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Herbal therapeutics for preventing postoperative peritoneal adhesions: a mechanistic review of preclinical evidence

Terapi Herbal untuk Pencegahan Adhesi Peritoneal Pascaoperasi: Tinjauan Mekanistik Studi Praklinis

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ABSTRACT

Background: *Postoperative peritoneal adhesions remain a common complication of abdominal and pelvic surgery and may cause bowel obstruction, infertility, chronic pain, and difficult reoperation.*
Objective: *This review synthesized evidence on herbal therapeutics for adhesion prevention.*
Methods: *A comprehensive search of PubMed, Scopus, and Google Scholar for 2015-2025 publications used keywords related to postoperative adhesions and herbal therapy. English-language full-text in animal experimental studies with peritoneal adhesion induction and herbal interventions were included; non-herbal interventions, duplicate reports, non-postoperative adhesions, abstracts only, non-English papers, and retracted articles were excluded.*
Results: *A total of 169 records were identified, and after duplicate removal, title and abstract screening, and full-text eligibility assessment, 29 studies were included in the qualitative review. Curcumin consistently reduced inflammatory signaling, oxidative stress, collagen deposition, and adhesion scores through NF-kB modulation and antioxidant effects. Ginger and gingerol lowered TNF-α, IL-6, TGF-β1, VEGF, and malondialdehyde, indicating anti-inflammatory, antifibrotic, and anti-angiogenic activity. Rosmarinus officinalis reduced cytokines, oxidative markers, and TGF-β1 in rat models. Bletilla striata, frankincense, and polyherbal formulas showed additional wound-healing, anti-inflammatory, and pro-fibrinolytic effects.*
Conclusion: *Herbal therapeutics appear promising as adjunctive strategies for preventing postoperative adhesions; however, the evidence remains heterogeneous and is dominated by animal and in vitro studies. Standardized formulations, safety evaluation, and well-designed clinical trials are needed before wider clinical application.*

Keywords: *antifibrotic, anti-inflammatory, herbal therapeutics, oxidative stress, postoperative adhesions*

ABSTRAK

Latar Belakang: Adhesi peritoneal pascaoperasi masih merupakan komplikasi umum setelah pembedahan abdominal dan pelvis serta dapat menyebabkan obstruksi usus, infertilitas, nyeri kronis, dan kesulitan saat operasi ulang.
Tujuan: Tinjauan ini mensintesis bukti mengenai terapi herbal untuk pencegahan adhesi.

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Metode: Pencarian komprehensif pada PubMed, Scopus dan Google Scholar untuk publikasi tahun 2015-2025 menggunakan kata kunci terkait adhesi pascaoperasi dan terapi herbal. Artikel full-text berbahasa Inggris berupa studi eksperimental hewan dengan perlakuan induksi adhesi intraperitoneal dan intervensi herbal dimasukkan; intervensi nonherbal, laporan duplikat, artikel yang tidak membahas adhesi pascaoperasi, abstrak saja, artikel non-Inggris, dan artikel yang diretraksi dikeluarkan.
Hasil: Sebanyak 169 rekaman ditemukan, dan setelah penghapusan duplikasi, skrining judul dan abstrak, serta penilaian kelayakan teks lengkap, 29 studi dimasukkan ke dalam tinjauan kualitatif. Kurkumin secara konsisten menurunkan sinyal inflamasi, stres oksidatif, deposisi kolagen, dan skor adhesi melalui modulasi NF-kB serta efek antioksidan. Jahe dan gingerol menurunkan TNF-α, IL-6, TGF-β1, VEGF, dan malondialdehida, yang menunjukkan aktivitas anti-inflamasi, antifibrotik, dan antiangiogenik. *Rosmarinus officinalis* menurunkan sitokin, penanda oksidatif, dan TGF-β1 pada model tikus. *Bletilla striata*, frankincense, dan formula herbal kombinasi menunjukkan efek tambahan berupa perbaikan penyembuhan luka, anti-inflamasi, dan peningkatan fibrinolisis.
Kesimpulan: Terapi herbal tampak menjanjikan sebagai strategi adjuvan untuk mencegah adhesi pascaoperasi; namun, buktinya masih heterogen dan didominasi studi hewan serta in vitro. Standardisasi formulasi, evaluasi keamanan, dan uji klinis yang dirancang dengan baik masih diperlukan sebelum aplikasi klinis yang lebih luas.

