

Review Article

Antibiofilm Activity of Certain Medicinal Plants Against Perianal Infection-Causing Pathogens: An Integrated Survey

Vettrivel Arul¹, Venkatesan Hariram², Sridevi Muruhan³

^{1,2}Vinayaka Mission's Homoeopathic Medical College & Hospital, Vinayaka Mission's Research Foundation (DU), Salem, Tamil Nadu, India

³Vinayaka Mission's Kirupananda Variyar Engineering College, Vinayaka Mission's Research Foundation (DU), Salem, Tamil Nadu, India

DOI: <https://doi.org/10.24321/0019.5138.202651>

I N F O

Corresponding Author:

Vettrivel Arul, Vinayaka Mission's Homoeopathic Medical College & Hospital, Vinayaka Mission's Research Foundation (DU), Salem, Tamil Nadu, India

E-mail Id:

Veldoc4565@gmail.com

Orcid Id:

<https://orcid.org/0000-0002-2319-726X>

How to cite this article:

Arul V, Hariram V, Muruhan S. Antibiofilm Activity of Certain Medicinal Plants Against Perianal Infection-Causing Pathogens: An Integrated Survey. J Commun Dis. 2026;58(3):191-199.

Date of Submission: 2025-12-03

Date of Acceptance: 2026-09-14

A B S T R A C T

Background: Perianal infections such as abscess, fistula, and post-surgical wound sepsis are predominantly polymicrobial and strongly biofilm-driven. Major pathogens including *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella* spp., *Enterococcus* spp., and *Bacteroides fragilis* develop dense extracellular polymeric substance (EPS) matrices that confer 100-1000-fold antibiotic tolerance and drive chronicity, recurrence, and poor healing outcomes. Plant-derived phytochemicals possess multi-target antimicrobial and antibiofilm actions that may overcome these limitations.

Objectives: To integrate evidence on ten medicinal plants with documented antibacterial, antibiofilm, and mechanistic activity against major perianal pathogens, and to map their functional roles across biofilm development, persistence, and resistance.

Methods: An integrative review was conducted using Scopus, PubMed, and Google Scholar, covering literature from 2001-2025. Studies reporting *in vitro* antimicrobial/antibiofilm effects, *in vivo* wound-infection models, and *in silico* docking interactions (Sortase A, FtsZ, DNA gyrase, β -lactamases, quorum-sensing regulators) were included. Phytochemical data from gas chromatography-mass spectrometry (GC-MS) and Fourier-transform infrared (FTIR) spectroscopy analyses were synthesised to support mechanistic interpretation.

Results: Across all ten plants, consistent multi-target actions were observed: adhesion inhibition, quorum-quenching, EPS disruption, efflux-pump attenuation, β -lactamase suppression, membrane destabilisation, and restoration of antibiotic susceptibility. Berberine-rich species, garlic organosulfurs, neem limonoids, triterpenoids, and flavonoid-rich extracts showed strong inhibitory effects on biofilm initiation, maturation, and existing matrix architecture. Several demonstrated the ability to collapse mature biofilms and counteract resistance phenotypes.

Conclusion: These phytochemicals exhibit broad antimicrobial activity with convergent antibiofilm mechanisms highly relevant to chronic perianal infections. Their potential suitability for mucoadhesive, topical, and nano-enabled formulations highlights a promising translational pathway for managing biofilm-associated perianal disease.

Keywords: Perianal infections, Biofilms, Medicinal plants, Antibiofilm activity, Phytochemicals

Introduction

Perianal infections, which include abscesses, fistulae, cellulitis, and post-surgical wound infections, are the most common infection present in the colorectal patients. It is rare that they are due to a single organism but rather from polymicrobial communities, mainly dominated by *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella species*, *Enterococcus species*, and anaerobes including *Bacteroides fragilis*.¹ A characteristic feature of these organisms in chronic perianal disease is the formation of a mucoid matrix-reinforced biofilm, which develops within fistula tracks, crypt glands, and perianal wound surfaces.² Biofilms are formed when the microbial cells are embedded within an extracellular polymeric matrix and are known to offer a high degree of protection to the bacteria against antibiotics and host immune response at the site of local infection even after clinical drainage is conducted along with appropriate antimicrobial therapy.³

The biologic activity of biofilm is responsible for the remarkable failure rates that are regularly seen with treatment of perianal infection. In biofilms, bacteria can cooperate as well as communicate with one another by means of quorum-sensing systems and switch to slow-growing metabolic modes where they overexpress efflux pumps, adhesins, β -lactamases, and matrix-forming proteins.⁴ These adaptations can decrease susceptibility to antibiotics by as much as 100 – 1000-fold, so that conventional agents such as β -lactams, fluoroquinolones, and metronidazole are no longer fully effective.⁵ Regardless of the apparent treatment success, biofilm remnants can reseed infection to create chronic discharge, recurrent abscess formation, and non-healing fistula.

