-specific models.

Coptis chinensis

C. chinensis (Coptidis rhizome, Huang Lian) is one of the important plants in traditional Chinese medicine, and is widely used in traditional medicine for diarrhea, gastrointestinal disorders, inflammatory conditions, fever, toothache, diabetes, and skin diseases.[96–98] Its pharmacological activity is associated with several isoquinoline alkaloids, including berberine, sanguinarine, chelerythrine, and coptisine.[96–98] Preclinical studies showed that the sanguinarine–chelerythrine fraction of *C. chinensis* inhibited carrageenan-induced paw edema, reduced PGE2 release, TNF-α production, and MMP-9 levels, and showed a safer gastric profile than indomethacin in rats. In another preclinical study, sanguinarine, chelerythrine, and their fraction demonstrated analgesic and anti-inflammatory effects in tail-flick and formalin pain models without evident gastrotoxicity. Separately, coptisine improved diarrhea, bleeding, intestinal inflammation, and mucosal barrier function in a DSS-induced colitis model, partly through modulation of the cPLA2/TRPM8/CGRP-1 pathway. However, these findings should be interpreted as

indirect mechanistic support rather than direct clinical evidence for hemorrhoid treatment.[96–98]

Terminalia catappa L.

T. catappa, commonly known as ketapang in Indonesia and Indian almond in international literature, belongs to the Combretaceae family and is widely distributed in tropical and subtropical regions, including Indonesia.[99] Previous studies have reported its traditional or experimental relevance in anti-inflammatory, antiulcer, and wound healing contexts.[99,100] These effects may be partly attributed to its phytochemical constituents, including tannins, phenolics, flavonoids, saponins, kaempferol, and quercetin.[99,100] Tannins may contribute to local astringent effects, tissue contraction, reduced exudation, and mild bleeding control, whereas phenolic and flavonoid compounds may provide anti-inflammatory and antioxidant-related support.[99,100]

Preclinical evidence further supports the pharmacological relevance of *T. catappa* leaves. In an *in vitro* red blood cell membrane stabilization assay, a gel formulation containing 25% catappa leaf extract showed the highest membrane stability among the tested concentrations, reaching 99.7%.[100] In an *in vivo* mouse wound model, topical ointment containing 20% ethanolic extract of green leaves accelerated wound repair and achieved complete wound closure by Day 12.[99] However, these findings should be interpreted as indirect mechanistic support rather than direct clinical evidence for hemorrhoid treatment.

Thymus vulgaris L.

T. vulgaris (thyme), a member of the Lamiaceae family, contains thymol and carvacrol, which may contribute to antinociceptive effects through modulation of TRP channels and inhibition of COX-2, prostaglandin, and TNF-α signaling.[101] In mice, thyme tincture and syrup increased hot-plate response latency, with effects comparable to paracetamol.[101] Thyme-based nanofibers also promoted wound closure and reduced bacterial burden in infected wound models,[102] while thyme honey improved aphthous ulcer healing and pain.[103] Although these studies were not conducted in hemorrhoid models, they provide indirect support for further evaluation of thyme in hemorrhoid-associated pain and tissue repair.

Musa paradisiaca

M. paradisiaca (plantain/cooking banana) is known in Indonesia as *pisang ambon* or *pisang kepok*.[104,105] This plant thrives in tropical and subtropical regions and has traditionally been used to treat wounds, ulcers, and swelling, in line with recent pharmacological findings.[104] Its pharmacological efficacy is driven by a broad spectrum of bioactive metabolites, notably tannins, saponins, phenolics, and cycloeucalenone.[104–107]

Mechanistically, cycloeucalenone exerts potent anti-inflammatory effects by inhibiting phospholipase-A2 (PL-A2) and the NF-κB pathway, which synergizes with the antioxidant capacity of phenolic compounds to reduce vascular oxidative stress.[104] Preclinically, these molecular actions translate into accelerated tissue repair; *in vivo* wound models demonstrate that 10% peel extract and stem sap gels significantly reduce inflammatory infiltration, elevate PDGF-BB expression, and promote both epithelialization and collagen deposition.[105–107] This dual capacity to suppress vascular inflammation while actively stimulating mucosal and connective tissue regeneration makes *M. paradisiaca* a highly rational therapeutic candidate for hemorrhoidal tissue damage.

Discussion

Details of the literature review results on medicinal plants with potential as anti-hemorrhoidal agents are described systematically in Tables 1–4. Figure 1 presents a summary diagram of the primary pharmacological mechanisms underlying the anti-hemorrhoidal activity of these plants to facilitate conceptual understanding and provide a more concise overview.

Plant bioactive compounds exhibit anti-inflammatory effects through suppression of the NF-κB and AP-1 pathways, which reduce inflammatory mediators. Antioxidant activity enhances the cellular defense system against oxidative stress. Venotonic and vasodilatory effects help improve blood flow and alleviate venous stasis. In addition, astringent, hemostatic, and analgesic effects play a role in stopping bleeding, relieving pain, and accelerating wound healing, thereby supporting rectal tissue recovery and improvement of hemorrhoid symptoms.