Kata kunci: adhesi pascaoperasi, anti-inflamasi, antifibrotik, stres oksidatif, terapi herbal

INTRODUCTION

Postoperative peritoneal adhesions are pathological fibrous bands that develop after abdominal or pelvic surgery. They remain a major cause of small bowel obstruction, difficult reoperation, chronic pelvic pain, and infertility, and they continue to generate substantial clinical and economic burden.[1–3] Despite the use of modern surgical techniques, adhesions remain a common postoperative complication, occurring in as many as 50–95% of all surgical procedures.[4–6] One study reported that the incidence of readmission related to adhesions ranges from 5% to 20%, and approximately 6% of patients who undergo surgery require repeat operations up to two times because of adhesion-related complications.[7] In the United States, 70% of small bowel obstruction cases are caused by adhesions.[6]

Adhesion formation begins with mesothelial injury, exudation of fibrin, inflammatory-cell recruitment, and impairment of local fibrinolysis. When fibrin persists, fibroblasts, myofibroblasts, collagen deposition, angiogenesis, and tissue remodeling convert temporary exudates into permanent fibrous bands.[8–10] Despite meticulous surgical technique and the use of physical barrier agents, current prevention remains incomplete. Available adhesion barriers can reduce some clinically relevant outcomes, but they do not eliminate risk and their benefit depends on procedure type, application constraints, and cost.[1,2,11]

Because adhesion formation involves intersecting inflammatory, oxidative, fibrotic, angiogenic, and fibrinolytic pathways, herbal therapeutics have attracted attention as multi-target adjuvants. Curcumin, ginger, rosemary, *Bletilla striata*, frankincense, and polyherbal formulas have all shown anti-inflammatory and antifibrotic effects in experimental models.[12–14] However, existing evidence remains fragmented, varies in methodology, and is dominated by preclinical studies, with no comprehensive synthesis comparing mechanisms across different herbal agents. To our knowledge, no recent review has systematically compared the mechanistic pathways of various herbal agents in preventing postoperative adhesions. Therefore, this review aimed to synthesize recent

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evidence on herbal therapeutics for preventing postoperative adhesions, compare their major mechanisms, and identify implications for future clinical translation.[15]

METHODS

Study design

This study was conducted as a systematic literature review with qualitative synthesis. The search and study-selection process were designed to be transparent and reproducible, and the reporting was prepared with attention to the PRISMA 2020 statement. Because of heterogeneity in animal models, herbal interventions, dosages, routes of administration, and outcome measures, the findings were synthesized narratively rather than by meta-analysis.[16]

Search strategy

The literature search was conducted using PubMed, Scopus, and Google Scholar for studies published between 2015 and 2025. The search used the following Boolean combination: ("surgical adhesion" OR "postoperative adhesion" OR "peritoneal adhesion") AND ("herbal" OR "plant extract" OR phytotherapy) AND (animal OR rat OR mice). The search was limited to English-language articles. Reference lists from relevant articles were also checked manually to identify additional eligible studies.

Eligibility criteria

Studies were included if they: (1) evaluated herbal compounds, plant extracts, phytochemical preparations, or herbal formulations for preventing or reducing postoperative adhesions; (2) used animal experimental models, such as rat or mouse models; and (3) reported adhesion-related outcomes, including adhesion score, histopathology, fibrosis, inflammation, oxidative stress, or angiogenesis. Studies were excluded if they involved non-herbal interventions, were not focused on postoperative adhesions, were review or meta-analysis articles, conference abstracts without sufficient data, duplicate publications, non-English articles, retracted papers, or preprint/non-peer-reviewed articles.