Quorum sensing (QS) is the density-dependent chemical signalling system by which bacteria coordinate their behavior as a population. Growing cells continuously release small diffusible signal molecules: acyl-homoserine lactones in Gram-negative organisms such as *Escherichia coli*, *Klebsiella spp.*, and *Pseudomonas aeruginosa*, autoinducing peptides in Gram-positive organisms such as *Staphylococcus aureus*, and the interspecies signal autoinducer-2 generated through LuxS. Once these signals accumulate above a

threshold concentration, they bind their cognate regulators (for example, LasR and RhIR in *P. aeruginosa* or the agr system in *S. aureus*) and switch on the genes governing adhesin expression, extracellular polymeric substance (EPS) synthesis, swarming motility, toxin release, and biofilm maturation.⁴ Anti-quorum sensing (anti-QS) activity, also termed quorum quenching, is therefore the ability of a compound to interrupt this dialogue rather than to kill the organism outright. It is achieved in three principal ways: by suppressing synthesis of the signal molecule, by enzymatically degrading or chemically inactivating the signal once released, and by competitively occupying the receptor so that the signal can no longer bind.²⁰ The relevance to chronic perianal infection is that a pathogen whose QS circuit has been silenced remains viable but is effectively disarmed: it adheres poorly, produces a thin and loosely organized EPS matrix, and forms a biofilm that is far more accessible to antibiotics and to host phagocytes. Because anti-QS agents exert no direct kill-or-die pressure, they are also considered less likely than conventional bactericidal antibiotics to drive the emergence of resistance.⁴⁰

These challenges of therapy options have revived interest in plant-based phytochemicals, several of which display multi-targeted antimicrobial and antibiofilm activities. In contrast with the one-target fighting single-tactics of antibiotics, phytochemicals comprise a plethora of diverse molecules: alkaloids, flavonoids, tannins, and terpenoids, which target using a multitasking approach on bacterial membranes, QS mechanisms, virulence regulators, resistance enzymes, and adhesion proteins like Sortase A, but also essential ones like FtsZ and DNA gyrase.⁶ There are multiple classes of medicinal plants with a history of use in wound care, inflammation, or skin infections demonstrating potential activities against biofilm-forming pathogens associated with perianal disease. The potential to prevent adhesion, disrupt the matrix architecture, and interfere with QS or restore antibiotic susceptibility means that they are promising adjuncts or starting points for new treatments.⁷ (Figure 1)

With a wide range of evidence available, an integrative review is needed to pull together the mechanistic, experimental, and computational knowledge on these plants. This strategy combines the *in vitro* activity of antimicrobials, and antibiofilms, including the *in vivo* wound-infection models and *in silico* docking interaction modulations to molecular targets, as well as phytochemical information based on analytical methodologies such as gas chromatography-mass spectrometry (GC-MS) and Fourier-transform infrared (FTIR) spectroscopy.⁸ Combining these complementary layers provides a unique opportunity to gain an in-depth understanding of how medicinal plants function at each stage of biofilm development and pathogen resistance. The objective of this full-integrated review is

to collect and summarize evidence on ten medicinal plants with established antimicrobial / antibiofilm action against major perianal pathogens, discuss the molecular bases of their efficacy, and provide insight into their potential use for treating long-lasting biofilm-related perianal infections.

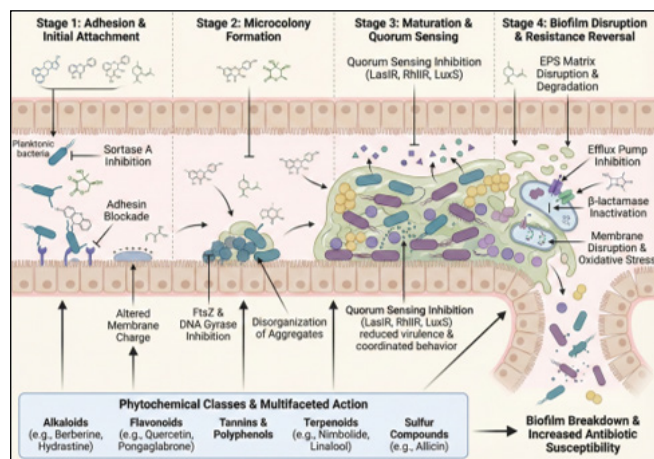


Figure 1. Multi-Targeted Antibiofilm Mechanisms of Medicinal Plants Against Perianal Pathogens

Methodology

Review Design

This review was designed as an integrating review, which made it possible to incorporate theoretical concepts, experimental results, mechanistic studies, and computational evidence published in the last two decades. This method ensures the full spectrum of phytochemical activity from early foundational research to the most evolving molecular-docking and biofilm-pathogen interaction studies is described.

Data Sources and Search Strategy

Scopus served as the principal database, PubMed for biomedical experimental research, and Google Scholar for secondary reference tracing. Papers from 2001 up to the near future (2025) were taken into the scope since much of the biofilm-focused phytochemical research that has solidified and grown during this time is relatively new. Search terms were grouped in four conceptual domains, which were:

- Perianal infection-associated biofilm-forming pathogens, including *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella species*, *Enterococcus species*, and *Bacteroides fragilis*.
- List of the ten medicinal plants used for analysis.
- Mechanism-based themes such as biofilm, QS, EPS modulation, Sortase A inhibition, FtsZ targeting, and DNA gyrase targeting.

- Investigational models comprising *in vitro* antimicrobial and antibiofilm assays, wound or infection animal models, and *in silico* docking of (protein) target interaction analysis.

Inclusion Criteria

Only Scopus-indexed papers of 2001-2025 studies reporting well-defined experimental or computational approaches, antibacterial, antifungal, antibiofilm findings, phytochemical profiling, or mode-of-action data and published in English were taken into account.

Exclusion Criteria

We excluded studies using unidentifiable or no standardized extracts, not clearly described methods, without assessment of biofilm-related outcomes, and with information presented in such a way that we were unable to interpret the data.