Among the various plants reviewed, *A. vera* and *T. vulgaris* have the most comprehensive pharmacological profiles. *A. vera* lowers inflammation and pain by blocking the COX pathway and inactivating bradykinin,[88] while simultaneously boosting mucosal tissue regeneration through the activity of glucomannan and growth factors that have been clinically proven to accelerate wound healing.[30,93] *In vivo* studies confirm its capacity to significantly lower proinflammatory cytokines TNF-α and IL-6 in hemorrhoidal tissue.[29] Meanwhile, *T. vulgaris* has spasmolytic and vasoprotective properties through the modulation of calcium channels and transient receptor potential vanilloid three by thymol and carvacrol,[67,68] as well as anti-inflammatory activity equivalent to diclofenac.[53]

Although preclinical evidence indicates strong potential, the development of natural anti-hemorrhoidal agents is limited by insufficient hemorrhoid-specific clinical validation and a lack of standardization. Most available clinical evidence originates from non-hemorrhoidal conditions, limiting direct efficacy extrapolation and precise dose determination for hemorrhoidal therapy. Variations in extraction methods also pose a constraint, as the choice of solvent has been shown to significantly affect the bioactivity profile, as seen in the differences in the antioxidant activity of *A. conyzoides*[31] and the anti-edema efficacy of *A. hippocastanum*.[60] Furthermore, inconsistencies in formulation and route of administration, such as differences in efficacy between topical and oral

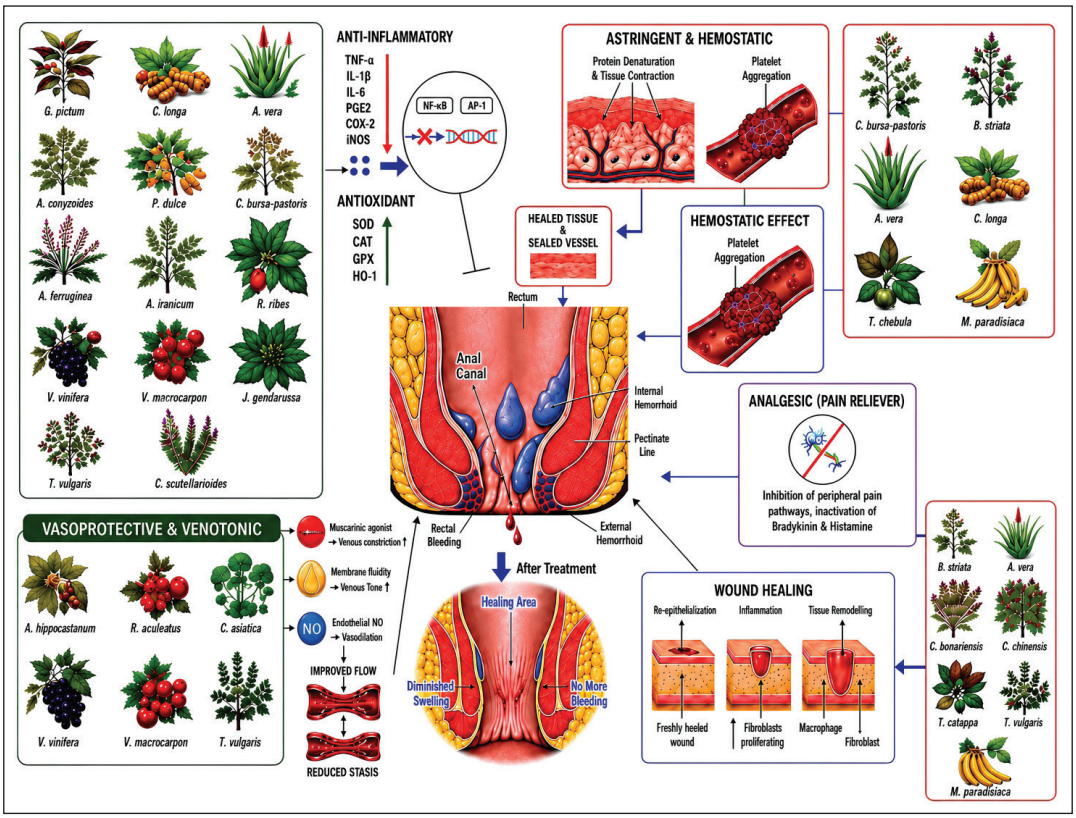

Figure 1. The Potential of Medicinal Plants as Anti-hemorrhoids Through Anti-inflammatory-antioxidant, Venotonic-vasodilatory, Astringent-hemostatic-analgesic, and Wound Healing Mechanisms.