Study selection process

Titles and abstracts were initially screened based on relevance to the review topic. Potentially eligible studies were subsequently assessed through full-text review. In the identification stage, 169 records were retrieved from PubMed, Scopus, and Google Scholar. After removing 39 duplicates, 130 records remained for screening. Following title and abstract screening, 41 full-text articles were assessed for eligibility. Of these, 12 articles were excluded because 4 full texts were unavailable, 4 did not evaluate herbal interventions, 2 did not report adhesion-related outcomes, and 2 were preprint or non-peer-reviewed articles. Finally, 29 studies were included in the qualitative review. The study selection process is presented in a PRISMA-style flow diagram in Figure 1.

Data extraction

The main data extracted from the included studies consisted of author, publication year, herbal intervention, experimental model, proposed mechanism, and the main anti-adhesion outcomes.

Quality assessment/risk of bias

A formal risk of bias assessment was not conducted in this review. Therefore, the findings should be interpreted cautiously, as the included studies may contain potential sources of bias, and the overall strength of evidence remains limited.

Data synthesis

Due to variations among the included studies in terms of animal models, dosage, routes of administration, and outcome measurements, the findings were synthesized qualitatively rather than through meta-analysis.

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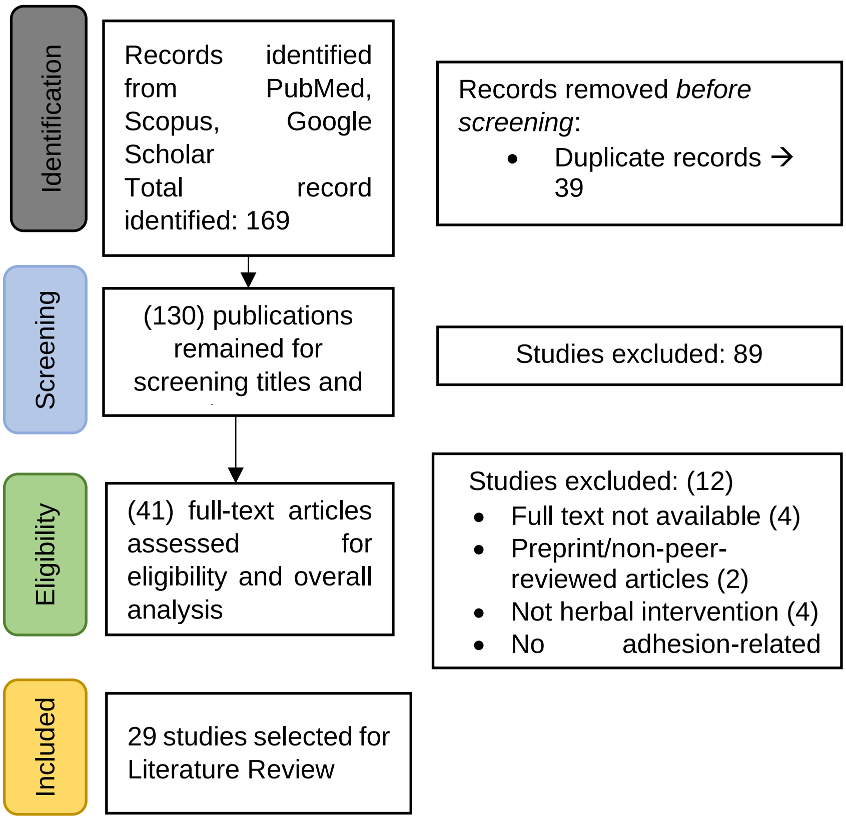

Figure 1. PRISMA-style flow diagram of study selection used in this review

RESULTS

Twenty-nine articles met the eligibility criteria for the qualitative review. All included studies were preclinical animal studies, predominantly rodent models of postoperative adhesions. No human clinical trial directly evaluating herbal agents for routine postoperative adhesion prevention was identified in the final corpus.