Data Evaluation and Quality Assurance

Every qualified study was appraised using a structured evidence-extraction matrix. Evidence from *in vitro*, *in vivo*, and *in silico* studies was weighted according to methodological strength, consistency, and biological plausibility. The preference was given to let it be mechanistic evidence such as QS interference, biofilm regulatory protein inhibition, or computational docking studies against Sortase A, FtsZ, DNA gyrase, or β -lactamases. Phytochemical evidence supported using GC-MS, FTIR, or other analytical methods to support biological plausibility.

Synthesis Method

The integrative synthesis was structured in terms of direct antimicrobial activity, interference with biofilm development (subtypes: inhibition and disruption), QS inhibition, molecular docking patterns, and phytochemical framework, as well as ecological significance with respect to the behavior of perianal biofilm agents. This also made it possible to have a consistent view on the mode of action of plant-derived molecules at biofilm initiation, maturation, resistance, and persistence.

Results

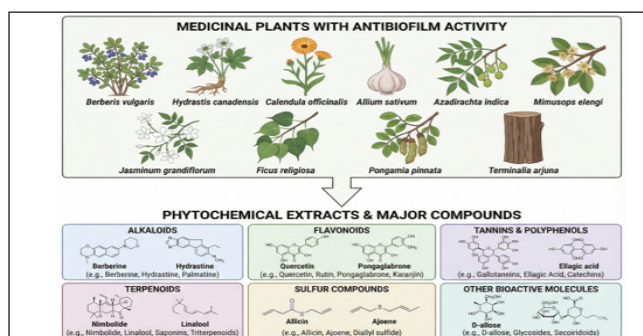


Figure 2. Overview of Medicinal Plants with Antibiofilm Activity and Their Major Phytochemical Classes

Berberis vulgaris (Common Barberry)

Major perianal pathogens such as *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA) strains, and *Escherichia coli* were shown to be sensitive to the *B. vulgaris* extract in a dose-dependent manner with a non-specific effect rather than a specific action against several species of microorganisms. Minimum inhibitory concentration (MIC) values ranging from 100 to 400 µg/mL were recurrently found for berberine-rich fractions, pointing out powerful inhibition even at relatively low concentrations. Biofilm formation assays, however, demonstrated significant decreases in bacterial adhesion, early biofilm formation, and mature biofilm mass.⁹ Berberine inhibited not only biofilm formation but also removed the existing biofilms through eliminating biomass and inducing striking collapse of the extracellular polymeric matrix. Mechanism studies indicated tight binding to Sortase A (involved in the anchoring of surface adhesins), FtsZ (essential for bacterial cell division) and DNA gyrase & topoisomerase IV, indicating a multi-targeting mechanism.¹⁰ Berberine, palmatine and synergetic tannins/flavonoids are mainly responsible for the pharmacological action, including their increased ability to permeate cellular membranes and to block efflux-mediated resistance.¹¹

Hydrastis canadensis (Goldenseal)

Hydrastis canadensis showed good antimicrobial effects, particularly for *S. aureus*, MRSA, and *E. coli*.¹² Moreover, complete plant extracts exerted stronger capacities when compared to single berberine isolates, designating synergistic effects between the specific phytochemicals of the plant extract. While relatively few investigations specifically addressed biofilm activity, altered biofilm structure with decreased cell attachment and impaired virulence gene expression was described. Molecular docking also showed very good binding values for hydrastine and berberine alkaloids against Sortase A, efflux pump proteins, and membrane-binding domains, consistent with their counteractive potential against adhesion and drug-resistance mechanisms.¹³ One of the great advantages of this extract is its high content of hydrastine and canadine, as well as phenolic compounds responsible for both antimicrobial and antibiofilm activities.¹⁴

Calendula officinalis (Pot Marigold)

Calendula officinalis demonstrated strong antibacterial activity against *E. coli*, *Salmonella*, *Shigella*, and the other enteric pathogens that are commonly seen in polymicrobial perianal infections. The extracts exhibited broad inhibition zones and low MICs, indicative of substantial potency.¹⁵ *C. officinalis* was found to have significant biofilm inhibitory effects, as it inhibited early bacterial adherence over 70% and decreased the preformed biofilm biomass

by approximately 60%.¹⁶ Mechanistic effects of these extracts might be associated with interfering with EPS formation, disrupting bacterial membrane integrity, and down-regulating of adhesion-related mechanisms. Its pharmacological effects are related to its content of quercetin, rutin, saponins, and triterpenoids that exhibit potential as antimicrobial and antiadhesive mediators.¹⁷

Allium sativum (Garlic)

Allium sativum was reported to have the most pronounced antibiofilm and antimicrobial activity among the plants discussed. The extracts of garlic exhibited strong antimicrobial activities against *S. aureus*, *E. coli*, *Klebsiella* spp., and *Pseudomonas aeruginosa*, including multidrug-resistant (MDR) strains.¹⁸ Antibiofilm efficacy was substantial: Both ajoene and allicin abolished >90% of *P. aeruginosa* biofilm mass, disintegrating EPS networks and killing biofilm-imbedded bacterial cells within mature biofilms.¹⁹ Such effects are possibly mediated by the inhibition of QS systems (LasI/LasR and RhlI/RhlR), the formation of oxidative cysteine-rich proteins in bacteria, and an extensive disruption of bacterial membranes. The action is attributed to derivatives of allicin, ajoene, and diallyl sulfide.²⁰