Source: This figure was created with Canva (Url: https://www.canva.com/).

application of *A. vera*, require further research to establish optimal and stable dosage standards.[28,29]

The combination of *G. pictum* and *C. bursa-pastoris* plants has significant pharmacological potential. *G. pictum* plays a role in relieving inflammation, swelling, and pain in the anal area, while *C. bursa-pastoris* supports the cessation of bleeding through its astringent properties and its capacity to constrict blood vessels. Clinical studies on *C. bursa-pastoris* also show a considerable reduction in bleeding volume, which would be particularly beneficial when combined with the anti-inflammatory effects of *G. pictum*.[20,39,69] The second therapeutic combination focuses on the use of venotonic agents combined with wound healing agents. Weakness of the vein walls and damage to the extracellular matrix are major factors in the occurrence of hemorrhoidal prolapse. Extracts of *A. hippocastanum* and *R. aculeatus* have strong scientific evidence as venotonics that can increase blood vessel tone and reduce capillary permeability.[61,63] However, in cases of hemorrhoids accompanied by lesions or ulceration, the addition of regenerative agents, such as *C. asiatica*, is highly recommended. *C. asiatica* can stimulate collagen synthesis and angiogenesis through increased VEGF expression,[64] which works synergistically with the vasoprotective effects of *A. hippocastanum* to strengthen and restore the structure of the anal cushion.

Even though medicinal plants have great therapeutic potential, the main challenges in their development lie in the variation in active compound content and limited data on long-term safety. This review confirms that phytochemical profiles are greatly influenced by geographical factors and the extraction methods used. For example, the chemical composition of *A. conyzoides* shows significant differences based on the location of growth and the type of solvent used.[31] Similar findings were also found in the extraction of *A. hippocastanum*, where the use of glycerol produced stronger anti-inflammatory and anti-edema activities and lower irritation effects compared to ethanol solvents.[60] These findings underscore the importance of strict standardization based on marker compounds, such as escin content in *A. hippocastanum* or curcuminoids in *C. longa*, to ensure consistency and reproducibility of therapeutic effects in each production batch.

In addition to standardization, safety evaluation, particularly chronic and sub-chronic toxicity testing, remains an area that has received insufficient attention. Most studies focused on acute or short-term toxicity effects, even though hemorrhoids are a chronic disease that requires repeated or long-term therapy. Some plants show a relatively good safety profile. For example, *C. chinensis* has greater gastrointestinal tolerability than NSAIDs, such as indomethacin,[96] and *Allium*

spp. is known to have a wide safety margin with a high lethal dose.[46] Conversely, plants containing bioactive alkaloids still require strict monitoring of dosage and duration of use to prevent potential cumulative toxicity.

Conclusion

Overall, natural products derived from medicinal plants show significant potential in improving hemorrhoid conditions through various mechanisms. Their main therapeutic effects include stimulation of hemostasis and coagulation, inhibition of inflammatory pathways, improvement of venous tone, and acceleration of tissue regeneration processes. Although conventional therapies such as micronized purified flavonoid fractions (MPFF) have been widely used, this review highlights that several other plant species also contain bioactive components that have the potential to serve as effective, economical, and more holistic therapeutic alternatives. Several plants, such as *A. hippocastanum* and *R. aculeatus*, have strong pharmacological evidence regarding their venotonic effects. However, most other plant candidates are still being studied at the *in vitro* or animal model level. Thus, clinical evidence in humans is insufficient. In addition, stronger data is still needed on optimal dosage, potential long-term toxicity, and standardization of extraction methods, especially since solvent variations have been shown to affect pharmacological activity, as in *A. conyzoides* and *A. hippocastanum*.

Despite its limitations, this review provides important references for the development of herbal hemorrhoid therapies. The literature synthesis identified promising compounds: curcumin from *C. longa* for anti-inflammatory effects, polysaccharides from *B. striata* and *A. vera* as hemostatics and wound healers, asiaticoside from *C. asiatica* for angiogenesis and tissue regeneration, and *G. pictum* and *T. vulgaris* showing anti-inflammatory-analgesic effects comparable to synthetic drugs. In the future, research should focus on increasing the number and quality of clinical trials, as well as on standardizing marker compound-based extracts to ensure consistency in therapeutic effects. Further exploration of molecular mechanisms, especially interactions with vascular endothelium and inflammatory cytokines, is also crucial. This approach will establish a strong scientific foundation for the development of new hemorrhoid drug formulations that integrate anti-inflammatory, antioxidant, vasoprotective, venotonic, astringent, hemostatic, analgesic, and regenerative properties.

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Authors' Contribution

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work. All the authors are eligible to be authors as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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Not applicable.

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All the data is available with the authors and shall be provided upon request.

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This study does not involve experiments on animals or human subjects.

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The authors used generative artificial intelligence tools (ChatGPT, OpenAI Inc.) solely for language editing and improvement of readability during manuscript preparation. All scientific content, interpretations, analyses, and conclusions were developed by the authors. No AI-generated data, results, or scientific conclusions were used in this study. All AI-assisted text was critically reviewed, revised, and approved by the authors, who take full responsibility for the final content of the manuscript. Canva was used for graphical design and layout. The conceptual framework, scientific content, mechanistic illustration, and final verification were entirely developed, reviewed, and refined by the authors to ensure scientific accuracy.

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