The included studies investigated a wide range of herbal interventions, including single plant extracts, isolated phytochemical compounds, and multi-herbal formulations. Several studies evaluated curcumin-related preparations, ginger, rosemary, *Bletilla striata*, pomegranate-derived preparations, *Portulaca oleracea*, *Salvia miltiorrhizae*, and other herbal compounds. Overall, most studies reported reduced adhesion severity, lower inflammatory response, less fibrosis, and improvement in oxidative stress-related markers, although the degree of benefit varied across interventions and experimental models. [12,13,15,17–27]

Across the intervention studies, the most frequently reported anti-adhesion mechanisms were suppression of pro-inflammatory cytokines, attenuation of oxidative stress, and reduction of profibrotic mediators such as TGF-β1 and collagen deposition. Several herbal therapies also influenced VEGF-related angiogenesis or restored fibrinolytic balance, indicating that postoperative adhesion prevention is a multi-pathway therapeutic target rather than a single-mediator process.[9,12,17,20,28–34] However, the overall body of evidence remains entirely preclinical and methodologically heterogeneous. A summary of the included studies and their main findings is presented in Table 1.

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Vol 18 No 1, Mei 2026
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Table 1. Summary of Herbal Compounds and Their Effects on Postoperative Adhesions

No	Researcher, year, citation	Herbal intervention and model	Dose	Main mechanism	Main outcome
1	Mahmoudieh, 2020[28]	*Punica granatum* flower; rat peritoneal burn model	100, 200, or 400 mg/kg/day orally	Anti-inflammatory and antifibrotic	Lower adhesion area and adhesion severity than the control
2	Jaafari, 2021[35]	*Portulaca oleracea* aerial parts; rat surgical peritoneal adhesion model	100 or 300 mg/kg/day orally	Anti-inflammatory, antifibrotic, reduced collagen deposition	Lower adhesion scores, fibrosis, and collagen deposition
3	Yahyazadeh, 2023[25]	Oral *Zingiber officinale* extract; rat peritoneal abrasion model	50, 150, or 450 mg/kg/day by gavage	Anti-inflammatory, antioxidant, antifibrotic, anti-angiogenic	Lower adhesion scores; lower IL-6, TNF-α, TGF-β1, VEGF, and MDA; higher GSH
4	Liu, 2023[36]	Jiawei Xiaochengqi decoction; rat ischemic button model	6.2 or 18.6 g/kg/day orally	Anti-inflammatory, reduced ECM accumulation, inhibition of STAT3/AKT signalling.	Reduced incidence and score of adhesions; less collagen deposition
5	Wu, 2018[37]	Daikenchuto; mouse cecum cauterization and abrasion models	22.5 mg, 45.0 mg, or 67.5 mg/ mouse	No clear anti-adhesion effect demonstrated	No significant inhibitory effect on adhesion formation
6	Zou, 2023[38]	Glycyrrhetinic acid from *Glycyrrhiza uralensis*; rat cecum abrasion model	28mg as lavage	Anti-adhesion, likely through anti-inflammatory and antifibrotic effects	Lower adhesion score than the comparison groups
7	Rakhshandeh, 2025[39]	*Punica granatum* seed lavage; rat peritoneal abrasion model	2mL of 0.1%, 0.3%, 1%, or 3% w/v as lavage	Reduced profibrotic and angiogenic markers	Biomarkers improved, but adhesion scores were not significantly different
8	Karatepe, 2025[34]	*Rosmarinus officinalis*; rat colon anastomosis model	2 mL of 2% extract	No clear anti-adhesion benefit in this model	No significant difference in macroscopic adhesion score
9	Yahyazadeh, 2024[24]	Ginger extract and gingerol lavage; rat peritoneal abrasion model	ginger extract (0.6, 1.8, 5 %w/v), and gingerol (0.05, 0.1, 0.3, and 1 %w/ v)	Anti-inflammatory, anti-angiogenic, antifibrotic	Reduced adhesion formation and improved inflammatory, angiogenic, and fibrotic markers
10	Raisi, 2021[40]	*Salvia miltiorrhiza* extract; rat celiotomy model	3 ml of 1% or 5% extract	Anti-inflammatory and antifibrotic	Lower adhesion and granulation tissue scores
11	Roohbakhsh, 2020[20]	*Rosmarinus officinalis* lavage; rat peritoneal abrasion model	2 mL of 4% w/v, 2% w/v, and 1% w/v	Anti-inflammatory, antioxidant, antifibrotic	Lower adhesion score and lower inflammatory/oxidative markers
12	Liu, 2019[18]	*Bletilla striata* extract; rat cecum abrasion model	15% as lavage	Anti-inflammatory and antifibrotic; lower TGF-β1 and	Lower adhesion score and reduced collagen thickness