Azadirachta indica (Neem)

The extract of *Azadirachta indica* strongly inhibited the growth of MRSA, *Helicobacter pylori*, and other biofilm-producing Gram-negative pathogens. Neem fractions not only significantly prevented early adhesion and decreased EPS thickness but were also able to disorganize the *P. aeruginosa*, *Vibrio cholerae*, and *S. aureus* biofilm architecture.²¹ Mechanistic studies provided evidence of the binding between neem limonoids (mainly nimbolide) and several virulence- and resistance-related targets, such as QS regulators, efflux pumps, and β -lactamase enzymes.²² A variety of different phytochemicals were identified, such as nimbolide, azadirachtin catechins, and flavonoids, which contribute to the multi-pronged antibiofilm and antimicrobial activities.²³

Mimusops elengi (Spanish Cherry, Bakul)

Antimicrobial efficacy of *Mimusops elengi* against *S. aureus*, *Enterococcus faecalis*, and *Streptococcus mutans* was significant, especially in polymicrobial biofilm models that are associated with chronic perianal infections. Extracts inhibited bacterial adherence and profoundly disturbed dentin and mixed-species biofilms.²⁴ The effects observed are due to the protein-precipitation characteristics of tannins and membrane-destabilizing properties of triterpenoids. These phytochemicals destroy the integrity of EPS, lower bacterial force and bound adhesion capability, and decrease biofilm stability.²⁵ This effect is further amplified by the plant's high flavonoid and polyphenol concentration, which boosts its antimicrobial properties.

***Jasminum grandiflorum* (Spanish Jasmine)**

Jasminum grandiflorum exhibited significant antibacterial efficacy with ethanolic extracts that strongly inhibited *S. mutans* at an MIC of approximately 6.25 µg/mL. Vapor-phase experiments showed that essential oils inhibited biofilm formation by *E. coli* and *Klebsiella* to an extent of 74% based on reduction in biofilm mass.²⁶ Mechanistic predictions proposed membrane disruptive activity of volatile terpenes linalool and benzyl acetate, as well as potential inhibition of DNA gyrase and QS-modulating LuxS enzymes by secoiridoids.²⁷ In fact, the interspecific profile of the plant's aromatic esters, terpenoids, and phenolics constitutes an excellent mechanistic root to account for its antibiofilm action.

***Ficus religiosa* (Sacred Fig, Peepal)**

The extracts of *Ficus religiosa* were found to be effective in controlling numerous pathogens, viz., *S. aureus*, *E. coli*, *Shigella* spp., *Salmonella* spp., and *Pseudomonas* spp.²⁸ In biofilm assays, the plant extract inhibited the swarming motility of *Proteus mirabilis*, which is a significant virulence factor in chronic infection, and it was also able to restore antibiotic sensitivity in CTX-M-15 β-lactamase-producing *E. coli* and *Klebsiella* pathogens.²⁹ The high concentration of quercetin, rutin, gallotannins, and other polyphenols in the plant may explain its antiadhesive, enzyme inhibitory, and motility-suppressive activities.³⁰

***Pongamia pinnata* (Indian Beech, Karanja)**

Pongamia pinnata exhibited a strong antibacterial and anti-biofilm response, particularly on *Staphylococcus epidermidis*. Inhibition of biofilm formation was noted to the extent of 97.4%, with collapse of the biofilm matrix observed by microscopy among extracts.³¹ The potent bioactivity is due to furanoflavones, including pongaglabrone, karanjin, and pongamol, which inhibit polysaccharide intercellular adhesin (PIA), inactivate Sortase A-mediated adhesion, and disturb the assembly of FtsZ, indispensable for septum ingression during cell division.³² These multivalent associations underscore the multifaceted nature of the plant in biofilm management and infection abatement.

***Terminalia arjuna* (Arjuna)**

The bark extract of *Terminalia arjuna* was found to have significant activity towards several wound-infecting bacteria and silver nanoparticles were developed from this extract for enhanced antimicrobial activity.³³ A rare sugar, D-allose, could greatly repress *S. aureus* biofilm formation by targeting adhesion systems and the regulatory pathways associated with staphylococcal accessory regulator A (SarA) and Sortase A, while in catheter-associated biofilm models of *E. coli* and *S. epidermidis* colonization, it was declined.³⁴ The plant's phytochemical profile, particularly ellagic acid,

gallotannins, glycosides, and D-allose, gives an array of mechanisms for antiadhesive/enzyme inhibitory/biofilm-disrupting activities.

Discussion

Converging Themes Across All Plants

A similar trend is observed across the 10 medicinal plants, all of which appear to follow multifaceted modes of action that go beyond mere growth inhibition. These plant extracts exhibit consistently broad-spectrum antibacterial activity while interfering with some of the multiple mechanisms underpinning biofilm life. One of the few common themes in the evidence base is potent anti-QS activity, especially against signalling regulators such as LasI/LasR, RhII/RhIR, and LuxS and other communication circuits necessary for biofilm cooperation.²⁰ Potent inhibition of Sortase A, an enzyme taking part in anchoring surface adhesins to the bacterial cell wall and directly compromising primary biofilm attachment steps, is another mechanism these compounds share. Practically all impact the architecture of EPS by decreasing its density, by modifying its chemical structure, or by enhancing its degradation, and this is important because the EPS layer is the first physical barrier protecting biofilm communities from both host immune response and antibiotic action.³⁵ In addition to these actions, multiple plants impaired the activity of efflux pumps and β-lactamases, compromising resistance strategies used by both Gram-negative and Gram-positive bacteria in mature biofilms. Reversal of the resistance/susceptibility was observed for all *Ficus religiosa*, *Azadirachta indica*, *Allium sativum*, and *Berberis vulgaris*, which stresses not only their direct antibiofilm potential but also their use as adjuncts to available antibiotic therapies.³⁶ This convergent mechanistic pattern argues for an integrated approach to plant phytochemicals as a strategy against biofilm-driven perianal infections.

Biofilm Breakdown Model (Cross-Plant Analysis)

When analyzed together, it is clear that each of the ten plants is disrupting every stage of biofilm development, forming an overview disruption model that easily applies across species. In the first stage of adhesion, all plants that inhibit Sortase A, block adhesin expression, or change bacterial membrane charge drastically reduce the pathogen's capacity to cling to epithelial or wound surfaces.¹⁹ This sets a weak foundation where biofilm can be developed. For microcolony formation, plants such as *Calendula officinalis*, *Pongamia pinnata*, and *Berberis vulgaris* disrupt cell-division pathways or disorganize initial micro-aggregates to prevent organized clusters from forming a stable community. The third stage of quorum-regulated biofilm formation is strongly inhibited by the anti-QS activity, of *Allium sativum*, *Azadirachta*

indica, and *Jasminum grandiflorum*, which suppresses signal molecules needed for coordinated amassment, virulence expression, and EPS production.³ EPS formation in the mature stage is targeted through membrane-active terpenoids, polyphenols, and sulfur compounds that disrupt the matrix's physio-chemical stabilizing factors. For already embedded cells, young terpenoids also disrupt the cell envelope, resulting in direct killing.³⁷ Further plants' inhibition of resistance strategies, revolving around β -lactamase secretion, efflux pump activation, and oxidative stress counterattack, reduces their survival prospects once embedded deep within the biofilm.³⁸ The models form a cross-plant portfolio of actions that collectively attacks biofilm at its structural, biochemical, regulatory, and genetic base.

Relevance to Perianal Infections

Perianal infections with anal fistulas, chronic abscesses, and persistent discharging sinuses are particularly difficult to treat, as they are invariably polymicrobial and predominantly biofilm-related. Pathogens, such as *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella spp.*, *Enterococcus spp.*, and *Bacteroides fragilis*, are able to persist due to the shield created by a dense EPS layer coating the fistula tract.³⁹ These organized microbial communities exhibit resistance to antibiotic penetration and decreased metabolic activity, maintaining chronic inflammation even after extended treatment. The biofilms responsible for perianal disease are also characterized by high levels of genetic exchange contributing to the development of resistance and survival in hypoxic areas. The plants discussed in this review fit straight on into this ecological madness.³ Their multi-mechanistic antiadhesion, quorum-quenching, EPS-degrading, enzyme-inhibiting, and membrane-disrupting modes of action correlate with those that are well documented for perianal pathogens to obtain sustained colonization. Sortase A inhibitors and EPS synthesis inhibitors weaken the scaffold of biofilm in fistula tracts.⁴⁰ Compounds with established activity against β -lactamase or efflux pumps might be useful to reactivate susceptibility to conventional antibiotics that are widely employed for perianal infections.³⁸ By targeting both sessile and planktonic bacterial populations, such botanicals might afford a therapeutic dimension that aligns with the complex nature of perianal biofilm ecology.

Translational Significance

Altogether, the data picture a rosy future in favour of translating these phytochemicals into interventions in the clinic for perianal disease. Topical applications would be the most direct method; these could include ointments, suppositories, irrigating solutions or post-surgical gels that could take these compounds to fistula tracts or abscess cavities that harboured biofilms.⁴¹ Additionally, their anti-

inflammatory and tissue-calming activity is a bonus in comparison to standard antibiotics, which can be irritating or disruptive to the microbiome.

Advanced delivery systems are also promising. Wrapping of plant-derived molecules in nanoparticles, hydrogels or mucoadhesive carriers might facilitate biofilm penetration and increase permanence time on the perianal region.⁴² Nano-delivery systems also provide some extra merits like enhanced solubility, controlled release and specifically targeted interaction with microbial membranes. Significantly, these phytochemicals are safe with low systemic toxicity and are also compatible with standard antibiotics to be used in combination or synergistic therapy alongside the existing synthetic chemo-therapeutic agents.⁴³ Integration of these approaches could potentially lower the rate of recurrence and time to healing and perhaps most importantly tackle the underlying issue of biofilm persistence that has been associated with failure to treat chronic perianal infections.

Conclusion

This comprehensive overview integrates and combines experimental, mechanistic, and computational evidence to demonstrate the complex, multifaceted activities of the ten medicinal plants tested against biofilm-resident pathogens known etiological agents in perianal infections. Instead of working through one single antimicrobial mechanism, these natural products are sustaining a systematical attack on a variety of components in the biofilm defensive system, including impairment of adhesion, interference with QS networks, disorganisation of microcolonies formation, degradation of the architecture in EPS and attenuation of drug resistance such as efflux pumps and β -lactamases.⁴⁴ That this phenomenon is occurring in phytochemically unrelated species emphasises the benefit of a multi-target strategy in response to chronic and polymicrobial infections that repeatedly evade traditional antibiotics.