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No	Researcher, year, citation	Herbal intervention and model	Dose	Main mechanism	Main outcome
				α-SMA	
13	Jomezadeh, 2018[33]	*Malva sylvestris* flower extracts; rat peritoneal button model	0.2 g with various extraction methods	Anti-inflammatory and antifibrotic	Reduced fibrosis and inflammation; ethanolic extract showed the best macroscopic improvement
14	Sahbaz, 2015[41]	*Pinus pinaster*; rat caecal abrasion model	10 mg/kg/BW intraperitoneal inj.	Anti-inflammatory, antifibrotic, anti-neovascular	Lower macroscopic adhesion score and improved histopathology
15	Sahbaz, 2015[42]	*Ananas comosus* (bromelain); rat caecal abrasion model	10 mg/kg/BW intraperitoneal inj.	Anti-inflammatory, antifibrotic, anti-neovascular	Lower macroscopic adhesion score and improved histopathology
16	Emre, 2018[43]	*Calendula officinalis* extract; rat cecal abrasion model	3mL intraperitoneal applied	Wound-healing support and anti-inflammatory effect	Reduced incidence of adhesions, although scoring differences were limited
17	Liang, 2024[32]	*Ligusticum chuanxiong*; rat caecal abrasion model	5mg/kg intraperitoneal applied	Antifibrotic and anti-EMT via TGF-β1/FOXC2-related pathway	Lower adhesion score than the untreated adhesion group
18	Javanmard, 2017[44]	*Silybum marianum* (silymarin); rat cecal abrasion model	50 mg/kg intraperitoneal inj.	Proposed antioxidant, anti-inflammatory, and antifibrotic effects	Lower macroscopic adhesion scores and lower histopathological adhesion grades than the control
19	Rezvan and Saghaei, 2024[45]	*Dracocephalum kotschyi* extract; rat caecal abrasion model	40, 80, or 120 mg/kg by gavage	Anti-inflammatory, antioxidant, and anti-fibroblast activity	Most treated groups showed lower adhesion index and inflammatory markers
20	Askarnia-Faal, 2023[46]	*Curcuma longa* rhizome/curcumin; rat cecal abrasion model	25mg/kg/day orally	Anti-inflammatory and antifibrotic	Lower incidence and severity of fibrotic adhesion bands
21	Deynez, 2025[47]	Multi-herb extract/fractions (*Asphodeline lutea*, *Rheum ribes*, *Rubia tinctorum*, and *Rumex nepalensis*); rat uterine horn abrasion model	100 mg/kg intraperitoneal applied	Anti-adhesion and antifibrotic	All treatment groups except the aqueous subextract significantly reduced adhesions
22	Gao, 2017[31]	Paeoniflorin; rat caecal abrasion model	10, 20, or 40 mg/kg by gavage	Anti-inflammatory and antifibrotic	Reduced the extent and severity of adhesions, especially at moderate and high doses
23	Khalili-Tanha, 2024[48]	*Ganoderma lucidum* and *Ziziphus jujuba*; rat peritoneal	*G. lucidum* (800 mg/kg) and *Z. jujuba* (400 mg/kg) by	Anti-inflammatory and antifibrotic through modulation of	Reduced adhesion bands and inflammatory cell infiltration