In addition, the results show robust potential for translation. Some of these plants (or their crude extracts or bioactive compounds) are also suitable for formulations in different platforms (topical, mucoadhesive and nano-enabled), which might be more effective to treat perianal disease with its complex anatomy. Their capacity to increase antibiotic susceptibility places them as additional good adjuncts of current therapies.⁴⁵ Combined, this evidence argues a convincing case for the development of phytochemistry-derived antibiofilm treatments and complex formulations to minimise recurrence, advance healing success and mitigate the ongoing therapeutic void in chronic perianal infections.

Limitations and Directions for Future Research

Despite the fact that this umbrella review offers robust summaries on phytochemical, antimicrobial

and antibiofilm evidence of perianal infections, there are a number of limitations to consider. Most of the published literature is based on *in vitro* assays, which do not comprehensively depict the complex polymicrobial anaerobic host-interactive biofilm conditions found in anal fistula and chronic perianal sepsis. The conflicting practice of preparing the extracts in different solvent systems and choosing plant parts has led to wide variations in the studied extracts, which complicates study comparisons, rendering findings less generalisable.⁴⁶ Furthermore, although anaerobic pathogens, especially *Bacteroides fragilis*, are known to play a key role in the pathophysiology of perianal disease, they have been infrequently studied.

To progress the field, future research should focus on developing uniform plant extracts with well-defined phytochemical profiles to conduct reproducible and clinically scaled studies. There is an urgent requirement for relevant animal models that resemble anal fistula biofilms well and enable the testing of phytochemicals in anatomically and microbiologically relevant environments. Concomitant studies of phyto-nanoformulations such as nanoparticles, hydrogels and targeted drug delivery systems may provide enhanced penetration into mature biofilms and longer maintenance within the fistula tracts.⁴⁷ Ultimately, studies in patients with recurrent perianal sepsis are needed to validate these botanical interventions and determine safety/efficacy and the utility of botanicals as supportive or alternative therapies.

Acknowledgements

The authors are thankful to the Vinayaka Mission's Homoeopathic Medical College and Hospital, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, for all the academic ambience and institutional support extended in the development of this integrated review.

Source of Funding: None

Conflict of Interest: None

Reference

1. Conner JN, Eren S, Tuma F. Perianal abscess. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025 <http://www.ncbi.nlm.nih.gov/books/NBK459167/>
2. Włodarczyk M, Włodarczyk J, Sobolewska-Włodarczyk A, Trzeciński R, Dziński Ł, Fichna J. Current concepts in the pathogenesis of cryptoglandular perianal fistula. *Journal of International Medical Research*. 2021 Feb 17;49(2):0300060520986669. [Google Scholar] [PubMed]
3. Sharma S, Mohler J, Mahajan SD, Schwartz SA, Bruggemann L, Aalinkel R. Microbial biofilm: a review on formation, infection, antibiotic resistance, control measures, and innovative treatment. *Microorganisms*. 2023 Jun 19;11(6):1614. [Google Scholar] [PubMed]
4. Preda VG, Săndulescu O. Communication is the key: biofilms, quorum sensing, formation and prevention. *Discoveries (Craiova)*. 2019;7(3):e100. [Google Scholar] [PubMed]
5. Belay WY, Getachew M, Tegegne BA, Teffera ZH, Dagne A, Zeleke TK, et al. Mechanism of antibacterial resistance, strategies and next-generation antimicrobials to contain antimicrobial resistance: a review. *Frontiers in Pharmacology*. 2024 Aug 16;15:1444781. [Google Scholar] [PubMed]
6. AlSheikh HMA, Sultan I, Kumar V, Rather IA, Al-Sheikh H, Tasleem Jan A, et al. Plant-based phytochemicals as possible alternative to antibiotics in combating bacterial drug resistance. *Antibiotics (Basel)*. 2020 Aug 4;9(8):480. [Google Scholar] [PubMed]
7. Mulat M, Banicod RJS, Tabassum N, Javaid A, Karthikeyan A, Jeong GJ, et al. Multiple strategies for the application of medicinal plant-derived bioactive compounds in controlling microbial biofilm and virulence properties. *Antibiotics (Basel)*. 2025 May 29;14(6):555. [Google Scholar] [PubMed]
8. Omar AM, Mohammad KA, Almalki M, Abulnaja KO, Ibrahim SRM. Integrative experimental and computational dataset for repurposed antibiofilm drug candidates targeting quorum sensing. *Data in Brief*. 2025 Sep 2;62:112025. [Google Scholar] [PubMed]
9. Barbarossa A, Rosato A, Tardugno R, Carrieri A, Corbo F, Limongelli F, et al. Antibiofilm effects of plant extracts against *Staphylococcus aureus*. *Microorganisms*. 2025 Feb 19;13(2):454. [Google Scholar] [PubMed]
10. Zhang C, Li Z, Pan Q, Fan L, Pan T, Zhu F, et al. Berberine at sub-inhibitory concentration inhibits biofilm dispersal in *Staphylococcus aureus*. *Microbiology (Reading)*. 2022 Sep;168(9). [Google Scholar] [PubMed]
11. Aghayan SS, Mogadam HK, Fazli M, Darban-Sarokhalil D, Khoramrooz SS, Jabalameli F, et al. The effects of berberine and palmatine on efflux pumps inhibition with different gene patterns in *Pseudomonas aeruginosa* isolated from burn infections. *Avicenna Journal of Medical Biotechnology*. 2017;9(1):2-7. [Google Scholar] [PubMed]
12. Cech NB, Junio HA, Ackermann LW, Kavanaugh JS, Horswill AR. Quorum quenching and antimicrobial activity of goldenseal (*Hydrastis canadensis*) against methicillin-resistant *Staphylococcus aureus* (MRSA). *Planta Medica*. 2012 Sep;78(14):1556-61. [Google Scholar] [PubMed]
13. Eliwa D, Ibrahim ARS, Kabbash A, El-Aasr M, Tomczyk M, Bin Jordan YA, et al. Biotransformation of modified benzyloquinoline alkaloids: boldine and berberine and in silico molecular docking studies of metabolites on

- telomerase and human protein tyrosine phosphatase 1B. Pharmaceuticals (Basel). 2022 Sep 28;15(10):1195. [Google Scholar] [PubMed]
14. Goldenseal (*Hydrastis canadensis* L.) and its active constituents: a critical review of their efficacy and toxicological issues. Pharmacological Research. 2020 Oct 1;160:105085. [Google Scholar] [PubMed]
15. Efstratiou E, Hussain AI, Nigam PS, Moore JE, Ayub MA, Rao JR. Antimicrobial activity of *Calendula officinalis* petal extracts against fungi, as well as Gram-negative and Gram-positive clinical pathogens. Complementary Therapies in Clinical Practice. 2012 Aug;18(3):173-6. [Google Scholar] [PubMed]
16. El-Ganiny AM, Shaker GH, Aboelazm AA, El-Dash HA. Prevention of bacterial biofilm formation on soft contact lenses using natural compounds. Journal of Ophthalmic Inflammation and Infection. 2017 Dec;7(1):11. [Google Scholar] [PubMed]
17. Nguyen TLA, Bhattacharya D. Antimicrobial activity of quercetin: an approach to its mechanistic principle. Molecules. 2022 Apr 12;27(8):2494. [Google Scholar] [PubMed]
18. Magryś A, Olender A, Tchórzewska D. Antibacterial properties of *Allium sativum* L. against the most emerging multidrug-resistant bacteria and its synergy with antibiotics. Archives of Microbiology. 2021;203(5):2257-68. [Google Scholar] [PubMed]
19. Asma ST, Imre K, Morar A, Herman V, Acaroz U, Mukhtar H, et al. An overview of biofilm formation-combating strategies and mechanisms of action of antibiofilm agents. Life (Basel). 2022 Jul 23;12(8):1110. [Google Scholar] [PubMed]
20. Singh S, Bhatia S. Quorum sensing inhibitors: curbing pathogenic infections through inhibition of bacterial communication. Iranian Journal of Pharmaceutical Research. 2021;20(2):486-514. [Google Scholar] [PubMed]
21. Mahmoud GAE, Rashed NM, El-Ganainy SM, Salem SH. Unveiling the neem (*Azadirachta indica*) effects on biofilm formation of food-borne bacteria and the potential mechanism using a molecular docking approach. Plants (Basel). 2024 Sep 23;13(18):2669. [Google Scholar] [PubMed]
22. Katola FO, Olajide OA. Nimbolide targets multiple signalling pathways to reduce neuroinflammation in BV-2 microglia. Molecular Neurobiology. 2023;60(9):5450-67. [Google Scholar] [PubMed]
23. Wylie MR, Merrell DS. The antimicrobial potential of the neem tree *Azadirachta indica*. Frontiers in Pharmacology. 2022 May 30;13:891535. [Google Scholar] [PubMed]
24. Tuon FF, Suss PH, Telles JP, Dantas LR, Borges NH, Ribeiro VST. Antimicrobial treatment of *Staphylococcus aureus* biofilms. Antibiotics (Basel). 2023 Jan 4;12(1):87. [Google Scholar] [PubMed]
25. Srinivasan R, Jin X, Lin X, Zhao Z. Essential oil compounds as antibiotic alternatives: a comprehensive review of antibacterial, anti-quorum sensing, and antibiofilm effects against *Vibrio* spp. in aquaculture. Reviews in Aquaculture. 2025;17(4):e70065. [Google Scholar]
26. Galovičová L, Čmíková N, Vuković N, Vukic M, Kowalczewski PŁ, Bakay L, et al. Chemical composition, antioxidant, antimicrobial, antibiofilm and anti-insect activities of *Jasminum grandiflorum* essential oil. Horticulturae. 2022 Oct;8(10):953. [Google Scholar]
27. Hachlafi NE, Benkhaira N, Zouine N, Fadi M, Jeddi M, Jeddi S, et al. Exploration of novel antibacterial and anti-adhesive formulations from three chemically characterized essential oils: optimization using experimental design methodology. Scientific African. 2023 Nov 1;22:e01927. [Google Scholar]
28. Murugesu S, Selamat J, Perumal V. Phytochemistry, pharmacological properties, and recent applications of *Ficus benghalensis* and *Ficus religiosa*. Plants (Basel). 2021 Dec;10(12):2749. [Google Scholar] [PubMed]
29. Veisi M, Hosseini-Nave H, Tadjrobehkar O. Biofilm formation ability and swarming motility are associated with some virulence genes in *Proteus mirabilis*. BMC Microbiology. 2025 Jul 2;25:388. [Google Scholar] [PubMed]
30. Zielińska D, Starowicz M, Wronkowska M, Zieliński H. Multifaceted biological activity of rutin, quercetin, and quercetin's glucosides. Molecules. 2025 Jun 11;30(12):2555. [Google Scholar] [PubMed]
31. Rajput M, Bithel N, Vijayakumar S. Antimicrobial, antibiofilm, antioxidant, anticancer, and phytochemical composition of the seed extract of *Pongamia pinnata*. Archives of Microbiology. 2021 Sep;203(7):4005-24. [Google Scholar] [PubMed]
32. Waqas M, Saddique T. *Pongamia pinnata*-derived phytochemicals as potent antibacterial and anti-biofilm leads against multidrug-resistant pathogens. SciForum [Internet]. 2025 Dec 3 [cited 2025 Dec 30]. Available from: <https://sciforum.net/paper/view/27663> [Google Scholar]
33. Khichar S, Dashora S, Patel DK, Chowdhury A, Patel S, Soni KV, et al. Bio-functionalization of Chitosan@ Ag nanoparticles using *Terminalia arjuna* and their antioxidant, antibacterial and cytotoxic activity. International Journal of Biological Macromolecules. 2025 Apr 1;301:140507. [Google Scholar] [PubMed]
34. Peng Q, Tang X, Dong W, Sun N, Yuan W. A review of biofilm formation of *Staphylococcus aureus* and its regulation mechanism. Antibiotics (Basel). 2022 Dec 22;12(1):12. [Google Scholar] [PubMed]
35. Bhat AH, Nguyen MT, Das A, Ton-That H. Anchoring