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No	Researcher, year, citation	Herbal intervention and model	Dose	Main mechanism	Main outcome
		abrasion model	gavage	TNF-α, IL-6, IL-1β, and TGF-β	
24	Jamshidi-Adegani, 2022[49]	Frankincense n-hexane extract (*Boswellia sacra* resin); mouse post-surgical intra-abdominal adhesion model	60 µL FHE/mice intraperitoneal applied	Anti-inflammatory and antifibrotic	Lower adhesion score, improved histology, and lower TNF-α/TGF-β1 expression
25	Süntar, 2021[29]	*Rumex crispus* extracts/fractions; rat surgically induced intra-abdominal adhesion model	30, 60, or 100% methanol fractions extract intraperitoneal applied	Anti-inflammatory, antioxidant, antifibrotic	Lower adhesion score, less fibrosis, and improvement in inflammatory/oxidative markers
26	Zhou, 2016[50]	Intestine Function Recovery Decoction; rat postoperative intra-abdominal adhesion model	7.55 or 15.1 g/kg/day by gavage	Anti-inflammatory, antifibrotic, anti-neovascular	Improved adhesion score and histology; lower α-SMA, TGF-β1, and IL-6
27	Goret, 2018[51]	Pycnogenol (*Pinus pinaster* bark extract); rat peritoneal adhesion model	10 mg/kg intraperitoneal applied	Expected antioxidant/anti-inflammatory effect was not confirmed	Did not reduce adhesions and was associated with increased inflammation/free oxygen radicals
28	Ozmen, 2020[52]	*Extractum cepae* (onion extract); rat postoperative peritoneal adhesion model	As intraperitoneal lavage	Evaluated anti-inflammatory and antifibrotic potential	Assessed adhesion score, fibrosis, inflammation, and tissue hydroxyproline
29	Çalışkan and Emin, 2022[30]	Macerated garlic oil (*Allium sativum*); rat postoperative intra-abdominal adhesion model	1.2 g/mL intraperitoneal applied	Evaluated anti-adhesion and matrix-modulating potential	Assessed macroscopic/histopathologic adhesion scores and fibrosis-related matrix changes

Abbreviations: α-SMA = alpha-smooth muscle actin; AKT = protein kinase B; ECM = extracellular matrix; EMT = epithelial-mesenchymal transition; FOXC2 = forkhead box protein C2; GSH = glutathione; HFE = hexane fraction extract; IL = interleukin; MDA = malondialdehyde; NF-κB = nuclear factor kappa B; STAT3 = signal transducer and activator of transcription 3; TGF-β = transforming growth factor-beta; TNF-α = tumor necrosis factor-alpha; VEGF = vascular endothelial growth factor.

DISCUSSION

Overall, the reviewed studies suggest a consistent pattern that herbal therapeutics may reduce postoperative adhesion formation primarily through anti-inflammatory, antioxidant, and antifibrotic mechanisms, with additional anti-angiogenic or pro-fibrinolytic effects reported in selected agents. This supports the concept that adhesion prevention is a multi-target process rather than a single-pathway intervention.

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p-ISSN:1979-8253

Anti-inflammatory activity was the most consistently reported finding. Curcumin, ginger, rosemary, *Bletilla striata, Portulaca oleracea, Salvia miltiorrhiza*, frankincense, and *Punica granatum* repeatedly reduced inflammatory mediators such as TNF-α, IL-1β, and IL-6. This is biologically relevant because early postoperative inflammation promotes fibrin persistence, fibroblast activation, and subsequent adhesion formation.[12–14,20,21,24–27,35,36,40,46,49]