- surface proteins to the bacterial cell wall by sortase enzymes: how it started and what we know now. *Current Opinion in Microbiology*. 2021 Apr;60:73-9. [Google Scholar] [PubMed]
36. Touani FK, Seukep AJ, Djeussi DE, Fankam AG, Noumedem JAK, Kuete V. Antibiotic-potential activities of four Cameroonian dietary plants against multidrug-resistant Gram-negative bacteria expressing efflux pumps. *BMC Complementary and Alternative Medicine*. 2014 Jul 21;14:258. [Google Scholar] [PubMed]
 37. Singh B, Dahiya M, Kumar V, Ayyagari A, Chaudhari DN, Ahire JJ. Biofilm and antimicrobial resistance: mechanisms, implications, and emerging solutions. *Microbiology Research*. 2025 Aug;16(8):183. [Google Scholar]
 38. Dulanto Chiang A, Dekker JP. Efflux pump-mediated resistance to new beta lactam antibiotics in multidrug-resistant gram-negative bacteria. *Communications Medicine (London)*. 2024 Aug 29;4:170. [Google Scholar] [PubMed]
 39. Hong JC, Chen JS, Jiang ZJ, Chen ZC, Ruan N, Yao XP. Microbiota in adult perianal abscess revealed by metagenomic next-generation sequencing. *Microbiology Spectrum*. 2023;12(4):e03474-23. [Google Scholar] [PubMed]
 40. Sikdar R, Elias M. Quorum quenching enzymes and their effects on virulence, biofilm and microbiomes: a review of recent advances. *Expert Review of Anti-infective Therapy*. 2020 Dec;18(12):1221-33. [Google Scholar] [PubMed]
 41. Scoglio D, Walker AS, Fichera A. Biomaterials in the treatment of anal fistula: hope or hype? *Clinics in Colon and Rectal Surgery*. 2014 Dec;27(4):172-81. [Google Scholar] [PubMed]
 42. Karnwal A, Jassim AY, Mohammed AA, Sharma V, Al-Tawaha ARMS, Sivanesan I. Nanotechnology for healthcare: plant-derived nanoparticles in disease treatment and regenerative medicine. *Pharmaceuticals (Basel)*. 2024 Dec 18;17(12):1711. [Google Scholar] [PubMed]
 43. Petrovic S, Bitá B, Barbinta-Patrascu ME. Nanoformulations in pharmaceutical and biomedical applications: green perspectives. *International Journal of Molecular Sciences*. 2024 May 27;25(11):5842. [Google Scholar] [PubMed]
 44. Lu L, Yu T, Wang H, Zhu X, Liao L, Zhu J, et al. Virulence-arresting drug discovery by strategies targeting bacterial virulence: mainly focusing on quorum-sensing interference and biofilm inhibition. *Journal of Pharmaceutical Analysis*. 2025 Dec 1;15(12):101310. [Google Scholar]
 45. Sanjai C, Gaonkar SL, Hakkimane SS. Harnessing nature's toolbox: naturally derived bioactive compounds in nanotechnology enhanced formulations. *ACS Omega*. 2024 Oct 18;9(43):43302-18. [Google Scholar] [PubMed]
 46. Jaiswal P, Sharma S, Pratap A, Ansari M, Shukla VK, Basu S, et al. Significant presence of biofilm-producing gut-derived bacteria in anal fistula of chronic duration. *International Wound Journal*. 2021 Feb 5;18(4):519-24. [Google Scholar] [PubMed]
 47. Delgado-Pujol EJ, Martínez G, Casado-Jurado D, Vázquez J, León-Barberena J, Rodríguez-Lucena D, et al. Hydrogels and nanogels: pioneering the future of advanced drug delivery systems. *Pharmaceutics*. 2025 Feb 7;17(2):215. [Google Scholar] [PubMed]
 45. Sanjai C, Gaonkar SL, Hakkimane SS. Harnessing nature's