Antioxidant and antifibrotic effects were also frequently observed. Curcumin, rosemary, *Portulaca oleracea*, and *Salvia miltiorrhiza* reduced oxidative injury markers and/or improved endogenous antioxidant defenses. In parallel, curcumin, ginger, rosemary, *Bletilla striata*, frankincense, and pomegranate-derived preparations were associated with lower TGF-β1 expression, reduced collagen deposition, lower hydroxyproline content, or decreased α-SMA activity. Taken together, these findings suggest that many herbal agents act not only during the early inflammatory phase but also during the progression from temporary fibrinous attachment to mature fibrous adhesions.[12–14,20,21,24–27,35,36,40,46,49]

Some herbal agents demonstrated broader multimodal effects. Ginger appeared to combine anti-inflammatory, antifibrotic, and anti-angiogenic properties, partly through reduction of VEGF-related signaling.[22,24,25] *Bletilla striata* was notable because it combined anti-inflammatory and antifibrotic activity with possible wound-healing support, which may help promote more organized tissue repair.[18,19,36,53] Polyherbal formulas such as Jiawei Xiaochengqi decoction and HuoXueTongFu formula also deserve attention because they appeared to target multiple pathways simultaneously, including cytokine signaling, extracellular matrix remodeling, macrophage polarization, and fibrinolytic balance.[36,54] These findings support the view that postoperative adhesion prevention is unlikely to depend on a single target, and that broader pathway modulation may be advantageous.

However, the results were not fully uniform across studies. The apparent benefit of some agents depended on the plant part, extraction method, formulation, dose, and route of administration. This was particularly evident for *Punica granatum*: flower extract reduced adhesion area and severity, whereas seed-based lavage improved biomarkers without a statistically significant reduction in gross adhesion scores, suggesting formulation-dependent efficacy.[28,39] Similarly, not all herbal interventions were effective. Daikenchuto showed no significant anti-adhesion effect in one mouse model, and pycnogenol did not reduce adhesions and was associated with increased inflammation and oxidative stress.[37] These negative findings are important because they indicate that herbal origin alone does not ensure anti-adhesion efficacy.

Among the reported mechanisms, anti-inflammatory and antifibrotic effects appear to be the most consistent across studies, whereas antioxidant, anti-angiogenic, and pro-fibrinolytic effects may provide additional benefit in selected agents.[12–14,20,21,24–27,35,36,40,46,49] From a translational perspective, these agents are best viewed as adjunctive multi-target strategies rather than substitutes for meticulous surgical technique or established physical barriers.[1–3] Local delivery systems, including lavage solutions and hydrogels, may be particularly promising because they can concentrate the active agent at the injury site while limiting systemic exposure.[13,20,24]

This review has several limitations. Most included studies were animal experiments, and substantial heterogeneity existed in herbal formulations, standardization of active constituents, dosage, administration routes, adhesion models, and outcome measures. These differences limit direct comparison and make it difficult to identify the most effective agent or protocol. In addition, biomarker improvement did not always correspond to a clear macroscopic benefit. Therefore, although the available preclinical

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p-ISSN:1979-8253

evidence is encouraging, further standardized animal studies and well-designed clinical investigations are needed before herbal interventions can be recommended for routine surgical use.

In summary, herbal therapeutics demonstrate multi-target anti-adhesion effects, primarily through anti-inflammatory, antioxidant, and antifibrotic pathways, although heterogeneity across studies remains a major limitation to translation.

CONCLUSION

Current evidence suggests that herbal therapeutics—especially curcumin, ginger, rosemary, *Bletilla striata*, and selected polyherbal formulations—can reduce postoperative adhesion formation in preclinical models through anti-inflammatory, antioxidative, antifibrotic, anti-angiogenic, and pro-fibrinolytic mechanisms. These findings support their potential as adjunctive anti-adhesion therapies. Nevertheless, translation into clinical practice should await standardized formulations and robust clinical trials demonstrating safety and efficacy in humans.

Future research should prioritize standardized extraction and characterization of herbal preparations, dose-response studies, optimized local-delivery formulations, comparison with established adhesion barriers, formal safety and drug-interaction assessment, and well-designed clinical trials in high-risk surgical populations. At the present stage, herbal therapeutics may be considered investigational adjuvants rather than routine preventive therapy.

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